Postcesarean Pulmonary Embolism, Sustained Cardiopulmonary Resuscitation, Embolectomy, and Near-Death Experience

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BACKGROUND: Survival after surgical embolectomy for massive postcesarean pulmonary embolism causing sustained cardiac arrest is rare.

CASE: One day after an uneventful cesarean delivery, a woman developed cardiac asystole and apnea due to pulmonary embolism. Femoral-femoral cardiopulmonary bypass performed during continuous cardiopulmonary resuscitation allowed a successful embolectomy. Upon awakening, the patient reported a near-death experience. Pulmonary embolism causes approximately 2 deaths per 100,000 live births per year in the United States, and postcesarean pulmonary embolism is probably more common than pulmonary embolism after vaginal delivery.

CONCLUSION: Massive pulmonary embolism is a potentially treatable catastrophic event after cesarean delivery, even if continuous cardiopulmonary resuscitation is required until life-saving embolectomy is done. (Obstet Gynecol 2005;106:1153–5)

Pulmonary embolism is the leading cause of maternal death following a live birth.1 The few reported cases of successful surgical pulmonary embolectomy after cesarean delivery have not occurred in the United States. Additionally, near-death experiences after pulmonary embolectomy have not been previously reported in the medical literature. We conducted a systematic, all-language literature review using Ovid (MEDLINE, Fulltext, and Cochrane), Inspire, MD Consult, and UpToDate search engines, and other expert search strategies, from 1966 to December 2004.

CASE

Under epidural anesthesia a 31-year-old G2, P2, Ab0 woman underwent a repeat cesarean delivery and delivered a 3.178-kg male infant. She had no complications until 1040 the next morning when she collapsed after standing up. Her blood pressure initially was unobtainable and then rose to 50 to 60 mm Hg systolic. Her pulse rate was 130 to 140; she appeared breathless and complained of substernal chest pain. Her nail beds were blue. She was alert, cooperative, and anxious. Breath sounds were equal on both sides of the chest. Oxygen, intravenous fluids, heparin, and dopamine were administered, but her blood pressure remained at 60 mm Hg.

An electrocardiogram showed severe right-axis deviation. A radial arterial line was placed and a pulmonary arteriogram was performed. During the pulmonary angiogram, which showed bilateral pulmonary emboli with complete obstruction of the right pulmonary artery and essentially complete obstruction of the left pulmonary artery except for a small upper lobe branch (Fig. 1), she suddenly stopped breathing, and her electrocardiogram monitor displayed many premature ventricular contractions and then asystole. Cardiopulmonary resuscitation (CPR) was begun, and the patient was transferred to the operating room with continuous CPR. Her pupils were dilated and unresponsive to light.

While she was having closed chest cardiac massage, the left inguinal region was prepared, draped, and incised. Two large cannulas were inserted into her femoral artery and vein, and cardiopulmonary bypass was begun at 1210—approximately 90 minutes from the time she collapsed in her room and 45 minutes after CPR had begun. Initial bypass flows were 2 to 2.5 L/min. The chest was then prepared and draped, and a sternotomy was performed while core cooling was done by cardiopulmonary bypass. The right heart appeared massively dilated and was not beating. A second venous cannula was inserted into the right atrium to augment venous return and to decompress the right heart. Cardiopulmonary bypass flows then increased to 4 L/min. The aorta was cross-clamped and blood cardioplegia was instilled into the aortic root. The main pulmonary artery was clamped proximally and then opened distally. Both pleura were then opened and both lungs were compressed manually to express the emboli out retrograde through the pulmonary arteriotomy. Twenty-six blood clots measuring up to 1.5 cm in diameter and 6 to 12 cm long were extracted. Pathologic examination showed...
the clots to be of different ages, some fresh and some organized with layers of white cells. After instilling a second dose of warm blood cardioplegia the pulmonary arteriotomy was sutured, the aortic cross-clamp was released, and the patient was rewarmed. Her heart returned into sinus rhythm, and she was weaned from cardiopulmonary bypass. The total cross-clamp time was 35 minutes; bypass time was 70 minutes. The chest was closed, the femoral cannulas were removed, the left femoral vessels were repaired, and she was transferred to the cardiac recovery room.

The next morning a brain scan and an electroencephalogram showed normal results. While still intubated in the recovery room, she then awoke and moved her hand in a way that indicated she wanted to write something. Her handwritten note described details of her near-death experience: “I saw Jesus when I fell in the floor the 1st time. I went to heaven out the window. Other room. I saw a cross. Then He came and got me.” Then she turned the paper over and drew a picture of the diamond cross.

Later that day she was extubated and described the near-death experience in more detail; she had died 3 times, had gone to heaven, and had seen Jesus and 2 deceased relatives. Heaven was described as a very pleasant place from which she did not care whether she returned to earth, but Jesus told her to return to take care of her children. Her oral description of the near-death experience was tape-recorded soon after she could talk.

To prevent recurrent pulmonary emboli, 2 days after her pulmonary embolectomy a “Bird’s Nest” venous filter was placed percutaneously in the inferior vena cava just below the renal veins. Anticoagulation was continued with heparin until

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**EMBOLECTOMY FOR POSTCESAREAN PULMONARY EMBOLISM NEEDING CARDIOPULMONARY RESUSCITATION (CPR)**

A. Outcomes when cardiopulmonary bypass started during continuous CPR
   3. Retrograde amnesia, discharged 9 days postoperatively—Marty et al. Present report. (United States)

B. Outcomes when surgery done for unstable hemodynamics after CPR(s)
her prothrombin times became therapeutic on warfarin. She was discharged on her ninth postoperative day and had no leg swelling and normal lower extremity venous duplex examinations thereafter. She continued to take warfarin.

Not unexpectedly, for many months after her prolonged cardiac arrest, she experienced severe amnesia, and at first she did not even remember having given birth to her son. Besides her amnesia, she developed posttraumatic stress syndrome and panic attacks, but these resolved after a few months. During the next 14 years of her life, the psychological impact of her near-death experience caused her to lose her fear of death and to speak publicly about her experience.

COMMENT
Pulmonary embolism is still the leading cause of maternal death in the United States, causing death in about 2 women per 100,000 live births each year. The box summarizes the previously reported cases of successful pulmonary embolectomy for massive postcesarean pulmonary embolism causing cardiac arrest, all of which happened outside of the United States. About one half of women who die of postpartum pulmonary embolism die within 24 hours of delivery. Although some authors disagree, women who undergo a cesarean delivery may have a 3- to 9-fold greater risk of pulmonary embolism compared with those who deliver vaginally.

Although any physician would be reluctant to operate on a patient while she is undergoing CPR, especially if the CPR had been in process for 45 minutes, 2 other “successful” examples were found in the literature (see box, “Embolectomy for Postcesarean Pulmonary Embolism Needing Cardiopulmonary Resuscitation” [CPR]). One of these patients survived, whereas the other suffered brain death, and her heart later served as a donor organ. Our patient antedates these cases, because we performed her surgery in February 1990. As the box also indicates, neurologic damage is a common complication in postcesarean pulmonary embolectomy patients, as is prolonged hospitalization. Liver lacerations may occur because the swollen liver that results from massive pulmonary embolism–induced venous congestion is easily injured if the patient requires CPR.

Our search of the medical literature did not reveal other near-death experiences after pulmonary embolectomy. However, in a recent prospective study, about 10% of people who suffered a cardiac arrest described a near-death experience. One of us (B.G.) investigated our patient’s experience and found that she scored 20 points on a standardized scale where a score of 7 or higher defines an experience as a true near-death experience. None of the anesthetic agents that our patient received in very low doses (fentanyl, midazolam, or scopolamine) have been reported to excite a reaction similar to near-death experience. Neuroscientists have proposed that such religious–numinous experiences involve endorphin-induced limbic lobe activity or Nmethyl-D-aspartate receptor blockade by putative endogenous neuroprotective molecules. Ketamine-induced hallucinatory experiences, which differ markedly from near-death experiences, also result from blockage of the Nmethyl-D-aspartate receptor, but our patient did not receive ketamine.

As in our patient, most individuals with near-death experiences endorse a religious or spiritual model for understanding their experience, and no amount of theorizing about the possible scientific explanations will change their minds. The particular religious elements in our patient’s experience corresponded to her religious beliefs and practice before her delivery. Cross-cultural research has shown that the particular “Being of Light” or religious figure seen in near-death experiences varies, depending on the individual’s ability to process an event that is largely ineffable.

REFERENCES
Massive Pulmonary Embolism in Pregnancy Treated With Tissue Plasminogen Activator

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BACKGROUND: Systemic thrombolysis with tissue plasminogen activator (t-PA) in pregnancy is still considered an experimental treatment. Several reports have described the successful use of t-PA in the setting of hemodynamic instability in gravids with massive pulmonary emboli.

CASE: A 34-year-old woman received a diagnosis of severe pulmonary embolism at 23 weeks of gestation. She developed pulmonary hypertension and became hemodynamically unstable. Thrombolytic therapy using t-PA was administered. The patient tolerated thrombolysis well and delivered at term. No placental abnormalities were identified on ultrasonogram or after delivery. The patient was also found to be a heterozygous carrier of prothrombin G20210A mutation.

CONCLUSION: We describe the successful thrombolysis with t-PA of a massive, life-threatening pulmonary embolism without complications followed by a term delivery.

(Obstet Gynecol 2005;106:1156–8)

Pulmonary embolism remains one of the most common causes of direct maternal mortality and is responsible for up to 20% of all maternal death during pregnancy. Pregnancies induce a hypercoagulable state, further increasing the risk for thromboembolism. Traditionally, thromboembolic disease in pregnancy has been treated with unfractionated heparin and more recently with low-molecular-weight heparin. The treatment options for patients with severe, life-threatening pulmonary embolism, for whom conservative management with heparin failed, include embolectomy, thrombolytic therapy, and localized catheter-directed thrombolytic therapy. Surgical options, however, require cardiac bypass and are associated with significant maternal and fetal mortality (2% and 10%, respectively).

Thrombolytic therapy is relatively contraindicated in pregnancy because of the presumed risk of maternal bleeding, placental abruption, and fetal loss. The teratogenic effects of systemic thrombolyis in humans are uncertain. There is some concern that elevated plasmin level can precipitate premature labor. However, it has not been proven in clinical practice.

In 1995, 3 first cases of thrombolysis with tissue plasminogen activator (t-PA) during pregnancy were reviewed by Turrentine et al. Several authors have recommended the use of thrombolysis in situations of life-threatening compromise in maternal hemodynamic functions. We report a case of successful treatment of massive life-threatening pulmonary embolism in the second trimester of pregnancy with t-PA.

CASE

A 34-year-old female, gravida 3, para 2, presented at 23 weeks of gestation with acute shortness of breath and chest pain. She also complained of sudden onset of dizziness and presyncope. She had been previously well. She denied a history of exertional chest pain, orthopnea, or paroxysmal nocturnal dyspnea. She had been normally active during pregnancy and was a nonsmoker. There was no history of hypertension during pregnancy, diabetes, or family history of cardiomyopathy or sudden death. She was on no medications.

Examination revealed a pale, ill-looking patient. Blood pressure was 85/59 mm Hg, heart rate 131 beats per minute (bpm), and respiratory rate 30 per minute. Temperature was 35.8°C, with an O2 saturation of 90% on room air. Jugular venous pressure was 9 cm above the sternal angle. Heart sounds revealed sinus tachycardia, a normal S1, and loud P2 component of S2. There was no S3 or S4. Lungs were clear to auscultation. Abdominal examination was normal; uterine fundus size was consistent with dates. Pelvic and neurologic examinations were normal. Fetal heart tones were reassuring. The right calf was mildly tender and warm with a palpable cord. Electrocardiogram demonstrated sinus tachycardia with Q wave and T wave inversion in lead III. Lower extremity Doppler studies showed no evidence of deep vein thrombosis above the calf. Clinical presentation was highly suggestive of pulmonary embolism, and therefore spiral computed tomography (CT) of the chest was ordered. In the meantime, the patient received one dose of low-molecular-weight heparin for anticoagulation. The spiral CT demonstrated massive bilateral pulmonary emboli extending from the left and right pulmonary arteries into bilateral upper and lower lobar segmental vessels. Subsequently, the patient developed an episode of hypotension with systolic blood pressure of 30 mm Hg and a diastolic of palpable. She was successfully resuscitated with intravenous fluids and epinephrine. Following the episode of hypotension, an echocardiogram was performed and de-
The patient received a bolus of 10 mg of t-PA intravenously and 90 mg of t-PA intravenously over 90 minutes. She had an excellent response to t-PA. Tachycardia and dyspnea resolved, and blood pressure and heart rate normalized. Respiratory rate was 20–22 per minute and PO₂ saturation was 97% on 4 L of oxygen per minute. A repeat echocardiogram 4 hours later demonstrated only slight enlargement of the right ventricle and resolution of pulmonary hypertension. Pulmonary artery pressure was 28 mm Hg. The thrombus in the right ventricle resolved completely.

During and after t-PA administration, fetal heart tones remained reassuring. No contractions or vaginal bleeding were noted. After t-PA administration, anticoagulation with intravenous heparin was continued for one week. Subsequently, the patient was placed on a weight-based dose of low-molecular-weight heparin twice a day. She was discharged home on day 9 of the hospital stay. Obstetric ultrasound examination 1 week after t-PA administration demonstrated no placental abnormalities. The fetus demonstrated appropriate growth throughout the pregnancy. During the remainder of her pregnancy, she had no complications. The plan for the patient was to change from low-molecular-weight heparin to heparin coagulation at 36 weeks of gestation. The patient, however, was noncompliant with clinic appointments and continued low-molecular-weight heparin until the day before labor onset. She presented to the emergency room with spontaneous rupture of membranes in labor and had uncomplicated vaginal delivery at 38 0/7 gestational weeks. A vigorous female infant was born with Apgar scores of 9 at 1 minute after delivery and 9 in 5 minutes. The newborn weighed 2,550 g. Estimated blood loss during delivery was 300 mL. Initial examination of the newborn was normal. The placenta was normal on ultrasound examination 1 week after delivery. We believe the placenta was normal during ultrasound examination 1 week after t-PA administration and at delivery.

The case we report demonstrates that pulmonary embolism should always be considered in the differential diagnosis for any pregnant patient presenting with acute onset of shortness of breath. Echocardiography is extremely helpful in the assessment of patients with dyspnea and is a good tool for evaluating response to therapy in this case. Unlike most patients in previously reported case series, our patient delivered at term. In both cases patients received extensive thrombolysis with streptokinase followed by t-PA. In our case, the placenta was normal during ultrasound examination 1 week after t-PA administration and on delivery.

The placenta was normal on ultrasound examination 1 week after thrombolysis and at delivery. We believe t-PA administration was life saving in this case and is an acceptable alternative for treatment of life-threatening thromboembolism in pregnancy.
Massive Pulmonary Embolism in Pregnancy Treated With Catheter Fragmentation and Local Thrombolysis

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BACKGROUND: Catheter-directed thromboembolus fragmentation and thrombolysis is used with success for treatment of pulmonary embolism with hemodynamic decompensation in nonpregnant patients, but information on its use during pregnancy is limited. We report successful treatment of massive bilateral pulmonary emboli in the third trimester of pregnancy.

CASE: A 29-year-old multigravida at 30 weeks of gestation presented with dyspnea, chest pain, heart palpitations, and syncope. A computed tomographic angiogram demonstrated massive bilateral central pulmonary emboli. Despite heparin and oxygen therapy, aggressive fluid resuscitation and pressor treatment, hypotension persisted, and there were prolonged, deep fetal heart rate decelerations. Emergency percutaneous pulmonary artery catheter thrombus fragmentation, followed by local infusion of tissue plasminogen activator, was performed. The patient recovered rapidly and was discharged from the hospital on subcutaneous low-molecular-weight heparin. She was delivered of a normal, healthy infant at term.

CONCLUSION: Catheter-directed mechanical fragmentation and local thrombolytic infusion therapy is a treatment option for pulmonary embolism with hemodynamic decompensation in pregnancy. Advantages are rapid clot lysis with consequent return of normal hemodynamics and uterine perfusion and avoidance of systemic thrombolytics and associated risk of bleeding complications.

Pulmonary embolism is a leading cause of maternal death during pregnancy. Anticoagulation with unfractionated heparin or low-molecular-weight heparin has been the standard of treatment for pulmonary thromboembolism during pregnancy. However, pulmonary embolism with circulatory compromise requires rapid resolution to prevent maternal and fetal mortality. Mechanical thrombus fragmentation with local thrombolytic infusion has the advantage of rapid clot lysis and avoidance of hemorrhagic complications of systemic thrombolysis, but there is little experience with this technique in pregnancy. We report successful treatment of massive bilateral pulmonary emboli with circulatory collapse by using percutaneous catheter-directed thrombus fragmentation and local thrombolytic infusion in the third trimester of pregnancy. Despite evidence of fetal compromise secondary to maternal hypotension, an infant with normal Apgar scores was delivered at term.

CASE

A 29-year-old gravida 5, para 2, at 30 weeks gestation presented to our hospital complaining of dull chest pain, heart palpitations, dyspnea and 2 near-syncopal episodes. She had recently returned from a 1,300-mile automobile trip, during which she experienced intermittent pain and swelling in the left leg. She had 2 previous uncomplicated term pregnancies. She did not smoke, and there was no family history for clotting disorders. Physical examination revealed an ill-appearing, gravid female with an initial blood pressure of 116/70 mm Hg, pulse rate 135 per minute and respiratory rate of 30 per minute. The lungs were clear to auscultation, and there was a loud S4 cardiac gallop. The legs were soft and nontender, without edema. Fundal height was 30 cm. Fetal heart rate was 130–140 beats per minute (bpm), with no decelerations. There were uterine contractions every 3 minutes, lasting 45 seconds. Doppler ultrasound examination of the lower extremities revealed a large deep venous thrombus in the left femoropopliteal and peroneal veins. There appeared to be a 10-cm free-floating clot in the left femoral vein. A computed tomographic (CT) angiogram showed extensive bilateral cen-
Pulmonary Embolism in Pregnancy

Intravenous heparin therapy was begun immediately, and the patient was transferred to the intensive care unit. Central venous and peripheral arterial catheters were placed. A Greenfield inferior vena cava filter was placed percutaneously to prevent further pulmonary emboli. The patient required 100% oxygen by mask. She developed progressive hypotension, with blood pressure 60/40 mm Hg, which was treated with intravenous 500-mL saline boluses and dopamine to a rate of 15 \( \mu g \cdot kg^{-1} \cdot min^{-1} \). Uterine contractions were more frequent during dopamine therapy, and there were deep, prolonged fetal heart rate decelerations, late decelerations, and absent variability. Frequency of uterine contractions was not reduced by intravenous magnesium sulfate at a rate of 3 g/h. It was clear the patient would not survive cesarean delivery, and the parents were informed that the fetus might expire. After a run of supraventricular tachycardia with a heart rate of 190 bpm, dopamine was discontinued and norepinephrine infusion started. The patient complained of severe back pain, but there was no evidence of retroplacental hemorrhage or bleeding around the caval filter by ultrasonography. Echocardiogram (EKG) showed right ventricular enlargement, with estimated pulmonary artery pressure of 55 mm Hg, determined from tricuspid regurgitation velocity. The condition of the mother and fetus continued to deteriorate despite oxygen, heparin, and pressor therapy, with systolic blood pressure falling to the low 60s mm Hg and fetal heart rate decelerations to 50 bpm.

The patient’s condition rapidly improved. Within 5 hours postprocedure, the norepinephrine infusion was tapered off, and at 8 hours postprocedure, she required only 4.5-L/min nasal oxygen. Fetal heart rate returned to a baseline of 140 with accelerations and no decelerations. Uterine contractions stopped. The patient recovered completely and was discharged from the hospital on subcutaneous low-molecular-weight heparin (enoxaparin 1 mg/kg subcutaneously, twice daily). Eight weeks later, she had an uncomplicated vaginal delivery of a healthy male infant with Apgars of 8 and 9 and birth weight of 6 lb, 5 oz.

COMMENT

Pulmonary embolism occurs in approximately 1/1,000 pregnancies and causes 11% of maternal deaths during pregnancy.1 Most patients with deep venous thrombosis or pulmonary embolism in pregnancy can be treated successfully with unfractionated heparin or low-molecular-weight heparin.2 However, massive pulmonary embolism with hemodynamic decomposition requires rapid dissolution of the embolus to restore adequate blood flow to prevent maternal and fetal morbidity and mortality. Although both systemic thrombolysis and local therapy for massive pulmonary embolism in pregnancy have been described,3–6 there are so few published reports that no conclusions can be made regarding the superiority of one method over the other. Systemic thrombolysis is easy to administer, but it is associated with maternal hemorrhage (8%), pregnancy loss (6%), and preterm delivery (6%).7 Local therapy has the theoretic advantage of immediate removal or fragmentation of the obstructing clot while avoiding the potential bleeding complications of systemic therapy, but it is invasive and requires a sophisticated radiology or cardiac laboratory. Experience with t-PA use in pregnancy is limited, but because it is more thrombin-
specific than streptokinase, it has the advantage of more localized thrombolysis at the site of the thrombus and less systemic coagulopathy than other agents.8 The treatment described in this report included both mechanical fragmentation of the thrombus and local infusion of t-PA. Immediate improvement in pulmonary blood flow occurred during thrombus fragmentation, with further improvement after infusion of t-PA. Sofocleous et al4 reported a case of massive pulmonary embolism in early pregnancy treated with a combination of mechanical thrombectomy and local thrombolysis with t-PA. In contrast to our case, improvement in pulmonary blood flow was not observed until after t-PA infusion. Nonetheless, it seems reasonable to use both mechanical and medical lytic therapy. Mechanical fragmentation increases the surface area of thrombus available for lytic activity, thus improving the efficiency of thrombus dissolution. If appropriate facilities and expertise are available, catheter fragmentation and local thrombolytic therapy using t-PA should be considered for treatment of pulmonary embolism with cardiovascular decompensation in pregnancy.

REFERENCES

Second-Trimester Rudimentary Uterine Horn Pregnancy
Rupture After Labor Induction With Misoprostol

Terri-Ann Samuels, MD, and Awoniyi Awonuga, MD, FRCOG

BACKGROUND: Uterine anomalies are often first suspected after bimanual or ultrasonographic examination. Currently there are no specific recommendations for further evaluation of asymptomatic women with suspected uterine anomalies in pregnancy.

CASE: A young primigravida with a history of an ultrasound diagnosis of bicornuate uterus presented with mild abdominal pain. An ultrasound examination showed a viable 18-week fetus with anhydramnios in the left uterine horn. Labor induction with misoprostol culminated in uterine rupture. At laparotomy, a ruptured left noncommunicating rudimentary uterine horn of a unicornuate uterus was noted.

CONCLUSION: Pregnanacies within noncommunicating uterine horns significantly increase the risk of potentially catastrophic outcome, therefore, consideration should be given to performing 3-dimensional ultrasonography and/or magnetic resonance imaging examinations to determine the nature of uterine anomalies. Caution should be exercised if prostaglandins are considered for use in this setting.

(Obstet Gynecol 2005;106:1160–2)

Congenital uterine anomalies affect 1 in 201 women in the general population and are present in 1 in 594 fertile women.1 However, only approximately 1 in 76,000 pregnancies resides in a rudimentary horn.2,3 They are often initially suspected after bimanual or ultrasound pelvic examination or exploration of the uterine cavity during hysteroscopy or dilatation and curettage. Although percentages vary based on the type of uterine anomaly, most women with undiagnosed anomalies go through pregnancy unaware of their diagnosis and without complications.4

Unicornuate uterus comprise 5% of all uterine anomalies, and the vast majority of these have a contralateral rudimentary uterine horn of the noncommunicating

See related editorial on page 1150.
type (between 74% and 86%) that is often diagnosed at exploratory laparotomy after pregnancy-related uterine rupture.\textsuperscript{1,2} The consequences of a ruptured uterus can be devastating to both mother and fetus.

In recent years a variety of new prostaglandin agents have been used for labor induction and as abortifacients. These agents have been associated with increase in the rate of uterine rupture during attempts at vaginal birth after cesarean.\textsuperscript{6} However, with a PubMed and OVID search from September 1963 to June 2005, using search terms such as “uterine anomaly,” “misoprostol and uterine anomaly,” “mullerian anomaly,” “rudimentary uterine horn,” “uterine abnormalities,” “bicorne uterus,” we were unable to locate any reports suggesting a risk from the use of these agents in the setting of a uterine anomaly. We present a case of uterine rupture after induction of labor with misoprostol in a patient with ultrasound diagnosis of inevitable midtrimester fetal loss, with a pregnancy in a horn of a suspected bicornuate uterus. At laparotomy, a ruptured noncommunicating left rudimentary horn of a unicornuate uterus, with a fetus in the peritoneal cavity, was found. This report highlights the importance of determining the precise status of a uterine anomaly before the use of prostaglandin agents.

CASE

A young primigravida at 18 weeks of gestation with a history of an ultrasound diagnosis of bicornuate uterus at 16 weeks presented with mild, throbbing left lower quadrant abdominal pain of sudden onset. The patient was afebrile, and her other vital signs were stable. Her abdomen was soft, with no rebound, guarding, or rigidity. An abdominal ultrasound examination showed a viable 18-week sized fetus, compatible with her dates. The pregnancy was in the left horn, and anhydramnios was also noted. There was no free fluid in the abdominal or pelvic cavity. The placenta seemed compressed, with signs of separation consistent with an abruption.

After extensive counseling, a decision was made to terminate her pregnancy with intravaginal misoprostol. Ninety minutes after intravaginal placement of 200 μg of misoprostol, the patient’s pain became constant, increased to a pain score of 10 of 10, and the patient seemed pale. A bedside ultrasonogram was performed that showed free fluid in the peritoneal cavity, with demise of the fetus in the left uterine horn. A repeat complete blood count revealed that the hematocrit had dropped from 27% to 11%. A blood transfusion was started and the patient was taken to the operating room. At laparotomy, the fetus was found in the abdomen with 2 L of hemoperitoneum. A ruptured left noncommunicating rudimentary uterine horn was found and excised. The patient was managed in the intensive care unit postoperatively subsequent to transfusion-related acute lung injury after 7 units of packed red blood cells. Subsequently, she made an uneventful recovery and was discharged home on postoperative day 5. Surgical pathology confirmed an 18-week grossly normal fetus with a 3-vessel cord and placenta accreta in the ruptured noncommunicating rudimentary horn of a unicornuate uterus.

COMMENT

This case illustrates the need for caution in managing pregnant patients with uterine anomalies, especially when considering the use of prostaglandins to induce labor. Obstetricians should be wary of uterine rupture because prostaglandin agents may pose more risk to patients with uterine anomalies, similar to the reported increased risk associated with their use in patients having a trial of vaginal delivery after cesarean delivery.\textsuperscript{7,8}

Ultrasound is now used as a first-line diagnostic modality for investigating pelvic pathology.\textsuperscript{9} It is also increasingly used in early pregnancy for dating and for evaluating pregnancy associated pelvic pain and bleeding. Not coincidentally, more uterine anomalies are detected than ever before.\textsuperscript{10} Most obstetricians feel that it is unnecessary to proceed with an exhaustive investigation in an asymptomatic, pregnant patient with an incidental finding of a uterine anomaly. However, it is universally accepted that these patients should have imaging of the urogenital tract to rule out the associated anomalies that occur in approximately 60% of cases.\textsuperscript{3,9}

Our patient was first diagnosed at ultrasound examination as having a bicornuate uterus with a pregnancy in a left horn that did not seem hypoplastic. However, ultrasound cannot always characterize the exact nature of a uterine abnormality, and although a bicornuate uterus was diagnosed, the fact that the patient’s pregnancy was in a noncommunicating horn was not. Indeed, before the advent of ultrasound, 80–90% of rudimentary horn pregnancies were diagnosed after rupture, and only 5% of the reported cases were diagnosed preoperatively.\textsuperscript{7,11} Given that ultrasonography cannot always precisely characterize uterine anomalies, it may be appropriate in certain circumstances to proceed with further investigation such as 3-dimensional ultrasonography\textsuperscript{8} and/or magnetic resonance imaging\textsuperscript{12} to detail the nature of an anomaly, especially in nulliparous patients. In our case, these modalities might have helped in reaching a diagnosis before the use of misoprostol.

Misoprostol has been used in the mid trimester for pregnancy termination and has been reported to be safe.\textsuperscript{13} Letterie et al\textsuperscript{14} reported a case of mid trimester pregnancy in a woman with a noncommunicating uterine horn in which prostaglandin was used for induction without success, but also without any unto-
ward effect. However, most obstetricians would consider its use to be contraindicated in that circumstance. In that case the pregnancy in the left noncommunicating rudimentary horn that was not ruptured was detected at laparotomy for failed induction of labor.

Although maternal outcomes subsequent to rupture have continued to improve secondary to prompt surgical intervention and improved access to intensive care facilities, we believe that it may be prudent to use magnetic resonance imaging and 3-dimensional ultrasound to characterize uterine anomalies in pregnancy when the ultrasound findings are not definitive. In that manner, some ruptures may be avoided by prompt laparoscopy and or laparotomy. It would also enable clinicians to avoid the danger associated with the use of prostaglandins for induction of labor, even in the second trimester, in women with a uterine anomaly, as illustrated by our case, who may also be at increased risk for rupture.

REFERENCES

Percutaneous Transluminal Coronary Angioplasty and Stent Placement in Pregnancy

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BACKGROUND: Myocardial infarction (MI) is uncommon during pregnancy. As the average maternal age increases and assisted reproductive technology allows for very advanced maternal ages, so too may the incidence of MI during pregnancy. Percutaneous transluminal coronary angioplasty (PTCA) with stent placement is an attractive option for treatment of MI in pregnancy when revascularization is required.

CASE: We present a gravida with an ST elevation MI during the third trimester, who was treated with emergent PTCA, stent placement, and platelet inhibitors, and we discuss the patient’s subsequent obstetric and anesthetic management.

CONCLUSION: Percutaneous transluminal coronary angioplasty with stent placement may be used during the third trimester with successful outcome.

Myocardial infarction (MI) occurs in 1 of 10,000 pregnancies. This incidence is likely to increase as assisted reproduction enables pregnancy in older women. Non-ST elevation MI is managed medically. However, ST elevation myocardial infarction requires expedient revascularization for optimal outcome. Options for revascularization include thrombolysis, percutaneous transluminal coronary angioplasty (PTCA), and coronary artery bypass grafting. Newer PTCA technology includes stent placement, which is associated with a decreased need for subsequent revascularization and
better overall clinical outcome. Thrombolytic medications have been associated with obstetric complications, and coronary artery bypass grafting is maximally invasive. Percutaneous transluminal coronary angioplasty with stent placement is an attractive option for treatment of MI during pregnancy.

Only 6 cases of PTCA with stent placement in pregnancy have been described in the English literature. To our knowledge, there is only one other case reported that uses modern antiplatelet therapy with clopidogrel and aspirin postoperatively rather than ticlopidine and aspirin or heparin alone. Clopidogrel (class B) is a potent antiplatelet agent used to prevent thrombosis. The choice of clopidogrel and aspirin to prevent stent thrombosis avoids well-known hematologic complications such as neutropenia, associated with the older drug, ticlopidine. Clopidogrel and aspirin are the current antiplatelet standard of care after stent placement. The other case reported by Sullebarger et al in 2003 described PTCA, stent placement, and subsequent treatment with clopidogrel and aspirin in a woman at 6 weeks of gestation. Thus, labor management was not a concern in this case as it was in ours. (See the Appendix for description of the literature review.)

CASE

A 41-year-old gravida (G8P4–0-3–4), at 34 weeks and 6 days of gestation, presented to the emergency department with severe substernal chest pain, nausea, diaphoresis, and shortness of breath.

The patient’s pregnancy was poorly dated by a third-trimester ultrasonogam alone. The pregnancy had been complicated by diet-controlled gestational diabetes. Her medical and surgical histories were unremarkable, although she had had minimal previous medical care. She took no medications. Her obstetric history was remarkable for 1 cesarean followed by 3 vaginal deliveries, all of which were full term. Coronary artery disease risk factors included a 15-pack-year smoking habit and a family history of early onset MI. The patient had quit smoking 8 months before presentation. She worked as a manual laborer.

On the day of presentation, the patient was cutting vegetables at the kitchen counter when she developed sudden severe nonradiating substernal chest pain and shortness of breath. In the emergency department her electrocardiogram revealed ST-segment elevations in the anterior leads consistent with an anterior MI. Her peak troponin was 440 ng/mL, and her peak creatine kinase was 2,253 U/L. She was transferred emergently to a medical center where coronary catheterization was available.

Upon coronary catheterization, a single lesion was found with 100% occlusion of the mid left anterior descending artery. She thus underwent PTCA and placement of a 2.5 mm × 18 mm bare metal stent (Medtronic, Minneapolis, MN). Special precautions were taken during the procedure to protect the fetus, such as draping the maternal abdomen with a lead shield and performing continuous electronic fetal monitoring. The procedure was otherwise unaltered to accommodate the pregnancy. After the procedure, the patient was placed on clopidogrel, aspirin, and atenolol. Immediately postoperatively, she had multiple episodes of spontaneously resolving nonsustained ventricular tachycardia. When stable, she was transferred to a tertiary care center for cardiac and antenatal care.

Subsequent echocardiogram revealed an ejection fraction of 46%, with apical akinesis and a probable patent foramen ovale versus an atrial septal defect. Given the possibility of a patent foramen ovale, a Doppler ultrasonogram of the lower extremities was performed, which was negative for a potential source of paradoxical embolism. The patient was monitored on telemetry for 1 week. She had no further episodes of chest pain or arrhythmia and was transferred to the antepartum unit for continued observation. Because the patient’s home was located several hours’ driving distance from the hospital, she was ultimately transferred to nonmedical hospital housing for proximity to care. The patient was discharged on clopidogrel 75 mg daily, aspirin 81 mg daily, and β blockade with atenolol 25 mg daily.

Clopidogrel requires 7–14 days for elimination to avoid significant bleeding complications. Because of the risk of spontaneous labor and the fact that the patient was grand multiparous, the timing of clopidogrel treatment was crucial. After a multidisciplinary team meeting that included cardiology, obstetric anesthesiology, and maternal-fetal medicine specialists, the decision was made to stop clopidogrel at approximately 37 weeks of gestation, 14 days after the stent placement rather than the usual 21–28 days. Aspirin alone was continued to prevent stent complications.

The patient underwent induction of labor with oxytocin at 39 weeks and 5 days of gestation. Before the induction, a repeat echocardiogram was performed, which showed persistent apical akinesis and no change in cardiac function. She received an early epidural catheter, continuous external cardiac monitoring, and an arterial line. The patient was continued on aspirin and β blockade. Ten hours after the induction began, the patient underwent a planned, uncomplicated, vacuum-assisted vaginal delivery of a 3,180 g neonate with Apgar scores of 8 and 9. Arterial cord gas showed pH 7.23, PO2 67, PCO2 14, bicarbonate 27.3, and base excess of –2.5. The patient was monitored with telemetry for the first postpartum day. Her postpartum course was unremarkable.

COMMENT

Myocardial ischemia in pregnancy is uncommon. The highest incidence has been reported among multigravidas older than 33 years of age during the third trimester. Anterior wall infarctions are the most common. In Roth and Elkayam’s 1996 review, 21% of cases were associated with thrombosis without other evidence of...
atherosclerosis, as was the case with our patient. Other reported etiologies included atherosclerotic plaque rupture, coronary dissection, paradoxical embolism, and coronary artery vasospasm from Methergine.

Management of myocardial infarction during pregnancy is complicated. In the case of an ST-elevation myocardial infarction, revascularization is imperative. There is very little data regarding the use of thrombolytic agents during pregnancy. These medications are unlikely to cross to the placenta but have been associated with first-trimester pregnancy loss, preterm labor, maternal hemorrhage, abruptio placenta, and fetal death. 1 Percutaneous transluminal coronary angioplasty is a good alternative. Conventional balloon angioplasty carries a risk of acute vessel closure and restenosis (30–50%).2 Stent placement increases the immediate diameter of the lumen, reduces the rate of acute vessel closure and restenosis, and increases the clinical success rate, thus decreasing the need for subsequent revascularization.2 Stent placement is now performed in at least 77% of percutaneous coronary interventions in the United States.4

Bare metal stent placement traditionally commits patients to at least 21 days of treatment with clopidogrel. However, clopidogrel carries the risk of obstetric and surgical hemorrhage. A 1–2 week drug elimination period is generally regarded as sufficient for return of platelet function to avoid surgical hemorrhage.5 Regional anesthesia is contraindicated before clopidogrel elimination. According to the American Society of Regional Anesthesia and Pain Medicine Consensus Conference in 2002,5 regional anesthesia is generally regarded as safe after 1 week of clopidogrel elimination. Given our patient’s advanced gestational age and poor dating, our concern for imminent delivery was high. Thus, we elected to use 14 days of clopidogrel rather than the traditional 21–28 days, anticipating the 1–2 week elimination period and hoping that labor would occur after the drug was eliminated. The patient was continued on aspirin alone to protect her stent from thrombosis. Aspirin is associated with significantly less surgical hemorrhage than clopidogrel and does not complicate regional anesthesia.3

If our patient had gone into labor before clopidogrel elimination, obstetric or surgical hemorrhage could have been treated with platelet transfusion. With regard to anesthesia, we planned to administer a short-acting narcotic via patient-controlled analgesia. General anesthesia would have been required for cesarean delivery.

After MI in pregnancy, the mode of delivery does not appear to impact maternal mortality among the relatively small number of cases reported and should be determined by the usual obstetric indications.1 The mode of delivery in this case was a complex decision because of the patient’s prior cesarean. We recommended a vaginal birth after cesarean delivery because she had had 3 subsequent successful vaginal deliveries and had a favorable cervix the day of induction. Ultimately, 2 weeks after the clopidogrel was stopped, regional anesthesia was administered and oxytocin induction was successful.

Stent placement with obligatory clopidogrel administration offers cardiac benefits among patients with acute ST-elevation MI, but it carries obstetric and anesthetic risks. However, the benefits may outweigh the risks in carefully selected patients.

REFERENCES


APPENDIX

A comprehensive search of MEDLINE, from the early 1950s through September 6, 2004, was undertaken with the help of a professional librarian. MEDLINE was searched for the following MeSH terms and text words: “angioplasty,” “transluminal,” “percutaneous,” “coronary” or “PTCA” or “myocardial infarction” AND “angiography” AND “stents” AND “pregnancy.” An additional search of MeSH and text words including “angioplasty” AND “pregnancy” AND “case report” was performed. These searches revealed 6 cases involving PTCA and stent placement during pregnancy. Of these 6, one case used a heparin infusion for anticoagulation therapy after stent placement. Four cases used ticlopidine and aspirin as antiplatelet therapy. Only one case used clopidogrel and aspirin as antiplatelet therapy. This case involved a myocardial infarction at 6 weeks gestation. Thus, PTCA, stent placement, and antiplatelet therapy with clopidogrel and aspirin did not complicate delivery of the fetus.7
Management of Interstitial Pregnancy Using Selective Uterine Artery Embolization

Philippe Deruelle, MD, Jean-Philippe Lucot, MD, Christophe Lions, MD, and Yann Robert, PhD

BACKGROUND: Interstitial pregnancy is a rare and dangerous form of ectopic pregnancy which is treated by surgery, medical treatment, or both. Management options are not standardized. Currently, conservative nonsurgical treatment seems to be an alternative method in case of interstitial pregnancy.

CASE: A right interstitial pregnancy was diagnosed in a 28-year-old woman. She was successfully treated by 2 courses of systemic methotrexate (1mg/kg) 24 hours apart followed by selective uterine artery embolization. The postembolization course was uneventful, and no rupture occurred. Ten weeks after embolization, human chorionic gonadotropin level was negative.

CONCLUSION: Uterine embolization associated with methotrexate can be used successfully in treating selected cases of early interstitial pregnancy. We hypothesize that this procedure combined with methotrexate could reduce hemorrhagic risk.

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Interstitial pregnancy is a rare condition and accounts for approximately 2% of all ectopic pregnancies. Despite management improvement, maternal mortality remains high, approximately 2% to 2.5%.

Because of its low incidence, most authors have only published case reports or small studies. Therefore, no standard therapeutic protocol has been suggested. Surgical treatment has been used, consisting of a laparotomy or laparoscopy. More conservative techniques have been proposed, including laparoscopic cornuostomy, hysteroscopic procedures, or medical treatment by methotrexate.

We report a case of interstitial pregnancy that was treated by combination of systemic methotrexate and selective uterine artery embolization.

CASE

A 28-year-old woman was referred to our center for an interstitial pregnancy occurring at 6 weeks and 5 days of amenorrhea. Three years before, she had been treated for a right tubal pregnancy by laparoscopic salpingectomy. She also had an appendectomy in childhood.

The urine pregnancy test was positive. She complained of an episode of lower abdominal pain that had resolved spontaneously. On admission, hemodynamic variables were stable. Abdominal examination was normal. Vaginal examination revealed a right adnexal tenderness. Pelvic abdominal and transvaginal ultrasonography (Toshiba SSA-350 A/CoRevision, Toshiba Corporation, Tokyo, Japan) showed an empty uterus with an endometrium 13 mm thick. In the right cornual area, a 22-mm gestational sac was detected with an 8-mm viable embryo. The whole dilated uterine horn measured 28 mm. The chorionic sac was surrounded by an asymmetric and thin layer. Color Doppler showed a highly vascularized mass. There was a left corpus cyst of 45 × 28 mm. The diagnosis of interstitial pregnancy was made according to the criteria of Timor-Trisch et al. Serum ß-hCG quantitative assay was 17,785 mIU/mL. Hemoglobin concentration and hematocrit were within normal values.

Management options were discussed. The patient was given 2 courses of methotrexate 1 mg/kg intramuscularly 24 hours apart. The day after the second injection, ß-hCG level was 20,458 mIU/mL and a selective uterine artery embolization was performed. A 4 French arterial sheath was introduced into the right femoral artery. Angiography was performed. A 4 French arterial sheath was introduced into the right femoral artery. Angiography was obtained, and right uterine artery embolization was performed with 300–600 µm and 900–1200 µm particles (Contour-PVA, Boston Scientific Corporation, Natick, MA) until blood flow ceased and interstitial pregnancy was excluded. After the procedure, the patient complained of low abdominal pain. Forty-eight hours after embolization, ultrasound control showed the mass with small echogenic spots corresponding to pledges. The mass size was identical but without any flow with color Doppler. The embryo displayed no heart activity. Beta-hCG level was 16,811 mIU/mL.

Six days after embolization, ultrasonic examination revealed a flattening of the gestational sac and ß-hCG level was 14,375 mIU/mL. The patient was asymptomatic and was discharged home. Serum ß-hCG levels were followed up weekly and decreased gradually. They became undetectable 10 weeks after embolization (Fig. 1). Ultrasound follow-up showed that the decrease of the interstitial pregnancy size was slower than the decrease of the ß-hCG level. The sac was collapsed and measurements unchanged for several weeks between 15 mm and 18 mm. Nine months afterward, there was a round nonvascular structure of 10 mm × 8 mm with an echogenic ring and a tiny central hypoechoic area. Gynecologic examination was normal and the patient was regularly menstruating.

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COMMENT

Usually, the treatment of interstitial pregnancy consists of cornual resection or hysterectomy by laparotomy. Because of an earlier diagnosis and improvement in surgical procedures, a more conservative treatment has been suggested using laparoscopy. Surgical treatment is very successful, but it is associated with an increased risk of severe hemorrhage. The actual risk of uterine rupture in subsequent pregnancies is unknown. The uterine horn seems to be more fragile, particularly when it has been operated on. We hypothesize that the risk of uterine rupture is higher after surgical treatment than after conservative treatment. Uterine rupture has been described not only after surgery at the site of a previous interstitial pregnancy but also after conservative treatment. Because the risk after medical treatment cannot be definitively excluded, patients must be counseled carefully, and elective cesarean delivery is advised.

The conservative medical treatment using methotrexate has been proposed for ectopic pregnancies, including interstitial forms, and has allowed minimally invasive treatment. Systemic or local injection or the combination of both can be applied. The most commonly used dosing regimen includes 1 or 2 courses of intramuscular methotrexate injection. The overall success of local, systemic, and combined therapy ranges from 62.5% to 83%. Nevertheless, unlike tubal pregnancies, there is no consensus for criteria that can predict the success of medical treatment and determine when methotrexate can be used safely.

To preserve fertility and to avoid uterine scar, conservative management was considered in the present case. Because of the size of the interstitial pregnancy and its highly vascularized feature, a severe hemorrhage in surgical or local treatment was feared. Because of the high β-hCG level and the evolution of the pregnancy, systemic methotrexate treatment could have been unsuccessful, if applied alone. Thus, it has been suggested to add selective uterine embolization to prevent the risk of hemorrhage and to favor ectopic pregnancy arrest.

Uterine embolization is regularly used in obstetrics or gynecology for bleeding conditions. It can be used as an alternative method for surgical treatment or associated with it to prevent major bleeding. Pregnancy after embolization is possible, but the risk for malpresentation, preterm birth, cesarean delivery, and postpartum hemorrhage is increased. However, most data derive from case reports or case studies, and further data are necessary to draw conclusions regarding the safety in women who wish to become pregnant.

Recently, Ophir et al described a successful case of interstitial twin ectopic pregnancy treated by selective uterine artery embolization after failure of systemic methotrexate treatment in a 23-year-old woman. This case and ours showed that selective uterine embolization could be an effective treatment for the conservative management of interstitial ectopic pregnancy. In our report, we hypothesize that embolization treatment has been a useful adjunct to

![Fig. 1. Beta–human chorionic gonadotropin (HCG) evolution after treatment. Deruelle. Interstitial Pregnancy and Uterine Embolization. Obstet Gynecol 2005.](image-url)
Splenosis, the heterotopic autotransplantation of splenic tissue, is a rare complication after splenic trauma and splenectomy. The factors supporting or suppressing the growth of splenic implants in patients after splenic trauma are unknown.

In most cases, the splenic implants, referred to as “splenules,” cause no clinical symptoms and diagnosis is made incidentally. Hypersplenism and relapse of hematologic disease, mainly autoimmune thrombocytopenia, may occur in this period. The implanted splenic tissue frequently occurs in the abdominal cavity, and may give rise to masses in the chest (after thoracic trauma), abdomen or pelvis, which is misinterpreted as tumors or other pathologic masses such as endometriosis or hemangiomas. In addition, the splenic tissue, which is well vascularized, may bleed spontaneously or after trauma or may even spontaneously rupture.

We describe a patient who was diagnosed with a pelvic mass, and afterward multiple splenic implants were identified at exploratory laparotomy.

**CASE**

A 34-year-old woman was admitted to our gynecology clinic complaining of abnormal vaginal bleeding. She had primary infertility due to male factor lasting 14 years. Additionally, she had menometrorrhagia for 2 years, the intensity of which was increased during the last 2 months. Her pelvic examination revealed a huge, fixed pelvic mass undifferentiated from uterus and adnexa. Her abdomen was soft and nontender. A well-healed surgical scar was noted in the left upper quadrant. The only remarkable aspect of the patient’s past medical history was splenectomy after blunt abdominal trauma at the age of 7 years.

Her transvaginal ultrasonogram revealed uterine enlargement (108 × 81 × 130 mm) and multiple myomas, the largest of which was 93 × 94 mm, consisting of intramural, subserous components also displacing the endometrium. The left ovary was normal in size, but in the right adnexal region, a 67 × 36 mm cystic, anechoic mass originating from the right ovary was observed (Fig. 1).

At admission, blood analysis of the patient showed hemoglobin value of 5.9 g/dL, hematocrit of 21.6%, and platelet count of 470,000/mm³. The peripheral smear confirmed microcytic, hypochromic anemia. Her laboratory tests for liver and renal functions were at the normal limits. Tumor markers were Ca 125 147 U/mL (normal <30), carcinoembryonic...
antigen 0.1 ng/mL (normal 0–5), Ca 19–9 19 U/mL (normal <36.2), Ca15–3 9 U/mL (normal <35), alpha-fetoprotein 1 ng/mL (normal 0–5), and β-HCG 0.7 mIU/mL (normal <10).

An endometrial biopsy specimen was obtained. On histologic examination, stromal predecidual changes of the endometrium were observed.

Exploratory laparotomy was planned for the resection of the pelvic mass. The patient had a hemoglobin value of 8.6 g/dL after administration of 4 units of packed red blood cells preoperatively. On the seventh hospital day, the patient underwent exploratory laparotomy. Exploration of the abdominopelvic cavity showed multiple myomatous uterus of 12 weeks of gestation in size and hydrosalpinx of the right tube. Multiple, reddish-purple, vegetative masses up to 5 cm in diameter were observed in ileocecal region, including the appendix (Fig. 2A–C). Similar tumor plaques up to 2 cm in diameter were scattered over colonic serosa, small bowel serosa, and peritoneum. Primary splenic tissue was not observed in left upper quadrant of the abdominal cavity at exploration. The frozen section of the mass, excised from the ileocecal region, revealed splenic tissue, consistent with splenules (Fig. 3). Total hysterectomy, right salphengectomy, and appendectomy were performed.

During the postoperative period, the patient had hemoglobin value of 9.6 g/dL after transfusion of 1 unit of blood. Computed tomography (CT) of the thorax was normal. Abdominal CT scan showed multiple, nodular intraperitoneal masses of homogeneous density similar to the CT appearance of primary splenic tissue in the subdiaphragmatic peritoneal cavity, adjacent to the right kidney, and in the splenic cavity, with well-defined borders (Fig. 4). On the fourth postoperative day, the patient was discharged without further complications.

**COMMENT**

The incidence of splenosis in patients who have undergone splenectomy after trauma has been reported to be 76% at maximum. Most of the ectopic splenic tissues are found in the peritoneal cavity as in our patient, or rarely in liver parenchyma and in brain.

Splenosis generally does not cause clinical symptoms. Our patient had a 27-year interval between her splenectomy and presentation. The splenic implants may mimic hepatic or gastric tumors and benign or malignant tumors of the pelvis, as was the case in our patient. In
many cases they are diagnosed only by surgical exploration. If suspected preoperatively, the diagnosis of splenosis can be made in most cases. The most sensitive test employs the reinfusion of technetium-99m-labeled, heat-damaged autologous erythrocytes, which may detect only those nodules smaller than 1–2 cm and identified as composed of functioning splenic tissue.²

The histologic appearance of the splenules has been described as lacking normal splenic architecture or a well-formed capsule.⁵ In patients with multiple splenic fragments, differentiating splenosis and accessory spleen is not difficult. However, in cases where few splenic fragments are present, identifying whether the vascular supply of the splenic tissue is different from that in accessory spleens can only be possible by receiving their blood supply from the branches of the splenic artery and splenules and from the surrounding tissues.⁷

In patients with symptoms, surgical treatment may be necessary, but there is no need to attempt to remove all identified splenules, because most will cause no problems.²

REFERENCES

Laparoscopic Management of Abdominal Pelvic Splenosis

Eli Serur, MD, Neeti Sadana, MD, and Alecia Rockwell, MD

BACKGROUND: Splenosis is an unusual cause of pelvic pain.

CASE: A 37-year-old nulligravida presented with a 10-year history of chronic pelvic and abdominal pain that was diagnosed as splenosis via laparoscopy. The patient was previously advised against surgical intervention. We report our experience with laparoscopic excision of the above splenosis.

CONCLUSION: Splenosis should be considered in patients with a history of splenic injury and abdominal pain. Laparoscopic excision of splenic nodules with the argon beam coagulator is a well-suited method of treatment for symptomatic splenosis.

(Obstet Gynecol 2005;106:1170–1)

Splenosis is the autotransplantation of splenic tissue or nodules following trauma. Splenosis was originally described at autopsy in 1896, and in 1910 the first case of splenosis known to have followed trauma was discovered. Later, Buchbinder and Lipkoff coined the term splenosis and recorded the first case in the United States in 1939. Interestingly, in Buchbinder and Lipkoff’s case, a young woman thought to have endometriosis was found at surgery to have multiple peritoneal implants after undergoing splenectomy for trauma. Since then, few cases of splenosis have been reported in the literature; even fewer cases have been related to gynecologic symptoms. We report a case of abdominal/pelvic splenosis, presenting as chronic pelvic pain, successfully treated by laparoscopic excision.

CASE

A 37-year-old white woman (P0000) was admitted for surgery at St. Vincent’s Medical Center Staten Island Campus with a history of lower abdominal and pelvic pain for over 10 years. The patient’s pain was unresponsive to medication and lasted 12–14 hours, usually on a daily basis. She had a regular 30-day menstrual cycle with 7-day flow. The patient’s history is significant for a motor vehicle accident in 1970 that resulted in splenic injury and subsequent splenic removal. The patient recovered without complication. She began to experience lower abdominal and pelvic pain in 1994. She described her pain as originating in the periumbilical region and radiating to the right lower quadrant and pelvic regions with a tearing, shearing quality. The pain worsened 1 week before onset of menses.

The patient was evaluated with transvaginal and transabdominal ultrasound examinations in 1994, which revealed 3 solid masses superior and inferior to the right ovary and one solid mass inferior to the left ovary. There was no evidence of cul-de-sac fluid collection or abnormal endometrial thickening. At the time, a probable diagnosis of endometriosis was given. The patient was treated initially with ibuprofen and later with acetaminophen plus oxycodone, without relief. She experienced a 50-pound weight loss over the course of her illness, most of which occurred in the past year.

A transvaginal ultrasound examination repeated in 1995 was also suggestive of endometriosis. In late 1995, the patient underwent diagnostic laparoscopy, and a diagnosis of splenosis was made. The patient consulted several physicians, and the consensus was to avoid surgery for fear of intra-abdominal bleeding.

The patient’s pain continued, and a repeat pelvic ultrasound examination was performed on February 2, 2004, which revealed multiple pelvic nodules adjacent to the uterus with increased vascularity. She was referred to our gynecologic oncology service for further management. Physical examination was essentially normal. The uterus was normal in size and tender to palpation. The cervix was 2 × 3 cm and without lesions. The adnexal examination revealed right lower-quadrant tenderness. Results of the complete blood count, urinalysis, electrocardiogram, and chest X-rays were within normal limits. The patient also received abdominal and pelvic computed tomography (CT) scans with contrast that were consistent with intraperitoneal splenosis with multiple nodules scattered throughout the abdominal pelvic cavity.

Diagnostic laparoscopy was performed and revealed a normal-appearing uterus and adnexa, with extensive splenosis throughout the abdominal peritoneal cavity. The lesions varied in size and appeared purplish, vascular, and lobulated (Fig. 1). Laparoscopic excision was performed with the argon beam coagulator. Hasson open laparoscopy was used to enter the peritoneal cavity. A 1-cm incision along the superior umbilical fold was made, and a 10-mm trocar was placed. Three additional 5-mm ports were placed under direct visualization in the right and left lower quadrants and symphysis pubis areas, respectively. The bowel and omentum were mobilized from the anterior abdominal wall. Extensive and careful dissections were required to deal with the multiple peritoneal adhesions. The argon beam coagulator was useful in dissecting the splenic lesions from the underlying structures, avoiding injury to the splenic capsules in the process, and...
minimizing bleeding. The lesions were placed in an Endo-pouch (Endo-Surgery, Inc., Cincinnati, OH), which was retrieved via the 10-mm umbilical port. A total of 15 implants were excised, ranging in size from 5 mm to 6 5 cm, in a procedure that required 3.5 hours and resulted in 150 mL blood loss. Splenic lesions were removed from the right pelvic sidewall, cul-de-sac, anterior peritoneal surfaces, posterior peritoneal surfaces, and both the large and small bowel surfaces. Minimal residual splenic implants were left in the small bowel serosa in the upper abdomen to avoid a small bowel resection. The postoperative course was unremarkable, and the patient was discharged on the third postoperative day.

The patient’s own estimate of pain before and after the procedure revealed a dramatic reduction in her pain scores from 8/10 before surgery to 1–2 10 postoperatively. She resumed her full daily activities within 1 week after surgery.

COMMENT

The autotransplantation of splenic tissue is thought to result from the spillage of cells from the pulp of the damaged spleen. It is hypothesized that this splenic tissue is functional and may prevent patients from developing sepsis and meningitis from encapsulated bacteria. This retained splenic tissue may also have another function. Patients with splenosis are still able to remove defective red cells in the form of Howell-Jolly bodies and “pitted” cells. These red cell inclusions are lower in patients with splenectomy following trauma than in those after elective splenectomy.

The differential diagnosis for splenosis includes endometriosis, carcinomatosis, hemangiomas, and accessory spleen. It is essential to differentiate splenosis from accessory spleen. Splenosis results from implants of spleen that have no hilus and also derive their blood supply from circumferential vessels. Accessory spleens, on the other hand, are usually present from birth, tend to be fewer in number than splenic implants, and tend to occur more specifically in the left side of the dorsal mesogastrium. Splenic implants occur usually throughout the peritoneal cavity and are found most likely in 1) the small bowel serosa or mesentry, 2) the omentum, 3) the parietal peritoneum and the large bowel serosa, and 4) the diaphragmatic surface. Splenic implants also have a thinner capsule with a decreased amount of normal elastic tissue. The white pulp area also tends to be diminished compared with accessory spleen. Splenic implants characteristically appear as multiple reddish-blue nodules on the abdominal and pelvic peritoneum. Implants tend to be multiple in number, with an average diameter of 3 cm. Presentations of the implants can be quite varied, ranging from asymptomatic to acute abdominal pain with intra-abdominal hemorrhage to bowel obstruction.

Splenosis has rarely been reported in gynecologic cases. Possibly, other cases of splenic implants are found incidentally at gynecologic surgery. Our patient was misinformed about the symptomatic management of splenosis and, when her quality of life was no longer tolerable, decided to explore surgical intervention. We feel that the argon beam coagulator is the ideal instrument to use, laparoscopically, for removal of these lesions. Its superficial penetration allows the mobilization of implants without violating the splenic capsules and minimizes bleeding and time of dissection. We believe that asymptomatic lesions do not need excision and may in fact be immunologically active. However, if symptoms are present, laparoscopic excision is well suited for surgical management. Gynecologists should consider splenosis in the differential diagnosis of any patient presenting with chronic pelvic pain, especially in the context of a history of trauma and splenic rupture. Minimally invasive surgery via laparoscopy is ideal for diagnosing and treating such patients.

REFERENCES


Fig. 1. Photograph of the pelvis, with arrows showing multiple splenic nodules.

Iatrogenic Fetal Injury

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Ronald M. Zuker, MD, FRCSC

BACKGROUND: Iatrogenic fetal injury during cesarean delivery is a serious but underreported complication.

CASE: A distal iatrogenic amputation of a digit occurred during a cesarean delivery.

CONCLUSION: Obstetricians should be aware of this potential complication.

The incidence of iatrogenic fetal birth trauma during cesarean delivery has been reported in the literature to be 0.1–1.9%. The most common form of this injury is a laceration, which could be either superficial without the need of any surgical intervention or deep enough to be fatal. Other reported injuries are fractures, soft tissue contusion, and nerve injury caused by compression. A case was recently managed at our institution, which has spurred us to look at this topic further. Reporting this type of case should increase the awareness of both obstetricians and neonatologists about such possible complications.

CASE

A male child was born at 29 weeks of gestation. He was the larger child of a monochorionic, diamniotic twin pregnancy and had a cephalic presentation. Spontaneous rupture of membranes had taken place the day before birth, and antibiotics had been commenced. The biophysical profile was 6 out of 8. The weights of the twins were 1,050 g and 670 g. The discordant growth was thought to be secondary to twin-to-twin transfusion. Because of premature rupture of membranes and oligohydramnios, the decision was made for an emergency cesarean.

The larger child was the first fetus to be removed and was soon followed by his brother. The apgar scores were 8 and 9 at 1 and 5 minutes, respectively.

Physical examination at birth showed amputation of the distal phalanx of the right middle finger (Fig. 1). It was presumed that the injury happened accidentally during the cesarean delivery, and the obstetrician was notified. The distal stump (Fig. 2) was recovered from the uterine cavity, and the plastic surgeon on call was notified. The tip was reattached as a composite graft. The level of amputation was just distal to the distal interphalangeal joint. The child was taken to the neonatal intensive care unit (NICU) as part of the routine protocol for prematurity and was on antibiotics for 2 weeks. The fingertip appeared as though it might take with a positive capillary refill for 2 days. Unfortunately, thereafter the tip became nonviable. It was retained as a biological dressing and the mummified tip fell off 3 weeks later to leave a completely healed fingertip (Fig. 3). There was no obvious deficit in the range of motion of the joints of the digit. The child appeared to thrive well and left the NICU having nearly doubled his birth weight.

COMMENT

Despite improvements in the medical management of patients and surgical techniques, fetal trauma continues to take place around the time of birth. There have
been over 50 reported cases of iatrogenic fetal injury since 1974.3 The majority of these cases were not identified initially, and in one case this delay was as late as 1 week after birth. In this particular case, the child was diagnosed to have a fractured radius and tibia.4 The incidence of fetal injury during cesarean delivery appears to be variable and has been reported to occur in 0.1–1.9% of births.1,5

Several risk factors have been suggested. The lack of surgical experience of the obstetrician has been implicated as a causative factor in injury during cesarean delivery.6,7 Because of the thinning of the lower part of the myometrium, labor itself seems to be a risk factor for causing a laceration injury to the fetus. In addition, rupture of the membranes reduces the amount of the amniotic fluid and results in greater proximity of the underlying fetal parts to the uterine wall. The combined effect is a significant reduction of the safety cushion that would normally exist between the fetus and the uterine wall.8

Lacerations to the fetus do not result from scalpel use alone. Scissors have caused significant injuries.2,9 In one case, spreading of scissors resulted in skull fracture and a penetrating brain injury, which was ultimately fatal.2 Fetal laceration has also been reported from the use of fetal monitoring probes10 and as a complication of episiotomy.11

Iatrogenic finger injuries during cesarean delivery have been reported only twice in the literature. In the first case, there was injury to the flexor digitorum profundus, one slip of the flexor digitorum superficialis, and the ulnar digital nerve in a little finger.12 In the second case, extensor tendons of index and middle fingers were injured.13 Both cases needed primary repair of the structures involved and had satisfactory outcomes.

Finger amputation, as a complication of cesarean delivery, has not been reported previously in the literature (as determined by PubMed search, with the search terms “fetal injury/laceration” and “cesarean section,” in all languages, from 1966 to 2004). Distal finger amputations can be treated by reattachment of the tip as a composite graft, but the outcome is difficult to predict. In this case, the composite graft consisted of skin, pulp fat, the inserting part of the flexor digitorum profundus tendon, and the cartilage of the distal phalanx. Microsurgical techniques were not considered suitable in this case because the level of amputation was too distal and the fingertip was too small. Even although the amputated distal tip did not survive, it acted as a biological dressing. The resultant healed finger was shorter, but the proximal interphalangeal joint had been spared and had a full range of movement.

Gerber3 proposed a few simple surgical techniques to minimize the risk of fetal laceration. It was suggested that, once the myometrium was incised, the insertion of a digit could be useful to separate the myometrium from the underlying fetal part, before extending the incision. Allis forceps could also be used to elevate the uterine wall, and all retractors should be removed before delivery of the fetus. Ishii and Endo14 even designed a special blade with a blunt edge and notches to minimize the risk of fetal laceration during cesarean delivery.

Cesareans, be they elective or emergency, are performed to reduce both maternal and fetal complications of labor. The literature demonstrates that it is not a procedure without risks. Clearly, when considering the stressful circumstances of an emergency cesarean delivery, it is not surprising that the probability of complications is greater than in elective cases. The incidence of iatrogenic fetal injury is high enough to warrant inclusion as a specific complication when obtaining consent.

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Endometrial Carcinoma After Endometrial Resection for Dysfunctional Uterine Bleeding

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BACKGROUND: Endometrial destruction is an accepted conservative surgical approach for women with dysfunctional uterine bleeding. However, this procedure cannot guarantee complete removal of the entire endometrium. The possibility exists that endometrial carcinoma may develop even years after such procedure.

CASE: We report on a case of endometrial carcinoma, which was diagnosed 3 years after hysteroscopic resection of the endometrium for dysfunctional uterine bleeding in a patient with no risk factors.

CONCLUSION: Endometrial carcinoma after hysteroscopic endometrial ablation is still a possibility even when strict selection criteria are applied.

During the last 20 years, endometrial ablation has been frequently employed as an attractive alternative to hysterectomy in the treatment of medically intractable dysfunctional uterine bleeding. The option of destruction of endometrium offers women a less radical alternative to hysterectomy, especially for those who are at an increased risk for operative complications after hysterectomy or those who do not wish to undergo hysterectomy. One major concern is the potential subsequent appearance of cryptic endometrial adenocarcinoma and late diagnosis because of overlying scar tissue. We report on a patient who presented with vaginal bleeding and abdominal pain, in which endometrial carcinoma was found 3 years after hysteroscopic resection of the endometrium for dysfunctional uterine bleeding.

CASE

A 57-year-old, postmenopausal, multiparous woman was admitted to our department with irregular vaginal bleeding and abdominal pain that had persisted for the last 4 months. She was usually healthy, and her medical history revealed no classic risk factors for endometrial carcinoma, such as hypertension, diabetes mellitus, or obesity. Until 3 years before admission, she had been menstruating irregularly and heavily every 21–60 days. On examination, her uterus was normal in size. Following failure of medical treatment attempts, the patient underwent a diagnostic hysteroscopy which revealed a normal uterine cavity. An endometrial biopsy showed proliferative endometrium. Subsequently, she underwent an endometrial loop excision. The total weight of the resection specimen was 12 grams and contained myometrial tissue. The histopathological examination of the endometrial resection specimen showed secretory endometrium with focal benign glandular hyperplasia. The patient remained completely amenorrheic for 3 years. During the 2 years before the present admission, she had been suffering from mild hot flushes that did not require hormone replacement therapy. Transvaginal sonography on admission revealed an intrauterine hyperechogenic finding, 2 × 1.3 cm, in the mid-fundal region with irregularity of the endometrium-myometrium interface (Fig. 1). Increased blood flow was demonstrated by color Doppler, with a resistance index = 0.38. An attempt for endometrial biopsy and a diagnostic hysteroscopy was unsuccessful because of cervical stenosis and fibrotic adhesions. Therefore, a laparoscopically assisted vaginal hysterectomy and bilateral salpingo-oophorectomy were performed. A frozen section of the retrieved specimen demonstrated a well-differentiated endometrioid adenocarcinoma invading the outer third of myometrium. Consequently, the surgical procedure was extended to include laparoscopic pelvic and para-aortic lymph node sampling. A thorough investigation...
of the pelvis and the abdomen, including the liver and the diaphragm, revealed no metastatic spread. Final histopathology confirmed the initial frozen section report, and the disease was defined as International Federation of Gynecology and Obstetrics (FIGO) stage IC, well-differentiated (G1) endometrioid adenocarcinoma with no evidence of lymphatic invasion. The patient did very well postoperatively and was discharged on the second postoperative day.

COMMENT

Endometrial ablation has become an attractive alternative to hysterectomy for women with dysfunctional uterine bleeding who are unresponsive to medical therapy. The hysteroscopic electrosurgical operation is usually performed using a loop electrode or a rollerball device. This procedure is considered to be relatively safe and has a success rate of approximately 90%.\(^1\) Endometrial ablation is a less extensive surgical procedure and has a shorter recovery period than a hysterectomy. Moreover, the costs are reduced, and there are fewer complications than with hysterectomy, and therefore, many surgeons and patients prefer this procedure when appropriate.

Ideally, complete destruction or removal of the basal layer of the endometrium is attempted, leaving behind only the myometrium. However, no method of endometrial resection or ablation can guarantee such complete removal of the entire endometrium. The possibility exists, therefore, that endometrial carcinoma may develop after such a procedure, originating from deep crypts of remaining endometrial glands. This is particularly important when considering hormone replacement therapy for women who have undergone hysteroscopic endometrial ablation, and these women should not be treated with unopposed estrogen as opposed to those who have had a hysterectomy.

To the best of our knowledge, only 7 cases of the appearance of endometrial carcinoma following endometrial ablations have been published.\(^2\)–\(^5\) All women had at least one known risk factor for endometrial carcinoma. These risk factors included diabetes mellitus, obesity and hypertension, and associated factors, such as carcinoma of the colon, polycystic ovary disease, endometrial hyperplasia, and persistent hyperplasia of endometrium in spite of progestin treatment. It is noteworthy that endometrial hyperplasia was diagnosed before the ablation in 6 of the 7 cases reported.\(^2\)–\(^5\) Of those, 3 had associated atypia.\(^2\),\(^3\),\(^5\) Only one case had no association with endometrial hyperplasia,\(^6\) but this patient was obese, suffered from hypertension and diabetes mellitus, and had a uterus size comparable to that expected at 14 weeks of gestation.

In patients with predisposing factors for endometrial carcinoma, hysterectomy rather than endometrial ablation should be preferred. Endometrial hyperplasia without atypia is not considered a precancerous state\(^7\),\(^8\) and usually responds to progestin. When a response fails to occur, suspicion of a more severe lesion should be raised.

Our case is different from other reported cases because the patient had only focal benign glandular hyperplasia of endometrium and the endometrial biopsy before the procedure excluded atypia. It may be argued that the patient, who was not yet menopausal at the age of 54, could have been exposed to prolonged unopposed estrogens. In this case, however, we would have expected more distinct histopathological features of highly proliferative endometrium and not secretory endometrium in the resection specimen. It remains unclear whether a precancerous lesion was present at the time of endometrial resection and remained undetected or whether endometrial carcinoma developed de novo in an endometrial crypt that escaped destruction during the procedure. Whatever the case may be, the obvious conclusion is that, even when using strict selection criteria before endometrial destruction, the subsequent development of endometrial adenocarcinoma cannot be excluded.

REFERENCES

Delayed Leiomyoma Degeneration After Microwave Endometrial Ablation

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BACKGROUND: Microwave endometrial ablation is an effective treatment for dysfunctional uterine bleeding. Patients with leiomyomata, including submucosal leiomyomata up to 3 cm, may also be treated with microwave endometrial ablation.

CASES: A 46-year-old woman with multiple leiomyomata and menometrorrhagia underwent microwave endometrial ablation. Two months after microwave endometrial ablation, she developed signs of peritoneal irritation. A negative laparoscopy excluded a thermal bowel injury. Imaging and clinical examination ultimately determined that her symptoms were due to leiomyoma degeneration. A 38-year-old woman with menometrorrhagia and leiomyomata underwent microwave endometrial ablation. Fifteen days after microwave endometrial ablation, she developed signs of peritoneal irritation. With a presumptive clinical diagnosis of microwave endometrial ablation degeneration, the patient was expectantly managed with pain medications and observation.

CONCLUSION: Fibroid degeneration may have a delayed presentation after microwave endometrial ablation. Thermal bowel injury must be excluded in a patient presenting with signs of peritoneal irritation after microwave ablation of the endometrium before diagnosing leiomyoma degeneration, which can be managed expectantly.

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Microwave endometrial ablation has been found to be an effective treatment for dysfunctional uterine bleeding.1 Compared with first-generation endometrial ablative procedures, such as transcervical resection, microwave endometrial ablation is quicker and easier to perform.2,3 Although other first- and second-generation endometrial ablation procedures exclude many patients with uterine leiomyomata, most patients with leiomyoma are candidates for microwave endometrial ablation, except those with submucosal leiomyomata greater than 3 cm. We present 2 patients who developed signs of peritoneal irritation because of delayed onset of leiomyoma degeneration after microwave endometrial ablation.

CASE 1

A 46-year-old woman with menometrorrhagia and multiple uterine leiomyomata (all < 3 cm) underwent a microwave endometrial ablation. Her preoperative evaluation included an endometrial biopsy and a pelvic ultrasound examination, which demonstrated the myometrial wall to be thicker than 10 mm in all areas. In the operating room, hysteroscopy demonstrated no areas of perforation after cervical dilation to 9 mm. The microwave applicator (Microsulis Medical, Waterlooville, Hampshire, UK) was inserted into the uterine cavity. The length of the applicator used to reach the uterine fundus matched the previously measured cavity length. The microwave applicator then treated the endometrial cavity with microwave energy, starting with the fundus, then the cornua, then the lower corpus, moving slowly back and forth in a coronal plane. Information on a computer screen regarding a treatment temperature band guided the speed of the procedure. The patient was discharged home with a prescription for ibuprofen 600 mg every 6 hours as needed.

Two months after the ablation procedure, the patient presented to the emergency room with complaints of increasing abdominal pain, nausea, and vomiting for 2 days. She denied vaginal bleeding or discharge. In the emergency room, she was afebrile and hemodynamically stable but in significant discomfort. She displayed rebound and guarding on abdominal examination. Her right adnexa and uterus were tender to palpation. All laboratory tests, including a white blood cell count, were within normal limits. Radiography of the abdomen showed no free air.
Computed tomography (CT) images of the abdomen and pelvis revealed a prominent midline hypodense structure in the pelvis, with a slightly enhancing rim and a low-density center, possibly representing a degenerating leiomyoma (Fig. 1).

Although leiomyoma degeneration was our suspected diagnosis, given the possibility of a delayed thermal bowel injury, the patient was taken to the operating room for a laparoscopy and hysteroscopy. The bowel appeared healthy, with no compromised areas. The uterus was enlarged, with a blanched appearance on the anterior uterine serosa in a T-shape, consistent with the prior ablation area. Hysteroscopy revealed the endometrial cavity to be normal in appearance. Given the lack of other findings, the patient’s peritoneal symptoms were attributed to the degenerating leiomyoma visualized on the CT scan.

After pain relief from nonsteroidal anti-inflammatory medications, the patient was discharged home the next day. At a 4-week follow-up visit, she remained symptom free.

CASE 2
A 38-year-old woman with menometrorrhagia and uterine leiomyomata underwent microwave endometrial ablation with the same preoperative evaluation and surgical technique described above. A pelvic ultrasound examination described several intramural leiomyomata, all less than 3 cm.

After initially experiencing no postprocedure pain, on postoperative day 15 she developed increasingly severe cramping and pain, which led her to be evaluated in an emergency room. Similar to case 1, she had diffuse abdominal and uterine tenderness, along with rebound and guarding on physical examination. She was afebrile, with a normal white blood cell count. There were no specific findings on pelvic ultrasound examination or abdominal/pelvic CT scan. With a presumptive clinical diagnosis of leiomyoma degeneration, the patient was expectantly managed with nonsteroidal anti-inflammatory medications and observation. After several days her symptoms completely resolved.

COMMENT
With microwave endometrial ablation, cell destruction occurs to a depth of 6 mm, effectively destroying the basalis layer, minimizing the chance of regrowth of the endometrium. Targeted tissues are heated by microwaves to 70–80°C during the procedure. The advantages of microwave endometrial ablation, compared with other ablative techniques, are that it is safe, rapid, and simple to use. Additionally, it may also be used on patients with distorted uterine cavities due to leiomyomata, including submucosal leiomyomata that are less than 3 cm in diameter.

In a randomized controlled trial comparing outcomes after transcervical endometrial resection and microwave endometrial ablation, there were few treatment failures and needs for hysterectomy in both groups that were followed postprocedure for 2 years. The effects on dysmenorrhea, amenorrhea, and menstrual flow were not statistically different between the 2 groups. A small number of women required diagnostic laparoscopy because of pelvic pain after both treatment methods, but information about these women was not included in the paper.

Both of our patients were relatively asymptomatic after their microwave endometrial ablation procedures until their acute onsets, 2 weeks and 2 months postoperatively, of abdominal and uterine pain, most likely caused by leiomyoma degeneration. Although both displayed peritoneal signs, neither was febrile nor had an elevated white blood cell count. A clinical decision was made to perform a diagnostic laparoscopy in case 1 to rule out a thermal bowel injury. The patient in case 2 was merely observed, with this decision being made at a different institution. Both patients’ pain soon resolved without further incident.

Leiomyoma degeneration may be caused by an interruption of its blood supply causing ischemia. Theoretically, the thermal effects of the microwave endometrial ablation procedure may have compromised the vascular web surrounding a leiomyoma, ultimately leading to its delayed degenerative changes. Although leiomyoma degeneration is a known cause peritoneal irritation, it is normally a diagnosis of exclusion. In situations such as those experienced by these 2 patients after microwave endometrial ablation, it is crucial to initially exclude a thermal bowel injury. If the evaluation is negative and
the patient is diagnosed with leiomyoma degeneration, expectant management will typically suffice.

REFERENCES

Twin Pregnancy Complicated by Severe Hemolytic Disease of the Fetus and Newborn Due to Anti-G and Anti-C

Thomas N. Trevett Jr, MD, and Kenneth J. Moise Jr, MD

BACKGROUND: Hemolytic disease of the fetus and newborn caused by anti-G antibodies is rare, and in most previously reported cases, leads to a mild anemia. The RhG antigen is usually found in association with both RhD and RhC. We report a case of a twin pregnancy affected by both anti-G and anti-C alloantibodies leading to severe hemolytic disease of the fetus and newborn requiring multiple intrauterine transfusions and prolonged postnatal therapy.

CASE: A patient with a prolonged history of previously affected pregnancies due to anti-D and anti-C was subsequently found to be affected with anti-G instead. She required aggressive therapy during her pregnancy, initially with intravenous immune globulin and plasmapheresis until umbilical blood sampling and intrauterine transfusions were feasible.

CONCLUSION: Although hemolytic disease of the fetus and newborn due to anti-G antibodies is rare and usually mild, these pregnancies should be followed up closely and in utero therapy should be offered if necessary.

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See related case report on page 1180.

Trevett and Moise Twin Pregnancy and Hemolytic Disease

Severe red cell alloimmunization due to documented antibodies produced in response to the RhG red cell antigen is rare. There are few case reports of anti-G in pregnancy causing significant hemolytic disease of the fetus and newborn. This may in part be due to the difficulty in distinguishing anti-G antibodies from a combination of anti-D and -C antibodies.1 Most red cells that express the RhD or RhC antigen or both also express the RhG antigen.2 To accurately distinguish between anti-G antibodies and anti-D and -C antibodies, the blood bank must perform a separate elution assay with maternal serum against indicator red cells negative for the RhD and RhC antigens but positive for the RhG antigen.

In this case report we present a woman who was initially thought to have produced anti-D and -C antibodies but was found to have anti-C and -G antibodies. The implications for the management of such a pregnancy are discussed.

CASE

The patient was a 34-year-old gravida 7 para 2–0–4–2 who presented for management of her twin pregnancy complicated by red cell alloimmunization thought to be due to anti-D and anti-C. She was sensitized during her first pregnancy, an ectopic gestation for which she did not receive Rhesus immune globulin (RhIG). Her subsequent pregnancies included 2 additional ectopic pregnancies and the delivery of 2 term infants with no evidence of active hemolytic disease of the fetus and newborn. In her sixth pregnancy a presumed anti-D titer of 1,024 was associated with hydrops fetalis and an intrauterine demise at 21 weeks of gestation.

Parental phenotypes were determined using serologic methods. The maternal red cell phenotype was A, Rh dce/dce; the paternal phenotype was O, Rh DCe/Dce. She was referred to our institution for therapy at 12 weeks and had ultrasonography that revealed viable diamniotic, dichorionic twins. The first antibody screen done at our institution returned with an anti-G antibody at a titer of 512. An anti-C antibody was present at a titer of 1,024 and here was no evidence of an anti-D.

As she had experienced an early second trimester perinatal loss secondary to hydrops, intravenous immunoglobulin
Plasma exchange followed by IVIG (1 g/kg) was repeated at weekly intervals until 21 weeks of gestation. Weekly peak middle cerebral artery velocimetry remained stable in both fetuses during this period. At 21 weeks, the middle cerebral artery of twin A became elevated at 1.69 MoM, whereas that of twin B was 1.48 MoM. A percutaneous umbilical blood sampling/intrauterine transfusion was undertaken. The initial hematocrit for twin A was 23%. An intravascular transfusion of 7 mL of packed red blood cells resulted in a final hematocrit of 30%; an intraperitoneal transfusion was then performed with 10 mL of packed red blood cells (hematocrit 77%). The initial hematocrit on twin B was 33%, for which 10 mL of packed red blood cells were transfused intravascularly. A final hematocrit could not be obtained; no intraperitoneal transfusion was undertaken in twin B. Five days later, a repeat intrauterine transfusion was performed on twin A. No procedure was performed on twin B, because its repeat middle cerebral artery Doppler measurement was normal at 0.85 MOM. At 23 weeks of gestation, a third intrauterine transfusion was performed on twin A. Twin B had an elevated middle cerebral artery of 1.46 MoM, and although increased, it did not meet criteria for severe anemia after an intrauterine transfusion based on the work by Detti et al. A decision was made to repeat the middle cerebral artery of twin B in 1 week to prevent the missed detection of a developing anemia. At the follow-up ultrasound appointment, a fetal demise of twin B was diagnosed. There was evidence of gross hydrops that had not been noted on ultrasonography by the referring physician 3 days earlier. A repeat maternal titer was obtained and noted to be > 16,000 for anti-G, obscuring the anti-C titer. Twin A appeared viable without any evidence of distress or hydrops.

Four subsequent intrauterine transfusions were performed on the viable twin without complication. At 33 weeks of gestation the patient experienced the onset of spontaneous preterm contractions and delivered 1 viable female and 1 nonviable female neonate vaginally. Cord blood values of the viable twin revealed a hematocrit of 35.3%, 6% fetal red cells on flow cytometry, and a total bilirubin of 5.4 mg/dL. Postnatal serology confirmed the presence of anti-G and -C antibodies. The infant was admitted to the neonatal intensive care unit for 12 days and required only phototherapy, but no red cell transfusions. In the first 4 months of life, the infant required 3 red cell transfusions for recurrent anemia as well as supplemental erythropoietin injections, but was then exhibiting normal red cell production.

**COMMENT**

Allen and Tippett first described a novel red cell antigen in 1958 when they discovered an entire family whose blood samples produced very unusual reactions when crossed with standard grouping sera. They named it the “G” antigen. Work by Faas et al demonstrated that a single amino acid substitution at position 103 was encoded by exon 2 of both the RhD and RhC genes. This serine moiety is located in the second extracellular loop of both RhD and RhC proteins and results in the “G positive” phenotype. The presence of this serine at position 103 is necessary for both the antigenicity of the RhG protein as well as the conformation of the protein on the extracellular surface. Most RhD- or RhC-positive patients will also be G positive, and the converse is also true.

In many cases of maternal red cell alloimmunization, the anti-D antibody is often found in conjunction with an anti-C antibody of low titer. The likelihood that the outcome in this case was secondary to anti-C antibodies is low, because there are only 2 cases in the literature regarding severe hemolytic disease of the fetus and newborn due to anti-C. The clinician should suspect the presence of an anti-G antibody when the anti-C titer equals or surpasses the level of anti-D. In their review, Hadley et al described a woman initially thought to have a pregnancy sensitized to anti-D antibodies who subsequently delivered an RhD-negative child. On reanalysis, an anti-G antibody was discovered. This prompted a review of the serum of 28 other women with alloimmunization due to anti-D and -C antibodies. They found that 7 of 28 (25%) of these patients had titers of anti-G greater than anti-D titers. This work confirmed a previous report from Issitt and Tessel, who found 30% of anti-D- and -C patients had anti-G antibodies and a small percentage of those (6%) had anti-G as the predominant antibody.

Previous literature has suggested that anti-G antibodies are not likely to cause significant hemolytic
disease of the fetus and newborn. Indeed, a report by Cash et al\textsuperscript{2} described the first case of hemolytic disease of the fetus and newborn secondary to anti-G antibodies at a titer of 64; intrauterine and postnatal transfusions were not required for treatment. The virulence of the anti-G antibody is echoed in the case report by Shirey et al,\textsuperscript{2} who reported a case of anti-C and -G (maximum anti-G titer of 8) without anti-D that had a mild neonatal hemolytic course without need for phototherapy.

The presence of anti-G has another important implication for the clinician. Because the antibody is often mistaken for an anti-D, the patient may not receive appropriate RhIG when indicated. Potentially, this could result in the development of a new anti-D antibody, which could further exacerbate the hemolytic disease of the fetus and newborn caused by the anti-G. Our patient was given a total of 6 doses of RhIG during her pregnancy and postpartum.

This report demonstrates that although rarely reported and difficult to identify correctly, pregnancies affected by alloimmunization to the RhG antigen can lead to devastating consequences and should be managed identically to pregnancies affected by immune-mediated anemia from sensitization to other red cell antigens.

REFERENCES

The history of erythroblastosis fetalis has changed dramatically over the past 50 years. The perinatal death rate was 50% before the current evaluation and treatment methods and is considered by many to be a true perinatal success story. Because of the introduction of antibody titers, amniocentesis for determination of delta OD450 bilirubin levels, fetal transfusion, Rh-immunohyphylaxis, and middle cerebral artery peak systolic velocity measurements, hemolytic disease of the newborn secondary to isoimmunization today affects only 1–6 in 1,000 live births and rarely results in perinatal mortality.

Uncommon red blood cell antigens have become more clinically significant as pregnancies complicated by anti-D have decreased with the widespread use of Rh immune prophylaxis. The more common atypical antigens that are known to be capable of causing hemolytic disease of the newborn include Kidd, Kell, Duffy, c, E, and C. However, a number of rare atypical antigens have been reported to cause fetal hemolytic disease.

Cw is a low-frequency red blood cell antigen from the Rh antigen system (Rh8). It is usually inherited along with the common Rh haplotype, CDe, possibly showing reduced expression of the C antigen. At the molecular level, it is characterized by an Arg to Gln nucleotide substitution of the gene that encodes the Rh antigens. Approximately 2% of the United States population carries the Cw antigen. This uncommon antigen’s effect on pregnancy is largely unknown, but anti-Cw–sensitized pregnancies have been described in the literature. We report a case of anti-Cw isoimmunization that resulted in severe fetal anemia, requiring multiple intrauterine transfusions.

CASE

A 28-year-old multigravida transferred to our facility at 18 weeks of gestation during her fourth pregnancy. She had a cervical cerclage in place because of a history of cervical incompetence. She had a very complicated obstetric history, including 2 preterm deliveries at 32 and 34 weeks. Her family history was significant for thromboembolic disease and she was diagnosed with protein S deficiency at age 25. All of the prior pregnancies had been managed at a different obstetric clinic, and all resulted in the delivery of liveborn neonates without long-term complications.

Her third pregnancy was complicated by anti-Cw isoimmunization. Her initial antibody screen at 10 weeks of gestation revealed an anti-Cw titer of 1:64. A repeat titer at 14 weeks of gestation was 1:256. In addition she was found to have 2 other antibodies in low titers, anti-Kell (1:1) and anti-S (1:8). These antibodies required referral to a reference laboratory for identification. The anti-Kell and anti-S antibody titers remained less than 1:16 throughout that pregnancy. Her husband was heterozygous for the Cw antigen and negative for the Kell and S antigens. No laboratory could be found that was capable of performing fetal Cw determination using amniotic fluid. Her pregnancy was managed by serial ultrasound examinations and amniocenteses. The middle cerebral artery peak systolic velocity always remained less than 1.5 multiples of the median (MoM), corresponding to mild fetal anemia.

She delivered a healthy baby at 35 weeks of gestation secondary to preterm labor. The initial neonatal hematocrit was 32%, and the neonate had a positive direct antibody test and was found to be positive for the Cw antigen. The initial reticulocyte count was elevated to 7.6% and the lactate dehydrogenase (LDH) level was elevated to 277 U/L. The hematocrit decreased to 24% on postpartum day 2. The neonate was significantly affected and required several exchange transfusions. The patient was advised after delivery that future pregnancies would be more severely affected, with the possible need for intrauterine transfusion if the fetus was again Cw positive.

In her fourth pregnancy, the patient’s initial anti-Cw titer was 1:8. She was also found to have anti-V and anti-M antibodies, both with titers of 1:1 throughout the pregnancy. The previously identified anti-Kell and anti-S antibodies were not present. Her husband was negative for the V and M antigens. She was followed with weekly ultrasound examinations to assess the amniotic fluid volume and middle cerebral artery Doppler velocity and for evidence of fetal hydrops. Multiple attempts were made without success to locate a laboratory capable of identifying the Cw antigen on the fetus. At 18, 20, 21, and 22 weeks of gestation, the middle cerebral artery peak systolic velocity ranged from 24 to 40 cm/s, which corresponded to less than 1.5 MoM, thus representing mild fetal anemia. The middle cerebral artery Doppler peak systolic velocity increased to 60 cm/s (1.5–1.75 MoM) by 24 weeks of gestation, suggesting moderate-to-severe fetal anemia. An amniocentesis for optical density (OD)450 was performed with a value of 0.223, which corresponded to the intratropic death risk on the Queenan curve. No evidence of fetal hydrops was seen on ultrasonography. A fetal intravascular transfusion was then performed. The opening fetal hematocrit was 24%. The fetus was transfused with 30 mL of packed red blood cells, and the closing fetal hematocrit was 40.7%.

At 27 weeks of gestation, a repeat ultrasound examination revealed elevated middle cerebral artery peak systolic velocities without evidence of fetal hydrops. A second fetal intravascular transfusion was performed. The opening fetal hematocrit was 27%. An uncomplicated transfusion of 50 mL of packed red blood cells was performed. Before obtaining a posttransfusion hematocrit, the fetus moved and dislodged the needle.

The patient had preterm premature rupture of the membranes at 30 weeks of gestation and underwent an uncomplicated spontaneous vaginal delivery the same day. She had an uncomplicated postpartum course and was discharged home on postpartum day 2. The initial neonatal hematocrit was...
40%. The neonate was found to be direct antibody test–positive and a carrier of the Cw antigen. The initial reticuloocyte count was 1.8%, reflecting the recent transfusion. The LDH level was elevated to 259 U/L, and the peripheral smear revealed marked polychromasia. The neonate required 3 postdelivery blood transfusions, with no long-term therapy required. No other causes of fetal anemia were identified in the antepartum or postpartum period.

**COMMENT**
To the best of our knowledge, this case represents the first description of severe isoimmunization from Cw antibodies requiring intrauterine fetal transfusion. Severe isoimmunization was based on the definition from Mari et al. This case emphasizes the potential severity of atypical red blood cell antigens, many of which are not thought to cause severe hemolytic disease. The presence of the other atypical antibodies is somewhat confusing, but given that the titers of these antibodies were always low (<1:16), we believe that the fetal anemia was due to the presence of the anti-Cw antibodies. The work by Spong et al. demonstrated that the presence of more than one antibody confers a higher risk of severe isoimmunization, but in their study all severe cases were associated with the presence of anti-D. Despite the presence of multiple antibodies, a critical titer of 1:16 should still be used.

A MEDLINE search limited to English and humans, using the search terms “anti-Cw,” “isoimmunization,” and “pregnancy,” was performed (1966 to November 2004). Anti-Cw has not previously been reported to cause severe fetal anemia or require intrauterine fetal transfusion. Some cases of anti-Cw in pregnancy are due to naturally occurring antibodies, without antecedent exposure to Cw-positive red blood cells. In other cases, a history of transfusion or paternal Cw positivity offers an explanation for the finding of maternal antibodies. Clark and colleagues in 1999 found that 11% of their study group had “enzyme only” naturally occurring anti-Cw antibodies and that these antibodies were clinically insignificant. Mild-to-moderate hemolytic disease of the newborn has been associated with anti-Cw antibodies. Bowman and Pollack, from Winnipeg, reported the largest population of pregnancies complicated by maternal Cw isoimmunization. Most cases were associated with mild-to-moderate neonatal anemia requiring phototherapy or exchange transfusions after delivery.

Prior reports do not recommend further evaluation for fetal anemia during pregnancy complicated by Cw isoimmunization, only close postpartum surveillance. However, we believe that anti-Cw should be added to the list of atypical antibodies that have the ability to cause severe hemolytic disease during pregnancy. If anti-Cw antibodies are identified, the pregnancy should be managed the same as those complicated by the more common atypical antibodies. Management may include the use of antibody titers, paternal antigen determination, Doppler assessment of the peak systolic velocity of the middle cerebral artery, amniocentesis, and fetal intravascular transfusion when needed. The technology to evaluate amniotic fluid for Cw typing has been reported, but unfortunately it is not commercially available.

**REFERENCES**
Spontaneous Resolution of Mirror Syndrome

Allison M. Goeden, MD, and Dennis Worthington, MD

BACKGROUND: Mirror syndrome, a rare condition characterized by maternal anasarca in a pregnancy complicated by fetal hydrops, may have a devastating fetal outcome and significant maternal morbidity.

CASE: We report a case of mirror syndrome caused by parvovirus B19 infection, which resolved spontaneously with good fetal and maternal outcome.

CONCLUSION: The pathogenesis of mirror syndrome is not understood. The trigger for mirror syndrome may be derived from a compromised fetus or placenta.

(Mirror Syndrome)
Ultrasound examination showed the fetus to have grown appropriately, but it remained hydropic. At 24 weeks, the patient was given a course of corticosteroids to accelerate fetal maturation in the anticipation that early delivery was likely. Because the fetal heart rate and fetal biophysical profiles remained reasonable and maternal condition remained stable, delivery was delayed. At 26 2/7 weeks, ultrasound examination showed significant improvement in the fetal hydrops. Maternal blood pressure was in the range of 130–140/80–90 mm Hg. Maternal laboratory studies remained stable and serum uric acid fell to 5.9 mg/dL, although protein excretion persisted at 2,409 mg per 24 hours. The patient was discharged and followed as an outpatient.

At 28 3/7 weeks of gestation, an ultrasound examination showed complete resolution of the fetal hydrops (Fig. 2). The patient’s edema had resolved, with a weight loss of 12.7 kg, her blood pressure was normal, and 24-hour urine protein excretion was only 369 mg.

The pregnancy was followed closely, and there was no recurrence of fetal hydrops or signs of preeclampsia. At 36 6/7 weeks of gestation, due to a decreased amniotic fluid index and asymmetric growth restriction, induction of labor was carried out. Labor was uneventful, and the patient spontaneously delivered an infant female weighing 1,932 g, with Apgar scores of 8 and 9. The placenta was normal. The infant was discharged from hospital on day 10 of life. The mother’s immediate postpartum course was normal, and her postpartum serology for parvovirus B19 showed IgG levels slightly lower than in earlier pregnancy and undetectable IgM.

**COMMENT**

The clinical picture of mirror syndrome has several characteristics. It frequently presents in the late second or early third trimester at an average gestational age of 27 weeks. Carbillon et al. described the clinical picture of mirror syndrome as a “characteristic triad” of massive edema, oliguria, and hemodilution in the context of fetal hydrops. Also noted are mild albuminuria and slight elevations of blood pressure. The syndrome seems to simulate preeclampsia although there are distinguishing features. Patients with mirror syndrome have intravascular volume...
expansion that results in anemia, whereas patients with preeclampsia have hemoconcentration.\textsuperscript{1–3} Preeclampsia has been noted to develop in the course of mirror syndrome but not in all cases.\textsuperscript{2} Occasionally, preeclampsia may progress to become severe,\textsuperscript{2} but eclampsia is rare.\textsuperscript{1,3} The fetal prognosis for untreated mirror syndrome is poor, and its development usually indicates impending fetal death.\textsuperscript{1,2}

Many of the known causes of fetal hydrops can be associated with mirror syndrome. Carbillon et al\textsuperscript{1} reported that fetal hydrops of any etiology can be associated with mirror syndrome and that it manifests when the fetal status becomes severe. Some of the reported conditions include fetal cardiac arrhythmias, Ebstein’s anomaly, placental chorioangioma, aneurysm of the vein of Galen, a-thalassemia, sacrococcygeal teratoma, trisomy 13, erythroblastosis, and human parvovirus B19 infection.\textsuperscript{1,4}

There are reported cases of antepartum resolution of mirror syndrome. In each of these cases, improvement in the maternal condition was noted after treatment for the cause of the fetal hydrops was rendered. Heyborne and Chism\textsuperscript{5} described a case in which a twin pregnancy was complicated by mirror syndrome. Selective termination of the hydropic twin resulted in resolution of the mirror syndrome, and the pregnancy continued without complication. In another case reported by Midgeley and Harding,\textsuperscript{4} fetal hydrops caused by a tachyarrhythmia was associated with mirror syndrome, which resolved after treatment with flecainide. Duthie and Walkinshaw\textsuperscript{6} reported a case of reversal of mirror syndrome after in utero blood transfusion of a hydropic, anemic fetus due to infection with parvovirus B19.

Parvovirus B19 is a well-known cause of nonimmune hydrops fetaalis. It is reasonable to assume that fetal hydrops in our case was caused by parvovirus. The patient and her family had upper respiratory symptoms about 3 weeks before presentation. Her antibody levels for parvovirus were positive for infection, indeterminate for a recent infection, and both IgG and IgM levels were lower postpartum. Other causes of fetal hydrops were ruled out. Spontaneous resolution of nonimmune hydrops fetaalis secondary to human parvovirus B19 infection is known to occur. Pryde et al\textsuperscript{7} described 2 cases of nonimmune hydrops fetaalis secondary to human parvovirus B19 infection that were managed expectantly and resulted in healthy infants with no identified sequelae.

Mirror syndrome has been reported in association with parvovirus B19 infection.\textsuperscript{8} The case described by Ville et al\textsuperscript{8} involved a mother with acute respiratory distress syndrome and death of the fetus. There was no attempt to treat the fetal hydrops because the mother’s condition was unstable and the fetus died within hours of hospital admission. The other published case of parvovirus and mirror syndrome described resolution of the fetal and maternal condition after treatment by in utero blood transfusion.\textsuperscript{5} Other treatable causes of mirror syndrome have shown resolution after successful treatment of the fetal condition.\textsuperscript{2,4–6} Our case demonstrates reversal of the maternal signs of mirror syndrome after spontaneous reversal of fetal hydrops. Over a 5-week period of observation, during which time fetal pleural, pericardial, and intraabdominal effusions disappeared, significant maternal peripheral edema resolved (12.7-kg weight loss) while blood pressure and proteinuria improved.

Mirror syndrome is not common, and its pathogenesis is not understood. It has been suggested that placental pathology may contribute to the development of the condition,\textsuperscript{1,3} but the pathophysiology remains elusive. It is interesting to speculate that a “trigger,” from either a compromised fetus or placenta, could initiate a profound change in maternal condition that is potentially reversible. Although we did not intend to treat our patient conservatively, her refusal to undergo a second attempt at PUBS and possible intrauterine transfusion left us with no alternative. The fetal consequence when mirror syndrome develops is dire,\textsuperscript{1,2} and we fully expected fetal death to occur or deterioration in maternal condition to necessitate early delivery. Hypertension and significant proteinuria are not usually associated with mirror syndrome but likely develop in the latter stages of an untreated situation. Also, anemia, which is said to be a hallmark of the mirror syndrome,\textsuperscript{1–3} was not significant in our case. One would anticipate that expectant management would result in resolution of maternal pathology following fetal death. However, the fetal hydrops reversed, presumably as fetal anemia improved, and with this improvement, there was a marked maternal diuresis accompanied by improvement in blood pressure, proteinuria, and serum uric acid level. The relationship between fetal hydrops, mirror syndrome, and preeclamptic toxemia remains an unanswered question, but awareness of the condition by clinicians may allow further exploration of clinical and biochemical characteristics to help resolve this enigma.

REFERENCES

Preterm Torsion of a Gravid Uterus Didelphys Horn of a Twin Pregnancy

Fabien Demaria, MD,
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Dominique Cabrol, MD, PhD

BACKGROUND: Simultaneous pregnancy in each horn of a uterus didelphys is a rare and complex clinical situation.

CASE: Torsion of one horn of a gravid didelphic uterus during a twin pregnancy was diagnosed during cesarean delivery after erroneous diagnosis of abruptio placentae.

CONCLUSION: Localization of the placenta in a pregnancy complicated by uterine didelphys may improve the ability to diagnose hemiuterus torsion.

(Obstet Gynecol 2005;106:1186–7)

Simultaneous pregnancy in each horn of a uterus didelphys is a rare and complex clinical situation.1 Hemiuterus torsion is a well-known complication of gravid uterus didelphys during labor, which requires cesarean delivery to treat fetal distress or failure of labor to progress.2 We report a case of gravid hemiuterus torsion during the third trimester in a didelphys uterus with twin pregnancy.

CASE

A 23-year-old woman, para 3, gravida 2, with a documented 2-horned, bicervical uterus, was diagnosed at 9 weeks with a twin pregnancy, with one embryo in each hemiuterus. The pregnancy was uneventful until 27 weeks, when sudden abdominal pain developed in the right groin radiating to the lumbar region. Physical examination was normal, with supple abdomen and no rebound tenderness, mild irregular uterine contractions with no major changes of the 2 cervixes at digital examination and no vaginal bleeding. Fetal tracing and ultrasonography were normal for both fetuses. Blood analyses revealed moderate anemia (10.4 g/dL); platelet count and liver enzymes were normal. No proteinuria was detected. Thinking the patient was in preterm labor, we administered an intravenous tocolytic agent (nicardipine 2 mg/h) and intramuscular betamethasone (12 mg) for fetal lung maturation. Uterine contractions ceased rapidly, but the patient still complained of abdominal pain, which intensified the following day. Hemoglobin had declined to 8.5 g/dL. Platelet count, prothrombin time, and activated clotting time were normal, but the D-dimer level was elevated. Liver function tests showed no hepatic cytolysis, but total hyperbilirubinemia, mostly the free form, and hemolysis were present. The urinary dipstick became protein positive. Despite tocolysis, irregular uterine contractions reappeared and vaginal bleeding occurred.

Abruptio placentae in the right horn was suspected, and an elective cesarean was determined to be necessary. The twins were delivered through transversal hysterotomies, performed on both hemiuteri, but the incision in the right horn proved to be transplacental. The placenta was removed, and no evidence of abruptio placentae was found. Externalization of the uterus didelphys revealed a 180° clockwise torsion of the right hemiuterus. Upon retrospective review of all ultrasound reports, the placenta in the right horn was found to be inserted in the posterior wall on the last examination, performed 48 hours before the delivery, thereby confirming that the posterior wall of the right horn, erroneously thought to be the anterior wall, was incised during the cesarean. Both neonates had uneventful postnatal outcome and were discharged at 6 and 8 weeks.

COMMENT

Pregnancies in uteri with symmetric congenital malformations are at higher risk of spontaneous abortion,
premature labor, abnormal fetal presentation, abnormal placental insertion, and abruptio placentae. More specific to uterus didelphys is the risk of hemiuterus torsion, which has only been reported during labor. In that case, the diagnosis was made during the cesarean performed in response to abnormal fetal tracing and failure of labor to progress.

Our observation illustrates that torsion of one uterine horn can also occur before labor starts. Unlike the torsion described during labor, that occurring during pregnancy might be difficult to recognize because it may mimic more common complications associated with this type of uterine malformation [ie, abruptio placentae or premature labor]. Indeed, the association of abdominal pain, irregular uterine contractions, vaginal bleeding, and hemolytic syndrome made the diagnosis of abruptio placentae the most likely. However, this case illustrates the importance of accurate localization of the placenta(s) at midgestation in uterus didelphys. All of our patient’s ultrasonography reports before she developed abdominal pain had mentioned that the placenta in the right hemiuterus was inserted posteriorly. However, during the cesarean delivery, because of the torsion, it was found to be inserted into what had been thought to be the anterior wall of the right hemiuterus, leading to unavoidable translaplacental hysterotomy. The vaginal bleeding and hemolytic syndrome were probably the consequence of the torsion-induced ischemia of the right hemiuterus and made cesarean delivery the only valid option to avoid any major fetal or maternal morbidity.

REFERENCES

Herpes Simplex Virus Hepatitis Causing Acute Liver Dysfunction and Thrombocytopenia in Pregnancy

Rebecca H. Allen, MD, MPH, and Ruth E. Tuomala, MD

BACKGROUND: Herpes simplex virus (HSV) hepatitis in pregnant women is a rare condition. We report a case confirmed by liver biopsy and successfully treated with empiric intravenous acyclovir.

CASE: A 25-year-old primigravida at 34 weeks of gestation presented with fever, thrombocytopenia, and markedly elevated liver enzymes. The patient was treated empirically and was delivered by cesarean. After delivery failed to correct her condition, a liver biopsy revealed HSV hepatitis. The fetus was unaffected and the patient recovered with an extended course of acyclovir.

CONCLUSION: Pregnant women are susceptible to disseminated HSV causing hepatitis. A high index of suspicion is necessary to diagnose HSV hepatitis and begin appropriate treatment with acyclovir. Herpes simplex virus hepatitis should be included in the differential diagnosis for liver failure during pregnancy.

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Herpes simplex virus (HSV) hepatitis in pregnancy is a rare condition that can be a difficult diagnosis to make. Inclusion of HSV hepatitis in the differential diagnosis of liver dysfunction, liver biopsy, and administration of acyclovir can decrease morbidity and mortality rates for both mother and fetus.

CASE

A 25-year-old healthy primigravida at 34 weeks of gestation presented with the complaint of 1 week of fevers, chills, malaise, myalgias, and diffuse abdominal pain. The patient denied nausea, vomiting, diarrhea, constipation, dysuria, vaginal discharge, headache, blurry vision, contractions, leakage of fluid, and vaginal bleeding.

The patient’s prenatal course was notable for negative prenatal screens, including antibody to human immunodeficiency virus (HIV) and a urine culture significant for β-hemolytic Streptococcus bacteria, for which treatment with oral cephalixin was initiated 7 days before presentation. Her gynecologic history included prior chlamydia infection, pelvic inflammatory disease, and cervical dysplasia but no history of HSV disease. Use of tobacco, alcohol, or illicit drugs was denied.
Vital signs included a temperature of 102°F and normal heart rate, blood pressure, and respiratory rate. Heart and lung examination were normal, and abdominal examination was significant for a gravid nontender uterus and nonpalpable liver edge. Baseline fetal heart rate was 150 with reactivity. The cervix was 1 cm dilated, 50% effaced, and in a posterior position.

Initial laboratory studies included normal electrolytes and trace protein on urinalysis. A complete blood count revealed a white count of 6,400/µL with 20% band forms, hematocrit of 32.6%, platelets of 143,000/µL, and bunn cells on peripheral smear. Coagulation parameters showed a prothrombin time (PT) of 10.7 seconds and partial thromboplastin time (PTT) of 41.4 seconds. Hepatic panel revealed aspartate aminotransferase (AST, normal range 0–40 U/L) of 643 U/L, alanine aminotransferase (ALT, normal range 0–40 U/L) of 279 U/L, and normal bilirubin levels. Urine, blood, and amniotic fluid cultures subsequently returned as negative. Imaging revealed a normal chest X-ray, an enlarged hyperechoic liver on ultrasonogram, with thickened gall bladder wall but no gallstones, and a well-grown fetus (2,175 g) with normal amniotic fluid.

Empiric broad-spectrum antibiotics were begun. Because of the worsening of her condition, on hospital day 4 the patient was transferred to a tertiary care facility. Upon presentation, laboratory studies revealed worsening coagulopathy and liver failure, with platelets of 83,000/µL, PTT 44 seconds, PT 16 seconds, AST 2,240 U/L, ALT 980 U/L, and lactate dehydrogenase (LDH, normal range 107–231 U/L) of 2,045 U/L. Bilirubin, fibrinogen, and electrolytes remained within normal range. The patient’s white count was 3,000/µL, with 7% band forms. Her vital signs were stable; physical examination now revealed mild right upper-quadrant tenderness. The external fetal monitor tracing documented a baseline fetal heart rate of 150, no accelerations, and minimal variabilty. Shortly after presentation, irregular, spontaneous contractions were noted, with associated persistent moderate variable decelerations and loss of variability.

Because of worsening hepatic failure that was consistent with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP), in addition to other diagnostic possibilities, and because the fetus was at 34 weeks of gestation, delivery was contemplated. Due to the deterioration in fetal heart rate pattern, the patient was taken for an urgent cesarean delivery. She received 2 units of fresh frozen plasma before her surgery and received spinal anesthesia without complication. A 4-pound, 7-ounce male infant was born, with Apgar scores of 8 at 1 minute and 9 at 5 minutes.

Postpartum, temperature elevations continued, reaching a maximum of 102.3°F. Her platelets reached a nadir of 68,000/µL; AST and ALT peaked at 955 U/L and 2,360 U/L, respectively. The patient was started on empiric intravenous ampicillin, ceftriaxone, metronidazole, and acyclovir. Serum antibody titers were negative for HIV, hepatitis A, B, and C, cytomegalovirus, toxoplasmosis, and Epstein-Barr virus. Abdominal computed tomography (CT) scan performed on postpartum day 1 showed numerous low attenuation lesions throughout the liver, possibly representing microabscesses. A CT-guided transcutaneous liver biopsy was performed, which was found to be diagnostic of HSV by pathology, special stains, and culture. Enzyme immunoassay for anti-HSV types 1 and 2 immunoglobulin G (IgG) was positive, with an index value of 1.69 (≥ 1.0 positive). Acyclovir was continued, and the patient was discharged home on postpartum day 8 to complete 3 more weeks of antiviral therapy. Infant cultures were negative for HSV, and he was discharged home with his mother. The placenta showed no signs of infection histologically, and HSV stains were negative.

**COMMENT**

To date, 27 cases of HSV hepatitis during pregnancy, including the current case, have been reported. Disseminated HSV infection causing hepatitis is rare in adults. It has been documented in immunocompromised adults, including renal transplant patients and those receiving steroid therapy. Pregnant women are also susceptible. Herpes simplex virus hepatitis may result from both HSV serotype 1 and serotype 2, as well as both primary and latent infections.

The differential diagnosis includes severe preeclampsia/HELLP syndrome and acute fatty liver of pregnancy, as well as hepatitis due to other viral pathogens or exposure to exogenous substances, including drug reactions. Distinguishing characteristics of HSV hepatitis include markedly elevated transaminases with normal bilirubin levels and coagulopathy. Leukopenia and thrombocytopenia may be associated. Half of cases lack the presence of typical HSV mucocutaneous lesions. Patients with no known history of genital or oral HSV may present with the disease. Clinicians must maintain a high index of suspicion for the possibility of HSV hepatitis in any pregnant woman with hepatic failure.

Appropriate antepartum management when the diagnosis of HSV hepatitis is suspected includes the empiric administration of acyclovir pending results of confirmatory diagnostic tests. Acyclovir is the drug of choice for treatment and is considered to improve the survival rate. Percutaneous liver biopsy is the recommended method of diagnosis. As in this case, immuno histochemical studies for the HSV antigen secure the diagnosis. Additional diagnostic techniques that can suggest the diagnosis of HSV hepatitis include CT scan, which can show low-density areas of necrosis in the liver, and serologic studies. In this case, if concern about fetal status had not intervened, the CT
scan might have indicated the need for liver biopsy and empiric acyclovir as opposed to preterm delivery.

Even in the face of progressive liver failure with coagulopathy, the diagnostic work up for HSV should proceed, and acyclovir should be instituted in an effort to both avoid unnecessary preterm delivery and maximize maternal outcome. A recent review of the literature reported a maternal mortality rate of 39% due to HSV hepatitis, with an associated neonatal mortality of 39%. The cause of fetal death is difficult to ascertain because many reports do not report the neonatal HSV infection status or fetal status before delivery. It is unknown whether delivery improves neonatal survival in this condition.

**REFERENCES**


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**Life-Threatening Maternal and Fetal Macrocytic Anemia From Antiretroviral Therapy**

*Stephen A. Myers, DO, Sandra Torrente, MD, Daniel Hinthorn, MD, and Perry L. Clark, MD*

**BACKGROUND:** Antiretroviral therapy is recommended for human immunodeficiency virus (HIV)-infected patients during pregnancy to reduce the vertical transmission to the newborn. Complications from this therapy are uncommon.

**CASE:** A 38-year-old HIV–positive pregnant woman was treated with lamivudine and zidovudine. At 28 weeks of gestation, her hemoglobin had fallen to 4.6 g/dL with an mean corpuscular volume (MCV) of 126 μm. At 36 weeks the fetal biophysical profile was abnormal. A pale hydropic infant was delivered via emergency cesarean, with a hemoglobin of 2.1 gm and MCV of 131 μm. The newborn hemoglobin normalized after withdrawal of the neonatal retroviral therapy.

**CONCLUSION:** Maternal-fetal macrocytic anemia may complicate antiretroviral therapy.

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The Centers for Disease Control and Prevention estimate that nearly 7,000 women infected with the human immunodeficiency virus (HIV) deliver each year in the United States. Therapy is aimed at not only maximizing maternal well-being, but also reducing the risk of vertical transmission from mother to fetus.

Since the publication of the Pediatric AIDS Clinic Trial Group (PACTG) Protocol 076 in 1994, it is clear that significant reduction in vertical transmission with monotherapy can be accomplished. That regimen consists of antenatal treatment with zidovudine (AZT), beginning as early as 12–13 weeks of gestational age, continuing AZT treatment throughout the pregnancy, intrapartum AZT infusion, and finally neonatal AZT treatment for 6 weeks after delivery. The current guidelines published by the Public Health Service regarding prevention of maternal-fetal transmission of the disease are based on those results. Recent therapies include multiple drug antiretrovirals aimed at more aggressive virus suppression and prevention of viral resistance. Macrocytic anemia (hemoglobin < 8 gm/dL) occurs in 1.1% of asymptomatic patients taking zidovudine and in 4% of pediatric patients given combination zidovudine and lamivudine. Although usually mild, more severe forms can develop requiring either transfusion therapy and/or adjustment of antiretroviral regimen. Transient neonatal macrocytic anemias, some requiring transfusion, have also been reported. The following report documents a case in which severe maternal macrocytic anemia developed as a result of antiretroviral therapy. Concomitantly, life-threatening macrocytic fetal anemia was also present. A MEDLINE review of the English-language literature (1966 to December 2004), using the terms “HIV,” “anemia,” and “pregnancy,”
failed to report such severe maternal and fetal anemia occurring together. If confirmed by other studies, the findings have significant implications for the evaluation of effected pregnancies. We report our findings and discuss suggestions for additional approaches to patients receiving antiretroviral therapy.

**CASE**

This 38-year-old multipara was identified as being HIV-positive on initial prenatal laboratory assessment performed in the eighth week of her pregnancy. All other initial prenatal laboratory values were within normal limits. Following confirmation, CD4 count of 215 with a viral load of 17,925 copies was determined. The patient’s spouse was HIV-negative. The patient was started on 150 mg lamivudine (3TC) and 300 mg AZT in the form of Combivir (GlaxoSmithKline, Research Triangle Park, NC) twice daily and 200 mg nevirapine (Viramune; Boehringer-Ingelheim, Ridgefield, CT) twice daily. By the 28th week of her pregnancy, the patient began experiencing fatigue and poor weight gain, and a macrocytic anemia developed. Fetal surveillance, in the form of weekly biophysical profile was begun. By the 34th week of pregnancy, persistent severe macrocytic anemia was present, resulting in a worsening of the patient’s symptoms. Serum hemoglobin had fallen to 4.6 gm/dL, with an mean corpuscular volume (MCV) of 126 μm.³ Serum iron, erythropoietin, folate, and B12 studies were within normal limits. Parvovirus B19 immunoglobulin (Ig)G was found to be positive, but polymerase chain reaction and IgM were negative. The patient received a 3-unit packed red cell transfusion resulting in a hemoglobin of 8.4 gm/dL. The anemia was thought to be secondary to myelosuppressive effects of AZT, and as a result, the AZT dose was reduced to 100 mg 3 times daily (one half of the previous dose), while lamivudine and nevirapine were unchanged. At the 36th week of pregnancy, the patient reported decreased fetal movement. Fetal biophysical profile was 2 of 10 (with points for amniotic fluid only); the finding of hydrops was not appreciated. The patient received immediate parenteral AZT therapy, per Pediatric AIDS Clinic Trial Group protocol, as well as an additional 2 units of packed red blood cells, and an urgent cesarean delivery was performed. The patient’s viral load at delivery was undetectable.

Upon delivery, the baby was pale, hydropic, floppy, with poor respiratory effort, and had significant hepatomegaly. Apgar scores of 2, 4, 6, and 8 at 1, 5, 10, 15 minutes, respectively, were recorded. Umbilical artery cord blood pH was 6.78. Initial complete blood count values for the infant were as follows: hemoglobin 2.1 g/dL, hematocrit 6.4%, white blood cell count 8,900/mm3, platelets 161,000/mm2, and MCV 131 μm.³ Within an hour, a partial volume-exchange transfusion was performed, and the infant’s hematocrit increased to 14%. Further laboratory evaluation to determine the etiology of the infant’s anemia was inconclusive. Blood type was O/Rh+ with negative antibody screen, total bilirubin was less than 0.1 mg/dL, and the uncorrected reticulocyte count was 0.3%. A Kleihauer-Betke smear of maternal blood found no fetal cells. Blood and urine cultures were negative for an infectious etiology, including cytomegalovirus. Finally, HIV polymerase chain reaction, parvovirus B19 polymerase chain reaction, and IgM were negative after an elevated parvovirus IgG, consistent with passive transfer during pregnancy. After transfusion the infant’s hemoglobin stabilized, and his condition quickly improved and was normal at the time of discharge home at 29 days of age. Zidovudine was continued for a total of 6 weeks. The infant hemoglobin at 6 weeks of age was 11.3, with an MCV 84.5 μm,³ and uncorrected reticulocyte count was 0.3%. A repeat HIV polymerase chain reaction was negative, and the AZT was discontinued at this time.

**COMMENT**

Contemporary management of HIV-infected pregnant patients focuses on reduction of viral load, restoring satisfactory immune competence, and prevention of vertical transmission of the HIV to the fetus and newborn. The current case, as well as isolated reports in the literature, point to potentially serious complications related to an antiretroviral regimen, which includes AZT. Although significant maternal anemia is easy to recognize and treat, the same has not been traditionally true for the fetus. As such, obstetric management could include an assessment of fetal hemoglobin.

The use of middle cerebral artery peak Doppler flows has been found to reliably detect severe fetal anemia in a noninvasive manner.⁵,⁶ As described by Mari et al,⁶ the middle cerebral artery blood flow responses to reduced oxygen-carrying capacity with a resultant increase in the peak systolic velocity as determined with duplex Doppler. If fetal anemia had been suspected, measurement of middle cerebral artery peak systolic velocities could have been used to monitor the fetal hemoglobin status. If a declining fetal hemoglobin had been noted at an earlier stage, more intensive surveillance could have been instituted, delivery could have been attempted sooner, and/or fetal transfusion could have been employed—all before the nearly fatal anemia that developed in the fetus. A reasonable approach in such cases would conform to the assessment and management of severe fetal anemia in other disease states, Rh isoimmunization and parvovirus being the most common examples. Although no published reports document the usefulness of middle cerebral artery peak flows to evaluate fetal anemia from other causes, there is no reason to think it would not be effective.

An additional question raised by these observa-
tions relates to the potential appearance of the anemia in the fetus or in the absence of maternal anemia. Of note is a case reported by Watson et al,7 which reports profound neonatal anemia with a hematocrit of 11% (roughly double of the above case). As in the case reported above, it was the conclusion of the authors that this profound neonatal anemia was the result of antiretroviral therapy that the patient received during her pregnancy. Of interest, their report does not note any significant maternal anemia. Shaw and colleagues,8 in an elegant in vitro experiment, examined the effects of zidovudine on erythroid progenitors and found that progenitor cells from fetal and neonatal sources were more sensitive to the effect of AZT than those from the marrow of adults. Based on this case report and those of Watson and Shaw, it may be suggested that significant fetal anemia develop even in the absence of significant maternal anemia. Routine surveillance for fetal anemia, even in the absence of significant maternal anemia, may be considered, given the noninvasive nature of such assessments.

It is hoped that the current report stimulates the obstetric/medical community to begin examining in a more comprehensive fashion mothers, fetuses, and neonates for the possible hematologic effects of retroviral therapy. If the observations we have reported are confirmed by others, periodic assessment of middle cerebral artery peak flows could become part of routine surveillance during the management of patients receiving antiretroviral therapy.

REFERENCES

Budd-Chiari Syndrome, Systemic Lupus Erythematosus, and Secondary Antiphospholipid Antibody Syndrome in Pregnancy

Gary M. Joffe, MD, Gary A. Aisenbrey, MD, and Kent F. Argubright, MD

BACKGROUND: Hypercoaguable states such as the antiphospholipid antibody syndrome may be associated with thromboses in any vascular bed.

CASE: This case report demonstrates clinical manifestations of Budd-Chiari syndrome during pregnancy, diagnostic dilemmas, and suggestions for prevention of serious thromboembolic complications.

CONCLUSION: Patients with antiphospholipid antibody syndrome and previous thromboses in any vascular bed who are considering pregnancy should be considered candidates for full anticoagulation throughout the entirety of gestation and the puerperium. Anti-Xa levels may reflect inadequate dosing of low molecular weight heparin, particularly during the first trimester, and should be monitored frequently. In patients with suspected hepatic venous thrombosis, Doppler evaluation may be inadequate to establish the diagnosis.

The defining feature of the antiphospholipid antibody syndrome is thromboembolism. Any vascular bed is susceptible, and altered hormonal states such as pregnancy may exacerbate the process. Thromboembolism prevention in the form of prophylaxis or anticoagulation...
should be considered in a patient with multiple risk factors for development of this disease. The following case of thrombosis of a venous bed demonstrates some of the challenges faced when managing this potentially life-threatening disease.

CASE

A 28-year-old gravida 3 para 0020 at 15 weeks of estimated gestational age developed midepigastric pain, nausea, and intermittent vomiting. Her epigastric pain intensified over the next 7 days, and she presented to the emergency room. Physical examination at admission revealed normal blood pressure, mild tachycardia, and mild tachypnea, and she was afibrile. Doppler fetal heart tones were 140–160 beats per minute. She appeared thin and pale, with no jaundice, rash, or Raynaud's disease.

She had moderate right upper quadrant pain with palpation, and the absence of hepatosplenomegaly. She was experiencing moderate left upper quadrant pain with palpation. Admission laboratory values included a white blood cell count 11.8, hemoglobin 12.9, hematocrit 38%, platelet count 228, aspartate transaminase 99, and alanine transaminase 98. Admission lipase was 61, amylase 58, and D-dimer 1.03. Her presumptive diagnosis at admission was cholelithiasis.

Her past medical history was significant for systemic lupus erythematosus, which was diagnosed in 1999. She developed a lower extremity deep vein thrombosis while taking oral contraceptive pills. She was noted to have + antinuclear antibodies, lupus anticoagulant, anticardiolipin antibodies, and anti–double-stranded DNA. Her intermittent lupus flares manifested as arthralgia, and Raynaud’s disease. She was intermittently treated with cyclophosphamide (Cytoxan, Bristol-Myers Squibb, Princeton, NJ) and corticosteroids.

Her pregnancy history included blighted ova in 2001 and 2002. She received a preconception consultation in 2003 that revealed a thrombophilia workup that was negative. Repeat laboratory values confirmed a positive lupus anticoagulant, and strong positive anticardiolipin immunoglobulin G. She was advised to begin enoxaparin (Lovenox, Rhone-Poulenc Rorer Pharmaceuticals, Inc, Collegeville, PA) and aspirin 81 mg daily before pregnancy. In late 2003, she developed a spontaneous superior sagittal sinus thrombosis.

During the index pregnancy she presented for early prenatal care and was normotensive during the 1st trimester. She had started enoxaparin 30 mg subcutaneously twice daily and aspirin 81 mg orally daily, before conception. The goal of providing anticoagulant medication was to achieve thromboembolism prophylaxis, but not full anticoagulation. An anti-Xa value of 0.36 (0.50–1.0 U/mL) was noted at 9 weeks. Enoxaparin was increased to 40 mg 2 times daily at 13 weeks. §bauto1§aauto1

Admission right upper quadrant ultrasound was completely within normal limits. Serial laboratory evaluations were significant for rising liver enzymes. She continued to experience increasing right upper quadrant and epigastric pain with no relief with patient-controlled anesthesia narcotic administration. Her peak liver function test results were aspartate transaminase 490 and alanine transaminase 536. Other values included an lactic acid dehydrogenase of 662 and a total bilirubin of 1.2, with an indirect fraction of 1.0. A noncontrast computed tomographic scan of the abdomen showed normal results with the exception of moderate splenomegaly. (Fig. 1). Repeat right upper quadrant ultrasound (36 hours after admission) demonstrated marked thickening of the gallbladder wall, “sludge balls” within gallbladder lumen, and fluid in Morison’s pouch. Based upon splenomegaly and new onset of ascites, hepatic venous thrombosis was suspected, but Doppler evaluation of the portal venous circulation was normal. Along with a laparoscopic cholecystectomy, liver biopsy was performed due to a congested and mottled appearance of the liver surface. During the first 24 hours postoperatively, there was significant reduction in her pain, but after 24 hours her pain returned to preoperative levels. Liver biopsy was notable for periportal necrosis and numerous thromboses within presinusoidal capillaries. (Fig. 2). The gallbladder revealed chronic cholelithiasis and cholecystitis. She was given the presumptive diagnosis of hepatic vein thrombosis. However, repeat Doppler examination again revealed normal hepatic venous flow. Magnetic resonance venography was used to confirm thromboses in right and left branches of the hepatic vein plus portal and splenic vein thrombosis. (Fig. 3). Dilution and evacuation was performed with patient’s consent due to persistent hepatic dysfunction, intractable pain, and risk of embolization into the inferior vena cava without a viable alternative therapeutic option. She was ultimately discharged home in stable condition on warfarin (Coumadin, DuPont Pharma, Wilmington, DE). Twelve weeks after delivery, repeat magnetic resonance venography demonstrated complete resolution of Budd-Chiari syndrome.

COMMENT

Budd-Chiari syndrome is an occlusive process of the right, middle, or left hepatic veins. It is usually thrombotic, with or without extension of thrombus into the inferior vena cava. Twenty percent of patients are women either pregnant, postpartum or taking oral contraceptive pills. Another 20% will demonstrate a hypercoagulable state, for example the antiphospholipid antibody syndrome. Cardinal signs of Budd-Chiari include abdominal pain, ascites, and hepatomegaly. Some patients, as in this report, will develop splenomegaly. Diagnosis is made with computed tomography, magnetic resonance imaging, Doppler, or liver spleen scan. Treatment is based on the underlying cause. Antithrombotic treatment (heparin, warfarin, thrombolytic agents) is of little use.1

The major questions raised by this case are as follows: what is the role of Doppler evaluation of the hepatic circulation in pregnancy? Was the patient...
adequately anticoagulated? Were there alternative treatments to dilation and evacuation?

On 2 occasions during her workup, the patient was found to have normal Doppler venous flow values. Possible explanations might include a wide distribution around the mean value for “normal” hepatic venous flow or “normal” flow through collateral venous circulation.

In terms of her dosing regimen for enoxaparin, she was likely underdosed to achieve even prophylaxis at the time of initial presentation. Pharmacokinetic studies during pregnancy have demonstrated that the volume of distribution of enoxaparin is highest in first trimester, with greater clearance, lower concentration, and lower mean residence time compared with the latter 2 trimesters and postpartum. Therefore, to achieve the desired level of anticoagulation, it is necessary to monitor anti-Xa levels frequently and adjust dosing accordingly. Conversely, patients in late second and third trimesters may be overly anticoagulated due to declining clearance of the medication, so close monitoring should continue.

In terms of whether “prophylaxis” or “full anticoagulation” should be recommended for patients with systemic lupus erythematosus and secondary antiphospholipid syndrome, “Most experts feel there is no evidence that women with APS [antiphospholipid syndrome] and prior thrombosis of any location should be fully anticoagulated.” (D. Ware Branch, MD, personal communication).

Dilation and evacuation was offered to this patient after consultation with gastrointestinal specialists, who thought that the probability for successful alternative therapy was unlikely. We have subsequently learned of a case of portacaval shunt placement in a patient with Budd-Chiari syndrome and the prothrombin gene mutation. She delivered a healthy child at 31 weeks but subsequently died after “clotting of the shunt, which occurred in the face of full anticoagulation”; death occurred 10 months after liver transplantation.

Fig. 1. Abdominal computed tomographic scan demonstrating moderate splenomegaly.

Fig. 2. Photomicrograph of the liver. Four separate fields show thrombi within presinusoidal capillaries.

Fig. 3. Magnetic resonance venography with thrombi in the portal vein (large arrow) and right and left hepatic veins (small arrows).
In summary, this patient with multiple risk factors for development of thromboembolism presented with signs and symptoms of Budd-Chiari syndrome. Doppler evaluation of her hepatic venous circulation was insensitive to the development of thrombosis. She likely was inadequately anticoagulated, based upon the volume of distribution of enoxaparin during the first trimester of pregnancy. Randomized trials of prophylactic dosing compared with full anticoagulation are not currently available in patients who have had thrombosis in the presence of systemic lupus erythematosus and secondary antiphospholipid syndrome. Until such trials are available, expert opinion suggests that these individuals should be considered candidates for full anticoagulation throughout pregnancy and the puerperium. Portacaval shunt in the presence of acute Budd Chiari syndrome may allow prolongation of pregnancy to achieve a successful neonatal outcome, but may not be associated with long-term maternal survival.

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Acute Onset of Polymyalgia Rheumatica in Pregnancy

Hiroko Sasaki, MD, Motoo Washio, MD, Noriyuki Ohara, MD, and Takeshi Maruo, MD

BACKGROUND: Polymyalgia rheumatica is uncommon in young women and remains a diagnostic challenge for pregnant women.

CASE: A 28-year-old pregnant woman developed polymyalgia rheumatica in the third trimester. Laboratory investigations revealed elevated erythrocyte sedimentation rate and C-reactive protein levels with normal muscle enzyme levels and seronegativity for rheumatoid factor. Although her symptoms deteriorated as pregnancy progressed, she drastically improved by treatment with prednisone. She underwent cesarean delivery at 39 weeks. She was relapse-free of polymyalgia rheumatica after discontinuation of prednisone on the 50th postoperative day.

CONCLUSION: The diagnosis of polymyalgia rheumatica is important to properly manage pregnancy.

(Obstet Gynecol 2005;106:1194–6)

Polymyalgia rheumatica is an inflammatory condition of unknown cause that is characterized by pain and stiffness in the musculoskeletal structure, including the neck, shoulder, and pelvic girdle. This disorder mainly affects patients aged older than 50 years. The development of polymyalgia rheumatica in patients aged younger than 50 years remains infrequent. A MEDLINE search for English-language articles published from 1973 to 2004 using the keywords “polymyalgia rheumatica” and “pregnancy” revealed no case reports on pregnancies complicated by polymyalgia rheumatica. The influence of polymyalgia rheumatica on pregnancy outcome and optimal treatment for polymyalgia rheumatica in pregnant women remains to be defined. Here, we present a report of a woman whose pregnancy was complicated by polymyalgia rheumatica.

CASE

The patient was a 28-year-old nulliparous woman with a past history of hyperthyroidism at 24 years of age. She had been receiving propylthiouracil 300–400 mg daily. The antenatal course was uneventful until 34 weeks of gestation, when she presented with an acute onset of muscle aches involving bilateral deltoid, triceps brachii, and biceps brachii. At 36 weeks of gestation, her pains in the bilateral upper extremities and thighs increased, with worsening on the right side. She complained of difficulty in walking and had a sore throat and a low-grade fever at night. At 37 weeks of gestation, she was hospitalized due to gait disturbance, nausea, vomiting, and appetite loss. Physical examination demonstrated muscle weakness and polymyalgia of the proximal muscles of the upper and lower extremities. At neurologic examination, no abnormal deep tendon reflexes or sensory disturbances were noted. There were no signs of
temporal artery tenderness, jaw claudication, or visual impairment. At pelvic examination, the cervix was 3 cm dilated and uneffaced. A nonstress test showed reassuring fetal heart rate pattern. Laboratory investigations revealed an elevated erythrocyte sedimentation rate of 83 mm in the first hour and C-reactive protein at 3.5 mg/dL (normal range < 0.5 mg/dL). Liver function tests, electrolytes, and thyroid function tests were normal. Muscle enzymes including creatine phosphokinase (27 IU/L, normal range 25–190 IU/L), aldolase (1.6 IU/L, normal range 1.7–7.5 IU/L), lactate dehydrogenase (112 IU/L, normal range 106–211 IU/L), and myoglobin (11 ng/mL, normal range < 60 ng/mL) were within the normal ranges. Serum CH50 (66.2 U/mL, normal range 30–45 U/mL), C3 (143 mg/dL, normal range 69–128 mg/dL), C4 (47 mg/dL, normal range 14–36 mg/dL) were slightly elevated. The rheumatoid factor, antinuclear antibody, and anti-DNA antibody revealed negative results. Sputum culture yielded no bacilli. Five days later, she could not stand up by herself due to the progression of polymyalgia. At 39 weeks of gestation, she had difficulty in raising her upper limbs and grasping chopsticks. Finally, she could not get up out of bed by herself.

A presumptive diagnosis of polymyalgia rheumatica was made on the basis of the typical clinical features, including progressive polymyalgia in the shoulder and pelvic girdles as well as laboratory data showing an elevated erythrocyte sedimentation rate and C-reactive protein levels. Normal muscle enzyme levels, seronegativity for rheumatoid factor, normal electrolyte levels, and normal thyroid function excluded the possibility of polymyositis, rheumatoid arthritis, and periodic paralysis. We recommended that she undergo muscle biopsy, but she declined. Prednisone was started at a dosage of 30 mg daily, followed by marked improvement in her symptoms as early as 5–6 hours after administration. However, general muscle weakness did not disappear completely. Method of delivery was discussed with the patient and her family. It was decided that a cesarean delivery would be more appropriate than vaginal delivery, because the latter mode could be unsuccessful due to sustained general muscle weakness. At 39 weeks of gestation, she underwent cesarean delivery. She delivered a live, full-term neonate with birth weight of 2,982 g. Apgar scores were 8 at 1 minute and 10 at 5 minutes. The neonatal course was uneventful, and the patient could breastfeed from the fourth postoperative day. Prednisone was gradually tapered from the fourth postoperative day, because her symptoms did not deteriorate. Serum levels in erythrocyte sedimentation rate and C-reactive protein normalized on the eighth postoperative day, and she was discharged home. Prednisone was discontinued on the 50th postoperative day. She continued to do well, without any signs of the relapse of polymyalgia rheumatica.

**COMMENT**

We have described an uncommon case of a pregnancy complicated by polymyalgia rheumatica. Our patient experienced an acute onset of polymyalgia in the upper and lower proximal muscles at 34 weeks of gestation, and her symptoms deteriorated as pregnancy progressed. Laboratory investigations revealed elevated erythrocyte sedimentation rate and C-reactive protein levels, with normal muscle enzyme levels and seronegativity for rheumatoid factor. The unexpected feature was drastic improvement of her symptoms in response to prednisone therapy.

Polymyalgia rheumatica often presents a diagnostic challenge because of many differential diagnoses, including steroid-responsive malignant neoplasms, seronegative arthritis, and polyarthritis. Although elevated erythrocyte sedimentation rate and C-reactive protein levels are included in the diagnostic criteria for polymyalgia rheumatica, 6% of patients with polymyalgia rheumatica have been shown to have a normal erythrocyte sedimentation rate at diagnosis. Salvarani et al showed that a normal erythrocyte sedimentation rate does not exclude a diagnosis of polymyalgia rheumatica and that C-reactive protein and interleukin 6 seem to be more sensitive indications of disease activity both at diagnosis and during relapse. In our patient, serum CH50, C3, and C4 were slightly elevated. Shintani et al demonstrated immunoglobulin G, immunoglobulin A, and fibrinogen deposits in the perimysium by immunofluorescence microscopy, suggesting that immune complexes play a role in the pathogenesis of polymyalgia rheumatica. Although pathologic findings in affected muscles are not included in the criteria for polymyalgia rheumatica, abnormal findings in biopsied muscle specimens have been reported to show perivascular and perifascicular infiltration of lymphocytes to the perimysium and type 2 fiber grouping.

Polymyalgia rheumatica is known to be closely related to giant cell arteritis, which is an immune-mediated disease characterized by granulomatous infiltrates in the wall of medium-sized and large arteries, including superficial temporal, occipital, ophthalmic, and posterior ciliary arteries. However, our patient did not show any clinical features of giant cell arteritis such as headache, scalp tenderness, or eye and central nervous system ischemic symptoms.

Corticosteroids are the standard drugs for the treatment of polymyalgia rheumatica. This disease shows rapid response to 20 mg/d of prednisone or its equivalent. A low-dose corticosteroid trial may be useful as the final step in the diagnosis of polymyalgia rheumatica. However, we initially treated our patient with a higher dosage of prednisone (30 mg/d) than a standard dosage to control her progressively worsening symptoms. Her rapid clinical response to prednisone therapy supported the diagnosis of polymyalgia rheumatica. The prognosis of polymyalgia rheumatica is generally favorable, but
some patients may relapse. Our patient remained relapse free after discontinuation of therapy at the time of writing this report. However, careful monitoring is necessary, because the natural course of polymyalgia rheumatica in young women remains unknown. Although polymyalgia rheumatica is uncommon in young women, the awareness of polymyalgia rheumatica is important to prevent delayed diagnosis and determine the mode of delivery, especially when polymyalgia rheumatica develops late in pregnancy.

REFERENCES

Goodpasture Syndrome in a Pregnant Woman

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BACKGROUND: Goodpasture syndrome, an immunologic disorder characterized by glomerulonephritis and pulmonary hemorrhage, rarely presents in pregnancy.

CASE: We describe a patient who was diagnosed with Goodpasture syndrome in her second trimester. She required daily hemodialysis, intermittent plasmapheresis, and immunosuppressive therapy. Her pregnancy was complicated by hypertension, and she delivered a low birth weight neonate prematurely at 26 4/7 weeks of gestation by cesarean due to nonreassuring fetal status. Deterioration in the fetal status may have been secondary to complications of hypertension, in addition to prematurity.

CONCLUSION: Goodpasture syndrome in pregnancy may be associated with significant maternal and fetal morbidity.

(Obstet Gynecol 2005;106:1196–9)

Goodpasture syndrome was initially described in 1919.1 It is classically defined as a triad of glomerulonephritis with pulmonary hemorrhage and anti-glomerular basement membrane (GBM) antibodies. It is a rare disorder in which circulating antibodies are directed against a type IV collagen antigen on the glomerular basement membrane.2 Expression of this antigen is highest in glomeruli and alveoli, is much lower in the renal tubular basement membrane, and is rare in tissues such as the placenta. Its expression is reflected in its presentation of rapidly progressive glomerulonephritis and pulmonary hemorrhage. Goodpasture syndrome can cause significant maternal and fetal or neonatal morbidity and highlights several important issues in management, including the use of renal biopsy and treatment with antihypertensives, corticosteroids, azathioprine, hemodialysis, and plasmapheresis during pregnancy.

CASE

A 34-year-old woman, gravida 2 para 0, presented at 18 weeks of gestation with a 2-week history of malaise, nausea, vomiting, diarrhea, pruritus, decreased urine output, and foamy urine. She also had occasional episodes of cough and mild hemoptysis. There was no peripheral edema.

Before this, she had several respiratory illnesses including asthma, nasal polyps, and 2 episodes of pneumonia. The last occurrence was 4 years before the index pregnancy. Her symptoms worsened despite antibiotic treatment, and a lung biopsy revealed chronic eosinophilic pneumonia with nonnecrotizing vasculitis and alveolar hemorrhage. She was treated with inhaled bronchodilators and prednisone that was tapered off over 1 year. Pulmonary function tests performed just before conception showed a
forced expiratory volume (FEV₁) of 2.85 L (92% predicted) and FEV₁/FVC (forced expiratory vital capacity) of 68%. A chest x-ray was normal. Her past medical history was also significant for anemia of chronic disease.

Upon presentation at 18 weeks of gestation, her blood pressure was 118/63 mm Hg, heart rate was 79 beats per minute, respiratory rate was 18 breaths per minute, and oxygen saturation on room air was 96%. The fetal heart rate was assessed with an external fetal monitor and had normal variability. Physical examination, including cardiopulmonary examination, was within normal limits. The hemoglobin level was 78 g/L, serum creatinine was 1306 μM and potassium was 7.6 mM, with peaked T waves on electrocardiogram. The patient was dialyzed urgently, transfused with 4 units of packed red blood cells, and then transferred to a tertiary perinatal center.

Urinalysis revealed proteinuria, trace glucosuria, and hematuria with an active sediment but no casts. She underwent a renal biopsy, which was consistent with rapidly progressive glomerulonephritis involving more than 80% of glomeruli. A crescentic pattern was noted, with mild to moderate interstitial fibrosis and necrotizing glomerular lesions. Immunofluorescence microscopy revealed diffuse linear staining for IgG along the glomerular basement membrane. Serum antinuclear antibodies, double-stranded DNA antibodies, and antineutrophil cytoplasmic antibodies were negative. Serum anti-GBM antibodies were present. Serum levels of complement C3 and C4 were normal. Serum levels of complement C3 and C4 were normal.

Treatment included daily hemodialysis over 4 hours. She underwent 2 courses of plasmapheresis (the first lasting 5 days and second lasting 1 day), and was started on methylprednisolone (Solu-Medrol, Pfizer, New York, NY) 1 g intravenously daily for 3 days, followed by 1 mg/kg/d of oral prednisone. As a result of steroid therapy, she developed gestational diabetes requiring insulin. She also had one episode of streaky hemoptysis. As a result, at 23 weeks of gestation, azathioprine 100 mg daily was added, and the prednisone was tapered. Her blood pressure remained high normal and varied from 125/80–144/96 mm Hg. Ten days after initiation of azathioprine, repeat pulmonary function tests showed normal lung volumes (FEV₁ of 3.2 L, FVC of 4 L, both at 113% predicted, and FEV₁/FVC of 78%) and normal lung diffusion capacity when corrected for hemoglobin (96%). Anti-GBM IgG titers continued to decrease. A 24-hour urine collection contained 740 mL total output, and showed a creatinine clearance of 7.8 mL/min and proteinuria of 2.57 g. However, her blood pressure was refractory to hemodialysis alone and varied from 148/86–162/106 mm Hg. Alpha-methylldopa, standard therapy for chronic hypertension complicating pregnancy at the institution, was initiated but her blood pressure continued to increase and peaked at 174/114 mm Hg at 26 weeks of gestation. Her anemia was managed with erythropoietin. Complete blood counts, renal function, and electrolytes were monitored regularly with dialysis. Liver function and coagulation studies were performed weekly to monitor for the development of preeclampsia.

Fetal ultrasonography performed at 24 weeks of gestation revealed normal fetal anatomy and biometry. Estimated fetal weight was 604 g (50th percentile for gestational age). Placental appearance, amniotic fluid volume, and umbilical Doppler studies were normal. At 25 of weeks of gestation, betamethasone was administered in 2, 12-mg intramuscular doses given 24 hours apart. At 26 weeks of gestation, the estimated weight was 730 g (12th percentile). The biophysical score was 8 of 10 based on the 10-point Manning scale, with 2 points lost for a nonreactive nonstress test. The placenta showed signs of chronic decreased perfusion with multiple calcified and infarcted areas. Umbilical Doppler ultrasonography was abnormal with absent arterial end diastolic velocity. The following morning, umbilical artery Doppler studies revealed intermittently absent and reversed end diastolic velocity. The umbilical vein Doppler waveform showed pulsations. A routine nonstress test was nonreactive with minimal heart rate variability. The biophysical score remained at 8 of 10 (2 points lost for a nonreactive nonstress test). External fetal monitoring showed the fetal heart rate ranging from 100 to 150 beats per minute with variable decelerations. The fetus was delivered by cesarean at 26 4/7 weeks of gestation due to nonreassuring fetal status.

A male neonate was born with a birth weight of 700 g in stable condition. The Apgar scores were 3 at 1 minute and 8 at 5 minutes. The neonate was intubated at birth and given prophylactic surfactant. Umbilical venous gas values at birth were as follows: pH 7.21, Paco₂ 41, PaO₂ 20, and bicarbonate 16. An arterial sample could not be obtained. At 76 minutes after birth, the arterial blood gas values were as follows: pH 7.20, Paco₂ 42, PaO₂ 48, and bicarbonate 16. The neonate required artificial ventilation for 24 hours and was extubated to nasal continuous positive pressure. The course during first 48 hours after birth was unremarkable, with stable blood pressure, urine output, and serum creatinine. Anti-GBM titers were negative. However, the first cranial ultrasound examination at 36 hours after birth revealed massive intraventricular hemorrhage on both sides and intraparenchymal hemorrhage on the right side. Subsequent cranial ultrasonography examination revealed continued ventricular enlargement and development of a communicating hydrocephalus, requiring a reservoir placement at 1 month of postnatal age. Neurodevelopmental follow-up at 12 months corrected age revealed a global delay, generalized hypotonia, and exaggerated reflexes. Gross and fine motor development were equivalent to 9 months of age, and expressive language, receptive language, and social adaptive skills were equivalent to 11 months of age. Visual impairment was found and thought to be secondary to optic nerve dysfunction. The ventriculoperitoneal shunt remained present for ongoing treatment of hydrocephalus.
The infant has shown failure to thrive, because weight and length remain below the third percentile and skull circumference at the 25th percentile at age 12 months. One week postpartum, the patient’s need for hemodialysis decreased. She was treated with weekly erythropoietin injections, calcium and vitamin D supplements, azathioprine, and a prednisone taper. Hemodialysis was discontinued. Repeat investigations showed improving renal function, with a total 24-hour urine collection of 1,311 mL and normalized creatinine clearance of 20.4 mL/min and proteinuria of 2.64 g. Four weeks after delivery, anti-GBM titers were at normal levels, and total urine output over a 24-period was 1,700 mL, with a normalized creatinine clearance of 18.6 mL/min and proteinuria of 3.55 g/L. Hypertension was controlled with metoprolol, amlodipine, and ramipril. Placental pathologic examination revealed placental weight less than 10th percentile, extensive fetal thrombotic vascu-lopathy, basal plate hematoma with adjacent infarcted tissue, as well as subchorionic, intervillous, and interlobu-lar septal hematomas.

COMMENT
A MEDLINE literature search of all languages from 1966 to the present, using search terms Goodpasture syndrome, anti-glomerular basement membrane disease, (anti-)glomerular basement membrane antibody (antibodies), and pregnancy (pregnant), revealed only 4 reported cases of Goodpasture syndrome occurring in pregnancy. In 2 cases, diagnosis and disease progression occurred during pregnancy as in our case.4,5 One of these cases resulted in a fetal death at 28 weeks of gestation, whereas the other resulted in a preterm delivery at 35 weeks of gestation, despite poor patient compliance. The other 2 cases describe pregnant women with a preconcep-tual diagnosis of Goodpasture syndrome and successful term deliveries.6,7 One of these women received a renal transplant years before pregnancy and went on to develop graft rejection, possibly due to poor compliance and superimposed preeclampsia. The other maintained stable renal function throughout the preg-nancy.

These cases suggest that disease presentation and initiation of treatment before conception lead to a favorable neonatal outcome, whereas presentation during pregnancy increases the risk of fetal and neonatal morbidity. Maternal outcome is less predict-able and may depend on the nature of therapy and patient compliance.

Our case describes a normotensive pregnant woman who developed hypertension in the second trimester after 20 weeks of gestation. The differential diagnosis included hypertension secondary to renal dysfunction, corticosteroid-induced hypertension, and preeclampsia superimposed on acute renal dysfunction. Although her initial fetal and placental survey were normal at 24 weeks of gestation, she was at high risk for developing placental insufficiency and preeclampsia, given the onset of renal insufficiency in early pregnancy. By the time of delivery, the placenta showed signs of chronic hypoperfusion, and the fetus was small for gestational age. The placental damage noted on patho-logic examination may have been mediated by maternal renal dysfunction, complicated by hypertension. Other possible sources of placental damage may be attribut-able to nonspecific binding of anti-GBM antibodies to the placenta, uremia secondary to renal dysfunction, and superimposed preeclampsia. One could speculate that hypertension refractory to dialysis may be an early sign of utero-placental insufficiency and should warrant high clinical suspicion, close fetal monitoring, and pa-tient counseling.

In pregnancies complicated by hypertension and proteinuria, preeclampsia must be differentiated from underlying renal disease such as Goodpasture syn-drome. Systemic manifestations of preeclampsia in-clude persistent headache, visual or other cerebral disturbances, thrombocytopenia, microangiopathic hemolytic anemia, elevated aminotransferase levels, and timing of presentation (usually in the third trimester). By comparison, anti-GBM antibodies in Goodpasture syndrome may lead to acute glomerulone-phritis (hematuria, red cell casts, and renal insufficiency), with pulmonary hemorrhage (presenting as hemoptyis) or pulmonary infiltrates with increased diffusion capacity on pulmonary function tests. These findings can also be seen in systemic vasculitis (for example Wegener’s granulomatosis), systemic lupus erythematousus, and poststreptococcal glomerulonephritis complicated by pulmonary edema. The definitive diagnosis is determined by serologic studies (including anti-GBM antibodies, antineutrophil cytoplasmic antibodies, antinuclear anti-bodies, antistreptococcal antibodies, or blood cul-tures) and renal biopsy. Renal biopsy during pregnancy is not associated with increased risk of complications and is indicated if there is sudden deterioration of renal function or nephrotic syndrome of unknown origin before 32 weeks of gestation.8

In conclusion, Goodpasture syndrome can result in serious maternal and fetal morbidity. Maternal compromise may arise from pulmonary or renal complications. Although very rare, severe pulmonary complications such as life-threatening hemoptyis or respiratory failure may occur and warrant antenatal discussion regarding emergent or perimortem cesarean delivery. Invasive procedures such as renal bi-
The transobturator tape procedure is one of the newer minimally invasive slings used for the surgical treatment of genuine stress urinary incontinence. This minimally invasive alternative to the tension-free vaginal tape operation for stress urinary incontinence, but it may be associated with vascular complications.

CONCLUSION: The transobturator tape procedure is one of the newer minimally invasive slings used for the surgical treatment of genuine stress urinary incontinence. This procedure has been reported to be associated with bladder, bowel and vascular injury due to the blind passage of needles through the retropubic space.

The transobturator tape sling is the most recent minimally invasive midurethral sling, which has been introduced with the hope of decreasing some of the complications associated with retropubic passage of needles. First introduced in France in 2001 by Delorme, the technique involves passage of needles through the medial portion of the obturator foramen, which then exit through an incision in the anterior vaginal wall under direct finger guidance. A synthetic tape is attached to the needles and threaded in place between the 2 obturator foramina, creating a hammock supporting the midurethra. The retropubic space is not entered during this procedure, and hence this method has the theoretical advantage of potentially decreasing the complications arising from the passage of needles in proximity to the retropubic structures. However, other complications, although infrequent, can occur. We report 2 cases of pelvic hematomas following the transobturator tape procedure.
CASE 1

A 57-year-old para 2 presented with a 4-year history of stress urinary incontinence requiring constant pad use. She denied significant symptoms of urge incontinence or pelvic organ prolapse. Her medical and surgical histories were otherwise unremarkable. Upon examination she was noted to have urethral hypermobility without significant pelvic organ prolapse.

Urodynamic testing revealed a stable detrusor, normal bladder capacity, and normal urethral pressure (maximum urethral closure pressure 56 cm H₂O). Uroflow and voiding studies were normal. The patient underwent a transobturator sling and cystoscopy under general anesthesia. There were no complications intraoperatively, and the estimated blood loss was less than 50 mL. She was discharged the day of surgery after successfully passing a postoperative voiding trial.

The patient presented on postoperative day 6 with left hip pain and diffuse bruising in the left hip, infraumbilical area, and inner thigh (Fig. 1). A computed tomography (CT) scan of the pelvis revealed a 7.4 × 7.9 cm pelvic hematoma in the retropubic space and extending behind the left obturator internus muscle. Her hematocrit at this time was normal. She was managed conservatively with analgesics and rest. A repeat CT scan 2 weeks later revealed that the hematoma was unchanged, and her hematocrit was stable. Her pain continued to decrease, and she was pain-free approximately 6 weeks after her surgery and remained continent. A CT scan done at this visit showed that the hematoma had decreased in size to 7 × 4.5 cm.

CASE 2

A 47-year-old multigravida presented with a 2-year history of stress urinary incontinence and symptomatic pelvic organ prolapse. She had previously had a hysterectomy for benign indications. Her medical and surgical histories were otherwise unremarkable. Upon examination she was noted to have a grade 2 cystocele, grade 1 vault prolapse, and urethral hypermobility. A simple cystometrogram revealed normal bladder capacity, and the result of her cough stress test was positive.

The patient underwent an anterior repair, bilateral sacrospinous ligament fixation of the vault, and a transobturator sling and cystoscopy. Because of the attenuation of the patient’s tissues and bilateral paravaginal defects noted intraoperatively, the anterior repair was augmented with a polypropylene mesh. The surgery was uncomplicated, and the estimated blood loss was 100 mL. After an uncomplicated hospital course, she was discharged home without a bladder catheter on the first postoperative day.

One week after the procedure, the patient presented with vaginal bleeding precipitated by an episode of straining due to constipation. Upon examination, there was minimal oozing from the anterior vaginal wall incision. Monsel’s solution was applied, and the vagina was packed for 24 hours. She had persistent bleeding after removal of the pack and hence was taken to the operating room. The vaginal incision was opened and thoroughly irrigated. There was minimal oozing noted from the paravaginal space. This bleeding decreased with pressure and the application of Surgicel (Ethicon, Somerville, NJ) but recurred the next day following removal of the pack. It was noted to be dark, old blood, as opposed to fresh bleeding. Her hematocrit remained stable at 32. A CT scan showed a 4.2 × 5.7 cm right pelvic hematoma located in the retropubic space, which was drained under CT guidance, and the patient’s vaginal bleeding resolved (Fig. 2). A repeat CT scan 2 days later showed complete resolution of the hematoma.

COMMENT

The original minimally invasive midurethral sling procedure, the tension-free vaginal tape (TVT), involves the transvaginal passage of needles through the retropubic space and has been associated with reports...
of rare bladder, bowel, and blood vessel injury. The procedure has also been reported to be associated with pelvic hematoma, ranging from 0.6–1.9% in published reports.2–4 The abdominal retropubic approach (suprapubic arc sling) has also been reported to have a mean decrease in hematocrit, from preoperative to postoperative day 1, of 7.1% (range 1–14%), with occasional retropubic hematomas requiring transfusion.5,6 Indeed, many patients may have small subclinical hematomas associated with blind needle passage through the retropubic space. The great majority of these patients remain asymptomatic and clinically silent. In rare cases of symptomatic hematoma, transfusion and evacuation have been reported.

The transobturator approach has been introduced to minimize risk of complications from retropubic passage of the needles. Although limited data are available regarding the safety and efficacy of this approach, current literature suggests that bladder and urethral injuries are extremely rare.1 No significant bleeding or hematoma complications have been reported to date. We have performed 60 transobturator sling procedures at our institution and have encountered 2 hematomas. We believe these hematomas were most likely caused by bleeding in the retropubic space.

To understand and prevent these complications, knowledge of the pelvic anatomy and obturator space with respect to the transobturator sling procedure is important. In females, the obturator foramen is a triangular aperture formed by the pubic and ischial rami. The obturator membrane covers the obturator foramen and is a site of origin for the obturator externus and the obturator internus muscles. Both of these muscles insert into the medial surface of the greater trochanter of the femur. The obturator canal is situated in the anterosuperior aspect of the obturator foramen and contains the obturator neurovascular bundle. The obturator artery exits the pelvis through the upper part of the obturator foramen where it terminates in anterior and posterior branches (Fig. 3).

With needle passage during the outside-in transobturator approach, the needle tip penetrates the obturator externus muscle, the obturator membrane, and then rotates around the medial aspect of the pubic ramus, skimming the obturator internus muscle. It is then contacted by the surgeon’s finger and exited through the vaginal incision under direct finger guidance. Failure to rotate the needle or a significant push of the needle before rotation may extend the needle tip fully through the obturator internus muscle, thereby entering the retropubic space and causing vascular injury.

In both the cases presented, there were no significant sequelae from the pelvic hematoma, and both patients did well without significantly compromising surgical efficacy. Early recognition of complications is the key to effective management. Imaging modalities, such as CT scan or magnetic resonance imaging, are useful for establishing the diagnoses and offering guided drainage in appropriate patients. We recommend a conservative approach to management of these hematomas if the patient is hemodynamically stable. In the case of expanding hematomas, percutaneous drainage or angiography and embolization may be preferable to laparotomy or laparoscopy because access to these spaces may be challenging.

To decrease the risk of vascular injury, the pelvic surgeon should pay attention to proper technique with the outside-in approach and have a high clinical suspicion under the appropriate circumstances. This complication is rare and is most often self-limited. An inside-out modification of the transobturator sling (TVT-Obturator, GYNECARE, Somerville, NJ) has been introduced and may further reduce the risk of vascular injury. To date, there is limited data on the
Hematometra in a Patient With Cornelia De Lange Syndrome

Joseph O. Doyle, Christopher D. Williams, MD, and Colleen A. Raymond, MD

BACKGROUND: Hematometra is usually the result of developmental anomalies or may be secondary to cervical obstruction. Abnormal uterine contractile function (atony) would be an uncommon cause of hematometra.

CASE: An 18-year-old female with Cornelia De Lange syndrome and abdominal pain was found to have a hematometra on ultrasound examination. On pelvic examination, her cervical canal was patent and was easily dilated, but the hematometra did not drain until suprapubic pressure was applied. Two weeks postoperatively, pelvic magnetic resonance imaging showed a markedly thinned uterine myometrium and a recurrent hematometra, prompting the decision to perform a hysterectomy.

CONCLUSION: Hematometra in a patient with Cornelia De Lange syndrome may be the result of abnormal uterine contractile function.

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Hematometra is a collection of blood within the uterine cavity resulting in uterine distension. Hematometrizes usually result from obstruction, typically from either developmental anomalies or postsurgical cervical obstruction. We present a case of hematometra secondary to an abnormal, atonic uterine myometrium in a patient with Cornelia De Lange syndrome.

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the anatomy. This study demonstrated a markedly thinned uterine myometrium and recurrent hematometra (Fig. 1). Based on the recurrence of the hematometra, the patient’s history, and a discussion with the patient’s parents (legal guardians), the decision was made to perform a hysterectomy. There was no evidence of endometriosis or other pathology in the pelvic or abdominal cavity when surgery was performed. The pathology report noted a hypoplastic cervix and a markedly thinned and dilated myometrium.

COMMENT

Cornelia De Lange syndrome (alternatively known as Brachmann–De Lange syndrome) is a disorder with a prevalence estimated as high as 1 in 10,000 individuals. Although debate still exists, the mostly likely defect resulting in this disease is located in a 1.1-Mb critical region on chromosome 5. Multiple cases of Cornelia De Lange syndrome are attributable to mutation of the NIPBL gene within in this region, which is analogous to an enhancer-promoter and signal regulator of multiple developmental pathways in the Drosophila homolog. Autosomal dominant inheritance is the most likely mode of transmission, with most cases thought to arise from spontaneous mutations. The sporadic nature of presentation is thought to reflect genetic lethality of the disorder in the majority of cases.

Because there is currently no biochemical or genetic test for this syndrome, the diagnosis is clinical, based upon distinctive facial features, upper extremity anomalies, severe prenatal and postnatal growth restriction, and severe mental retardation. The prepubertal facial findings of greatest diagnostic value are the combination of neat, well-defined, arched eyebrows, long philtrum, thin lips, and crescent-shaped mouth.

Endocrine abnormalities in Cornelia De Lange syndrome include risk for dysfunction of gonadotropin and prolactin secretion. Despite variable dysfunction of the hypothalamic-pituitary-gonadal axis, which is suggested by gonadotropin and sex steroid responses to gonadotropin-releasing hormone stimulation, most females have normal secondary sexual characteristics. No anatomical or functional abnormalities of the uterus or other müllerian structures have been described. Successful pregnancies have been reported, particularly in those individuals with milder phenotypes, suggesting that allelic heterogeneity has a role in this disease. Because of the autosomal dominant inheritance pattern, normal progeny are a possibility. However, the genetic lethality of this defect most often results in the spontaneous abortion of affected fetuses. This is probably due to the fact that the proposed gene is involved in multiple developmental pathways.

Northern blot analysis showed that the proposed NIPBL gene is strongly expressed in adult placenta, heart, and skeletal muscle, among other tissues. Unfortunately, analysis was not performed on uterine tissue. Multiple biopsies (including skeletal and cardiac muscle, liver, lung, and kidney tissue) of a hypotonic infant with Cornelia De Lange syndrome showed severe distortion of the mitochondrial architecture, with multiple mtDNA deletions identified. In the muscle biopsies, areas of myolysis were interspersed among intact myofibrils. Of note, gastroesophageal dysfunction was encountered in 13 of 17 adolescents in one study of Cornelia De Lange syndrome, with a strong correlation between gastroesophageal reflux disease severity and clinical phenotype. These results suggest the possibility of more pervasive smooth muscle dysfunction in this population, including, perhaps, the uterine myometrium.

Hematometras usually result from obstruction, typically from either developmental anomalies or cervical stenosis. In this patient no outflow tract obstruction was present. Because of atony of the uterine myometrium, the intrauterine pressure did not increase as the uterine cavity expanded to accommodate the increasing volume of menstrual debris. It is unclear whether, or how much, the atony in this case was due to smooth muscle dysfunction related to the Cornelia De Lange syndrome.

**Fig. 1.** Pelvic magnetic resonance image demonstrating a markedly thinned and dilated uterine myometrium and recurrent hematometra.

or if there was a contribution from the medications she was receiving. However, none of the medications she was taking are known to cause atony or hematometra. We conclude that, in some women with Cornelia De Lange syndrome, the uterine myometrium has impaired function and may be at risk to form hematometra.

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Acute Coronary Syndrome and Preeclampsia

Sepideh Nabatian, MD, Patrick Quinn, DO, Leslie Brookfield, MD, and Jeffrey Lakier, MD

BACKGROUND: Myocardial ischemia and infarction are rare during pregnancy. Approximately 150 cases of myocardial infarction during pregnancy have been documented in the literature worldwide (predominantly anterior wall). However, elevated troponin levels have been reported in patients with preeclampsia.

CASES: We describe 2 patients with preeclampsia who presented with acute myocardial ischemia; 1 with ST segment elevation and one non-ST segment elevation at EKG. Our patients clearly had acute coronary syndromes with troponin levels much higher than would be accounted for by preeclampsia.

CONCLUSIONS: From the existing body of literature regarding this patient population, it is unclear why there is a higher incidence of adverse myocardial events. It may be that coronary ischemia has been missed in patients with preeclampsia. Troponin I is now readily available for detection of myocardial damage and should be used in this patient population only when clinically indicated, such as when chest discomfort or new electrocardiogram changes are observed. Patients with preeclampsia may be at higher risk for coronary events, and troponin I levels could be a valuable tool with which to monitor women who develop related symptoms.

(Obstet Gynecol 2005;106:1204–6)

The incidence of myocardial infarction in women of reproductive age is less than 1%, with an estimated incidence of 0.01% during pregnancy. Approximately 150 cases of myocardial infarction during pregnancy have been documented in the literature worldwide (predominantly anterior wall). Elevated troponin I levels in women with preeclampsia and pregnancy-induced hypertension have been reported. We present 2 cases of women with preeclampsia and acute coronary syndrome, 1 with ST segment elevation and 1 with non-ST segment elevation myocardial infarction.

CASE 1

A 36-year-old healthy nullipara (gravida 2) at 28 weeks of gestation presented to an outlying hospital with chest pain. She described resting substernal chest pain, with radiation down both arms that lasted 10 minutes. She had had 2 similar episodes of chest pain associated with nausea and vomiting, each episode had lasted 5–10 minutes. On arrival at the emergency department, she was asymptomatic, and her electrocardiogram showed normal sinus rhythm, with T wave inversion in leads I and AVL; her blood pressure was 180/106 mm Hg. She had been followed up by her obstetrician and had no history of hypertension before or during her pregnancy. Her first troponin I was negative and a CT scan of her chest was negative for aortic dissection. Her repeat troponin, 6 hours after presentation was positive at 3.2 (normal < 0.1). She was subsequently transferred to our facility for further evaluation and was admitted directly to the cardiac intensive
infant boy did well on follow-up. EKG changes suggestive of ischemia. The patient and her maximal heart rate of 132 beats/min without symptoms or test; she completed 9 minutes of the Bruce protocol with a
of her hospital course was uneventful. Several weeks after her discharge from the hospital she had a treadmill stress test; she completed 9 minutes of the Bruce protocol with a maximal heart rate of 132 beats/min without symptoms or EKG changes suggestive of ischemia. The patient and her infant boy did well on follow-up.

CASE 2
A 26-year-old Hispanic multipara (gravida 3) was transferred from an outside hospital to our obstetric unit at 28 weeks gestation. She had a history of chronic hypertension and chronic placenta abruptio. She presented with vaginal bleeding and uterine contractions every 2–3 minutes. On arrival, her premature uterine contractions were treated with intravenous magnesium, and her hypertension with oral methyldopa (Aldomet, Merck, West Point, PA). Her blood pressure was 157/115 mm Hg; she was given labetalol 20 intravenously, with an adequate reduction of her blood pressure. There was no proteinuria in her urine, and her liver and kidney functions were normal.

The patient was treated with bed rest, intravenous magnesium, and labetalol. On the morning of the 9th day of admission, the patient complained of left chest and back pain, with radiation into her left arm and ear. Her blood pressure was 123/93 mm Hg. She was diaphoretic, but denied nausea or shortness of breath. The patient stated these symptoms lasted for approximately 1 hour before notifying the house staff. Physical examination showed clear lungs, and a holosystolic murmur (2/6) consistent with mitral regurgitation. An electrocardiogram done during the chest pain demonstrated sinus rhythm at 79 beats per minute with 1-mm horizontal ST depressions in the inferior leads and 2-mm horizontal ST depression and T wave inversion in the anteroseptal leads, suggestive of acute posterior myocardial infarction. A second electrocardiogram after spontaneous resolution of the chest pain showed sinus rhythm at 73 beats per minute, with resolution of the ischemic ST-T wave changes seen on previous electrocardiogram. An echocardiography study showed hypokinesis in the posterior lateral wall. Cardiac markers drawn 5 hours after resolution of the chest pain revealed a troponin level of 110 (normal < 0.1). Also noted was proteinuria (497 mg/24 hours), with normal renal and liver function.

The patient was transferred to the telemetry unit for observation. A calcium channel blocker (nifedipine) was added to the patient’s medical regimen for the presumptive diagnosis of vasospastic coronary artery disease. Eventually, β-blockade was initiated for both hypertensive and postinfarction management. Cardiac catheterization with possible intervention was not done due to the placental abruption. The differential diagnosis was ischemia due to prolonged vasospasm, coronary artery dissection, a thromboembolic event, and a vulnerable plaque rupture.

On the 17th day of admission, the patient had another echocardiogram, which was unchanged from the previous study (hypokinetic posterior wall). The following day, the patient developed hypertension (164/114 mm Hg), pulmonary edema, and orthopneic symptoms and proteinuria of 5,378 mg/24 hours. She denied chest pain. An emergency cesarean was performed without complication. She had a healthy 1,552 g male neonate. Postoperatively, the patient developed fulminate pulmonary edema and was aggressively diuresed under observation in the cardiac intensive care unit. After 2 days in the unit, the patient remained free of chest pain and without evidence of heart failure. Cardiac catheterization was performed and demonstrated normal coronary arteries. The patient was seen in follow-up several weeks later, and both mother and infant were doing well.

COMMENT
The estimated incidence of myocardial infarction during pregnancy is one per 10,000 pregnancies, which is lower than in the general population. Ginzel reviewed 39 pregnant patients with acute myocardial infarction and reported the mortality in patients aged younger than 35 years as 50% and 10.5% in women aged older than 35 years. Several factors have been linked with increased mortality rate: 1) patients aged younger than 35 years, 2) cesarean delivery, 3) delivery within 2 weeks of infarction, and 4) infarction occurring in the third trimester. There is a higher mortality reported with cesarean delivery (23%) compared with 14% with vaginal delivery in women with acute myocardial infarction.

Aglio et al reviewed 82 reported cases of myocardial infarction in parturient women and found that only 30% had defined coronary artery morphology: 40% had significant coronary artery atherosclerosis, 30% had normal coronaries with coronary thrombus, 10% had coronary aneurysm or dissection, 10% had normal coronaries, and 10–15% had probable coronary thrombus.

Fleming et al examined troponin I level in 69 women with preeclampsia or gestational hypertension. There were 43 controls, 20 patients with gestational hypertension, and 6 with preeclampsia. Troponin I levels were significantly higher in the gestational...
hypertensive group compared with controls (0.118 compared with 0.03ng/mL). They found higher mean troponin I levels in women with hypertension and proteinuria (0.155ng/mL) compared with those without proteinuria (0.089mg/mL). Our patients clearly had acute coronary syndromes with troponin levels much higher than would be accounted for by preeclampsia.

It may be that coronary ischemia has been missed in patients with preeclampsia. Troponin I is now readily available for detection of myocardial damage and should be used in this patient population only when clinically indicated, such as when chest discomfort or new electrocardiographic changes are observed. We do not believe that troponin I levels should be checked in all preeclamptic patients routinely, because Fleming et al reported that troponin levels are slightly elevated in this patient population. Patients with preeclampsia should be followed up closely and if symptoms suggestive of coronary ischemia (ie, chest pain or shortness of breath) are present, troponin I levels and electrocardiograms should be obtained. From the existing body of literature regarding this patient population, it is unclear why there is a higher incidence of adverse myocardial events. VanWijke et al reported that the numbers of T-cell and granulocyte microparticles are increased in preeclamptic patients as compared with nonpregnant and pregnant females without preeclampsia. They raised the question of vascular dysfunction due to the altered microparticle numbers.

Continued evaluation is needed to delineate the pathophysiology in this patient population and the occurrence of adverse cardiac events. Patients with preeclampsia may be at higher risk for coronary events, and troponin I levels could be a valuable tool with which to monitor women who develop related symptoms.

REFERENCES

Pregnancy Outcome in Patients With Pulmonary Arterial Hypertension Receiving Prostacyclin Therapy

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BACKGROUND: Pregnancy is contraindicated in cases of pulmonary hypertension, a highly morbid disease affecting young women of childbearing age.

CASES: We describe the pregnancies of 3 patients with pulmonary arterial hypertension (idiopathic, Eisenmenger syndrome, and related to systemic lupus erythematosus). They received epoprostenol and low-molecular-weight heparin throughout pregnancy. The patient with Eisenmenger syndrome started epoprostenol in gestational week 16. Cesarean delivery under general anesthesia was performed at 28–33 weeks of gestation; early delivery was necessary in the patient with Eisenmenger syndrome because of fetal growth restriction. All deliveries were uneventful, and birth weights were 1,700, 1,500, and 795 g. There were no postpartum complications.

CONCLUSION: Pregnancy in women with pulmonary hypertension should still be considered high risk for both mother and child, but stable patients on epoprostenol may successfully complete pregnancy.

(Obstet Gynecol 2005;106:1206–10)

Pulmonary arterial hypertension is characterized by elevated pulmonary vascular resistance and low cardiac output. It may be idiopathic or related to other conditions, such as collagen vascular disease or congenital heart defects (Eisenmenger syndrome). Before the introduction of prostacyclin therapy, pulmonary hyper-
tension was considered fatal, with a median survival of 3 years. Today, the course of the disease has changed. Prostacyclin improves exercise capacity, hemodynamic parameters, and short- and long-term survival.

Pregnancy is contraindicated in every patient with pulmonary hypertension, and particularly in those with Eisenmenger syndrome, because the disease precludes the appropriate adaptive responses to the circulatory changes of pregnancy and to the fluctuations during labor and the postpartum period. Eisenmenger syndrome, even when associated with mild cyanosis, can develop into severe life-threatening hypoxemia during pregnancy and postpartum. The reported pregnancy-related mortality in women with Eisenmenger syndrome is 30–50% (Kahn ML. Eisenmenger syndrome in pregnancy [letter]. N Engl J Med 1993;329:887).1 There is also considerable fetal morbidity and mortality in this setting. Premature delivery and restricted fetal growth occur in at least 50% of cases, and only 15–25% of pregnancies progress to term.

Prevention or early interruption is considered the usual measure to alleviate maternal hypertension, which commonly affects women of childbearing age. Although experience is still quite limited worldwide, the use of prostacyclin therapy may provide hope to stable patients with well-controlled pulmonary hemodynamics. The present work describes 3 cases of successful completion of pregnancy in patients with pulmonary hypertension treated with epoprostenol.

CASE 1
A 29-year-old woman with idiopathic pulmonary arterial hypertension, who was treated with warfarin and continuous intravenous epoprostenol (Flolan; GlaxoSmithKline, Research Triangle Park, NC) therapy through a Hickman catheter, was followed in our pulmonary hypertension clinic for the last 3 years. She was stable on treatment and decided to become pregnant, despite the known risk and against medical advice. She was placed under close medical surveillance by the obstetric and pulmonary team, with routine monthly checkups and echocardiography assessments. Warfarin was stopped, and low-molecular-weight heparin (clexane) was started. There was no change in either hypertensive symptoms or hemodynamic parameters until week 23 of gestation, when she began to complain of mild exertional dyspnea and chest pain. Improvement was noted with a progressive increase in the dose of epoprostenol, up to 20 ng/kg/min (Fig. 1). The echocardiogram showed a mild rise in pulmonary arterial pressure to 60 mm Hg with no evidence of right heart failure. In week 30 of gestation, the chest pain and palpitations worsened, and the patient was hospitalized in the high-risk pregnancy department. There was no sign of right heart failure; oxygen saturation was stable (96%), and there was no change in hemodynamic factors. Multidisciplinary consultation among physicians from the pulmonary, anesthesia, cardiology, obstetric, and pediatric departments led to a decision to perform cesarean delivery at 32 weeks of gestation. A Swan-Ganz catheter was placed for intraoperative pulmonary arterial pressure monitoring. After the patient was anesthetized, systolic pulmonary arterial pressure measured 40 mm Hg, with a mean of 30 mm Hg. The patient remained stable throughout surgery and did not need additional vasodilators. A healthy female baby was delivered, weighing 1,700 g; Apgar score was 9 at 1 minute and 10 at 5 minutes. Bilateral tubal ligation was performed at the patient’s request.

After extubation, the patient remained stable and was followed in the intensive care unit for 1 week. She was discharged on epoprostenol therapy and Coumadin (Bristol-Myers Squibb, New York, NY). One year after delivery, the patient is stable, and the baby is healthy and well developed.

Fig. 1. Relationship between pulmonary arterial pressure (right Y axis) and epoprostenol dose (left Y axis). At diagnosis, the dose of epoprostenol was progressively increased with a parallel decrease of the pulmonary arterial pressure. During pregnancy (shaded area), the pulmonary arterial pressure increased and so does the dose of epoprostenol. After delivery we were available to reduce the dose of epoprostenol to the prepregnancy level. Illustration: John Yanson.

CASE 2

A 33-year-old woman with Eisenmenger syndrome caused by an uncorrected ventricular septal defect was referred to our pulmonary hypertension clinic in the seventh week of pregnancy. She had previously undergone 2 abortions and was determined this time to continue her pregnancy despite medical advice. Examination revealed cyanosis, with oxygen saturation of 69% in room air and 79% with oxygen mask. The echocardiogram showed a large ventricular septal defect, with pulmonary arterial pressure equal to systemic arterial pressure (90–100 mm Hg). Epoprostenol was started through a Hickman catheter at 16 weeks of gestation, and the dose was gradually increased to 9 ng/kg/mn. She received continuous oxygen therapy. The patient felt well, and no clinical or hemodynamic deterioration was noted. She was closely monitored at the high-risk pregnancy clinic. Intrauterine growth restriction was noted from week 26 of gestation. In week 28, the absence of diastolic blood flow at the uterine artery led to a decision to perform cesarean delivery. The patient remained stable during surgery, with normal oxygen saturation after induction of general anesthesia (SaO2 of 94% on FiO2 100%). A male baby was delivered weighing 795 g. The baby was intubated and admitted to the neonatal intensive care unit. Mechanical ventilation was continued for a week, and surfactant was given prophylactically. The mother was monitored in the intensive care unit. She became more hypoxic, with oxygen saturation dropping as low as 45–50% on room air. The patient responded well to increasing doses of epoprostenol (up to 12 ng/kg/mn) and was discharged home 2 weeks after delivery. One-year postdelivery, the baby is healthy and shows no evidence of any systemic or neurological deficit.

CASE 3

A 23-year-old woman with pulmonary hypertension related to systemic lupus erythematosus (SLE) was referred to our clinic at 7 weeks of gestation. She was treated with warfarin and epoprostenol through a Hickman catheter for the last year. During pregnancy, she was in good condition, with no evidence of right heart failure. The dose of epoprostenol was gradually increased to 12 ng/kg/mn, and warfarin was replaced with subcutaneous low-molecular-weight heparin. Palpitations and dyspnea began at 30 weeks of gestation, but no change was noted on right ventricular size and function on repeated echocardiograms. Mild intrauterine growth restriction was noted at the same time. Cesarean delivery was performed at week 32. The operation was uneventful. A Swan-Ganz catheter measured a pulmonary arterial pressure of 52/26 mm Hg and a pulmonary vascular resistance of 143 dynes/s/cm5. The patient remained stable during delivery, with no need for additional vasodilators.

Table 1. Pregnancy and Pulmonary Arterial Hypertension Treated With Prostacyclin Therapy: Literature Review

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IPAH, idiopathic pulmonary arterial hypertension; SLE, systemic lupus erythematosus.
She delivered a healthy male baby weighing 1,530 g with normal Apgar scores. No significant complications were noted in the postpartum period in either mother or child.

**COMMENT**

Pulmonary arterial hypertension is characterized by an elevation in pulmonary vascular resistance and a consequent decrease in cardiac output, right heart failure, and death. In recent years, better understanding and treatment of the disease have significantly improved patient outcome. Histologic and molecular studies suggested that the abnormal proliferation of both endothelial and smooth cells plays a crucial role in the disease. It correlates with endothelial dysfunction, diminished prostacyclin and nitric oxide synthesis, and endothelin overexpression. It was later confirmed by the discovery that a mutation of the bone morphogenetic protein receptor type II (BMPR-II) is present in 50–60% of familial cases of pulmonary arterial hypertension and in 30% of sporadic cases. However, additional environmental factors may play a role because not all patients who carry the BMPR-II mutation develop the disease.

Pregnancy significantly aggravates pulmonary arterial hypertension because it causes a marked increase in demand on the cardiopulmonary system, as well as higher tendency for thromboembolism. In normal pregnancy, cardiac output increases by 30–50%, blood volume by 40%, and oxygen consumption by 20%. The heart enlarges, with myocardial hypertrophy and valvular regurgitation. The left systolic heart function, which is maintained until the third trimester, decreases in the last period of pregnancy. Any preexisting vascular disease reduces the hemodynamic reserve. The progressive increase in blood volume and the peripheral oxygen consumption with limited oxygen delivery exceed patient adaptation. Therefore, the third trimester and the first month of postpartum carry the highest risk of death. During delivery, the uterine contractions induce an additional elevation in cardiac output (40%). After delivery, the complete return of the cardiovascular system to the prepregnant state is a slow process, despite the rapid normalization of the blood volume, and there is an increased risk in right heart failure.2

There are a few reports in the literature of pregnancy in women with pulmonary hypertension. Usually the hypertension is discovered during pregnancy, and the outcome is fatal. Before the prostacyclin era, pregnancy, and particularly the postpartum period, was associated with a 30–50% risk of maternal death. In 2 reviews of Weiss et al,1,2 Eisenmenger syndrome was associated with a slightly higher maternal mortality rate than idiopathic primary pulmonary hypertension. Other factors affecting outcome were late diagnosis of the pulmonary hypertension, late admission to the hospital, severity of the disease, and cesarean delivery. Antithrombotic drugs increased the risk of bleeding, and no benefit was observed with the use of pulmonary artery catheter during delivery.

The prognosis of pulmonary arterial hypertension has dramatically changed with the introduction of prostacyclin therapy. Prostacyclin is a metabolite of arachidonic acid, which is produced by vascular endothelium. It is a potent vasodilator with antiplatelet aggregatory and antiremodeling effect. With the introduction of prostacyclin therapy, pulmonary hemodynamic values and exercise capacity improved, leading to a better quality of life. Although not well documented, there are several cases of successful pregnancy outcome. We reviewed the MEDLINE database, from 1994 through September 2004, using the key words “pulmonary hypertension/pregnancy” and “pregnancy/prostacyclin,” in the English language. We found 9 additional cases of pregnancy under prostacyclin therapy (Table 1).3-9 In most patients, prostacyclin was administered during delivery; only 2 were receiving long-term therapy. Two mothers have died among the 12 pregnancies reported. All but one underwent cesarean delivery. The pregnancy was more likely to succeed if the hemodynamic parameters were stable under prostacyclin therapy, and a planned multidisciplinary approach was used.

In summary, we describe our experience in 3 cases of pregnancy in women with pulmonary hypertension of different causes. Two of the women (cases 1 and 3) were treated with epoprostenol before pregnancy, and their clinical and hemodynamic improvement allowed for continuation of the pregnancy. The patient with Eisenmenger syndrome (case 2) started epoprostenol after she was already pregnant, with improved hemodynamic control. A multidisciplinary approach, close hemodynamic, medical and obstetric monitoring, increased epoprostenol dose over the pregnancy, and early termination of pregnancy led to a successful outcome in all 3 patients. Nevertheless, pregnancy in pulmonary hypertension still remains very risky to both mother and child and should be avoided, if possible.

**REFERENCES**

Burns in Pregnancy

Luis D. Pacheco, MD, Alfredo F. Gei, MD, James W. VanHook, MD, George R. Saade, MD, and Gary D. V. Hankins, MD

BACKGROUND: Treatment of a major burn injury during pregnancy must incorporate modifications in management resulting from gestational physiologic changes. 

CASE: A 25-year-old woman, at 34 weeks of gestation, sustained a major burn injury at home. She required ventilatory support, invasive hemodynamic monitoring, and massive fluid resuscitation. Labor was augmented and a spontaneous vaginal delivery of a healthy neonate was achieved. Later, wound autografting was performed.

CONCLUSION: Pregnancy-induced physiologic changes affect key factors in the management of the burned patient, including airway management and hemodynamic support. Multidisciplinary management is essential to achieve the best possible outcome.

A 25-year-old Hispanic woman (gravida 3, para 1) at 34 weeks of gestation sustained a severe burn injury during a house fire. She was intubated and transferred to our hospital, where she arrived 10 hours postinjury. The patient was admitted to the obstetric intensive care unit. Vital signs showed a maternal pulse of 122 beats per minute (bpm), blood pressure of 90/54 mm Hg, temperature of 38°C, and arterial oxygen saturation of 100%, with an inspired oxygen fraction of 0.8. She weighed 68 kg, with a body surface area of 1.76 m². Total body surface area burned was estimated to be 38%. Diagnostic bronchoscopy confirmed inhalation injury.

Initial management included ventilatory support, invasive hemodynamic monitoring, aggressive fluid resuscitation with lactated Ringer’s solution and 20% albumin infusions, analgesia, gastrointestinal bleeding prophylaxis with famotidine, and deep vein thrombosis prophylaxis with enoxaparin. Enteral nutrition was provided, and topical antibiotics were given. Continuous electronic fetal monitoring was done, and Biobrane (Bertek Pharmaceuticals Inc, Morgantown, WV) dressings were applied to the affected areas. Ultrasound revealed a singleton pregnancy in cephalic presentation with an estimated fetal weight of 2,175 g. Biophysical profile was 8/8. Fetal status was reassuring as evaluated by electronic fetal monitoring. Local wound care was carried out by the burn team.

Twenty-four hours postburn, the patient had received a total of 20 L of fluid. Maternal tachycardia persisted at a rate of 120 bpm, with a mean arterial blood pressure of 65 mm Hg, central venous pressure of 5 mm Hg, and urine output of 60 mL/h. A vaginal examination revealed 4 cm of cervical dilatation with 75% effacement in the presence of regular uterine contractions. Mild fetal tachycardia was noted (180 bpm), and labor augmentation was initiated with oxytocin. A male neonate was delivered with Apgar scores of 4 and 7 and umbilical artery pH of 7.31. A total of 35 L of fluids had been administered at this point.

 Twelve hours after delivery, the patient was transferred...
to the burns intensive care unit. She self-extubated later that day. Wound cultures were positive for *Pseudomonas* and *Enterobacter*, requiring antibiotic coverage. The patient was discharged 15 days postburn. During a second admission, autografting was performed. A follow-up appointment confirmed that the patient was healing as expected and that she had a healthy infant.

**COMMENT**

At the present time, there is insufficient data in the literature to generate any guidelines for the management of the pregnant burn patient. After reviewing the literature, we can make the following recommendations:

Pregnancy is a hyperdynamic state with an increase in cardiac output of 43% (6.2 ± 1.0 L/min) and a drop in systemic vascular resistances of 21% (1,210 ± 266 dynes/sec/cm$^2$). Intravascular volume is increased by 50%. As pregnancy progresses, there is a progressive fall in colloid osmotic pressure, making the pregnant patient more prone to extravasation. These changes, coupled with an increase in the total body surface area, predispose the pregnant burned patient for additional fluid loss beyond amounts seen in nonpregnant individuals—rendering the Parkland Formula inaccurate in estimating fluid requirement. According to the Parkland formula, the fluid requirement in the first 24 hours postburn is 4 mL/kg body weight per percent of body surface area burned. One half of the calculated fluids are given in the first 8 hours and the rest in the next 16 hours. The formula was originally described with the use of Ringer’s lactate. In our case, a total of 20 L of fluid was given to maintain hemodynamic stability during the first 24 hours postinjury. This is almost twice the amount of fluid required in the first 24 hours postburn according to the Parkland formula (10.3 L). Fluid resuscitation should be tailored by clinical characteristics such as urine output, heart rate, mean arterial blood pressure, central venous pressure, pulmonary artery occlusion pressure, and electronic fetal monitoring tracing.

Early intubation is strongly recommended if inhalation burn injury is suspected. Tracheal edema in late pregnancy (third trimester) may be significant, making intubation more difficult. Given the 30% to 50% increase in tidal volume during human gestation and concomitant 50% increase in minute ventilation, intubated burned pregnant patients may require higher tidal volumes compared with their nonpregnant counterparts (if pulmonary compliance allows it). Both the functional residual capacity and the residual volume are decreased by 20% in pregnancy, making ventilatory support particularly important. In this case, early intubation was performed and a relatively high tidal volume (10 mL/kg) was used.

Early enteral nutrition is vital in the management of the pregnant burn patient. In our case, enteral feeding was started soon after admission. To achieve a positive nitrogen balance, 36 kcal/kg/day with a protein supply of 1.5 to 2.0 g·kg$^{-1}$·day$^{-1}$ should be given. Particular attention to residual volumes is mandatory due to the delayed gastric emptying seen in pregnancy.

The procoagulant state of pregnancy is aggravated in the burn victim due to hemoconcentration and endothelial damage. The use of prophylactic doses of unfractionated heparin or low-molecular-weight heparin is strongly recommended. Our patient received deep vein thrombosis prophylaxis with both enoxaparin and sequential compression devices.

Viable pregnancies (24 weeks or more) should have continuous electronic fetal monitoring during the critical phase of burn management. When abdominal burns are present, sterile transducer covers should be used to decrease the risk of infection. Interpretation of fetal monitoring is important not only to assess fetal well being but also to provide information about the adequacy of resuscitation. In the case described, the development of fetal tachycardia was likely secondary to hypovolemia, because the patient was afebrile at that time. If more than 50% of the total body surface area is involved and the fetus is viable, some authors advocate delivery due to the high maternal and perinatal mortality. We recommend the use of steroids in pregnancies between 24 and 34 weeks to enhance fetal lung maturity, as long as the risk of infection is low. Mode of delivery should be dictated by obstetric indications. In emergent situations, a cesarean delivery can be performed over a burned abdomen.

There is minimal data regarding the safety of products such as Biobrane and Tranocyte (Smith & Nephew, Largo, FL) or grafts during pregnancy. The use of topical antibiotics such as nystatin, bacitracin, polymyxin B, and silver sulfadiazine is not associated with fetal malformations, and their use in pregnancy is not contraindicated. Early excision and skin grafting have been reported to improve the quality of wound healing, with pain-free stretching of the abdominal skin during the developing pregnancy to term, allowing adequate fetal growth and facilitating performance of cesarean deliveries when needed. Use of systemic antibiotics should be guided by results of frequent wound, blood, sputum, and urine cultures.

Narcotic use during pregnancy in critical care settings outweighs the fetal risks in most clinical situations. We recommend the use of short-acting agents such as fentanyl (as described in our case) as opposed to meperidine. The successful management of pregnant burn patients depends on the concerted interaction among obstetricians, maternal–fetal med-
Cavernous Hemangioma

Diffuse Enlarged Venous Spaces Within the Myometrium in Pregnancy

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Michele L. Monticello, MD,
Thomas W. Johnson, MD, and
Daniel Wechter, MD

BACKGROUND: Diffuse enlarged vessels throughout the myometrium are very rare. This case illustrates the diagnosis and clinical management of a pregnancy complicated by large vessels diffusely distributed throughout the myometrium.

CASE: A primigravida measured large for dates at 27 weeks gestation. Ultrasonography demonstrated tubular echolucent spaces throughout the myometrium. No flow could be detected within them by color or spectral Doppler. During cesarean delivery blood loss was 1,700 mL, but the uterus was successfully closed with 3 suture layers. A biopsy specimen showed myometrium containing large vascular spaces thought to be veins, consistent with a hemangioma.

CONCLUSION: Enlarged vascular spaces diffusely distributed throughout the myometrium proved to be a cavernous hemangioma. Cesarean delivery in the present case produced some additional bleeding that was easily controlled, and the uterus was closed without incident.

(Obstet Gynecol 2005;106:1212–4)

Localized abnormal vascular spaces in the myometrium have been reported in arteriovenous malformations and hemangiomas. Such vascular spaces diffusely distributed in the uterus, rather than localized, are even rarer.1–7 When seen in pregnancy they raise questions about diagnosis and management of delivery. The present such case is unusual because a biopsy specimen was taken of the myometrium at the time of cesarean delivery.

CASE

A gravida 1 para 0 patient measured large at 27 weeks, at which time a scan showed a diffusely thickened myometrium with tubular sonolucent areas. Referal ultrasonographic evaluation of the uterus at 32 weeks of gestation confirmed that the entire myometrium was markedly and diffusely thickened with numerous tubular echolucent areas (Fig. 1). The anterior wall of the uterus was quite compressible. Color, spectral, and power Doppler showed no flow in these tubular spaces. The preliminary diagnosis was that of vessels—either lymphatic or venous. The placenta was anterior.

The patient commented that some years before this pregnancy she had sought consultation regarding her very swollen legs. Venograms had been normal, and no diagnosis had been proffered. There was no pitting edema, difference in limb length, skin discoloration, varices, or other evidence for Klippel-Trénaunay-Webber syndrome.

During the present pregnancy, after failure to progress at 40 weeks of gestation, the patient underwent primary lower uterine transverse cesarean delivery, at which time the lower uterine segment was noted to be about 6 cm thick. Upon incision, copious venous blood welled up, obscuring the field of vision. A biopsy sample was taken of the myometrial edge (prior permission granted). The incision was closed, and at the
end of the procedure, the uterus contracted to the size of a term pregnancy. The neonate weighed 4,025 g, with Apgar scores of 8 and 9. Total operating time was 65 minutes, and estimated blood loss was 1,700 mL.

At the 6-week checkup the uterus was 14–16 weeks size. Microscopic evaluation of the myometrial biopsy showed multiple dilated thin-walled vessels, some of which were thrombosed, which appeared to be veins. There was increased fibrous tissue between them. The diagnosis was consistent with a cavernous hemangioma.

COMMENT

Benign vascular lesion terminology can be confusing. Hemangiomas consist of numerous single endothelial layer vessels—termed “capillary” when they are small in caliber and “cavernous” when large in diameter. They commonly have little connective tissue within the vessel walls, show intravessel thrombosis, and often also calcifications.8 Widespread capillary hemangiomas are termed “angiomyomatosis.” Cavernous hemangiomas usually show no blood flow by Doppler.9,10 This description of a cavernous hemangioma matches the pathologic description in the present case. Cavernous hemangiomas can also contain dilated lymphatics along with veins.7

Unlike hemangiomas, arteriovenous malformations are abnormal communications between arteries and veins in which the usual intervening capillaries are absent. The veins are usually arterialized, and spectral Doppler shows mixed arteriovenous velocities.9

A report similar to the present case was made in 1980 in which the anterior wall of the uterus demonstrated the same tubular pattern at 25 weeks of gestation. At cesarean delivery, the patient bled profusely from dilated channels, which seemed to be veins (estimated blood loss 1,500 mL).1 No biopsy was done. This same group also evaluated the uterine walls of 100 consecutive pregnant patients by gray-scale ultrasound and found the same tubular pattern in 20% of patients, almost always in the posterior fundal area and concurrent with the location of the placenta in 71%. However, in only 9% did it involve more than 1 quadrant of the uterus. There was no increase in incidence of this pattern with increasing gestation. They postulated that the tubular areas were myometrial veins.

Four cases with similar ultrasound appearances have been reported since that time and are summarized in Table 1.1,4–6 A biopsy was done in 1 case, which showed ectasia of the myometrial veins.5 However, as this pregnancy advanced, the veins in the anterior wall decreased in size and number except on the left. Because the uterine incision was vertical, it is probable that the biopsy was not through the portion of the uterus in which thickened large vessels persisted. No ultrasonography was performed in the case described by Gantchev.7 However, that case is notable because the patient underwent a Cesarean hysterectomy when several hematomas could not be prevented from expanding.

Richards and Cruz2 observed this same tubular pattern in a patient with Klippel-Trenaunay-Weber

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Table 1. Summary of Similar Cases With Diffusely Enlarged Myometrial Vessels

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>GA When First Enlarged</th>
<th>Color Doppler</th>
<th>Spectral Doppler</th>
<th>Delivery Type</th>
<th>Weight (g)</th>
<th>GA (wk)</th>
<th>EBL (mL)</th>
<th>Bx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hadlock et al</td>
<td>1980</td>
<td>25</td>
<td>NC</td>
<td>NC</td>
<td>Cesarean</td>
<td>3,140</td>
<td>40</td>
<td>1,500</td>
<td>N</td>
</tr>
<tr>
<td>Lotgerling et al</td>
<td>1989</td>
<td>14</td>
<td>NC</td>
<td>NC</td>
<td>Vaginal</td>
<td>1,880</td>
<td>35</td>
<td>NC</td>
<td>N</td>
</tr>
<tr>
<td>Weissman et al</td>
<td>1993</td>
<td>33</td>
<td>“blue and red”</td>
<td>NC</td>
<td>Vaginal</td>
<td>3,535</td>
<td>41</td>
<td>NC</td>
<td>N</td>
</tr>
<tr>
<td>Sutterlin et al</td>
<td>1998</td>
<td>17</td>
<td>“wild”</td>
<td>NC</td>
<td>Cesarean</td>
<td>3,320</td>
<td>41</td>
<td>500</td>
<td>Y</td>
</tr>
<tr>
<td>Gantchev</td>
<td>1997</td>
<td>34</td>
<td>ND</td>
<td>ND</td>
<td>Cesarean</td>
<td>2,250</td>
<td>34</td>
<td>NC</td>
<td>H</td>
</tr>
</tbody>
</table>

GA, gestational age; EBL, estimated blood loss; Bx, biopsy; NC, no comment; N, no; Y, yes; ND, not done; H, hysterectomy.
syndrome involving most of the uterus. Venous flow was seen in diffuse tubular structures in the majority of the uterus as early as 10 weeks. The anterior uterine wall measured 4 cm in thickness. A termination was performed because of fear that the patient would have life-threatening complications. However, others have found that bleeding from the angiomyomatosis (widespread hemangiomas) in Klippel-Trenaunay-Weber syndrome is not life threatening. Verheijen et al\(^9\) reported a case in which a healthy infant was delivered at term by classic cesarean. However, in that case report the abnormal vessels were limited to the lateral aspect of the uterus, and the dilated vessels were not transected. In fact, the uterine hemangiomas of Klippel-Trenaunay-Weber disease are usually localized. They can also be localized in patients without this syndrome; Kobayashi et al\(^9\) reported a localized hemangioma that they mistook for a fibroid, although it had the same tubular appearance as the present case and contained calcifications. Verheijen et al\(^3\) reviewed the course in pregnancy, which has been documented in the German literature.

A diffuse tubular pattern may also represent widespread AV malformations. Spectral Doppler will show arterial flow with low pulsatility, often over a wider area than suspected on gray scale. On section, the vessels consist of arteries and thick-walled arterialized veins.\(^9\)

Conceivably, dilated lymphatics could present the same picture. Congenital blockage of the lymph system in the pelvis has been noted to cause backflow into the uterus and vagina.\(^11\)–\(^12\) This was a consideration in the present patient because her legs were so enlarged. However, these patients usually present with watery vaginal discharge that comes from transudate from dilated vaginal lymphatics. No ultrasound evaluations of the uterus in these cases have been reported. A hydatiform mole has been mentioned as a possible diagnosis in several of these cases, but careful inspection shows that the Swiss cheese pattern involves only the uterine wall.

If there were increased arterial flow in enlarged vessels within the myometrium, as in arteriovenous malformations, incisions through these vessels would be expected to lead to severe bleeding. Venous flow, as in cavernous hemangiomas, in the angiomyomatosis of Klippel-Trenaunay-Weber syndrome, and as in the present case, can be expected to produce bleeding that is easily controlled.

The correct use of Doppler is the key to distinguishing arterial from venous flow and thus in managing these cases. Unfortunately, in several articles summarized here, flow was characterized as “wild” or “red and blue” (Table 1). This shows only that color Doppler was used. Color Doppler shows locations of vascular flow and identifies the direction—red toward the transducer and blue away from the transducer, but does not directly measure velocity and therefore does not distinguish arterial from venous flow. Power color Doppler is able to demonstrate flows slower than would be detected by regular color Doppler (as in veins), but does not show direction or velocity either. Spectral Doppler is displayed as a waveform and shows both direction and velocity and thus is the key to the differentiation between venous and arterial vascular spaces.

**REFERENCES**

An Unusual Cause of Sepsis During Pregnancy
Recognizing Infection With Chlamyphila Abortus

Gernot Walder, MD, MSc, Helmut Hotzel, PhD, Christoph Brezinka, MD, Walter Gritsch, MD, Robert Tauber, DVM, Reinhard Wurzner, MD, PhD, and Franz Ploner, MD

BACKGROUND: Chlamyphila abortus (formerly Chlamydia psittaci serovar 1) is a rare but severe cause of gestational septicemia, with particular problems in diagnosis and clinical management.

CASE: A 32-year-old woman in her fourth pregnancy (16th week of gestation) presented with progressive septicemia after extensive contact with abortive material from her goat flock. Treatment with levofloxacin could not prevent abortion. Multiorgan failure requiring catecholamines and artificial ventilation developed in the patient. After the agent was identified by polymerase chain reaction from acute-phase serum, macrolides were administered and yielded clinical improvement. The patient fully recovered. There were no sequelae in the subsequent 6 months.

CONCLUSION: Cp abortus must be considered in gestational septicemia after contact with ruminants. Polymerase chain reaction from acute-phase serum is a quick and easy way to establish the diagnosis. Macrolide antibiotics are still the treatment of choice.

Obstet Gynecol 2005;106:1215–7

Chlamyphila abortus (formerly Chlamydia psittaci serovar 1) is a major cause of abortion among ruminants and a rare but severe cause of septicemia in pregnant women, with a fetal mortality of 94% and maternal mortality of 6.3%. Until recently, diagnosis has either been confirmed retrospectively1–4 or by serology with a delay of a week or longer,1 but no method is available for its identification in the acute stage of illness. We describe polymerase chain reaction (PCR) from acute-phase serum as a rapid way of establishing the diagnosis, and discuss diagnostic pitfalls and clinical management strategies.

CASE

A 32-year-old woman in the 16th week of gestation of her fourth pregnancy was admitted to the emergency ward of the regional hospital in Sterzing, South Tyrol for a 3-day course of high fever. She reported extensive contact with abortive material from her goat flock, which had been affected by an epidemic of spontaneous abortions of unclear origin. Physical examination revealed fever of 40.8°C but was otherwise unsuspicious. Sonography showed a viable single unaffected fetus without signs of growth restriction. Laboratory investigations revealed an elevated level of C-reactive protein (29.8 mg/dL), pronounced thrombocytopenia (52,000/μL), low sodium (126 mM), and low potassium (3.2 mM); other measures including leukocyte count (6,800/μL) were within normal range. Antibiotic treatment with amoxicillin and clavulanic acid (Augmentin, GlaxoSmithKline, Verona, Italy) was initiated, but could not prevent further deterioration over the next 12 hours. The patient was transferred to the Department of Obstetrics at the University Hospital of Innsbruck.

Upon admission, fetal death had occurred. Because the patient experienced difficulty breathing and a respiratory infection could not be ruled out, levofloxacin (Tavanic, Aventis, Austria) was added to broaden the antibiotic coverage for gram-negative rods and atypical bacteria.

After local administration of 4 units of 3 mg dinoprostone (Vaginal Prostin estradiol, Pharmacia, Puurs, Belgium) at 6-hour intervals, a dead male fetus was delivered spontaneously. The patient’s condition rapidly deteriorated and she was transferred to the intensive care unit because of progressive septicemia, shock, and beginning multiorgan dysfunction. Intubation and mechanical ventilation were necessary, as was the administration of catecholamines and inotropic medication. Sonography and computed tomographic scans of the thorax, abdomen, and pelvic region revealed bilateral pulmonary edema, hepatosplenomegaly, effusions in the lower abdomen, and parenchymatous swelling of both kidneys. Fever was continuously above 40°C and repeated transfusion of erythrocyte and thrombocyte concentrates did not result in significant elevation of platelet and erythrocyte counts (9,000/μL and 2.78 × 106/μL).

Up to this moment, all efforts to identify the causative agent had been in vain. Blood cultures had remained sterile on agar-based media, cultures from vaginal swabs were unsuspicious for bacteria, ureaplasma, and mycoplasma, a commercially available PCR for Chlamydia had been negative from vaginal swabs, and acute phase sera and a wide panel of serologic tests including Chlamydia trachomatis and Chlamyphila psittaci failed to reveal a pathologic result.

A DNA sample was extracted from the patient’s acute
Recognizing Infection With Chlamydia phage serum 4 days after admission and retested for Chlamydiaceae by real-time PCR targeting the 16s-rRNA gene (primers: CTG AAA CCA RTA GCT TAY AAG CGG T and AYC TCG CCG TTT ARC TTA ACT CC, probe: FAM-CTC ATC ATG CAA AAG GCA CGC CG-TAMRA [tibmolbiol, Berlin, Germany]; PCR conditions were 10 minutes at 95°C followed by 50 cycles of 15 seconds at 95°C and 60 seconds at 60°C) and yielded a positive result. Subsequent PCR targeting the ompA-gene and sequence analysis of the resulting 390-bp fragment as previously described showed more than 99% identity to Cp abortus. Six days after admission, these findings were further supported by a 4-fold rise in the complement fixation test targeting Cp psittaci sensu latu. Testing of the patient’s placenta, the dead fetus, and abortive material from aborted goats by PCR was positive for Cp abortus, the sequence being identical to that derived from the patient’s serum. Clarithromycin (Klacid, Abbott, Vienna, Austria, at 2, 500-mg, doses) was administered immediately, resulting in marked improvement. Within 4 days C-reactive protein levels decreased from 26.97 mg/dL to 6.06 mg/dL, and after 4 days of treatment the patient became afebrile. A significant rise in liver enzymes was attributed to clarithromycin, so antibiotic was changed to doxycycline (VibraDox, Pfizer, Vienna, Austria, at 2, 100-mg, doses), which did not alter the process of convalescence. On day 12, artificial ventilation was terminated and the patient regained full consciousness. She was discharged in good general condition and with normal laboratory parameters after 21 days. Within 6 months, no sequela was observed.

**COMMENT**

Empirical first-line treatment in gestational septicemia is usually based on cephalosporin or β-lactam antibiotics combined with a β-lactamase inhibitor and clindamycin, because they cover a broad spectrum of agents and are considered safe in pregnancy. In gestational septicemia of zoonotic origin, however, no antibiotic is available that is sufficiently active against different pathogens as Listeria monocytogenes, Coxiella burnetii, and Cp abortus. Early identification of the causative agent is therefore crucial. Cp abortus represents a particular diagnostic challenge because it does not grow on common culture media, serologic reactions are usually too slow to confirm the diagnosis in a reasonable time, and commercial Chlamydia PCR systems almost exclusively target sequences specific for C trachomatis or Cp pneumoniae.

Clinical presentation and laboratory findings are rather nonspecific and include fever (87%), low platelets (100%), normal or moderately decreased leucocyte count (100%), elevated C-reactive protein level, positive lupus anticoagulant, low sodium levels, and elevated levels of neopterin. Febrile thrombocytopenia in the absence of leucocytosis may be misdiagnosed as a viral infection, causing delay in antibiotic treatment. If the patient confirms exposure to abortive material from ruminants, PCR from acute-phase blood, vaginal swabs, or if available, from abortive material of affected livestock is probably the fastest method to establish the correct diagnosis.

Because infections with Cp abortus are rare, maintaining a particular PCR for this agent is rather impractical. The use of broad-spectrum primers targeting all relevant members of the family Chlamydiaceae is probably a more suitable approach, because they can also be used in daily routine for detection of Cp trachomatis in vaginal swabs. Positive results can easily be corroborated by sequence analysis of the 16s-rRNA gene or the ompA-gene. Recently, quinolones have gained increasing importance in treatment of genital infections. The in vitro activity of levofloxacin against Cp abortus and Cp psittaci is comparable to that of erythromycin, so it might be considered a suitable first-line treatment in infection with Cp abortus. The findings in our patient do not encourage this strategy, because significant clinical improvement was not observed until 24 hours after administration of a macrolide antibiotic. Until clinical studies on the effectiveness of quinolones against agents of the Cp psittaci group are available, erythromycin should be considered the treatment of choice, particularly as long as the pregnancy is intact.

However, once the placenta is infected, neither macrolides nor tetracyclines have proven able to maintain the pregnancy: clinical recovery is not observed before this focus is removed. Because the parturition is often accompanied with a steep deterioration of the patient’s condition, probably due to a sudden release of bacteria into the bloodstream, patients should be transferred to a center where full-time critical care staffing and invasive hemodynamic monitoring are available. In late pregnancy, cesarean delivery under coverage with erythromycin would be the most promising strategy, whereas in earlier stages of pregnancy the fetus is usually doomed. Therefore, pregnant women who live on farms should be advised to stay away from flocks that are affected by abortions or preterm deliveries. After accidental exposure, early treatment with erythromycin should be considered. If treatment is started before the agent settles in the placenta, there might be a realistic chance to avoid the outbreak of the disease.

**REFERENCES**

Lichen Sclerosus Involving the Vagina

Mindy Longinotti, Yvette M. Schieffer, MD, and Raymond H. Kaufman, MD

BACKGROUND: A review of the English literature since 1940 did not reveal a reported case of lichen sclerosus involving the vaginal mucosa. Diagnosis of lichen sclerosus involving the vagina must thus be a rare occurrence.

CASE: This report presents the findings on a 54-year-old white woman with a history of lichen sclerosus involving the vulva. She was found to have lichen sclerosus involving the vaginal mucosa extending to the posterior vaginal fornix. The patient was started on the use of topical clobetasol ointment 0.05% to the vulva to be used twice daily for 1 month, at bedtime for 2 months, and every other day for 3 months. At follow-up, the vulvar and vaginal lichen sclerosus was unchanged, but the patient was asymptomatic. She was using the clobetasol 1 to 2 times per week.

CONCLUSION: Lichen sclerosus involving the vagina is a rare occurrence. Each case must be assessed separately and therapy initiated accordingly in each circumstance. Biopsy must be performed in all cases to identify the disease process and rule out malignancy.

(Obstet Gynecol 2005;106:1217–9)

Lichen sclerosus is an uncommon chronic inflammatory skin disease of poorly understood origin. When first reported by Hallopeau in 1887 it was described as an atrophic form of lichen planus; however, lichen sclerosus is now known to be a distinct nonneoplastic epithelial disorder usually in genitoanal distribution.1 Lichen sclerosus can occur at any age; however, it is uncommon before the age of 2 years and most commonly affects women in the fifth to sixth decades of life.

Although some patients are asymptomatic, the symptoms most often associated with lichen sclerosus include intense pruritus and irritation of the vulvar and perianal areas.1–3 Lichen sclerosus most commonly affects the anogenital area (85–98% of cases) and can occur in a figure-of-eight distribution.1,2,4 It occurs extragenitally in only 15–20% of cases,1,2,4 with rare oral mucosal lesions.5

We report a case of lichen sclerosus presenting both as a vulvar lesion as well as a vaginal mucosal lesion. A review of the English literature since 1940 did not reveal any reported case of lichen sclerosus involving the vaginal mucosa. The search engines used were both Ovid and PubMed. Limits were put on journals dating back to 1940, and the following search terms were used: lichen sclerosus, lichen sclerosus and vagina, lichen and vagina, lichen and vagina, lichen and location, lichen and location. The purpose of presenting this case is to contribute a report of lichen sclerosus involving the vaginal mucosa to the literature on this poorly understood disease.

CASE

The patient was a 54-year-old, gravida 2, para 2 white woman with a history of seasonal allergies and hypertension. Both deliveries were uneventful vaginal births. A hysterectomy had been performed for benign disease when she was aged 23 years. She was referred for examination of unimproved vulvar lichen sclerosus and evaluation of increased “leukoplakia” present on the vaginal vault. The patient was diagnosed 4 years before presentation with lichen sclerosus after a vulvar biopsy.

At the time of diagnosis, the patient had symptoms of vulvar pruritus, burning, and dryness. She was started on nystatin and triamcinolone intravaginal cream and vaginal estradiol tab therapy. Her symptoms of itching and burning improved, but she developed chronic vaginal wetness and discontinued use of the intravaginal estrogen. She was started at this time on a vaginal preparation of 3% testos-
terone and 1% hydrocortisone to be used twice daily as well as clobetasol propionate. At 1-year follow-up from this time, the patient complained of increased burning with urination and no improvement in her vulvar pruritus. On examination she was noted to have a white plaque now present on the vaginal vault. This white change on the vulvar area extended onto the anterior wall of the vagina below the urethra. A biopsy specimen was taken at this time from the abnormal vaginal mucosa. The biopsy slides were sent at the time of referral, and on review, the diagnosis of lichen sclerosus was confirmed.

At the time the patient was seen in consultation, she was complaining primarily of persistent vulvar pain exacerbated when she urinated. She stated that she had obtained some relief using 3% testosterone in Aquaphor (Beiersdorf, Inc., Wilton, CT) and had also been using clobetasol ointment 0.05% topically. On pelvic examination, a whiteness and thickening of the tissue was noted around the hood of the clitoris and in the region of the perineum and fourchette. Slight fissuring of the tissue was noted in the perineal region. Several small ecchymotic areas were noted along the upper inner labia majora. Within the vagina at the level of the vaginal vault (about 7–8 cm above the introitus), there was a thickened white plaque, and a biopsy specimen was taken from the vaginal vault. The specimen from the vaginal vault revealed lichen sclerosus (Fig. 1). The patient was started on the use of topical clobetasol ointment 0.05% to the vulva to be used twice daily for 1 month, at bedtime for 2 months and every other day for 3 months. She was advised to see the referring physician for follow-up examination in 3 months time; the vulvar and vaginal lichen sclerosus was unchanged, but the patient was asymptomatic. She was using the clobetasol 1 to 2 times per week.

**COMMENT**

Liver succes is a disease of poorly understood cause affecting less than 1% of women.6 Lichen sclerosus is known to affect the anogenital skin and various extragenital sites, including the inner thighs, submammary areas, shoulders, neck, wrists, and rarely the oral mucosa.1,2,5 A review of the English literature since 1940 revealed no reported cases of lichen sclerosus involving the vaginal mucosa.

Lichen sclerosus affects the anogenital area in 83–98% of affected women and occurs extragenitally in 15–20% of patients.1,2 It may involve any area of the vulva including perianal and inguinal skin and is usually bilateral and symmetric.7,8 Genital areas most commonly involved include the labia and fourchette, the perineum, the clitoris, periurethral tissue, and the inguinal folds.3,6,8,9 Patients often present with extreme pruritus, irritation, dysuria, dyspareunia, and intractable soreness of the vulvar and perianal areas. They may also complain of painful defecation or micturition. Traumatic tears can occur during intercourse or defecation.1,2 In severe cases, the labia minora may fuse or be entirely resorbed, the clitoris buried secondary to edema of the clitoral foreskin, and severe narrowing of the introitus or anus may occur, rendering intercourse impossible and defecation difficult.2,8 This narrowing can occur solely as a result of vulvar involvement, because vaginal and cervical tissues have not previously been found to be involved.2

The clinical and histopathologic features in the present case were characteristic of lichen sclerosus. The patient had been diagnosed 4 years before presentation with vulvar lichen sclerosus. When the patient was seen in consultation, a biopsy of the vagina revealed some classic changes of lichen sclerosus: thinning of the epithelium was present with pink staining acellular upper stroma, beneath which lay an inflammatory infiltrate of lymphocytes and plasma cells.

Of note, although we found no other case reports of involvement of the vaginal mucosa, there are
multiple reports of involvement of the oral mucosa. The white, homogenous, well-demarcated plaque seen on examination of the vaginal vault is also characteristic of oral mucosal lesions. Oral lesions appear as well-defined, white, flat lesions of sizes varying from small macules to involvement of larger mucosal areas. The white discoloration or oral mucosal lesion is thought to be a result of the thinned epithelium and hyaline changes of the underlying connective tissue. Oral mucosal lesions have been reported both in the presence and absence of genital lesions; however, in contrast to vulvar lesions, oral lesions are usually asymptomatic, only rarely producing symptoms secondary to epithelial atrophy and tightening. Due to the asymptomatic nature of oral mucosal lesions, they are often followed up clinically and left untreated or treated by simple excision alone. The same microscopic findings are present in oral mucosal lesions as in classic anogenital lesions.

Because lichen sclerosus involving the vaginal mucosa is rarely seen, its natural history and biologic behavior, and thus the best course of treatment, is unknown. It is unclear whether these mucosal lesions should be treated as oral mucosal lesions or as vulvar lesions. In this case, the patient was experiencing severe discomfort from her vulvar lesions, so treatment with topical clobetasol ointment was initiated to treat the vulvar and perirectal areas. The vaginal lesions were not treated. Although the causative relationship is unknown, there is an association between vulvar lichen sclerosus and squamous cell carcinoma with vulvar malignancy occurring in up to 5% of cases. However, the relationship of vaginal mucosal lichen sclerosus to malignancy is unknown. Excision of the vaginal lesion was not pursued at initial presentation. The lesion will be followed up clinically, because atypia was not present on biopsy.

It is our conclusion that each case must be assessed separately and therapy initiated accordingly in each circumstance. Biopsy must be performed in all cases to identify the disease process and rule out malignancy.

REFERENCES
**Pasteurella Multocida** Bacteremia and Tuboovarian Abscess

Kerry A. Myckan, MD, Christopher M. Booth, MD, and Eva Mocarski, MD

**BACKGROUND:** Tuboovarian abscess is commonly associated with sexually transmitted pathogens. We report a tuboovarian abscess caused by a rare pathogen, *Pasteurella multocida*, which was managed conservatively.

**CASE:** A 50-year-old sexually inactive woman presented with suprapubic pain and fever. Cat scratches were seen on her hand. Ultrasonography showed a 7.9-cm complex cystic adnexal structure. Her fever persisted despite broad-spectrum parenteral antibiotics. After placement of a transvaginal drain, the patient defervesced, and her pain improved. Both blood cultures and cyst aspirates grew *Pasteurella multocida*.

**CONCLUSION:** Tuboovarian abscess secondary to rare pathogens must be considered in the differential diagnosis of acute febrile pelvic illness in a non-sexually active woman. Minimally invasive drainage procedures may avoid surgery in patients failing initial antibiotic therapy.

*(Obstet Gynecol 2005;106:1220–2)*

Tuboovarian abscess occurs in association with pelvic inflammatory disease (PID), or as a complication after pelvic surgery. Pelvic abscess due to PID is frequently caused by ascending lower genital tract pathogens. However, tuboovarian abscess can also result from gastrointestinal organisms or from other rare organisms. It should therefore be considered in the differential diagnosis of acute febrile pelvic illness, even in women with no risk factors for PID. Treatment of tuboovarian abscess has traditionally been parenteral antibiotics, followed by surgery if the antibiotics fail. However, a minimally invasive drainage procedure, coupled with appropriate antibiotics, may offer a less morbid and fertility-sparing procedure, as well as ovarian conservation.

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**CASE**

A 50-year-old nulligravida perimenopausal woman was admitted to hospital with a 4-day history of fever and progressive pelvic pain. Her past medical history included a laparotomy 18 years ago for a ruptured endometrioma. She had no further symptoms related to endometriosis. She had also undergone previous appendectomy. She denied any chronic illness or immunosuppressive condition. Her only medication was the oral contraceptive pill for dysfunctional uterine bleeding. She had no known drug allergies.

The patient’s initial symptoms were mild suprapubic pain and fever. The pain increased over several days, leading to her emergency department presentation. On further history she reported nausea, but no vomiting, and some loose stool without blood or mucus. There was no recent travel history, no sick contacts, and no recent antibiotic exposure. She denied dysuria or hematuria. She was not sexually active. She did not have an intrauterine device. The only vaginal discharge was some intermittent spotting over the past 6 months. She reported a nonproductive cough but no dyspnea or chest pain. She denied headache or neck stiffness. There were no arthralgias or myalgias.

On initial examination her blood pressure was 110/60 mm Hg, pulse 110 beats per minute and regular, respiratory rate 16, and temperature 39.4°C. Oxygen saturation was 99% on room air. She did not seem toxic. Her neck was supple, and there were no focal neurologic deficits. There was no palpable superficial lymphadenopathy. Chest examination was unremarkable apart from a 2/6 systolic murmur best heard at the left lower sternal border. The abdomen was soft, with moderate bilateral lower quadrant tenderness on deep palpation. There were no peritoneal signs. Pelvic examination revealed mild cervical motion tenderness. The uterus was normal in size, mobile, and nontender. The right adnexa was normal. The left adnexa was moderately tender but without peritoneal signs. There was fullness but no discretely palpable mass in the left lower quadrant. There were several superficial abrasions on the surface of her right hand, which were attributed to her pet cats. There was no evidence of local skin infection.

Initial laboratory investigations revealed a white blood cell count of 9.4 × 10^9/L with 91% neutrophils. The blood work was otherwise normal. Urinalysis revealed 3+ red blood cells, 2+ white blood cells, and 1+ bacteria. A CT scan done in the emergency department showed a 7 cm × 4 cm left adnexal collection, at which point the gynecology service was consulted. A pelvic ultrasound showed a complex cystic structure in the left adnexa measuring 7.9 cm × 5.4 cm with normal Doppler flow (Fig. 1). The differential diagnosis included tuboovarian abscess or endometriosis. The patient was admitted to the hospital with a working diagnosis of urinary sepsis with concurrent endometrioma, or tuboovarian abscess. Tuboovarian abscess was considered less likely at this point given the absence of risk factors for PID and the physical examination finding of only mild cervical motion tenderness. Blood and urine cultures were obtained, and the patient was started on empiric broad-spectrum antibiotics with clindamycin and gentamicin.
During the course in hospital, the patient's pain improved; however, she continued to have intermittent fever. Preliminary blood cultures grew gram negative bacilli. On day 3 of hospitalization the blood cultures became positive for *Pasteurella multocida* in both the aerobic and anaerobic bottles. The Infectious Disease service was consulted.

Antibiotics were changed to penicillin G intravenously. Chest radiography revealed mild atelectasis but no infiltrate. Transthoracic echocardiography did not show any evidence of infective endocarditis. The patient continued to have intermittent low-grade fever. A repeat transvaginal ultrasound done on day 5 of admission showed the adnexal mass had increased in size to 8.7 cm × 6.2 cm × 7.3 cm. There were multiple cystic components with thin internal septations. Low-level internal echoes were seen. This was highly suggestive of a tuboovarian abscess. The following day a transvaginal aspiration was performed, which drained 60 mL of frank pus. Culture of the abscess fluid also yielded *Pasteurella multocida*. A vaginal drain was left in place, and the antibiotics were continued. The patient defervesced and her pain continued to improve. Repeat blood cultures on days 3 and 4 were negative. Urine and stool cultures from admission were also negative.

The patient developed urticaria on day 8, which was attributed to the penicillin. She was tried on cefazolin but the urticaria persisted. She was switched to doxycycline; however, this was poorly tolerated due to nausea and vomiting. Ciprofloxacin was also not tolerated. By this point the patient had been on antibiotics for 10 days, and had been afebrile for 4 days. Her pain was improved. The drain continued to put out small amounts of pus and blood. A repeat pelvic ultrasound showed the abscess to be decreasing in size, with the drain well positioned within the abscess cavity (Fig. 2). The antibiotics were stopped due to multiple intolerances and clinical improvement. The patient was discharged home with the drain in place.

The drain was removed 1 week later, and the patient felt well. At 4 weeks postdischarge, her left ovary felt normal on palpation apart from mild tenderness. The white blood cell count was 9.0 × 10⁹/L and the erythrocyte sedimentation rate was 11. An ultrasound showed 4 small cysts in the left ovary, the largest measuring 2 cm, and 3 smaller ones measuring 1 cm. The patient was reassessed clinically 2 weeks later, at which time she had mild persistent left lower quadrant discomfort. There was no cervical motion tenderness. She was to resume care with her community gynecologist. In an effort to prevent reinfection, the patient had her cat declawed.

**COMMENT**

*Pasteurella multocida* is an aerobic and facultative anaerobic gram-negative coccobacillus.² It is a part of the normal oral flora of domestic cats and dogs and is also common in wild animals. Human infections are relatively rare and are almost always associated with animal exposure such as bites and scratches. The most common manifestation is local skin and soft tissue infection. Occasionally this can progress to bone and joint involvement or respiratory tract infection. There have been reports of *Pasteurella multocida* abscesses in the brain, lung, liver, omentum, appendix, and kidney.³

Tuboovarian abscess is usually secondary to ascending infection from the lower genital tract. Common organisms classically include sexually transmitted pathogens such as *Neisseria gonorrhoea* and *Chlamydia trachomatis*; however, many different lower genital tract organisms can be involved. In addition, adjacent gastrointestinal infection can lead to pelvic or tuboovarian abscesses. *Pasteurella multocida* infection in the female genital tract is exceedingly rare. To
our knowledge, there are only 3 previous case reports in the literature of a Pasteurella multocida tuboovarian abscess. In the first reported case, the authors presented a healthy 47-year-old virginal woman who presented with fever and right lower quadrant pain over 3 weeks. She had multiple superficial lower extremity excoriations from her 12 cats. She underwent diagnostic laparoscopy which identified a 12-cm right-sided pelvic mass adherent to bowel. She then underwent laparotomy, which revealed the mass to be a tuboovarian abscess. A supracervical hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. The patient was treated with antibiotics postoperatively and rapidly improved. Cultures from the tuboovarian abscess yielded Pasteurella multocida. In the second case, the authors presented a 44-year-old woman who underwent dilation and curettage for menometrorrhagia. The following morning she was febrile and complained of severe right lower quadrant pain. She had an acutely rigid abdomen and underwent exploratory laparotomy. Intraoperatively, a ruptured tuboovarian abscess was found, and culture of the fluid grew Pasteurella multocida. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. The patient received 7 days of intravenous ampicillin, gentamicin, and metronidazole, and was discharged home on oral cephradine. However, she returned 3 days later with sepsis and required 2 more weeks of hospital care on intravenous antibiotics. The patient had close contact with 2 cats, but denied any history of scratches or bites.

In the third case, the authors presented a 37-year-old woman with fever and right lower quadrant pain over 2 days. She had several cat scratches on her legs. Diagnostic laparoscopy initially revealed a purulent exudate throughout the pelvis. The fallopian tubes were mildly hyperemic. She was treated with intravenous cefoxitin and doxycycline but did not improve. The antibiotics were changed to ampicillin, gentamicin, and metronidazole. Blood cultures grew Pasteurella multocida. Ultrasound then revealed a 5 cm x 6 cm x 7 cm mass in the right pelvis. Exploratory laparotomy showed a tuboovarian abscess, which required a right salpingo-oophorectomy. The patient improved and was discharged home on day 14.

In our case the patient presented with fever and pain, and an adnexal mass was seen on ultrasonography. We initially favored a diagnosis of endometrioma with coexisting urinary sepsis, because the patient had no risk factors for PID, and she was much less tender than is normally seen with tuboovarian abscess. However, urine culture was negative, and blood cultures revealed Pasteurella multocida bacteremia. The tuboovarian abscess aspirate subsequently grew the same. It is important to consider tuboovarian abscess secondary to uncommon organisms in the differential diagnosis of acute pelvic febrile illness in a non-sexually active woman. In addition to Pasteurella multocida, other rare causes of tuboovarian abscess include tuberculosis and Enterobius vermicularis.

In our patient, we hypothesize that she became bacteremic secondary to cat scratches. What is less clear, although possible, is whether her preexisting endometriosis or related scarring may have predisposed her to seeding of this organism into the pelvis. It is interesting that in the case presented by Teng et al there was also an underlying diagnosis of endometriosis.

Our patient ultimately did well with conservative management. Avoiding surgery was preferable in this case, because the patient had undergone 2 previous abdominal surgeries, including 1 for ruptured endometrioma. Minimally invasive drainage procedures may also serve as a fertility-preserving option as well as one to preserve the ovaries for endogenous hormonal support.

Patients with no risk factors for PID may still be susceptible to tuboovarian abscess from rare pathogens. This diagnosis must be considered in all women presenting with fever, pain, and a pelvic mass. Tuboovarian abscess from rare organisms may present atypically with less pain than is usually seen and minimal cervical motion tenderness. Conservative management in these patients is an option to avoid major surgery and to allow ovarian preservation.

REFERENCES