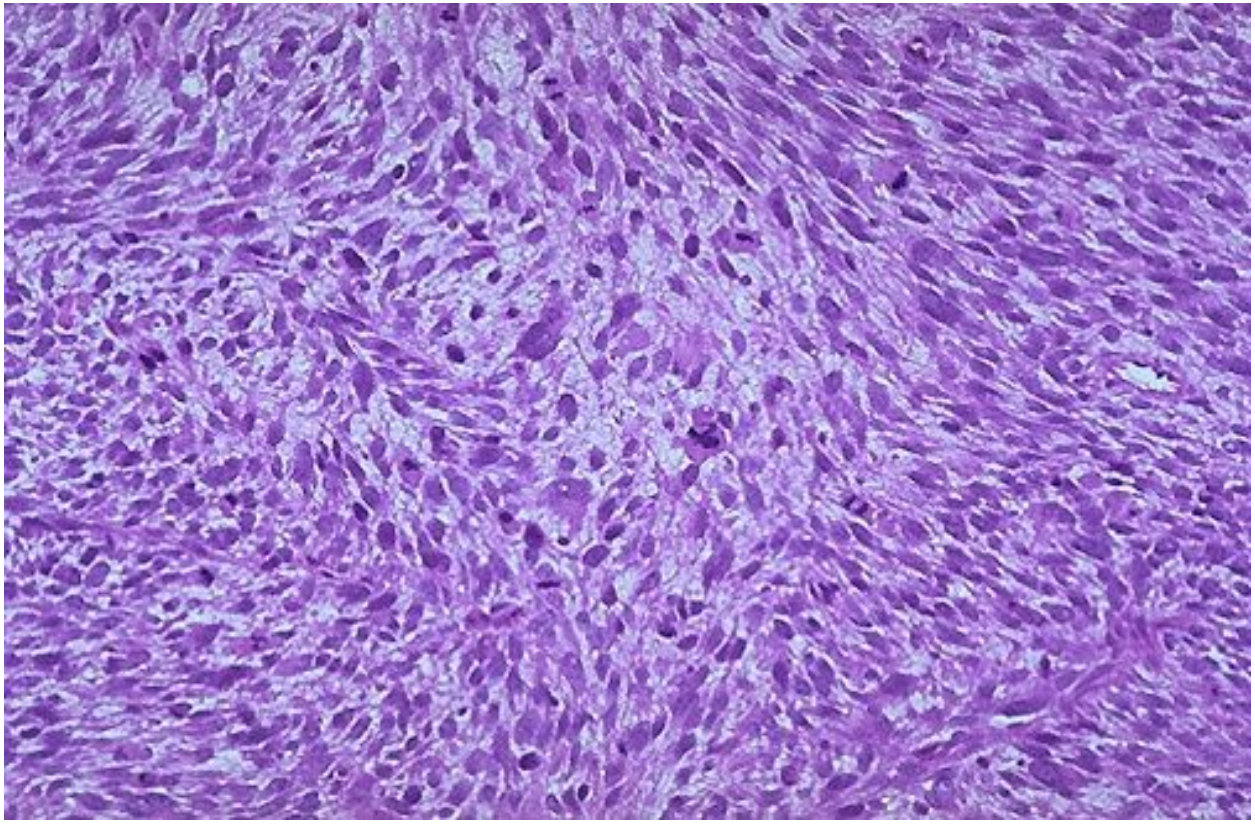
Uterine Leiomyosarcoma

A Case Presentation

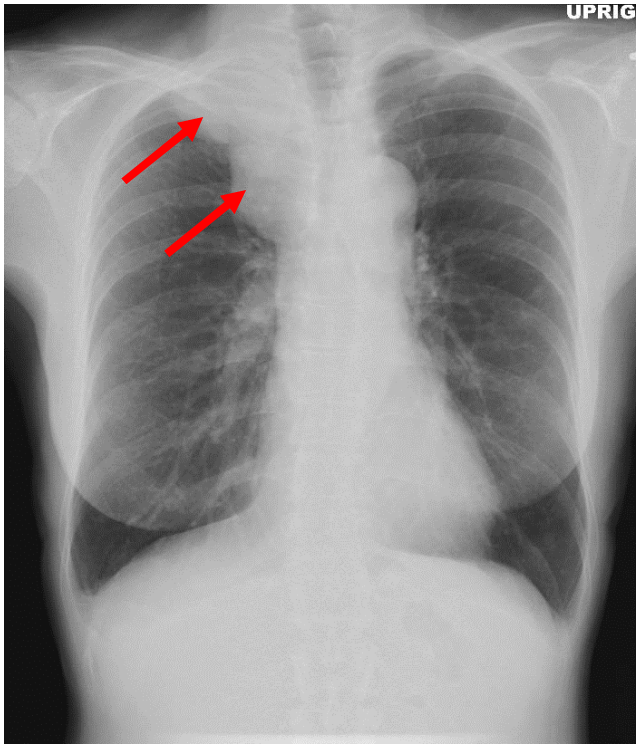


Patient Presentation

- 58 year-old female with history of fibroids presented to UVA Ob/Gyn clinic by self-referral in June 2014 for 9 months of intermittent post-menopausal bleeding
  - Endorsed progressive pelvic cramping, early satiety, and increasing abdominal girth
- Initially presented to primary care physician in September 2013
  - Pelvic ultrasound obtained at OSH in September 2013 demonstrated large fundal fibroid measuring 6.5 x 3.0 x 6.0 cm
  - Endometrial biopsy obtained in December 2013 was inconclusive

Clinical Course

- Repeat pelvic ultrasound performed June 2014
  - Uterine mass had doubled in size since last US in September
- Referred to UVA Cancer Clinic
  - Scheduled for total abdominal hysterectomy with BSO for removal of large uterine fibroid
  - CXR revealed multiple bilateral pulmonary nodules



Clinical Course (cont.'d)

- Intra-Op dx of uterine leiomyosarcoma on frozen section
  - Multiple nodule visualized throughout and removed from the peritoneum, omentum, and bowel

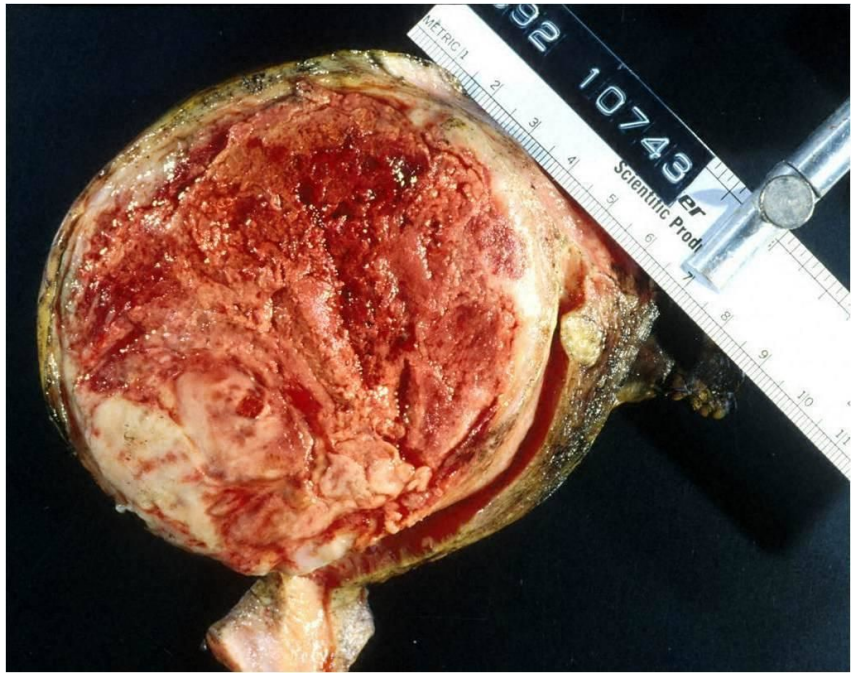
> *"The fundus of the uterus is diffusely involved by a tan-yellow infiltrative mass measuring 7.5 × 5.5 × 10.0 cm. Grossly the mass has a tan-yellow cut surface with areas of increased vascularity and rare areas of necrosis"*

Uterine Leiomyosarcoma

- Rare malignancy of uterine smooth muscle cells
  - Comprises 1-2% of all uterine sarcomas
  - Not derived from uterine fibroids
- Aggressive malignancy with poor prognosis and high rate of recurrence
  - 5 year survival of 40%; minimal if outside the uterus
  - Recurrence rate of 53-71%

Uterine Leiomyosarcoma

- Gross description fleshy tan-yellow mass with areas of hemorrhage and/or necrosis
  - Usually large (>6cm in diameter) and solitary



Clinical Course (cont.'d)

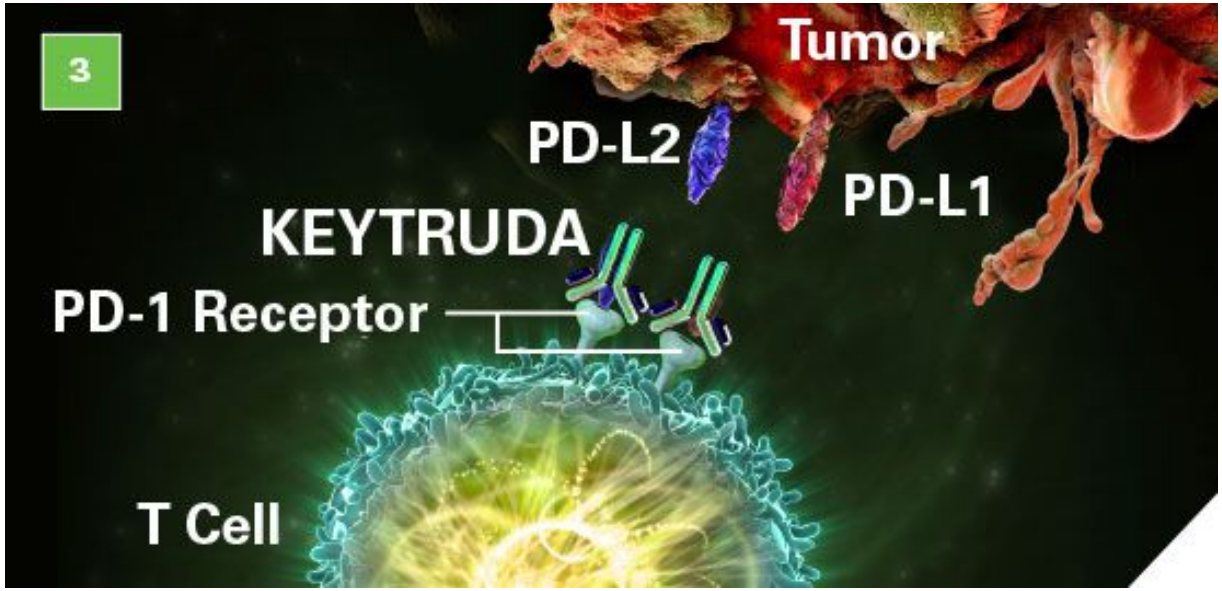
- Treatment with chemoradiation throughout subsequent years
  - Four rounds of chemotherapy: gemcitabine/docetaxel, carboplatin/doxorubicin, trabectedin, temazolamide, gemcitabine/docetaxel
  - Radiation therapy performed for control of hip lesions. Gamma knife for cerebellar lesions
- August 2017, chemotherapy stopped due to thrombocytopenia to 63, further tx deemed potentially harmful
  - Palliative lower colostomy performed d/t concern for impending BO
  - Patient expresses interest in XRT/pembrolizumab trial at UVA. Plan to irradiate painful RUQ abdominal wall lesion, neck mass, and perirectal masses.

Sites of Metastasis

Location	No. (%)
Lung	84 (74)
Peritoneum	46 (41)
Bones	37 (33)
Liver	30 (27)
Muscles	29 (26)
Lymph nodes	25 (22)
Subcutaneous	17 (15)
Kidney	6 (5)
Pancreas	6 (5)
Brain	5 (4)
Cardiac	5 (4)
Adrenal	2 (2)
Spleen	1 (1)
Thyroid	1 (1)
Breast	1 (1)
Vagina	1 (1)
Orbit	1 (1)
Total	297

Pembrolizumab

- Monoclonal antibody against PD-1 receptor
  - Prevents suppression of immune activity against tumor cells mediated by PD-L1 and PD-L2 expression
  - Currently approved for melanoma, NSCLC, H&N squamous CC, others

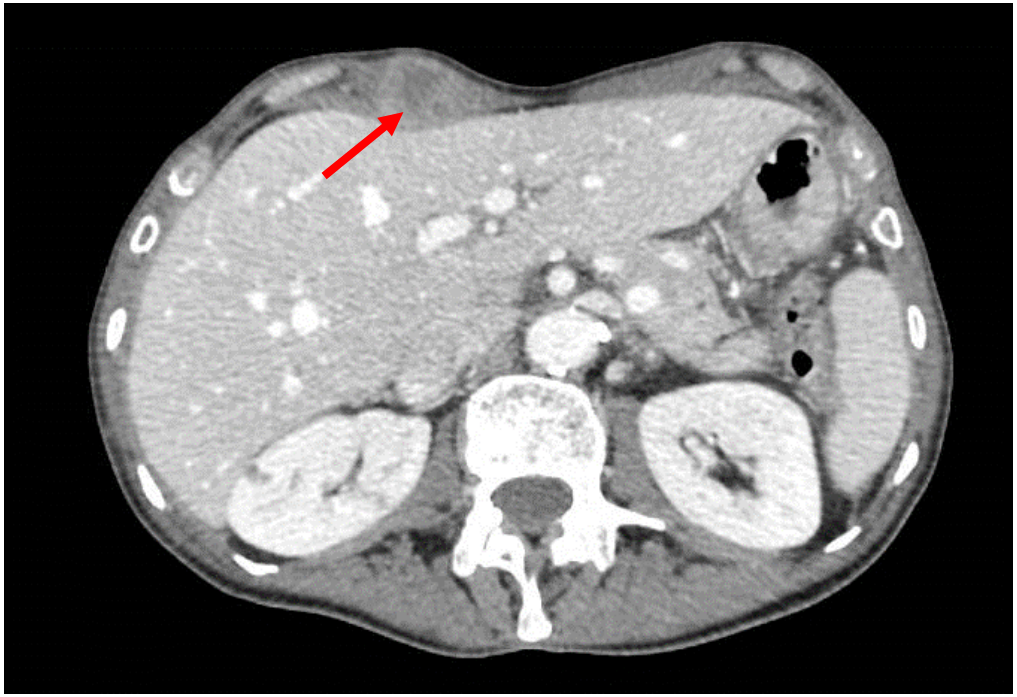


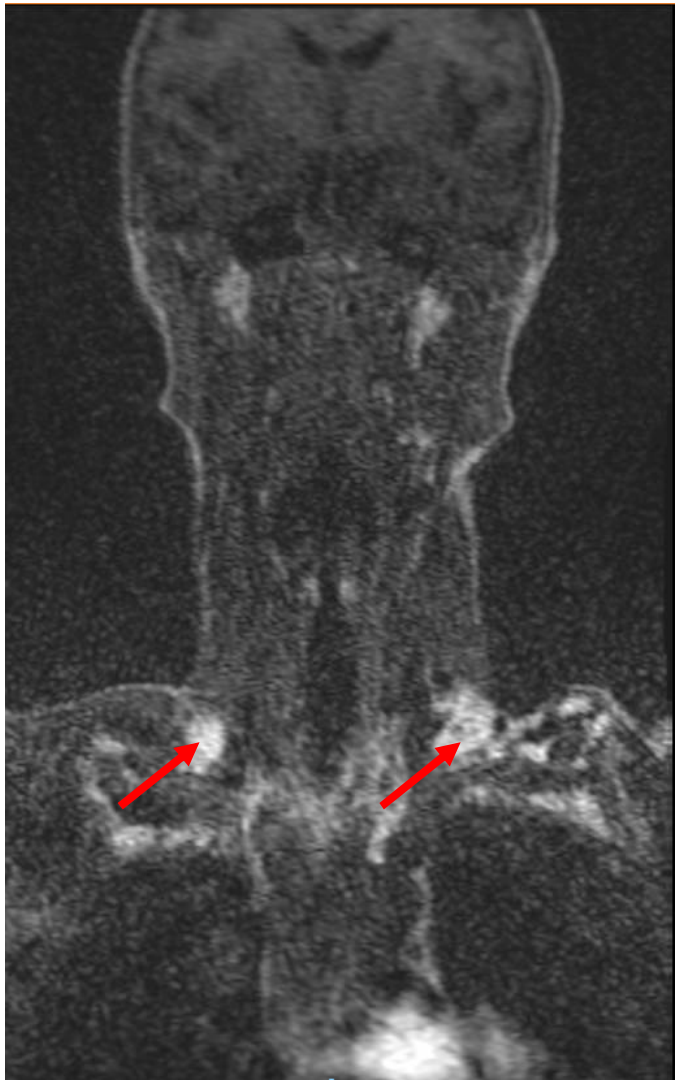
Pembrolizumab (cont.'d)

- UVA is undertaking Phase I safety trial of pembrolizumab with high-dose conformal radiation therapy
  - Primary outcomes include adverse event profile at 30 and 90 days and tumor infiltration by T-cell through day 43
- Notable inclusion criteria:
  - Must be able to provide tissue from 2-3 separate biopsy procedures
  - Patients must be resistant to at least 1 prior conventional chemotherapy regimen or other standard of care regimen
  - Patient must have no remaining conventional treatment options proven to provide long-term disease control

Most Recent Imaging

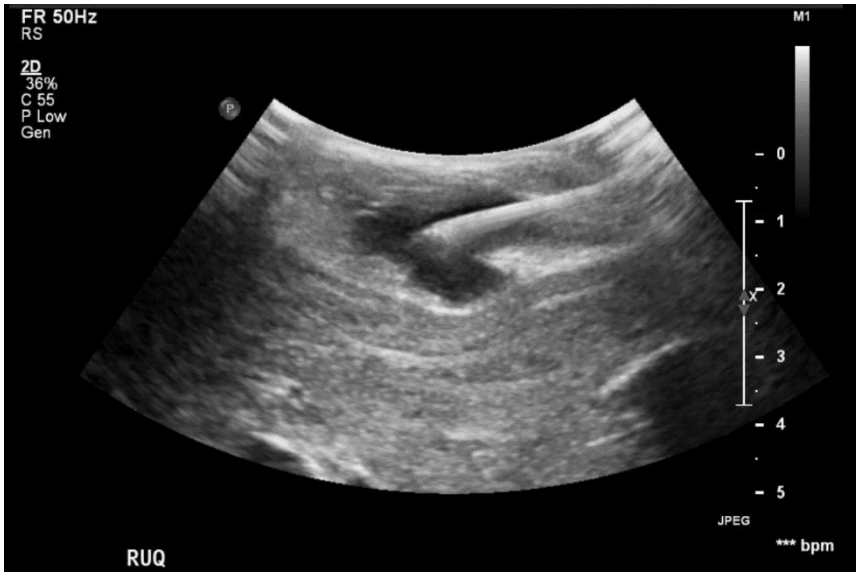
- Abdomen/pelvis CT
  - Interval enlargement of all pre-existing peritoneal implants and **right rectus abdominal implant**
  - New lesions of the liver and para-aortic lymph nodes
- Chest CT
  - Interval enlargement of all pre-existing lung nodules and 8th rib lesion, development of new lung nodules
  - **Enlarged cervical lymph nodes**
- MRI Brain
  - No abnormal enhancement in area of previous treated cerebellar lesion

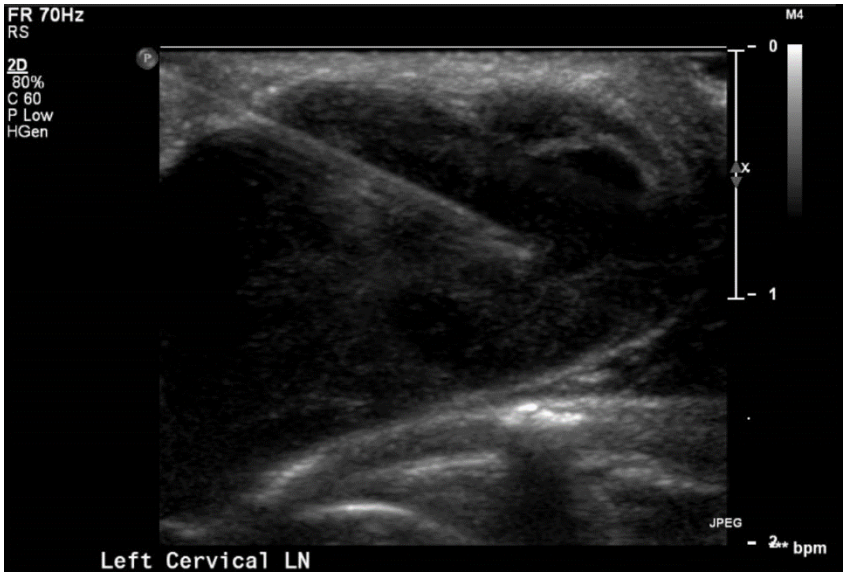




Procedure

- Ultrasound-guided FNA and core biopsies of RUQ abdominal wall mas and left cervical lymph nodes
  - 1 FNA and 4 core biopsies of rectus sheath mass
  - 1 FNA and 1 core biopsy of left ventral cervical LN

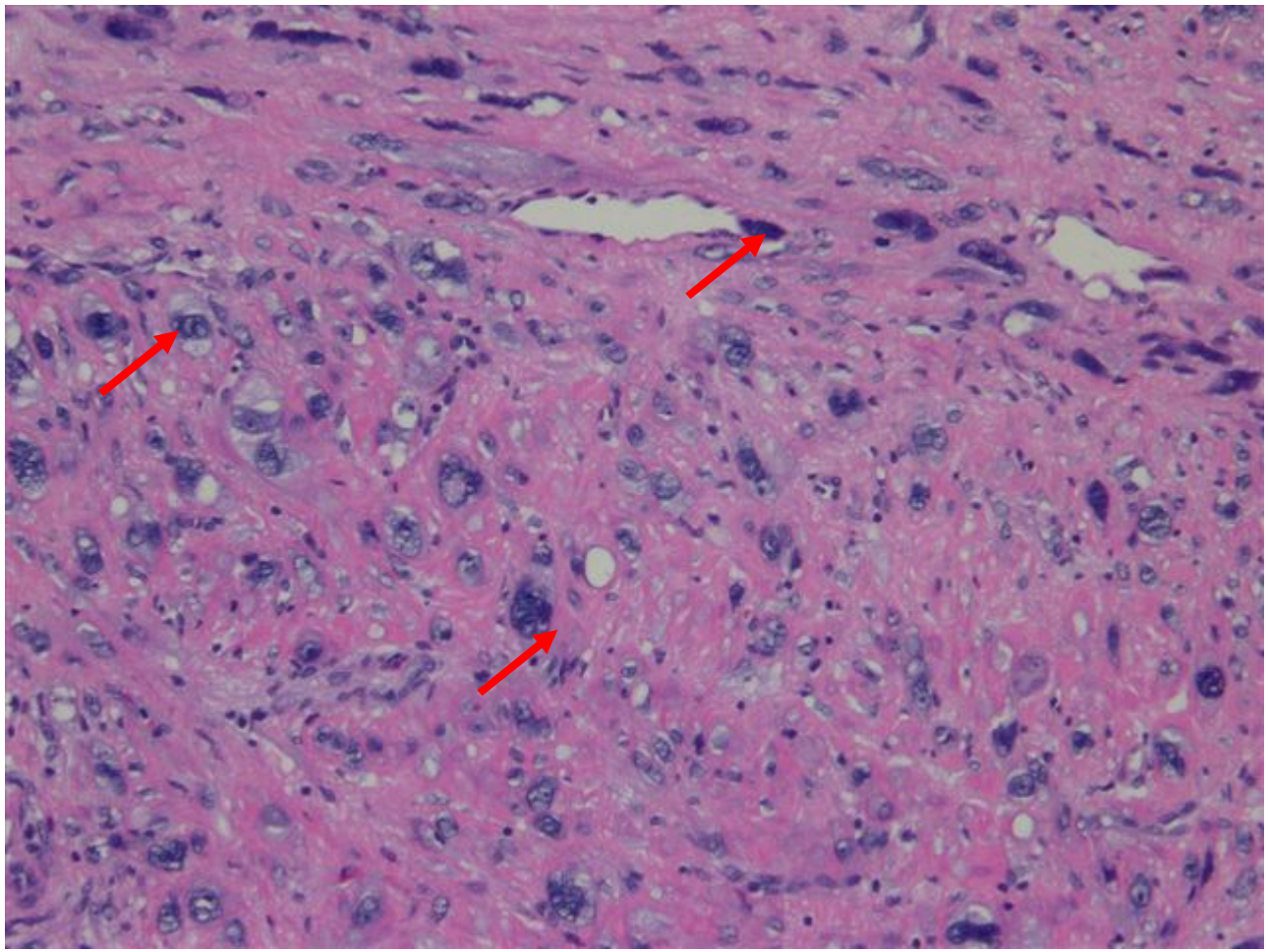




Cytology Findings

- Stanford criteria used in diagnosis
  - Cellular atypia, abundant mitoses (>10 figures per 10 hpf) , & coagulative necrosis
- Stains used for confimation
  - Smooth muscle markers: H-caldesmin, SMA, desmin
  - Hormone receptors: ER, PR
  - Others: Ki-67, EMA

Stanford Criteria



Hopeful News

JOURNAL OF CLINICAL ONCOLOGY
Official Journal of the American Society of Clinical Oncology

Response and oligoclonal resistance to pembrolizumab in uterine leiomyosarcoma: Genomic, neoantigen, and immunohistochemical evaluation.

Diana Miao , Dennis Adeegbe , Scott J. Rodig , Sachet Shukla , Ali Amin-Mansour , Scott L. Carter , ...Catherine Wu , Kwok-Kin Wong , Chandrajit P. Raut , Patrick Alexander Ott , Eliezer Mendel Van Allen , George D. Demetri , Suzanne George

"This patient exhibited complete pathologic response to pembrolizumab at all but one metastatic ULMS site. Genomic analysis of the resistant tumor revealed acquired bialllelic PTEN loss."

References

- D'Angelo E, Prat J. Uterine sarcomas: a review. Gynecol Oncol. 2010 Jan;116(1):131-9.
- Seagle BL, Sobecki-Rausch J, strohl AE, Shilpi A, Grace A, Shahabi S. prognosis and treatment of uterine leiomyosarcoma: A national Cancer Database study. Gynecol Oncol. 2017 Apr;145(1):61-70.
- Tirumani SH, Deaver P, Shinagare AB, et al. Metastatic pattern of uterine leiomyosarcoma: retrospective analysis of the predictors and outcome in 113 patients. Journal of Gynecologic Oncology. 2014;25(4):306-312.
- UpToDate. Treatment and prognosis of uterine leiomyosarcoma. Accessed October 2nd, 2017