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 x 5.5 x 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

<table>
<thead>
<tr>
<th>Location</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Lung</td>
<td>84 (74)</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>46 (41)</td>
</tr>
<tr>
<td>Bones</td>
<td>37 (33)</td>
</tr>
<tr>
<td>Liver</td>
<td>30 (27)</td>
</tr>
<tr>
<td>Muscles</td>
<td>29 (26)</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>25 (22)</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>17 (15)</td>
</tr>
<tr>
<td>Kidney</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Brain</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Adrenal</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Spleen</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Breast</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Vagina</td>
<td>1 (1)</td>
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<tr>
<td>Orbit</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>297</td>
</tr>
</tbody>
</table>
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 8\text{th} 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 mass 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 confirmation
  - Smooth muscle markers: H-caldesmin, SMA, desmin
  - Hormone receptors: ER, PR
  - Others: Ki-67, EMA
Stanford Criteria
Hopeful News

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 biallelic PTEN loss.”
References


- UpToDate. Treatment and prognosis of uterine leiomyosarcoma. Accessed October 2nd, 2017