Los Angeles Society of Pathologists
June 12, 2007

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Loma Linda University
Clinical History

- 33 year old female
- Presented with severe left arm pain
- H/O pain in both arms for six months
- Left thigh mass for one year
Radiological Findings

4.1 x 1.6 cm mass involving the distal humerus
9.5 cm mass involving the posterior part of the left thigh
Additional Radiological Findings

- 3cm adrenal mass
- Multiple small lung lesions
Work-up

- Touch imprints and core biopsy
- Followed by resection of left thigh mass (13.0 x 8.0 x 4.0 cm)
Focal diastase-resistant granular material in cytoplasm
# Immunohistochemical staining

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAM 5.2</td>
<td>Negative</td>
</tr>
<tr>
<td>Cytokeratin cocktail</td>
<td>Negative</td>
</tr>
<tr>
<td>S-100 protein</td>
<td>Negative except for scattered interspersed dendritic cells</td>
</tr>
<tr>
<td>HMB 45</td>
<td>Negative</td>
</tr>
<tr>
<td>Desmin</td>
<td>Moderate cytoplasmic staining of about 5% tumor cells</td>
</tr>
<tr>
<td>Myogenin</td>
<td>No nuclear staining</td>
</tr>
</tbody>
</table>
Electron Microscopy
Diagnosis

Alveolar Soft Part Sarcoma
Alveolar Soft Part Sarcoma

- First defined and named by Christopherson et al. in 1952
- Unknown histogenesis
- Unique because there is no benign counterpart
- Uncommon neoplasm (0.5-1.0% sarcomas)
Alveolar Soft Part Sarcoma
Clinical findings

- Typical age 15-35 years
- More common in females
- Adults - predominantly in lower extremities
- Children - most often in head and neck region
- Metastasis to the brain and lung may be first manifestation
Alveolar Soft Part Sarcoma

Age distribution of 102 alveolar soft part sarcomas

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>10-19</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>20-29</td>
<td>42</td>
<td>41</td>
</tr>
<tr>
<td>≥ 30</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>102</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

## Alveolar Soft Part Sarcoma

### Anatomic distribution of 102 Alveolar soft part sarcomas

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buttock/thigh</td>
<td>40</td>
<td>39.5</td>
</tr>
<tr>
<td>Leg/popliteal</td>
<td>17</td>
<td>16.6</td>
</tr>
<tr>
<td>Chest wall/trunk</td>
<td>13</td>
<td>12.9</td>
</tr>
<tr>
<td>Forearm</td>
<td>10</td>
<td>9.7</td>
</tr>
<tr>
<td>Arm</td>
<td>8</td>
<td>8.5</td>
</tr>
<tr>
<td>Back/neck</td>
<td>6</td>
<td>6.4</td>
</tr>
<tr>
<td>Tongue</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>102</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Alveolar Soft Part Sarcoma
Pathologic findings - Gross

- Variable appearance, often poorly circumscribed, soft, and friable
Alveolar Soft Part Sarcoma

Microscopic features

- Dense fibrous trabeculae divide the tumor into compartments of irregular sizes

- These are further divided into nests or islands of tumor cells

- Islands separated by thin walled vascular channels
Alveolar Soft Part Sarcoma

Microscopic features

- Tumor cells are large with eosinophilic granular cytoplasm

- Cellular aggregates may show pseudoalveolar pattern
Alveolar Soft Part Sarcoma Cytology

- Small groups of polyhedral cells
- Abundant granular cytoplasm
- Large round nuclei with prominent central nucleoli
- Binucleated and occasional multinucleated cells can be seen
- Numerous stripped tumor nuclei are a consistent feature
Alveolar Soft Part Sarcoma
Immunohistochemical staining

- Desmin sometimes +
- MyoD1 often cytoplasmic (but not nuclear) reactivity
- Myogenin consistently negative
- S100 protein or NSE + - 25% of cases
- Synaptophysin, chromogranin, neurofilament protein, cytokeratin, or EMA -
Alveolar Soft Part Sarcoma
Newer antibodies

- PAS-D resistant cytoplasmic granules associated with crystal formation are immunoreactive for MCT1 and CD147

- MCT1 is a monocarboxylate transporter

- CD147 functions in part as its chaperon protein
Alveolar Soft Part Sarcoma

Characterized by:
der(17)t(X;17)(p11;q25)

Results in the fusion of the *TFE3* transcription factor gene (from Xp11) with a novel gene at 17q25, named *ASPL*

*Fig. 9.47* Partial karyotype of ASPS showing the characteristic der(17)t(X;17)(p11.2;q25).
Balanced - translocation associated renal cell carcinoma

Unbalanced translocation - alveolar soft part sarcoma
Alveolar Soft Part Sarcoma

- Nuclear staining with the antibody to the carboxy-terminal portion of TFE3 retained in the fusion protein
Alveolar Soft Part Sarcoma
Electron Microscopy

Intracytoplasmic crystalloid inclusions in lysosomes
Alveolar Soft Part Sarcoma
Differential diagnosis

- Renal cell carcinoma
- Paraganglioma
- Granular cell tumor
Differential diagnosis
Renal cell carcinoma

- PAS-positive material is diastase-sensitive, and non-crystalline
- Alveolar pattern less developed
- Immunoreactivity for EMA, CD10, RCC in renal cell carcinoma
- Slightly older age on average
Differential diagnosis

Paraganglioma

- Patients over 40 years of age
- More vasculature around the nests
- Positive for neuroendocrine markers (synaptophysin, chromogranin)
- S-100 + in sustentacular cells
Differential diagnosis
Granular cell tumor

- Patients over 40 years of age
- Lack the rich vascular pattern of ASPS
- Well defined, distinctly granular cytoplasm
- S100, PAS - D +
Follow-up

- Given interferon, radiation therapy

- Alive 3 years later, with progressive disease
  - New lesion in right jaw region and base of skull
Alveolar Soft Part Sarcoma

- Rare sarcoma of undetermined histogenesis
- Malignant, indolent clinical course
- Distinctive nested growth pattern
- PAS + inclusions, crystalloids by EM
- Characteristic cytogenetic abnormalities
- TFE3, MCT1 and CD147 +
- DDx metastatic RCC, others
References:

- **Marc Ladanyi; et al.** The Precrystalline Cytoplasmic Granules of Alveolar Soft Part Sarcoma Contain Monocarboxylate Transporter 1 and CD147. *American Journal of Pathology.* 2002;160:1215-1221
- **Tornoczky T; et al.** Cytogenetic abnormalities of alveolar soft-part sarcomas using interphase fluorescent in situ hybridization: trisomy for chromosome 7 and monosomy for chromosomes 8 and 18 seem to be characteristic of the tumor. *Virchows Arch.* 2001 Feb;438(2):173-80
- **Sharon W. Weiss.** Alveolar Soft Part Sarcoma; Are We at the End or Just the Beginning of Our Quest? *American Journal of Pathology.* 2002;160:1197-1199
- **Ladanyi M; et al.** The der(17)t(X;17)(p11;q25) of human alveolar soft part sarcoma fuses the TFE3 transcription factor gene to ASPL, a novel gene at 17q25. *Oncogene.* 2001 Jan 4;20(1):48-57