Perspectives on Low-Grade Sarcomas: 
The Extraordinary Contributions of Sharon W. Weiss, M.D.

John R. Goldblum, M.D.
Chairman, Department of Pathology, Cleveland Clinic
Professor of Pathology, Cleveland Clinic Lerner College of Medicine
Cleveland, Ohio
Low-Grade Sarcomas
The Contributions of Sharon W. Weiss, M.D.
(A Partial List)

- Low-grade fibromyxoid sarcoma
- Hyalinizing spindle cell tumor
- Fibrosarcomatous DFSP
- Angiomatoid fibrous histiocytoma
- Soft tissue giant cell tumor
- Ossifying fibromyxoid tumor
- Myxoinflammatory fibroblastic sarcoma/IMHT
- ALT/dedifferentiated liposarcoma
- Spindle cell liposarcoma/fibrosarcoma-like lipomatous neoplasm
- Epithelioid hemangioendothelioma
- Kaposiform hemangioendothelioma
- ES-like hemangioendothelioma
- PHAT
SWW: Fellowship Legacy

- 1989-1995 University of Michigan
  - Surgical pathology fellowship with strong (and required) focus on soft tissue pathology

- 1996-present Emory University
  - Soft tissue pathology fellowship

- between these two programs, SWW has trained 35 fellows in soft tissue pathology
Low-Grade Sarcomas
The SWW / Fellow Connection

- Low-grade fibromyxoid sarcoma Andrew Folpe
- Hyalinizing spindle cell tumor Kathy Lane
- Well-differentiated/dediff liposarcoma Wally Henricks
- Epithelioid hemangioendothelioma Andrea Deyrup
- Fibrosarcomatous DFSP John Goldblum
Low-Grade Fibromyxoid Sarcoma and Hyalinizing Spindle Cell Tumor With Giant Rosettes

A Clinicopathologic Study of 73 Cases Supporting Their Identity and Assessing the Impact of High-Grade Areas

Andrew L. Folpe, M.D., Kathryn L. Lane, M.D., Gerson Paull, M.D., and Sharon W. Weiss, M.D.
Hyalinizing Spindle Cell Tumor With Giant Rosettes
A Distinctive Tumor Closely Resembling Low-Grade Fibromyxoid Sarcoma

Kathryn L. Lane, M.D., Randall J. Shannon, M.D., and Sharon W. Weiss, M.D.
<table>
<thead>
<tr>
<th>Molecule</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>S100</td>
<td>-</td>
</tr>
<tr>
<td>CD34</td>
<td>-</td>
</tr>
<tr>
<td>Bcl-2</td>
<td>-</td>
</tr>
<tr>
<td>CD99</td>
<td>-</td>
</tr>
<tr>
<td>SMA</td>
<td>-</td>
</tr>
<tr>
<td>EMA</td>
<td>+/-</td>
</tr>
<tr>
<td>MUC4</td>
<td>+</td>
</tr>
</tbody>
</table>
• Characteristic bland histology, frequently misdiagnosed as benign
• Paradoxically aggressive behavior
  • 68% local recurrence
  • 41% metastases
  • 18% died of disease
• Some cases with increased cellularity and atypia
• “The important feature of this neoplasm is that, despite its banal morphology, as many as 50% of cases eventually metastasize and pursue a fatal clinical course over a period of 10-30 years.” (CDM Fletcher, 2000)
LGFMS / HSCT
Folpe et al (2000)

• N = 73 cases
• 70/73 initially diagnosed correctly
• 3/73 with metastasis, previously diagnosed with “benign” tumors
LGFMS / HSCT
Clinical Behavior

• Follow-up: 2-192 mos (mean: 38 mos)
  • Local recurrence: 5/54 (9%)
  • Metastasis: 3/54 (6%)
  • Died of disease: 1/54 (2%)

Folpe et al. AJSP, 2000
Dedifferentiated Liposarcoma
A Clinicopathological Analysis of 155 Cases with a Proposal for an Expanded Definition of Dedifferentiation

Walter H. Henricks, M.D., Young C. Chu, M.D., John R. Goldblum, M.D., and Sharon W. Weiss, M.D.
**ALT/WDL: A Historical Perspective**  
**Weiss & Rao (1992)**

<table>
<thead>
<tr>
<th></th>
<th>Recur</th>
<th>Dediff</th>
<th>Mets</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep soft tissue</td>
<td>43%</td>
<td>6%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>(46)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>91%</td>
<td>17%</td>
<td>17%</td>
<td>33%</td>
</tr>
<tr>
<td>(23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Weiss SW et al, AJSP 1992
Weiss (1992)

- Subcutis: Atypical lipoma
- Deep soft tissues: WDL
- Retroperitoneum: WDL
ALT / WDL

Low-grade sarcoma
(no metastatic capability)

incomplete excision

Local recurrence

Tumor progression

Metastasis

complete excision

Cured!
## Dedifferentiated Liposarcoma

**Henricks et al: 155 cases**

<table>
<thead>
<tr>
<th>Site</th>
<th>Recurrence</th>
<th>Mets</th>
<th>Died of disease</th>
<th>Median f/u</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retroperitoneum (88)</td>
<td>41 (47%)</td>
<td>16 (18%)</td>
<td>30 (34%)</td>
<td>2.8 yrs</td>
</tr>
<tr>
<td>Accessible deep soft tissue (27)</td>
<td>9 (33%)</td>
<td>4 (15%)</td>
<td>3 (11%)</td>
<td>3.5 yrs</td>
</tr>
<tr>
<td><strong>Total (130)</strong></td>
<td><strong>53 (41%)</strong></td>
<td><strong>22 (17%)</strong></td>
<td><strong>36 (28%)</strong></td>
<td><strong>3 yrs</strong></td>
</tr>
</tbody>
</table>

Henricks et al. AJSP, 1997
Epithelioid Hemangioendothelioma of Soft Tissue:
A Proposal for Risk Stratification Based on 49 Cases

Andrea T. Deyrup, MD, PhD,* Mourad Tighiouart, PhD,† Anthony G. Montag, MD,‡
and Sharon W. Weiss, MD*
**EHE of Soft tissue**

**Low-Risk**
- \( \leq 3 \) MF/50 HPF
- AND
- Tumor size \( \leq 3 \) cm

**High-Risk**
- \( > 3 \) MF/50 HPF
- OR
- Tumor size \( > 3 \) cm

Deyrup et al. AJSP 2008
Nonparametric Survival Plot for Survival Mos
Kaplan-Meier Method
Censoring Column in DOD/DWD=1

Percent

Survival Mos

Table of Statistics
Mean Median IQR
73.3061 67 69

Deyrup et al AJSP 2008
Sarcomas Arising in
Dermatofibrosarcoma Protuberans

A Reappraisal of Biologic Behavior in Eighteen Cases
Treated by Wide Local Excision With Extended Clinical
Follow Up

John R. Goldblum, M.D., John D. Reith, M.D., and Sharon W. Weiss, M.D.
DFSP: 
Fibrosarcomatous Change

- Increased cellularity (gradual or sharp)
- Fascicular growth pattern
- Increased mitotic activity
- More nuclear pleomorphism
- Decreased / absent CD34 staining
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>20/31 (64%)</td>
</tr>
<tr>
<td>Metastasis</td>
<td>6/31 (19%)</td>
</tr>
<tr>
<td>Death</td>
<td>3/31 (9%)</td>
</tr>
</tbody>
</table>

Mentzel T et al. AJSP, 1998
# DFSP/Fibrosarcoma

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wide local excision</td>
<td>4</td>
</tr>
<tr>
<td>Incomplete excision</td>
<td>23</td>
</tr>
<tr>
<td>Unknown treatment</td>
<td>12</td>
</tr>
</tbody>
</table>

Mentzel T et al. AJSP, 1998
DFSP/Fibrosarcoma
Wide Local Excision

- Follow-up (N=18)
  - Range: 62 mos to 17 yrs
  - Median: 81.5 mos

- Local recurrence: 4/18 (22%)
- Metastasis: 0/18 (0%)
- Death: 0/18 (0%)

Goldblum JR et al. AJSP, 2000
Enzinger and Weiss's
SOFT TISSUE TUMORS
Sharon W. Weiss  John R. Goldblum
Fourth edition