Adult Fibrosarcoma

Background

Adult fibrosarcoma was once considered the most common soft tissue sarcoma in adults (1). However, the incidence of FS has declined dramatically over the past 7 decades, with recent SEER data showing it to account for only 3.6% of sarcomas arising from soft tissues (2). Even these data likely overstate the incidence of adult fibrosarcoma, however. A recent review of cases diagnosed as fibrosarcoma at a single institution over a nearly 50 year period showed strictly defined adult fibrosarcoma to account for <1% of adult soft tissue sarcomas (3).

Clinical Features

Adult fibrosarcoma is most common in middle-aged and older adults (median age 50 years), but may rarely occur in children. One recent series has reported adult fibrosarcoma to be more common in males (3). Fibrosarcomas most often involve the deep soft tissues of the extremities, trunk, head and neck. Visceral fibrosarcomas likely do not exist, and most retroperitoneal fibrosarcomas represents low-grade dedifferentiated liposarcomas. Fibrosarcoma presents as a mass with or without pain. In specific sites local symptoms relate to the effects of a mass. Some arise in the field of previous therapeutic irradiation, and rarely in association with implanted foreign material (3). Tumours with the histological features of adult fibrosarcoma may arise in dermatofibrosarcoma, solitary fibrous tumour and in well differentiated liposarcoma, either in the primary or in a recurrence, as a reflection of tumour progression.

Pathological Features

Fibrosarcomas are usually circumscribed white or tan masses, variably firm in relation to the collagen content. Hemorrhage and necrosis can be seen in high grade tumours. They are composed of relatively monomorphic spindled cells, showing no more than a moderate degree of pleomorphism. Tumors showing a greater degree of pleomorphism are better classified as undifferentiated pleomorphic sarcoma. The tumor cells are characteristically arranged in long, sweeping fascicles that are angled in a chevron-like or herringbone pattern. Storiform areas can be present, but the presence of large areas showing a storiform growth pattern should suggest fibrosarcoma arising from dermatofibrosarcoma protuberans. The cells have tapered darkly staining nuclei with variably prominent nucleoli and scanty cytoplasm. Mitotic activity is almost always present but variable. The stroma has variable collagen, from a delicate intercellular network to paucicellular areas with diffuse or "keloid-like" sclerosis or hyalinization. Some fibrosarcomas may contain relatively bland zones mimicking fibromatosis. By immunohistochemistry fibrosarcomas express vimentin and may occasionally show limited expression of smooth muscle actin, representing myofibroblastic differentiation. CD34-positive tumors showing fibrosarcoma
morphology likely represent fibrosarcoma arising in dermatofibrosarcoma protuberans or fibrosarcoma-like progression in solitary fibrous tumour.

**Genetic Features**

Adult fibrosarcoma has been reported to show multiple numerical and structural chromosomal abnormalities, without involvement of a specific locus or loci (4-6).

**Prognostic factors**

In the recent series of strictly defined adult fibrosarcomas reported by Bahrami and co-workers, over 80% of tumors were high-grade (FNCLCC Grade 2 or 3), with 1 of the 4 low-grade lesions progressing to a high-grade sarcoma in a local recurrence (3). These fibrosarcomas were aggressive, with multiple local recurrences, lymph node and parenchymal metastases, and overall survival of <70% at 2 years, and <55% at 5 years. Owing to the relatively small number of fibrosarcomas in the Bahrami et al series, no correlation could be made between clinicopathological variables (including grade) and outcome. In the older literature behaviour has been related to grade, tumour size and depth. The probability of local recurrence relates to completeness of excision, with historically reported recurrence rates of 12-79% (7, 8). Fibrosarcomas metastasize to lungs and bone, especially the axial skeleton, and rarely to lymph nodes. Widely variable metastatic and survival rates have been reported in older series of fibrosarcomas, likely reflecting diagnostic heterogeneity.

**Differential Diagnosis**

Adult fibrosarcomas should be distinguished from specific fibrosarcoma subtypes, such as low-grade fibromyxoid sarcoma, sclerosing epithelioid fibrosarcoma, low-grade myofibroblastic sarcoma, myxofibrosarcoma, and fibrosarcomatous dermatofibrosarcoma protuberans. They should also be distinguished from other monomorphic spindle cell sarcomas, including synovial sarcoma, malignant peripheral nerve sheath tumor, solitary fibrous tumor, spindle cell rhabdomyosarcoma, spindle cell angiosarcoma and the fibroma-like variant of epithelioid sarcoma. In superficial locations, spindle cell melanoma and sarcomatoid carcinoma also must be excluded. In general a limited panel of immunostains, to include some combination of cytokeratins, S100 protein, CD34, smooth muscle actin, desmin, myogenin, CD31, and SMARCB1 should allow these distinctions in most instances.

**References**


Fibrosarcoma: Where Do We Stand Now?

Andrew L. Folpe, MD
Professor of Laboratory Medicine and Pathology
Mayo Clinic, Rochester, MN
folpe.andrew@mayo.edu
RECENTLY, a review was made of the histories and pathological specimens in all available cases of known primary malignancy in the soft tissues of the extremities, exclusive of lymphosarcoma, malignant myeloma, and epithelioma, in which the patients had been operated on at The Mayo Clinic during the 21 year period from January 1, 1910, to December 31, 1930. There were in all 232 cases in which pathological material was available for study. Of the pathological specimens, 152 (65.5 per cent) represent fibrosarcomas. Fortunately, as a result of an efficient follow up system, there are complete data in 138 (90.8 per cent) of these 152 cases.
• Emphasized many potential mimics of fibrosarcoma
  • LPS, RMS, synovial sarcoma, MPNST, fibromatosis
• “There is little cause for wonder therefore that many malignant sarcomas of other sorts have been reported as fibrosarcomas…”
• Inherently a diagnosis of exclusion.
• First major “post-Stout” FS study
• Reviewed 330 tumors dx’ed as FS between 1910 and 1968
• Excluded over 33% of previously dx’ed FS
• 12% of soft tissue sarcomas

• 132 FS including 87 cases previously reported by Pritchard
• 96 cases reclassified
  • “Malignant fibrous histiocytoma” (40 cases)
  • MSS(19 cases)
  • MPNST (11 cases)
  • Other sarcomas (18 cases)
  • Non-sarcomatous fibroproliferative lesions (8 cases)
Identified 39 "FS - not otherwise specified" cases

Specifically excluded LGFMS and SEF

Limited IHC study

Genetic studies not performed

Median 56 years

Slight male predominance

Deep soft tissues of trunk > extremities

Local recurrences in 33%

Metastases and death from disease in 14%
Adult-type Fibrosarcoma: A Reevaluation of 163 Putative Cases Diagnosed at a Single Institution Over a 48-year Period

Armita Bahrami, MD and Andrew L. Folpe, MD

adult-type fibrosarcoma (FS) was once considered the most common adult sarcoma, but is now considered a diagnosis reserved for those patients with sarcomas with intermediate biological behavior. Recent studies have reclassified some of these tumors as fibroblastic/myofibroblastic sarcomas, synovial sarcoma, or even dermatofibrosarcoma protuberans. More recently, the clinicopathological and immunohistochemical features of adult-type FS have been better characterized. The objective of this study was to determine the incidence of adult FS at our institution in the modern era and to characterize the clinicopathological features of strictly defined adult FS. We studied all cases diagnosed as FS between 1960 and 2008 at our institution and excluded FS of bone, breast, and viscera and infantile FS. Individual case-specific IHC and FISH for SYT rearrangement were performed on selected cases.

Key Words: fibrosarcoma, sarcoma, immunohistochemical diagnostics

(Am J Surg Pathol 2010;34:1504-1513)

- Determine the incidence of adult FS at our institution in the modern era
- Characterize the clinicopathological features of strictly defined adult FS
- Studied all cases diagnosed as “FS” over 50 year period
- Excluded FS of bone, breast and viscera and infantile FS
- Individual case-specific IHC
- FISH for SYT rearrangement on selected cases
Diagnostic Criteria

• “Malignant tumor, composed of fibroblasts with variable collagen and, in classical cases, a herringbone architecture” (WHO 2002)
• Hyperchromatic spindled cells showing no more than moderate pleomorphism
• Fascicular, “herringbone” growth pattern
• Variable degree of interstitial collagen
• Absence of any morphologic features of myxofibrosarcoma, low-grade fibromyxoid sarcoma, sclerosing epithelioid fibrosarcoma or fibrosarcoma arising in DFSP
• Absent expression of any markers other than vimentin or very minimal smooth muscle actin
# Revised Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibrosarcoma</strong></td>
<td>26 (16%)</td>
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<tr>
<td><strong>Variants of Fibrosarcoma</strong></td>
<td></td>
</tr>
<tr>
<td>Myxofibrosarcoma</td>
<td>11 (7%)</td>
</tr>
<tr>
<td>Low grade fibromyxoid sarcoma</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Sclerosing epithelioid fibrosarcoma</td>
<td>4 (2.5%)</td>
</tr>
<tr>
<td>Fibrosarcomatous DFSP</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Myofibroblastic sarcoma</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td><strong>Undifferentiated pleomorphic sarcoma</strong></td>
<td>32 (20%)</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>21 (13%)</td>
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<tr>
<td>Solitary fibrous tumor</td>
<td>14 (9%)</td>
</tr>
<tr>
<td>MPNST</td>
<td>8 (5%)</td>
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<tr>
<td>Spindle cell melanoma</td>
<td>4 (2.5%)</td>
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<tr>
<td>Sarcomatoid carcinoma</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Spindle cell liposarcoma</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Desmoid-type fibromatosis</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Fibroma-like epithelioid sarcoma</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Cellular fibrous histiocytoma</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>17 (10%)</td>
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Fibrosarcomatous DFSP

PDGF-β

CD34
LG-Myofibroblastic Sarcoma

SMA
Undifferentiated pleomorphic sarcoma
Non-FS Monomorphc Spindle Cell Tumors

- Synovial sarcoma
- *Malignant peripheral nerve sheath tumor*
- Solitary fibrous tumor
- Spindle cell (sclerosing) rhabdomyosarcoma
- Spindle cell angiosarcoma
- Spindled (fibroma-like) epithelioid sarcoma
- Desmoid-type fibromatosis
Synovial Sarcoma

- ~10% of soft tissue sarcomas
- Young adults; may occur at any age
- Most common near knee; any location
- Biphasic (30%), monophasic (65%), and poorly differentiated (5%) variants
- Monomorphic spindled cells, alternating hyper and hypocellularity, wiry collagen
- Glands with eosinophilic debris, calcifications, mast cells
- High-grade sarcomas (FNCLCC/NCI 2-3 of 3)
Immunohistochemistry

- Cytokeratin expression may be very focal to absent, especially in PDSS
- HMWCK may be more sensitive
- EMA more sensitive but less specific
- Nearly 20% S100 protein-positive
- Essentially never CD34-positive
- TLE-1 positive
Genetics

- $t(X;18)(p11.23;q11)$ ($SS18-SSX1$): 65%
- $t(X;18)(p11.21;q11)$ ($SS18-SSX2$): 35%
- $t(X;18)(p11;q11)$ ($SS18-SSX4$): <1%
- $t(X;20)(p11;q13.3)$ ($SS18L1-SSX1$): <1%
Solitary Fibrous Tumor

- Middle aged adults
- Any location
- Large and highly vascular
- Hypoglycemia in 5-25%
- Uniformly distributed, branched and often hyalinized vessels
- Bland ovoid to spindled cells arranged in “patternless” pattern
- Collagen and fascicular growth in classic SFT
- May have myxoid change, mature fat, and multinucleated cells
- Usually CD34-positive; CD99, bcl-2 and bcl-6 may be of value
- Recently developed risk stratification system (DeMicco et al, Mod Pathol 2012; 25:1298) incorporating patient age, tumor size and mitotic activity may best predict outcome
Malignant Solitary Fibrous Tumor

CD34
Embryonal (Spindle Cell) Rhabdomyosarcoma

- Most frequent sarcoma of childhood; 70 to 75% of all RMS
- Usually occurs in children but also represents most common subtype of adult RMS
- Head/neck (50%), genitourinary (30%), soft tissue (10%)
- Poorly circumscribed, fleshy, hemorrhagic and/or necrotic masses
- Primitive round to spindled cells with varying degrees of rhabdomyoblastic differentiation
- Well-differentiated and poorly differentiated ERMS may mimic LG and HG-FS, respectively
- FS-like areas in sclerosing ERMS, in addition to OS, CS or AS-like areas
- Pediatric ERMS have an excellent prognosis; adults have worse prognosis
Angiosarcoma

CD31
Desmoid tumor
Final Fibrosarcoma Group

- 26 cases (16%); 15 M and 11 F
- Median age, 50 years (range, 6-74 years)
- Anatomic sites: lower extremities (12), head/neck (6), trunk (3), upper extremity (3), peritoneum and pleura (1 each)
- Tumor size: 2.5-17 cm
- Follow-up (24 of 26 cases, <1-35 years, median 5 years)
  - 11 DOD (<1-8 years, median 1 year)
  - 6 ANED (2.5-35 years, median 12 years)
  - 7 DOC (3-18 years, median 9.5 years)
Clinical Features

- Most common in middle-aged and older adults
- No clear sex predilection
- Deep soft tissues of the extremities, trunk, head and neck
  - The existence of visceral FS is debatable
  - Retroperitoneal cases likely represent low-grade dedifferentiated liposarcoma in most instances
- Unclear pathogenesis; some are irradiation or foreign material-associated
- “Secondary” FS arise in DFSP, SFT and WDL
Behavior

• Over 80% of strictly defined FS are high-grade (FNCLCC Grade 2 or 3)
• Aggressive, with multiple local recurrences, LN and lung metastases, and overall survival of <70% at 2 years, and <55% at 5 years
• In the older literature behaviour has been related to grade, tumor size and depth
• Local recurrence relates to completeness of excision, with historically reported recurrence rates of 12-79%
• Metastasize to lungs and bone, especially the axial skeleton, and rarely to lymph nodes
Summary

• Once the most common adult soft tissue sarcoma
• Incidence has declined dramatically over the past 7 decades
• Recent SEER data- 3.6% of soft tissue sarcomas
• Account for <1% of adult soft tissue sarcomas seen at Mayo Clinic over a 50 year period

Fibrosarcoma is a diagnosis of exclusion!