LEIOMYOSARCOMA OF THE BONE AND SOFT TISSUE: A REVIEW

An ESUN Article

Michael J. Weaver, MD
Harvard Combined Orthopedic Surgery Program
Boston, MA

John A. Abraham, MD
Center for Bone and Soft Tissue Oncology
Dana Farber Cancer Institute, Brigham and Women’s Hospital
Instructor of Orthopedic Surgery, Harvard Medical School
Boston, MA

INTRODUCTION
Leiomyosarcoma is an aggressive soft tissue sarcoma derived from smooth muscle cells typically of uterine, gastrointestinal or soft tissue origin. Sarcomas are malignant tumors arising from mesenchymal cell lines. They comprise a heterogeneous group of cancers, each with unique clinical, histologic, and radiographic characteristics. Soft tissue sarcomas account for 0.7% of malignancies. Sarcomas are generally classified according to the normal cell line that they most closely resemble. Of all soft tissue sarcomas, approximately 5-10% are leiomyosarcomas (1). Leiomyosarcoma of soft tissue is thought to arise from the smooth muscle cells lining small blood vessels. Leiomyosarcoma can also arise directly from the viscera, including the gastrointestinal tract and uterus. Leiomyosarcoma of soft tissue is discussed in this article, while the companion article addresses the uterine form of this disease. Gastrointestinal lesions are not included in this discussion. Primary leiomyosarcoma of bone is a distinct entity which is quite rare. While histologically similar, soft tissue leiomyosarcoma has classically been subdivided into three groups for prognostic and treatment purposes: leiomyosarcoma of somatic soft tissue, cutaneous leiomyosarcoma and leiomyosarcoma of vascular origin (4). A group of patients with leiomyosarcoma in the setting of immune dysfunction is also being discovered (5). Leiomyosarcomas are aggressive tumors that are often difficult to treat. The prognosis is poor, with survival rates among the lowest of all soft tissue sarcomas (7).

Somatic Soft Tissue: The term “somatic soft tissue” is an anatomic category that helps describe where a tumor is located or derived from. This term describes the entire category of normal tissues that, when altered, give rise to the class of cancers known as sarcomas. The term “somatic soft tissue” is another term for “connective tissue” and can be roughly thought of as the tissues that are responsible for holding the human body together. Examples of types of tissues that fall into this category include: muscle, nerve, fatty tissue, blood vessels, and fibrous tissue. Although visceral organs, such as the kidneys or liver, can be considered “soft”, they are made up of very specific types of tissues that have specific functions, enabling that organ to carry out its role in the human body. Cancers that arise from the cell that make up visceral organs are, in general, known as “carcinomas” and behave very differently from sarcomas, which have a different origin.

GENERAL CLINICAL FEATURES
There are no specific clinical features diagnostic of leiomyosarcoma of soft tissue that distinguish these tumors from other soft tissue sarcomas. Women are affected more than men (2:1), with the disease typically occurring in the 5th and 6th decades of life. This gender distribution may reflect the proliferation of smooth muscle that can occur in response to estrogen. Prognosis and treatment varies on the location, stage and grade of the primary tumor as well as the presence of
metastatic disease. The most common site of involvement of leiomyosarcoma is the retroperitoneum, accounting for approximately 50% of occurrences (8). In the case of retroperitoneal tumors, presenting signs and symptoms can include an abdominal mass, pain, swelling, weight loss, nausea or vomiting. Leiomyosarcoma of somatic soft tissues, like other soft tissue sarcomas, often present as an enlarging, painless mass. Although these tumors are generally associated with small blood vessels, they usually do not present with signs or symptoms of vascular compression. However, when leiomyosarcoma arises from a major blood vessel, symptoms of vascular compromise or leg edema may be present, as well as neurologic symptoms such as numbness from compression of an adjacent nerve. Soft tissue leiomyosarcoma typically affects adults, however it can present in childhood (2,3,5).

**IMAGING AND INITIAL WORKUP**

Typically, once a lesion suspicious for a sarcoma has been discovered, diagnosis and staging studies are performed simultaneously. Initial imaging should include plain radiographs of the affected area, an MRI of the lesion, and a chest CT scan. As with other soft tissue sarcomas in the extremities, MRI is the study of choice for the evaluation of the anatomic extent of the tumor. Important considerations are the involvement of adjacent structures such as bone, nerves or compression of vascular structures. CT imaging is useful in evaluating the extent of retroperitoneal tumors and specifically the involvement of adjacent structures. Angiography may be a useful modality in cases involving a major blood vessel. CT scanning of the chest is useful to evaluate for the presence of metastatic disease in the lungs. The role of PET scanning has not been studied in particular reference to leiomyosarcoma, but has been studied in other soft tissue sarcomas with early promising results. PET and PET/CT may prove particularly useful in evaluating patients who have undergone surgery in looking for local disease recurrence, or in the search for metastatic lesions. **Biopsy** is necessary to establish a specific diagnosis of leiomyosarcoma, and is often accomplished using a CT guided core needle biopsy. This technique can be performed in most cases with less morbidity than an open incisional biopsy.

**CLASSIFICATION**

Histologically, soft tissue leiomyosarcomas that arise in different anatomic locations are similar. However, based on the location of the tumor, prognosis and possible treatments differ. For this reason leiomyosarcoma of soft tissues is divided into four groups. Furthermore there are sporadic case reports of primary leiomyosarcoma of bone, a clinically distinct entity.

1. Leiomyosarcoma of Soft Tissue Retroperitoneal Somatic soft tissue
2. Leiomyosarcoma of Cutaneous Origin
3. Leiomyosarcoma of Vascular Origin (large vessel)
4. Leiomyosarcoma in the Immunocompromised Host
5. Leiomyosarcoma of Bone.

**LEIOMYOSARCOMA OF SOFT TISSUE**

Immunohistochemical analysis suggests that the cell line of origin of leiomyosarcoma is the smooth muscle cell. The most common site of leiomyosarcoma of soft tissue is the retroperitoneum, accounting for 50% of all cases (8). Smooth muscle sarcomas arising from the abdominal viscera or uterus are considered to be distinct disease entities. Other sites of involvement include the deep soft tissues of the extremities and are referred to as leiomyosarcoma of somatic soft tissue (4). Soft tissue leiomyosarcoma was at one time believed to arise from leiomyomas, however, this is now thought to be an extremely rare occurrence. Most malignant leiomyosarcomas arise independently, and are not associated with benign tumors. Histologic studies of somatic soft tissue leiomyosarcomas have shown that many, if not all, of these tumors arise directly from the smooth muscle cells lining small blood vessels.
Figure 1: Leiomyosarcoma of soft tissue of the wrist. The importance of MRI is demonstrated in this case, as the pathology was initially suggestive of a cutaneous leiomyosarcoma. This gadolinium enhanced T-1 weighted image with fat saturation shows the deep extension of the tumor nearly to the bone, placing this tumor in the category of leiomyosarcoma of soft tissue.

When the retroperitoneum is involved, presenting symptoms are usually vague abdominal discomfort, an abdominal mass and weight loss. Peripherally located masses present as an enlarging mass, often painless, with few constitutional signs. Due to the deep inaccessible location and large volume of the abdominal cavity, leiomyosarcomas of the retroperitoneum tend to be significantly larger than those of the extremities at presentation. Retroperitoneal leiomyosarcoma is an aggressive disease that is often not amenable to complete surgical resection.

Figure 2: Retroperitoneal Leiomyosarcoma. In this oral and IV contrast enhanced CT image, a large heterogeneous soft tissue mass arising from the retroperitoneum is demonstrated (red circle). Core needle biopsy confirmed the diagnosis of leiomyosarcoma.
LEIOMYSARCOMA OF CUTANEOUS ORIGIN
Leiomyosarcoma can arise within the dermis. When this occurs it is referred to as cutaneous leiomyosarcoma. Unlike other forms of leiomyosarcoma, men are affected more than women at a ratio of 2:1 (11). These lesions are typically small when first diagnosed (1-2 cm), and prognosis is generally good (12). When leiomyosarcoma develops within the dermis itself it is thought to be derived from the pilar arrecti (20). Tumors that develop within subcutaneous tissue arise from small or microscopic vessels and should be considered leiomyosarcoma of somatic soft tissue. The behavior of these tumors is more consistent with that of deeper tumors than intradermal tumors. When the lesion is confined to the dermis, metastasis typically does not occur (11). Deeper lesions can metastasize in up to 30-40% of cases, usually hematogenously to the lungs (12). Treatment consists of wide resection, and is often curative when the lesion is initially confined to the dermis, regardless of histologic grade.

LEIOMYSARCOMA OF VASCULAR ORIGIN
Leiomyosarcoma rarely arises directly from major blood vessels, however, when it does, it is termed leiomyosarcoma of vascular origin. There have been only a few hundred published reports of leiomyosarcoma of vascular origin. In one review of 86 cases, leiomyosarcoma of vascular origin was shown to have a propensity for lower pressure systems. Most commonly affected were the larger veins (68 cases), specifically the inferior vena cava (in 33 cases), and less commonly the pulmonary artery (10 cases) and rarely peripheral arteries (8 cases)(13).

If the tumor develops in the inferior vena cava in the supra-hepatic segment, Budd-Chiari syndrome develops: hepatomegaly, jaundice, and ascites. These tumors are usually not surgically resectable. Tumors that arise in the inferior vena cava below the liver present with lower extremity edema and vague abdominal pain. Symptoms are defined by the anatomic location of the lesion, and the local vascular physiology and drainage patterns.

Arterial leiomyosarcoma usually affects the pulmonary artery. Patients will typically complain of dyspnea and chest discomfort, relating to the arterial obstruction. Symptoms are related to the vascular distribution of the affected artery and the presence or absence of collateral blood flow.

LEIOMYSARCOMA IN THE IMMUNOCOMPROMISED HOST
Since the 1970s there have been a number of cases of leiomyosarcoma reported in immunocompromised patients having undergone transplantation and treated with immunosuppressive regimens (15). More recently, there have been further case reports involving people infected with the HIV/AIDS virus (6). There appears to be a relationship between these immunocompromised patients and super-infection with Epstein-Barr virus (EBV). Case reports of synchronous multiple leiomyosarcoma have been published where clonal analysis have shown that the individual tumors arose independently from each other (16). It is not known what interaction exists between immuno-incompentence and EBV infection that predisposes to leiomyosarcoma.

LEIOMYSARCOMA OF THE BONE
Primary leiomyosarcoma of bone is extremely rare. There have been approximately 90 cases reported since initially described in 1965 (22, 23). Many cases that are thought to represent primary disease of bone, after further investigation, actually represent metastatic disease from another site or bony invasion from a neighboring soft tissue lesion. Most cases of leiomyosarcoma of bone reported so far have been in the metaphysis of long bones. These lesions are thought to arise from the smooth muscle cells lining the intraosseous vessels or from pluripotent mesenchymal cells. The histology is the same as leiomyosarcoma of soft tissue. These tumors have an equal or slightly male-predominant gender distribution. The radiographic appearance of these tumors is typically a radiolucent lesion in the metaphysis of a long bone, although the tumor has been described in other locations as well. A permeative appearance is
There are no specific radiographic features that can diagnose leiomyosarcoma by radiography alone.

**Figure 3a and 3b:** Leiomyosarcoma of the distal radius. The permeative appearance often seen with leiomyosarcomas of bone is demonstrated in these AP and lateral radiographs of the wrist. This tumor had no extension outside the bone.

**STAGING**

Staging of leiomyosarcoma is important both in guiding treatment and in providing prognostic information. While many staging systems exist for soft tissue sarcoma, the most commonly used system is the AJCC system (9). This system classifies the tumor based upon histologic grade, the tumor size, location as superficial or deep, and the presence or absence of metastatic disease (see Table 1).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Histological Grade</th>
<th>Size</th>
<th>Location (Relative to fascia)</th>
<th>Systemic / Metastatic Disease Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Low</td>
<td>&lt; 5cm</td>
<td>Superficial or Deep</td>
<td>No</td>
</tr>
<tr>
<td>IB</td>
<td>Low</td>
<td>≥ 5cm</td>
<td>Superficial</td>
<td>No</td>
</tr>
<tr>
<td>IIA</td>
<td>Low</td>
<td>≥ 5cm</td>
<td>Deep</td>
<td>No</td>
</tr>
<tr>
<td>IIB</td>
<td>High</td>
<td>&lt; 5cm</td>
<td>Superficial or Deep</td>
<td>No</td>
</tr>
<tr>
<td>IIC</td>
<td>High</td>
<td>≥ 5cm</td>
<td>Superficial</td>
<td>No</td>
</tr>
<tr>
<td>III</td>
<td>High</td>
<td>≥ 5cm</td>
<td>Deep</td>
<td>No</td>
</tr>
<tr>
<td>IV</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The Surgical Staging System of the Musculoskeletal Tumor Society (MSTS) is also used. It is utilized for staging bone and soft tissue sarcomas, including leiomyosarcoma (10). This staging system classifies tumors as Ia, Ib, IIA, IIB, or III based upon the histologic grade of the tumor, its local extent and the presence or absences of macroscopic distant metastatic disease. If the tumor is localized to a single anatomic compartment, it is said to be confined. If it has spread locally beyond its initial compartment, then it is said to be unconfined (see Table 2).
TABLE 2: MSTS STAGING SYSTEM

<table>
<thead>
<tr>
<th>Stage</th>
<th>Histological Grade</th>
<th>Local Extent of Disease</th>
<th>Systemic / Metastatic Disease Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Low</td>
<td>Confined</td>
<td>No</td>
</tr>
<tr>
<td>Ib</td>
<td>Low</td>
<td>Unconfined</td>
<td>No</td>
</tr>
<tr>
<td>Ia</td>
<td>High</td>
<td>Confined</td>
<td>No</td>
</tr>
<tr>
<td>Ib</td>
<td>High</td>
<td>Unconfined</td>
<td>No</td>
</tr>
<tr>
<td>III</td>
<td>Any</td>
<td>Any</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Figure 4: Metastatic retroperitoneal leiomyosarcoma to bilateral proximal femurs. Non-contrast T-1 weighted MRI image demonstrates extensive disease in both femurs, which in this case necessitated surgical intervention to prevent fracture.

Staging: The American Joint Committee on Cancer (AJCC) was established to formulate and publish systems of classification of cancer, including staging and end results reporting, which will be acceptable to and used by the medical profession for selecting the most effective treatment, determining prognosis, and continuing evaluation of cancer control measures. The Enneking system of surgical staging of bone and soft tissue tumors is based on grade (G), site (T), and metastasis (M) and uses histologic, radiologic, and clinical criteria. It is the most widely used staging system and has been adopted by the Musculoskeletal Tumor Society.
**HISTOLOGY**

The histologic appearance of leiomyosarcoma of soft tissue exhibits significant variability. Typical features include a highly cellular field, with abundant pink to deep red cytoplasm on H&E staining. Cells are arranged in fascicles, and in well-differentiated tumors these fascicles are often arranged at right angles, allowing identification of both longitudinal and cross-sectional areas within one field. The nuclei are usually centrally located, and are classically described as cigar-shaped. One of the key features is the presence of myofibrils that are longitudinal and run the length of the cell. As the cells become increasingly de-differentiated, they become disorganized, and begin to lose their distinguishing characteristics.

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The concept of "Differentiation": Pathologists and oncologists often describe a particular tumor's potential for aggressive behavior in terms of "differentiation." Differentiation of any cell is a description that means that a given cell type has certain characteristics that make it unique, or "different" from other cell types. For instance, a fat cell is different from a cartilage cell, because these two cell types have many characteristics that differ from each other. Many types of connective tissue cells come from common precursor cells, but as they get signals to express certain proteins and develop certain characteristics, they fall into a unique cell type category. Sarcoma cells are cells that resemble or are derived from these cell types, but have undergone a transformation into a malignancy. That is, they have developed the capacity to metastasize.

Differentiation is a description of how closely the tumor resembles its cell of origin on the histologic (microscope) evaluation and gives a guide to the treating physicians of how aggressive a behavior to expect from a given patient's tumor. A well-differentiated tumor very closely resembles the cell line that it is derived from, whereas a poorly differentiated tumor has very few characteristics of its cell line of origin. This is an important distinction, as well-differentiated tumors have a lower potential for aggressive or aberrant behavior than poorly differentiated tumors, which can behave very aggressively. Additionally, the term "dedifferentiated" is usually used to describe a tumor that no longer has any detectable relationship to its origin cell line, and can only be diagnosed as being related to that cell line based on the background it is found in. For instance, a patient with a well-differentiated liposarcoma has a tumor that closely resembles adipose, or fat, tissue and has little propensity, if any, to metastasize. However, within that patient's well-differentiated liposarcoma if there were to be found a defined area that no longer has any resemblance to fatty tissue, but has the more characteristic appearance of an aggressive malignant spindle cell neoplasm, this area would then likely be considered a dedifferentiated area of the well-differentiated liposarcoma, or an area of dedifferentiated liposarcoma. It is important to note that these dedifferentiated tumors, since they behave differently from their related tumor type, may need to be treated quite differently than that related tumor type.

Leiomyosarcoma of somatic soft tissue has a number of histologic subtypes including epithelioid leiomyosarcoma, myxoid leiomyosarcoma, inflammatory leiomyosarcoma, granular cell leiomyosarcoma and dedifferentiated leiomyosarcoma. The clinical importance of these subtypes has not been well studied.
Figure 5a,b,c: Low grade Leiomyosarcoma of Soft Tissue: (a) Low, (b) Medium, and (c) High power. Classic features of leiomyosarcoma including cigar shaped nuclei and arrangement of cells in fascicles are seen.

Figure 6a,b,c: High grade Leiomyosarcoma of Soft Tissue: (a) Low, (b) Medium, and (c) High power. High grade tumors demonstrate marked atypia and cellularity with multiple mitoses present.

Histologic features under light microscopy are the most important factors in making the diagnosis of leiomyosarcoma. However, adjunctive modalities including immunohistochemistry and electron microscopy play an important confirmatory role. Immunohistochemistry helps support the diagnosis by demonstrating the presence of muscle specific markers including: desmin, muscle specific antigen (HHF35), cytokeratin (CK) and epithelial membrane antigen (EMA). While not required to make the diagnosis, one or more of these markers is usually found in specimens of leiomyosarcoma. Electron microscopy is useful in further elucidating the classic nuclear morphology seen in this tumor. Cytogenetic analysis of large series of soft tissue sarcoma, including leiomyosarcoma, has not shown a consistent chromosomal aberration or translocation (18).

Size, cellularity, atypia, necrosis, and mitoses per high power field are indicators that help define the difference between a benign smooth muscle tumor and leiomyosarcoma. Of these indicators, mitoses per high-powered field is considered the most reliable (25). It is important to note that the threshold of mitotic rates that would qualify a tumor as malignant in soft tissue leiomyosarcoma is lower than that used in uterine leiomyosarcoma. When considering soft tissue smooth muscle tumors, the presence of any mitotic figures should raise suspicion of a malignancy, especially in the presence of cellular atypia or focal necrosis.
TREATMENT

Due to the rarity of these tumors, and the need for a multi-specialty treatment team, treatment is best carried out in a specialized center with expertise in sarcoma care. At our institution, treatment planning begins with a multi-disciplinary review of the patient’s history, all available radiographic imaging, and the pathologic results from biopsy. A treatment plan is then formulated based upon the input from orthopedic and general surgeons, musculoskeletal radiologists, pathologists, medical oncologists, and radiation oncologists.

Surgery

Local control of soft tissue sarcomas is usually achieved with surgical resection. Pre-operative planning based upon radiographic and pathologic information is important to ensure adequate surgical margins. Achieving wide surgical margins is important in preventing local recurrence.

Radiation Therapy

Many tumors involve or are directly adjacent to vital structures. In these cases achieving a wide surgical margin is impossible. Radiation therapy is an important additional treatment for improving rates of local control when surgical margins are close, especially in high-grade sarcomas. Radiation therapy can be delivered either pre-operatively (neoadjuvant) or post-operatively (adjuvant). Radiation therapy can also be utilized as a means of palliative local control in cases where extensive metastasis has already occurred.

Chemotherapy

The primary role of chemotherapy is in the treatment of metastatic disease. While not curative, it may slow the progression of systemic disease. Agents that are used in some sarcoma centers include: doxorubicin and ifosfamide, gemcitabine and taxotere (docetaxel), dacarbazine, and ecteinascidin. There are currently investigational studies underway to identify other agents that may prove useful in the treatment of leiomyosarcoma. Chemotherapy is sometimes used as an adjuvant in the treatment of localized sarcomas. No clear survival benefit has been demonstrated in retroperitoneal leiomyosarcomas. However, pre-operative chemotherapy may help to shrink a tumor away from vital structures, and improve the ability of surgeons to successfully remove a large tumor. In localized leiomyosarcoma of the extremities, there may be a survival benefit for adjuvant chemotherapy using doxorubicin-based regimens (28). Both retrospective and prospective studies have shown a benefit for neoadjuvant doxorubicin and ifosfamide based regimens in patients with large (>8cm) high-grade sarcomas.
PROGNOSIS AND OUTCOMES

Retroperitoneal Leiomyosarcoma

In a recent review of smooth muscle tumors of soft tissue, Weiss has compiled data from the current series on retroperitoneal leiomyosarcomas (see table 3). These tumors seem to display very aggressive biology. Neither size nor mitotic activity correlated with outcome, which may represent a reflection of the fact that most of these tumors are quite large on presentation.

TABLE 3: SUMMARY OF PUBLISHED CASE SERIES OF RETROPERITONEAL/ABDOMINAL LEIOMYOSARCOMAS

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Cases</th>
<th>Atypia</th>
<th>Necrosis</th>
<th>Minimum Mitotic Rate</th>
<th>Size</th>
<th>Died of Disease (DOD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hashimoto</td>
<td>44</td>
<td>All</td>
<td>68</td>
<td>1-4/10HPF</td>
<td>&gt;10cm</td>
<td>79%</td>
</tr>
<tr>
<td>Rajani</td>
<td>17</td>
<td>All</td>
<td>12/17</td>
<td>3/10HPF</td>
<td>&gt;10cm</td>
<td>88%</td>
</tr>
<tr>
<td>Ranchod</td>
<td>13</td>
<td>12/13</td>
<td>7/13</td>
<td>0-4/10HPF</td>
<td>&gt;10cm</td>
<td>92%</td>
</tr>
<tr>
<td>Shmookler</td>
<td>36</td>
<td>?</td>
<td>?</td>
<td>1-4/10HPF</td>
<td>&gt;7cm</td>
<td>77%</td>
</tr>
<tr>
<td>Wile</td>
<td>16</td>
<td>?</td>
<td>?</td>
<td>2/10HPF</td>
<td>&gt;5cm</td>
<td>93%</td>
</tr>
</tbody>
</table>

(Table reproduced with permission from Weiss SW. Smooth muscle tumors of soft tissue. Advances in Anatomic Pathology. 9(6):351-359. Copyright 2002, Loppincott Williams & Wilkins.)

Soft Tissue Leiomyosarcoma

The patient numbers of most case series are small, and there is no published meta-analysis available to provide clear prognostic data. Small case series have been published, however, that do provide some insight into the prognostic significance of some patient variables. Deep soft tissue leiomyosarcomas are usually detected before they reach the large size of many retroperitoneal tumors. About half of these patients die of metastatic disease. The factors that are associated with worse prognosis include age >62 years, size greater than 4cm, tumor necrosis, French Federation Nationale des Centers de Lutte Contre le Cancer (FNCLCC) grade, vascular invasion, or previous intralesional surgery (1, 17). Mitotic rate has not been directly correlated to worse outcome, although mitotic rate is clearly a useful parameter in differentiating malignant tumors from benign ones. In a retrospective study of 66 patients with soft tissue leiomyosarcoma, Mankin, et al found a significant effect of MSTS stage and size on outcome but not gender, age, site, adjuvant therapy, or presence of local recurrence (7). Overall reported survival for patients diagnosed with soft tissue leiomyosarcoma range from 50% 3-year survival to 64% 5-year survival, making this tumor one of the more aggressive soft tissue sarcomas (1, 7).

Cutaneous Leiomyosarcoma

True intradermal leiomyosarcoma is thought not to metastatise, and therefore presents more of a local control issue than a problem of metastatic disease. Published series on this tumor have often included small subcutaneous tumors as well as truly intradermal tumors which alters the reporting of the natural history of this disease subtype. Wide excision of truly intradermal tumors, if achievable, is curative.
*Vascular Leiomyosarcoma*
Leiomyosarcoma of vascular origin has a poor prognosis. Because they are rare, definitive diagnosis is often delayed and complete resection is usually not possible. Local complications of the primary tumor are the main cause of morbidity and mortality. Metastatic disease to the liver and lungs occurs in 54%, in approximately the same percentage as other forms of leiomyosarcoma (14).

*Leiomyosarcoma in the Immunocompromised Host*
Little is known about the specific prognostic implications of this rare entity, as no case series have been compiled. However, as in most other cases of leiomyosarcoma it appears to behave aggressively.

*Leiomyosarcoma of the Bone*
The largest current series did not demonstrate any difference between wide surgical resection and surgery plus radiation and/or chemotherapy in the treatment of primary leiomyosarcoma of bone. In this study, local recurrences were seen in 24% of cases, and metastases developed in 24% of cases, all in the lung. Overall survival was 77% at 3 years and 68% at 5 years (29).

*Pediatric Patients*
Leiomyosarcoma in the pediatric age group is rare. In a series of 20 tumors in patients under 16 years of age, there was no gender predilection (5). Tumors were evenly distributed between the head and neck, upper extremity, lower extremity, and trunk. Most of the lesions (85%) in this series were considered low-grade. Local recurrence occurred in two patients, and none of the patients had died by the end of the study. The prognosis of children afflicted by leiomyosarcoma appears to better than adults (2, 3, 5).

**CONCLUSION**
Leiomyosarcoma is an aggressive sarcoma that can arise in a number of locations. Although advances have been made in treatment protocols, leiomyosarcoma remains one of the more difficult soft-tissue sarcomas to treat. Accurate diagnosis, classification, and multi-modality treatment by physicians who are familiar with these tumors are essential to favorable outcome.

The rarity of these tumors makes definitive studies difficult to perform. For instance, there is very little published data available on patients with leiomyosarcoma of somatic soft tissues. There have only been a limited number of small case series published. This fact has prompted us to look at the experience we have had with this tumor at our institution, and we are currently preparing to publish the treatment and outcome of over 120 patients with leiomyosarcoma of soft tissue. These types of reviews, along with carefully designed prospective randomized clinical trials, may help further define the best treatment of these tumors in the future.

Currently, however, in general local control is obtained with wide surgical excision. Neoadjuvant or adjuvant radiation therapy is appropriate in some circumstances where local control is an issue. Chemotherapy is employed for the treatment of systemic disease. Ongoing clinical trials may identify agents that may improve the overall and disease-free survival of patients suffering from this disease.
REFERENCES


