Large Monophasic Synovial Sarcoma: A Case Report and Review of the Literature

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Practice Points

- Synovial sarcoma is rare and requires a high index of suspicion for diagnosis.
- Biopsy is necessary for diagnosis of synovial sarcomas.
- Metastatic disease is common at the time of diagnosis.

Synovial sarcomas account for approximately 8% of all soft tissue tumors. The hallmark tumor marker is the t(X;18) translocation, which results in fusion of the SYT *gene of chromosome 18 to the* SSX *gene of the X chromosome, creating most frequently either an* SYT-SSX1 *or* SYT-SSX2 *transfusion transcript. Clinically, synovial sarcomas most often present on the extremities and average roughly 7 cm in diameter. Metastatic spread to regional lymph nodes and/or the lungs is common. Because the incidence of this tumor is low, most studies have been retrospective; therefore, management and prognostic interpretation has remained controversial. We report a case of a patient who presented with a slowly growing, unusually large mass on the left forearm of 10 years' duration. A diagnosis of monophasic synovial sarcoma was confirmed by biopsy. We also review the literature regarding management strategies for synovial sarcomas.*

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Although relatively rare, synovial sarcomas account for approximately 8% of all soft tissue tumors.[1] The term *synovial sarcoma* often is considered a misnomer because the cell of origin has not been clearly elucidated, synovial differentiation sometimes is not visualized, and the tumor occasionally can arise in sites other than the joints (eg, heart, lungs, pharynx).[2] The hallmark tumor marker is the t(X;18) translocation, which results in fusion of the *SYT* gene of chromosome 18 to the *SSX* gene of the X chromosome, creating most frequently either an *SYT-SSX1* or *SYT-SSX2* transfusion transcript, the products of which may behave as combined transcription activators-repressors that possibly interact with chromatin remodelers. Clinically, synovial sarcomas most often present on the extremities and average roughly 7 cm in diameter.[3] Historically, synovial sarcomas have been considered aggressive, though they also can be slow growing. Metastatic spread to regional lymph nodes and the lungs is common, especially in comparison to other soft tissue tumors.[4] Distant metastasis may occur in up to 53% of patients with primary synovial sarcomas of the extremities that are greater than 5 cm in largest dimension, with a 5-year tumor-related mortality rate of 37%.[5] Most studies have been retrospective given the low incidence of this tumor; therefore, management and prognostic interpretation has remained controversial.[6] We report a case of a patient who presented with a slowly growing, unusually large mass on the left forearm of 10 years' duration. A diagnosis of monophasic synovial sarcoma was confirmed by biopsy. We also review the literature regarding management strategies for synovial sarcomas.

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Case Report

A 50-year-old woman was referred to our clinic by a plastic surgeon for evaluation of a lesion on the left forearm. The patient reported that the lesion

had been present for the last 10 years, starting as a small nodule beneath the skin that had grown considerably in size. She denied any history of trauma to the area as well as any pain associated with the lesion, though she reported occasional numbness at night. Additionally, she reported a feeling of heaviness appreciated when supinating the forearm. No associated loss of function was noted. There were no lesions present in any other location on her body. The patient denied any systemic symptoms such as coughing, swollen lymph nodes, fever, or weight change. She was not currently taking any medications other than a daily multivitamin.

Physical examination revealed a 28×33-cm, firm, warm mass with prominent vasculature on the dorsal aspect of the left forearm (Figure 1). The lesion extended from the elbow to the dorsal wrist. A 6-mm, double-trephine punch biopsy revealed extensive fibrosis accompanied by a proliferation of spindle cells in a fascicular arrangement, many permeating between reticular collagen bundles with foci of calcification (Figure 2). The cells stained strongly positive for cytokeratin and were focally positive for prekeratin and epithelial membrane antigen. The cells stained negative for melan-A, S-100, CD34, and factor XIIIa. These findings were consistent with a monophasic synovial sarcoma. Magnetic resonance imaging (MRI) to assess the extent of tissue invasion revealed a large, heterogeneously enhancing mass as a dominant soft tissue in the forearm area with some sparing of the supinator surface. Computed tomography (CT) of the chest was negative for metastasis but notable for a single 2-mm nodule. A diagnosis of monophasic synovial sarcoma (T2bN0M0) was made. The consulting surgeons and radiation oncologists recommended preoperative radiotherapy with local excision in addition to lymph node biopsy, with the ultimate goal being surgical resection and postoperative chemotherapy and radiotherapy. The patient tolerated radiotherapy with no change in the dimensions of the tumor. After extensive counseling in favor of surgical resection and amputation of the forearm, the patient was lost to follow-up.

Comment

Synovial sarcomas usually present as palpable, soft tissue masses on the extremities with an average duration of 2 to 4 years, but lesions lasting as long as 20 years have been reported.[7] Unlike other soft tissue sarcomas, which usually are painless, synovial sarcomas frequently are associated with pain and tenderness. Constitutional symptoms are rare. Various patient and tumor characteristics have been determined to have prognostic significance and are described in the Table.[4-6,8-13]

Histologically, synovial sarcomas are divided into 3 subtypes: monophasic, biphasic, and poorly differentiated. The monophasic subtype predominantly shows spindle cells, while the biphasic subtype typically demonstrates epithelioid cells arranged in whorls or primitive glandlike structures along with the presence of spindle-shaped cells. The subtype influences the pathologic differential diagnosis, and final diagnosis often is aided by immunostaining, which is positive for keratin and epithelial membrane antigen in the majority of cases.[7]

Radiology has a role in evaluation of the primary lesion as well as detection of metastasis; however, radiographs may be normal in up to 50% of cases, especially if the lesion is small.[7] Calcification is

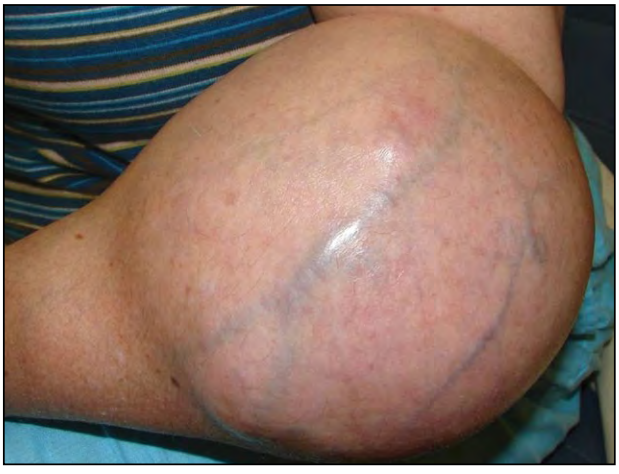

Figure 1. Large mass with prominent vasculature on the left forearm.

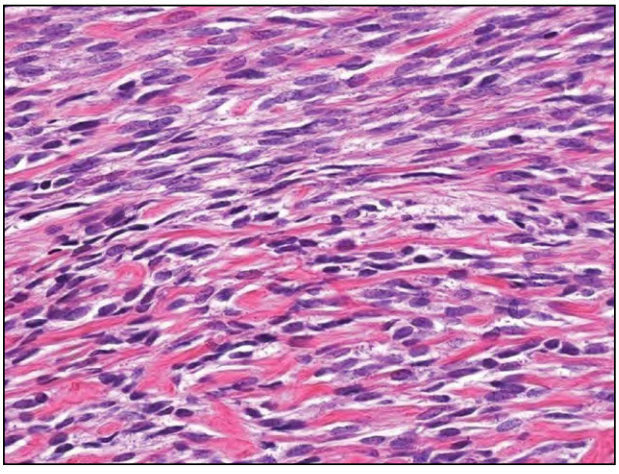

Figure 2. Proliferation of spindle cells in a fascicular arrangement (H&E, original magnification ×40).

Prognostic Markers in Synovial Sarcomas and the Data Supporting Their Significance

Marker	Prognostic Meaning	Quality of Data and Selected Studies
Tumor size	>5 cm in largest dimension most likely is prognostic for worse outcome	Consistently supported by numerous retrospective studies[4-6,8-10]
Patient age	Older age most likely is prognostic for worse outcome	Consistently supported by numerous retrospective studies[5,6,9,10]
Tumor grade[a]	Higher grade most likely is prognostic for worse outcome	Supported by retrospective studies[5,6,9,10]
Histology type	Monophasic may be prognostic for better outcome	Controversial; several retrospective studies both for and against prognostic significance[3,6,9,10]
Tumor site	On the extremities, proximal sites may be prognostic for better outcome than distal sites	Controversial; several retrospective studies both for and against prognostic significance[5,6,8-10]
Gene mutation	*SYT-SSX2* subtype may be associated with better long-term survival	Controversial; some studies suggest significance[11-13]

[a]As assessed by the French Federation of Cancer Centers (FNCLCC) grading system.[6]

found in up to 30% of synovial sarcomas. Magnetic resonance imaging is the preferred method for assessment of the extent of synovial sarcomas and may reveal a heterogenous multilobulated soft tissue mass with signal intensity similar to muscle. Involvement of the underlying bone is more common in synovial sarcomas than in other soft tissue sarcomas and is well assessed via MRI.[7] To detect lymph node metastasis, which is more common in synovial sarcomas than other soft tissue tumors, the utility of sentinel lymph node biopsy has been discussed.[4] A small prospective study of 15 patients found that a patient with a positive sentinel node had no metastasis on further regional resection, but another patient with node-negative disease demonstrated regional metastases.[14] A CT scan may be useful in the detection of metastasis. Because of the tumor's predilection for metastasis, MRI, sentinel lymph node biopsy, and CT scans often are utilized to plan the most effective treatment strategy.

The best combination of therapeutic modalities for treatment of synovial sarcomas remains to be elucidated. Complete surgical removal of the primary tumor continues as the mainstay of treatment, with clear postsurgical margins associated with greater 10-year, cancer-specific survival rates compared to microscopic-positive margins.[15] Metastasectomy historically has been a cornerstone in the treatment of soft tissue sarcomas, as beneficial effects on survival have been documented[16]; however, the utility of metastasectomy in treating synovial sarcomas specifically has been questioned. One study has found no change in outcomes for pulmonary metastasectomy.[17]

The role of adjuvant therapy continues to evolve. Several retrospective studies have found evidence for the beneficial effects of chemotherapy,[1,18] while others have not.[4-6,10] However, because these studies span many years, many of the chemotherapeutic regimens utilized across studies have been different, making it difficult to draw conclusions. The most commonly reported combination therapy in studies conducted over the last decade has been ifosfamide-doxorubicin-mesna.[1,18] One large study (N=104) observed a response rate of 58.6% with ifosfamide-doxorubicin combination therapy in patients with advanced disease; results from combination treatment were better than either agent alone.[17] This combination also has been reported to be beneficial in treating localized

disease.[3] To our knowledge, there are no randomized prospective trials of any chemotherapeutic regimens in the treatment of synovial sarcomas with sufficient power for comprehensive evaluation.

Radiation therapy also has found an evolving role in the management of synovial sarcomas through retrospective studies. Although there are studies that show no benefits associated with radiotherapy,[10] most studies have indicated some decrease in local recurrence in select groups with variable effects on long-term survival rates.[1,5,9,19] Prospective studies have evaluated the effect of radiation on all soft tissue sarcomas. One randomized trial of 91 patients with high-grade soft tissue sarcomas—26 patients with synovial sarcomas (the most of any single histologic type in the study)—appreciated a statistically significant reduction ($P<.05$) in local recurrence (not in survival rate) in patients who underwent satisfactory local excision followed by radiation therapy.[20]

Conclusion

Because the studies on synovial sarcoma treatment often are small and mostly retrospective, determining optimal management of patients is based on limited data. Additional study of the mechanisms of tumorigenesis by the *SYT-SSX* fusion protein may provide a more targeted approach to therapy. In this regard, there have been attempts to interrupt the *SYT-SSX* fusion protein in vitro.[21] Still, other studies have focused on the proteins overexpressed in synovial sarcomas, such as BCL2, epidermal growth factor receptor, and *ERBB2* (formerly *HER2/neu*), and preliminary studies are underway targeting such proteins. Thus it is possible to envision a more rationally derived therapeutic approach to this disease.

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