

Cystic Synovial Sarcoma of the Lower Extremity: A Case Report and Review of the Literature

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Abstract

Synovial sarcomas are rare tumors which most often present in the distal extremities of young adults and children. There are unique clinicopathologic features of this tumor which lend themselves to multidisciplinary treatment and translational research. We present a case of a primarily cystic synovial sarcoma and provide a thorough review of the available literature.

Keywords: Synovial Sarcoma, Multidisciplinary Treatment, Radical Resection

1. Introduction

Synovial sarcoma is a unique subtype of soft tissue sarcoma with a propensity for developing in the extremities of young adults. They have a characteristic histopathology and molecular genetic profile and are deemed high grade tumors. We report a case of a patient with a cystic synovial sarcoma involving the lower extremity and a review of the literature, with a focus on diagnosis, prognostic indicators, recent developments in management, and the future direction of therapy.

2. Case Report

A 49-year-old Caucasian female presented initially for evaluation of a left posterior thigh mass. The patient described a history of a pulled muscle six months prior followed by tightness in the back of her thigh. In the couple of months preceding presentation, the mass evolved, increasing in size and causing discomfort and pain. The patient noted difficulty with activity and bending her knee secondary to increased pain. The patient also reported a several month history of progressive fatigue. Physical examination revealed a solid, mobile mass in the posterior thigh compartment. The mass was slightly tender to the touch with no abnormalities in the overlying skin.

Radiographic evaluation of the left knee was normal. Ultrasound evaluation revealed the presence of a mass. MRI with and without intravenous contrast demonstrated

a complex, predominantly cystic mass measuring $6.8 \times 7.2 \times 9.7$ cm on the posterolateral aspect of the mid-thigh, deep in the muscle compartment (**Figure 1**). The mass was located in the region of the sciatic nerve and inferior gluteal vessels and found to medially displace the semimembranosus and semitendinosus muscles and posteriorly displace the long head of the biceps femoris head and encase the short head of the biceps femoris muscle. Breakdown products from prior hemorrhage were noted as well as inflammatory changes in the adjacent fat at the superior and inferior aspects of the mass. At this time, unable to specifically characterize the mass and with a differential including malignancy, biopsy was recommended. Due to the cystic nature of the mass, tissue diagnosis of the mass was obtained via excisional biopsy.

Following wide local surgical excision, where the mass was dissected free from the surrounding muscle and sciatic nerve with its pseudocapsule preserved, pathology revealed a 230-gram mass, measuring $9.0 \times 7.5 \times 6.0$ cm, surfaced by glistening red-tan membranous tissue. Sectioning showed multiple cysts filled with hemorrhagic fluid. Findings were consistent with synovial sarcoma with cystic change, measuring 9 cm and focally extending <0.1 cm from the margin. Immunohistochemistry was significant for stains positive for EMA, bcl-2, Ck5/6, and negative for CD34 (**Figure 2**). With negative margins surgically achieved, re-excision was foregone due to proximity to the sciatic nerve and high rate of systemic recurrence.

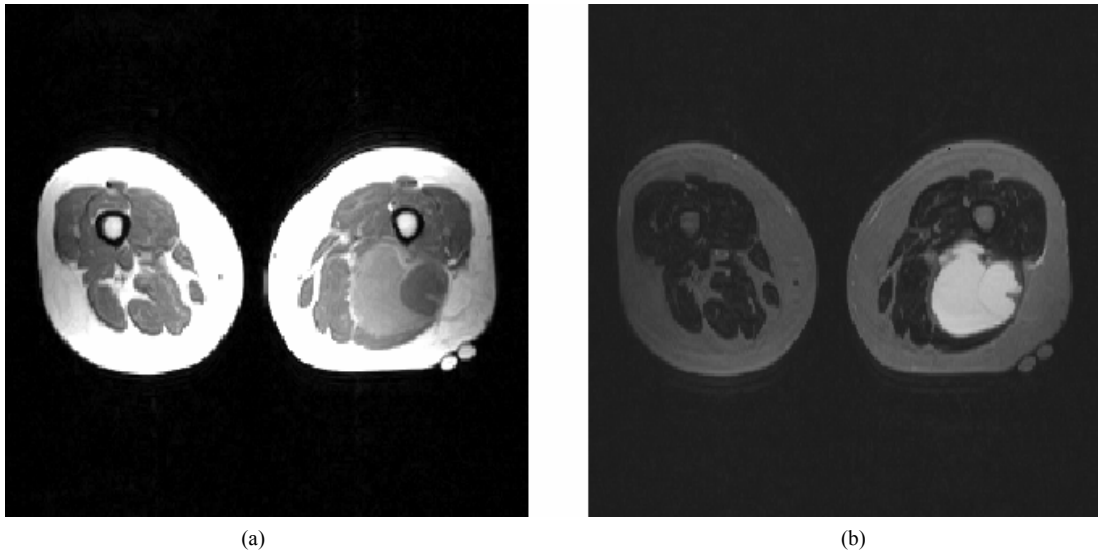


Figure 1. Cross-sectional MRI images reveal mostly cystic mass in the posterior compartment of the thigh on T1-weighted (a) and T2-weighted (b) images.

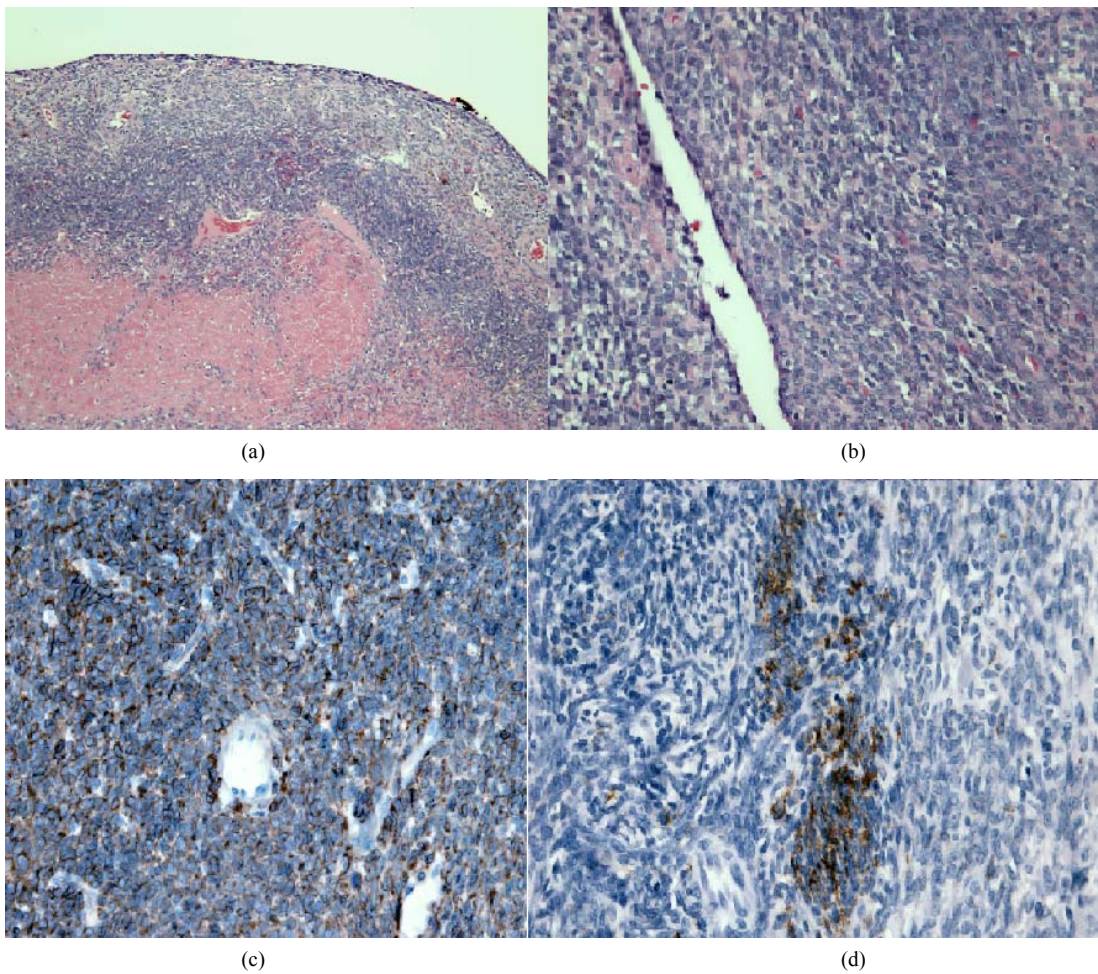


Figure 2. Histologic examination of synovial sarcoma. (a) shows 10x magnification using standard H&E staining; (b) shows 40x magnification with H&E staining as well; (c) shows positive staining under 40x magnification for bcl-2; and (d) reveals positive immunohistochemistry staining for smooth muscle actin.

The patient was referred to a medical oncologist and radiation oncologist for additional evaluation and treatment. A staging work-up, including a chest radiograph and computed tomography (CT) scan, demonstrated prominent bilateral axillary lymph nodes but no evidence of metastatic disease. Staging identified the lesion as a T2b N0 M0 synovial cell carcinoma. Due to the lesion size, the patient was determined to be at high risk for recurrence. As such, the patient was subsequently treated with a combination of adjuvant chemotherapy and radiation. Four cycles of ifosfamide and doxorubicin, which were tolerated well, were initiated prior to radiation therapy.

3. Discussion

Synovial sarcomas are rare malignant tumors historically regarded as high grade malignancies with significant metastatic risk. Synovial sarcoma accounts for 6-10% of all adult soft tissue sarcomas, rendering it the fourth most common type of sarcoma. Despite its name, this tumor is uncommon in joint cavities, instead occurring primarily in periarticular regions of extremities and often associated with tendon sheaths, bursae, and joint capsules. Principally affecting young adults aged 15-40 years, with the median age of patients in the third decade of life, synovial sarcoma most commonly presents as a palpable, deep-seated swelling or mass associated with pain or tenderness. The extremity is the most common site of primary disease, and the tumor tends to grow insidiously, frequently delaying diagnosis and therapy. [1,2]

Definitive diagnosis is often deferred until histopathologic examination of the surgical specimen upon resection. Pre-operative radiographs may exhibit calcifications within the tumor. Synovial sarcomas frequently appear as round or oval, lobulated, in close association with a large joint, and without involvement of the underlying bone. Computed tomography (CT) and magnetic resonance imaging (MRI) may be utilized in further elucidating the site of origin and extent of the mass. Synovial sarcoma represents a malignancy of two morphologically distinct cell types that form a characteristic biphasic pattern: epithelial cells and fibrosarcoma-like spindle cells. Synovial sarcomas may be classified into biphasic variant, monophasic fibrous variant, monophasic epithelial variant, and poorly differentiated variant. Large studies, however, have not demonstrated histologic type to be of prognostic or therapeutic significance. [3] Immunohistochemical stains further aid in the diagnosis of synovial sarcoma, the most useful of which are epithelial markers, including pankeratin, CAM 5.2, and EMA, as identified in our patient. These markers are less apparent in the spindle cell component of these tu-

mors, leading to the distinctive patchy staining pattern found in synovial sarcoma. In addition, in accordance with our findings, synovial sarcoma stains positively for bcl-2 and is consistently negative for CD34. Cytogenetic studies also indicate the presence of a translocation between chromosomes X and 18, t(X; 18) (p11.2; q11.2), in nearly all (>90%) cases of synovial sarcoma. This characteristic translocation involves the SYT gene on chromosome 18 and the SSX1 and SSX2 genes, located on the X chromosome, and leads to the creation of abnormal fusion proteins. [4]

Synovial sarcoma traditionally carries a poor prognosis. [3] In a retrospective analysis of synovial sarcoma in patients of all ages, Ferrari *et al.* [5] determined survival rates to vary significantly, measuring 5-year event-free survival to be 37 % for the study cohort as a whole, with the rate varying with age (66%, 40%, and 31% for patients age ≤ 16 , 17-30, and >30 years, respectively). Large tumor size has been consistently shown to be related to the progression to distant metastasis and decreased disease specific survival, and most studies demonstrate that prognostic indicators of distant recurrence parallel survival. [4] In a multivariate analysis of prognostic factors, Lewis *et al.* [6] demonstrated tumor size ≥ 5 cm and invasion of bone and neurovascular structures to be the only independent adverse predictors of distant recurrence and mortality.

Complete surgical resection remains the foundation of treatment for synovial sarcoma. Despite the frequent close proximity of the tumor to neurovascular structures, en bloc resection of the tumor is standard and these structures are usually spared. Adequate margins require that the resected specimen be tumor free at the margins, preferably with a margin of normal tissue. There is no role for non-curative surgery. [4] Achieving adequate surgical margins, however, must be balanced with maximal preservation of function and minimal morbidity. [3] Surgery is also the mainstay of treatment for locally recurrent disease. The role of surgery in treating metastatic synovial sarcoma is less well defined and limited to selected patients based on disease extent, length of disease-free interval, and response to systemic chemotherapy. [4]

Beyond surgery, the optimal therapeutic approach to synovial sarcoma has not yet been definitively established. However, prognosis is poorest in patients treated only with local excision with inadequate margins and no adjunctive therapy, with recurrence rates recorded as high as 70-83%. [2] As in the management of other soft tissue sarcomas, there is a role for adjuvant radiation therapy. Although good local control can be accomplished through surgery and radiation therapy, distant metastasis remains the limiting factor with regard to the

survival of patients with synovial sarcoma. [4] Despite adequate surgical resection, Lewis *et al.* [6] noted that distant metastasis developed in almost 40% of patients by 5 years, suggesting the need for adjuvant systemic therapy. Synovial sarcoma is known to be particularly chemosensitive. [4] Ferrari *et al.* [5] demonstrated the benefit of chemotherapy, showing that among patients with surgically resected tumors, 5-year metastatic-free survival rate in those receiving chemotherapy was 60% as compared to 48% in those who did not. The outcome advantage was noted particularly among those with high-risk synovial sarcoma (tumor size >5 cm), leading investigators to conclude that all patients with tumors >5 cm should be treated with chemotherapy. Multiple studies have revealed the utility of ifosfamide-based chemotherapy (+/- doxorubicin). In fact, it is the treatment of choice for patients with metastatic synovial sarcoma. Recent studies have shown ifosfamide-based therapeutic regimens to be effective in increasing disease-specific survival in patients with ≥ 5 cm, primary, extremity synovial sarcomas. [4]

Recent studies also indicate a role for sentinel lymph node biopsy in synovial sarcoma. Lymph node metastasis in soft tissue sarcoma in an extremity is considered to herald poor outcome. However, current literature suggests that complete surgical resection of involved lymph nodes may improve survival. [7] While the lung remains the most frequent site of metastasis, regional lymph node metastases have been demonstrated in 6-14% of synovial sarcoma cases. In a retrospective analysis of sentinel node biopsy in a cohort of eleven patients with synovial sarcoma, Tunn *et al.* [8] identified at least one node in each patient, and no patients developed complications post-procedure. Of a total of 15 sentinel nodes identified, only one was positive and 14 were negative.

4. Conclusion

In summary, we report herein the case of a woman with a 9 cm synovial sarcoma of the left lower extremity. Especially with such large tumor size, such a diagnosis is typically associated with a poor prognosis. However, future investigations hold promise. Surgery remains the

mainstay of treatment, but it is clear that obtaining more definitive data concerning the clinical management of this tumor, including the utility of radiation and chemotherapy and the possible development of more targeted therapeutic interventions, is warranted.

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