CHAPTER **48**

MALIGNANT SOFT TISSUE LESIONS OF THE FOOT AND ANKLE

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INTRODUCTION

Soft tissue is derived from mesoderm with some contribution of nonepithelial tissue comprised of the reticuloedothelial system, glia, and supporting tissue (Figure 1).[1] Within the various histologic categories, soft tissue tumors are divided into benign and malignant forms. Benign tumors more closely resemble normal tissue and exhibit little tendency to invade locally (Figure 2). Malignant soft tissue tumors, or sarcomas, are locally aggressive and capable of destructive growth and distant metastasis (Figure 3). Soft tissue sarcomas of the foot and ankle are rare, with the majority consisting of synovial cell sarcoma, fibrosarcoma, clear cell sarcoma, liposarcoma, and malignant fibrous histocytoma.[2,3] Of these 5 tumors, synovial sarcomas occur with the greatest

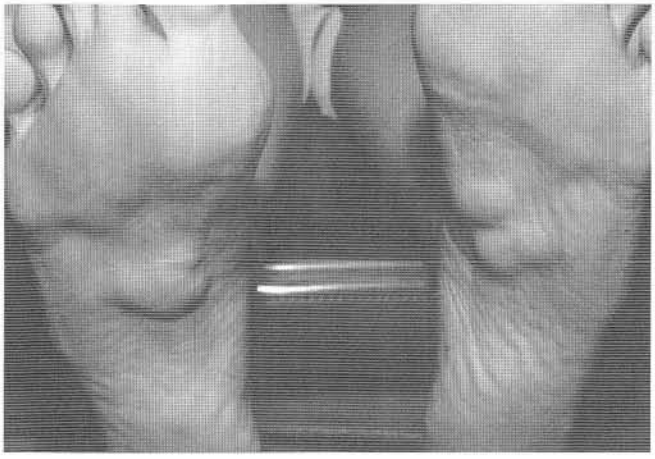

Figure 1. These soft tissue lesions are plantar fibromatoses. Fibrous dystrophic growths appear from the plantar fascia. Although benign, they can appear aggressive under a microscope and may be misread as malignant if the pathologist doesn't know the part of the body from where they came.

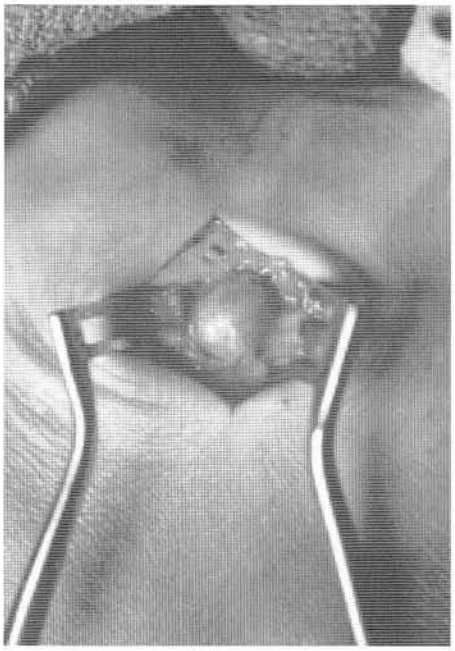

Figure 2. Benign tumors are generally distinct lesions that are well circumscribed and often encapsulated. They generally do not cross tissue planes.

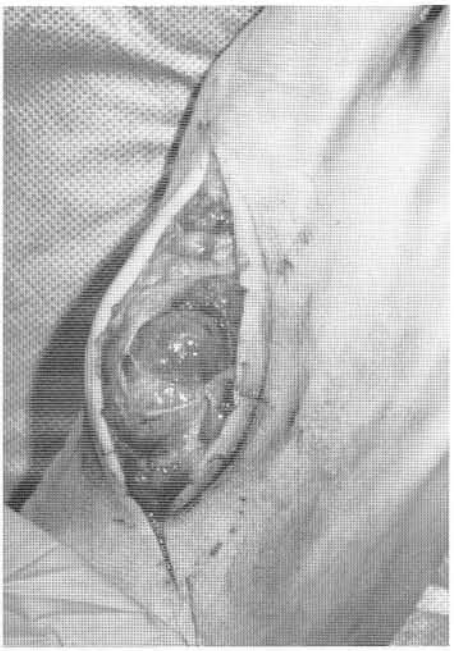

Figure 3. Malignant tumors such as this malignant fibrous hystiocytoma are often fast growing lesions that are not often distinct nor well circumscribed. They often have no regard for tissue planes as can be seen here.

frequency. Leiomyosarcoma, rhabdomyosarcoma, angisarcoma, and malignant schwannoma are also found in the foot and ankle, but with much less incidence.[3-5] Foot and ankle sarcomas have a more benign course than sarcomas at other locations.

INCIDENCE

Soft tissue tumors occur everywhere in the human body, however most arise in the trunk and proximal extremities because of the high tissue volume in these areas. In a retrospective review of 39,179 soft tissue lesions seen from 1980 to 1989 at the Armed Forces Institute of pathology, 8% of all benign soft tissue tumors and 5% of all malignant soft tissue tumors occurred in the foot and ankle.[5]

Kirby et al retrospectively analyzed 83 patients who had a soft tissue tumor in the foot and 72 (87%) of the lesions were benign, while the remaining 11 (13%) were malignant.[4] Five of the 11 malignant tumors were synovial sarcomas. The age of the patient and the location of the lesions were the most important factors that characterized the malignant tumors in this study. Duration of symptoms, history of trauma, and the size of the lesion were not useful discriminators between malignant tumors and benign lesions.[4]

In a more recent study, 252 cases of malignant soft tissue neoplasms of the foot were examined from a major medical center specializing in the treatment of cancer. The most common malignant soft tissue tumors were synovial sarcoma (24%) followed by clear cell sarcoma (12%), fibrosarcoma (11%), malignant fibrous histocytoma (9%) and liposarcoma (5%).2

The differential diagnosis for synovial sarcomas, clear cell sarcomas, fibrosarcomas, malignant fibrous histocytoma and liposarcomas are quite extensive and can include any subcutaneous soft tissue mass of the foot or ankle. The differential diagnosis includes but is not limited to ganglion cyst (the most common soft tissue lesion in the foot and ankle), lipoma, fibroma, synovial cyst, giant cell tumor of the tendon sheath, pigmented villonodular synovitis, neurofibroma, epidermal inclusion cyst, leiomyoma, leiomyosarcoma, rhabdomyoma, and rhabdomyosarcoma.[6] A detailed history, thorough exam, and adjunctive tests including radiographs, magnetic resonance imaging (MRI), and computed tomography (CT) are important for an accurate diagnosis. A definitive diagnosis is made by histological studies from a fine needle aspiration, core needle aspiration, or biopsy.[7,8]

SYNOVIAL SARCOMA

Synovial sarcomas are the most common sarcoma of the foot representing 6% of all soft tissue tumors, and compromising 25 to 56% of all malignant lesions.[9,10] The most common site of presentation is the knee followed by the foot and ankle region (Figure 4).[10,11] Synovial sarcomas are most commonly identified over the dorsum of the foot along the course of the extensor tendons, or near a joint, and are therefore often mistaken for a commonly occurring ganglion cysts upon first presentation.[11] This tumor does not originate from synovial structures, but rather has a true epithelial component distinguished by its histological keratin expression. A highly organized relationship exists between epithelial and spindle cell components.[11] The biphasic histological type contains both epithelial and spindle components, while the monophasic type is a spindle cell tumor with no epithelial component.[10]

Synovial sarcomas have a tendency to arise in young adults between the ages of 15 and 40 years.[8] On average, the delay between the onset of symptoms and subsequent treatment is 18 to 24 months because they usually remain quiescent for a long period of time.[11] As with all other soft tissue neoplasms of the foot or ankle, the most common clinical signs and symptoms are pain, tenderness, edema, and an enlarging mass. A careful sensory examination of the cutaneous innervation of the foot may provide the extent of neoplasm spread.[3]

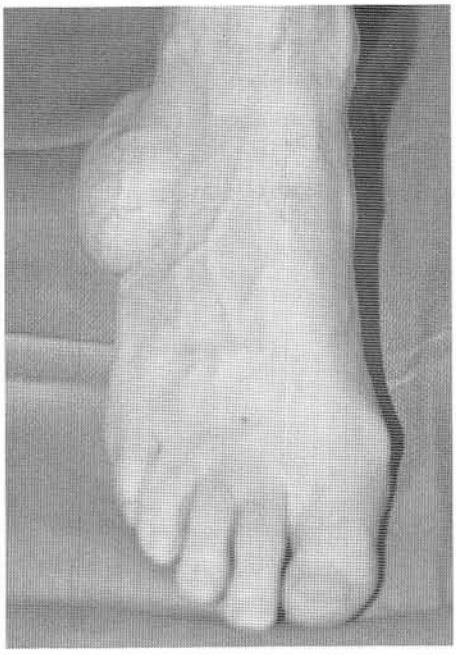

Figure 4. This synovial sarcoma is a solid lesion on the lateral midfoot rearfoot area. The patient waas having difficulty wearing shoes.

Immunohistochemistry studies are necessary in order to make a definitive diagnosis. Most poorly differentiated synovial sarcomas are immunoreactive for cytokeratin, epithelial membrane antigen, vimentin, CD99 and S100; negative for CD34, and negative for desmin.[12] Reactivity of CD99 is an important indicator for a poorly differentiated synovial sarcoma.[12]

Indications for tumor severity are not uniform among different studies. In a study by Scully et al of the 14 patients with synovial sarcoma of the foot or ankle, those with biphasic histological features of epithelial and spindle components had better outcomes than those with monophasic types.[8] Also, patients with prolonged symptoms before diagnosis had better outcomes. It was hypothesizes that patients with prolonged symptoms had slower growing, less aggressive tumors. In a different study where a prospective analysis was performed on 48 patients with extremity and truncal synovial sarcomas, tumor size, margin of resection and mitotic activity were prognostic factors for survival while grade, histologic subtype and tumor site were not.[9] The tumor will most often metastasize to the lungs followed by the lymph nodes and the bone marrow.[8] Once the lesion matastasises, the outcome is often fatal.[8] The five-year survival rate for synovial sarcoma is between 36% and 65% and has been found to metastasize or recur in 50% to 70% of cases.[12]

CLEAR CELL SARCOMA

Clear cell sarcoma (CCS) is a slow growing soft tissue tumor commonly associated with tendons and aponeuroses in the extremities of young adults between the ages of 20 and 40 years (Figure 5).[12] CCS represented 23 out of 189 (12%) of all soft tissue sarcomas of the foot and ankle in one study.[2] About 40% of all diagnosed clear cell sarcomas occur in the foot and ankle.[13] The mass is lobulated or multinodular, usually 2 to 6 cm in diameter and rarely encapsulated. CCS is melanocytic or mesenchymal in origin with the mesenchymal type closely resembling synovial sarcoma.[12] It is differentiated from synovial sarcoma by histopathologic criteria including the presence of spindle cells and clear cells, with abundant intracellular glycogen and occasional multinucleated giant cells.[12] The five-year survival rates are estimated between 48 and 67%.[13] Clear cell sarcoma is also referred to as malignant melanoma of soft parts.

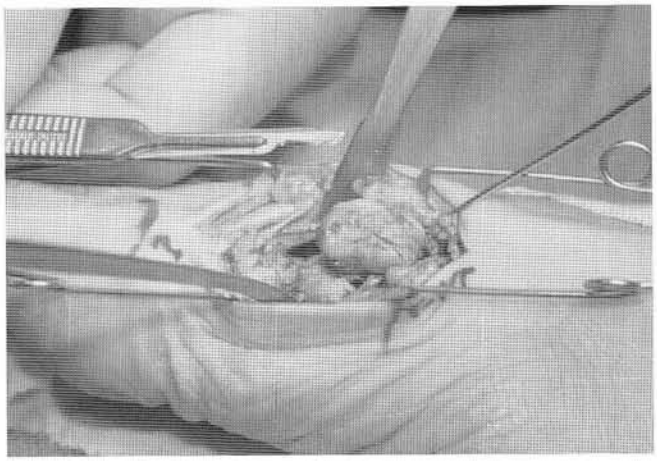

Figure 5. This clear cell sarcoma is somewhat unusual as it involved bone. This is often referred to as the malignant melanoma of soft tissue.

FIBROSARCOMA

Fibrosarcomas represent about 10% of all sarcomas in the foot and occur at any age but most commonly between the ages of 30 and 55 years.[2] This tumor occurs in fibrous tissue of fascial envelopes, aponeuroses, intramuscular septa and in tendons.[14] They arise from a slow growing painless mass more so than a painful rapidly growing mass. Malignant transformation of plantar fibroma to fibrosarcoma is rare, however distinction between a fibromatosis and low-grade fibrosarcoma may be difficult to make histologically (Figure 1). All fibrosarcomas have microscopic characteristics of fibroblastic cells in different levels of differentiation and collagen fibers.[14] High-grade fibrosarcomas have an irregular arrangement of spindle shaped fibroblastic cells and high mitotic activity as opposed to fibromas, which have differentiated fibroblast cells with rare mitosis.[14] The 2 most important determinants for five-year survival after tumor resection are histologic grade and size of the tumor.[14]

LIPOSARCOMA

Liposarcomas represent about 5% of all sarcomas in the foot.[2,4] Peak incidence is between the ages of 40 and 60 years with greater propensity for males.[6] Liposarcomas are usually large slow growing tumors in the intermuscular or periarticular planes, most frequently found in the thigh.[6] Grossly, liposarcomas are generally divided into distinct lobules formed by fibrous septa. They are composed of proliferating lipoblasts, a vascular network and a matrix of glycosaminoglycans and mucopolysaccharides.[15] Irregular calcifications may be seen on plain radiographs. MRI studies may display a low signal on T1 in some types of lipomsarcomas (myxoid liposarcomas) because these lesions contain less than 10% mature fat[6] Poorly differentiated tumors are highly aggressive and tend to

produce matastases in a high percentage of cases. The five-year survival rate of liposarcomas of the extremities is up to 70% with less aggressive types (myxoid and well-differentiated) having a much better prognosis than more aggressive (round cell and pleomorphic) types.[15]

MALIGNANT FIBROUS HISTOCYTOMA

Malignant fibrous histocytoma (MFH) are the most common soft tissue tumors in adult life, most commonly effecting individuals 50-70 years of age (Figure 3).[6] They represent about 4-9% of all sarcomas in the foot and ankle.[2,4] Men are affected twice as frequently as women. The lesions are solitary and multilobulated masses between 5 and 10 cm in diameter spreading along fascial planes.[16] MFH has a wide spectrum of cellular and tissue alterations. The histopathic features will display a mixture of fibroblastic and histiocytic elements with a cartwheel pattern of streaming spindle cells.[16] Because the tumor has a broad range of histological appearances, it is divided into the following subtypes: storiform-pleomorphic, myxoid, giant cell, inflammatory, and angiomatiod.[16]

IMAGING STUDIES

Radiographs may be useful by indicating the extent of bony involvement or calcifications occurring within the lesion. The soft-tissue mass and its relationship to bony structures can aid in the selection of further imaging modalities. While plain radiographs are generally negative for sarcomas, in 15% to 20% of cases of synovial sarcomas, periosteal reactions, superficial bone erosion or focal calcifications are seen.[17] To diagnose bone invasion by a soft tissue mass, the combination of plain film and MR imaging is adequate.

MRI is the examination of choice for soft tissue masses due to its ability to evaluate size, location, tumor margin, signal homogeneity, and signal changes in adjacent soft tissue (Figure 6).[18] Both benign and malignant tumors usually show a low signal intensity on T1-weighted images, therefore signal intensity provides little information about the histological grade of a given mass. Exceptions include lipomas, some liposarcomas and hemangiomas which all have high signal intensity on T1-weighted sequences because they contain either fat or blood.[18] Signal intensities on T2-weighted images are usually heterogeneous for sarcomas because of the variable amount of hemorrhage and necrosis occurring within the lesion.[8,18] A mass with a well-circumscribed smooth border is not necessarily indicative of benign because sarcomas tend to grow in a centripetal fashion along the path of least resistance and a smooth margin is usually seen.[1] Computed tomography provides excellent bony detail and show thinned cortices or calcifications that tend to occur in synovial sarcomas.[8] However, CT is usually not warranted in the case of soft tissue tumors. Angiograms or MRA studies may be helpful to differentiate vascular tumors (Figure 7) and bone scans may be helpful to determine metastasis (Figure 8).

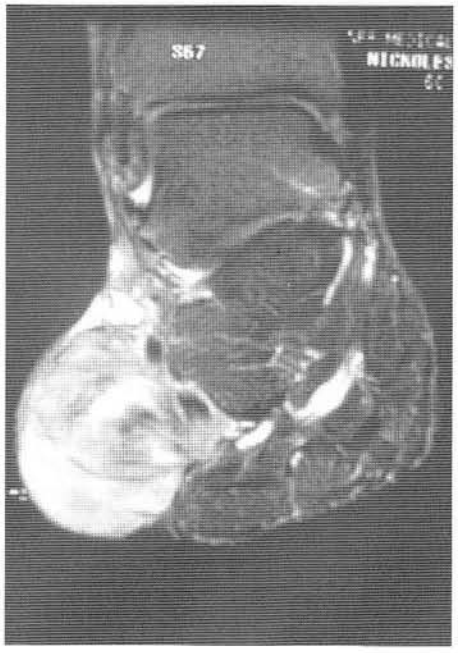

Figure 6. MRI of Synovial Sarcoma in the midfoot/rearfoot area.

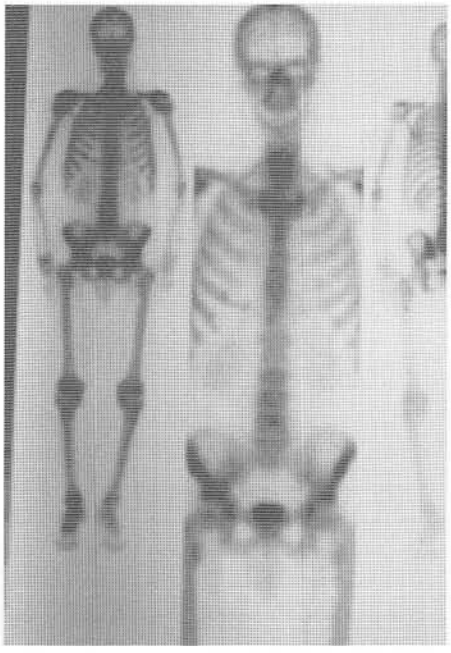

Figure 7. Full body bone scan.

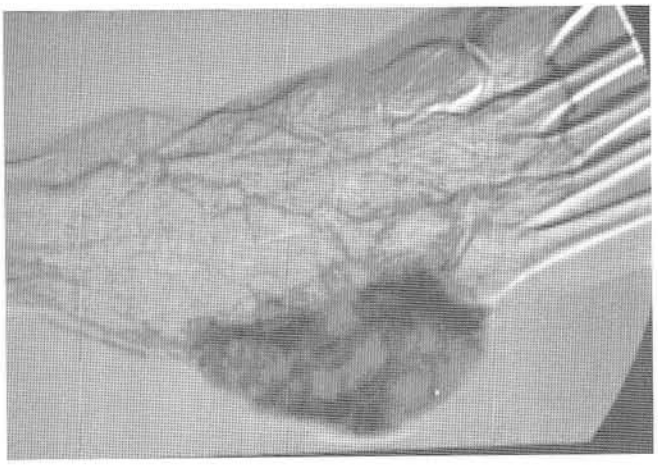

Figure 8. MRA study of the synovial sarcoma.

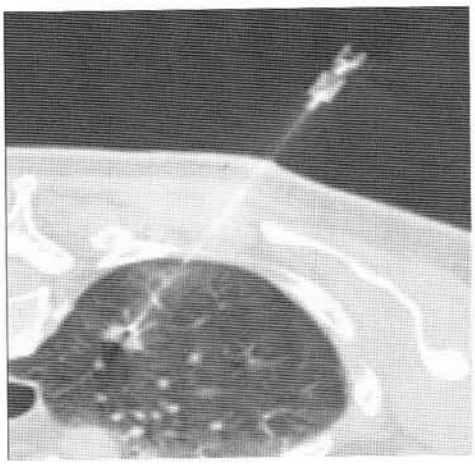

Figure 9. CT directed needle biopsy of tumor.

BIOPSY TECHNIQUES

Indications for the biopsy of soft tissue tumors include a size of greater than 5cm, tumors exhibiting growth, and masses present for longer than 4 weeks in duration.[2] When a lesion is questionable and a biopsy is needed, it is best to have the biopsy performed at a center that specializes in musculoskeletal tumors where the surgeon performing the biopsy will also perform the definitive care. Over a 15-year period, The Musculoskeletal Tumor Society noted a much higher incidence of biopsy related complications when the biopsy was not performed at the treating center.[7]

Fine needle aspiration involves using a fine-gauge needle to aspirate individual cells from a mass (Figure 9). The technique is relatively atraumatic and can be used to sample deep tumors minimizing the potential risk for tumor spillage. However, due to the limited amount of aspirate obtained it is sometimes difficult to discern the grade and histological type of sarcoma from the aspirate.[7]

Core needle biopsy is commonly performed with a Tru-Cut or a Craig needle obtaining a thin sliver of tissue (1 by 10 mm). If properly done, determination of both histological type and grade of a sarcoma has been correctly determined in over 90% of cases.[2]

Using the open biopsy technique, an incision is made to obtain the specimen. An excisional biopsy involves the removal of the entire mass and is best used for subcutaneous benign lesions. An incisional biopsy involves removing a portion of the tumor for pathological studies and leaving the remaining mass in situ. This procedure may be performed for masses suspected of being malignant because less tumor spillage will occur and the subsequent definitive tumor resection will be easier with the majority of the tumor in place.[7]

Table 1

AMERICAN JOINT COMMITTEE ON CANCER FOR THE STAGING OF SOFT-TISSUE SARCOMA

Stage	Grade	Tumor Size (T) and Location	Nodal Involvement	Metastasis
IA	Low	<5cm	No	No
IB	Low	>5cm, superficial	No	No
IIA	Low	>5cm, deep	No	No
IIB	High	<5cm	No	No
IIC	High	>5cm, superficial	No	No
III	High	>5cm, deep	No	No
IVA	Any	Any	Yes	No
IVB	Any	Any	No	Yes

STAGING

The purpose of staging a tumor is to determine the patient's progress and to direct treatment. The Musculoskeletal Tumor Society system of staging is based on grade, site and metastasis (Table 1).[19] Enneking considers the grade of a lesion to be an assessment of the biologic aggressiveness of the lesion requiring histologic, radiographic and clinical evaluation.[19] The site of the lesion is either within the borders of its compartment of origin,

contained within a compartment with extracapsular extensions, or extracompartmental. A superficial lesion in the skin and/or subcutaneous tissue that has not penetrated the deep fascia is considered intracompartmental. The extension of the tumor into adjacent anatomical compartments is considered a prognostic factor by some, but is not universally agreed upon.[1,19]

The American Joint Committee on Cancer for the Staging of Soft-Tissue Sarcoma focuses on three main events in the life cycle of a tumor: growth, as indicated by size of the tumor (T); spread to the lymph nodes (N); and distant metastasis (M).[1] In this system the sarcoma grade is determined according to the number of mitotic figures, and the extent of the necrosis. High-grade tumors have a higher likelihood of metastatic spread than low-grade tumors.

TREATMENT

The four general types of procedures used to excise tumors are: intralesional, marginal, wide, and radical.[7] Intralesional involves incising the tumor capsule and removing the lesion in sections. This approach is only appropriate for benign lesions. When performing a marginal excision, the tumor is shelled out around the reactive zone. This technique is also only appropriate for benign lesions because tumor cells can be left behind.[7,10] A wide excision involves the removal of viable tissue around the lesion and a radical surgery involves the removal of an entire anatomical compartment, which usually entails an amputation when dealing with the foot or ankle.[17] For high-grade sarcomas, only a radical approach with normal tissue at the reactive zone can be considered tumor-free.[7] Because of their tendency to recur, amputations of the involved part followed by radiation and or chemotherapy is the best treatment for aggressive soft tissue tumors of the foot and ankle. Chemotherapy with doxorubicin, cyclophosphamide and methotrexate prolongs both the absence of disease and survival in patients with high-grade soft tissue sarcomas of the extremities.[10] The use of chemotherapy and or radiation is especially crucial in cases of limb-sparing surgery such as ray resections, which have lead to functionally good results for less aggressive pseudoencapsulated sarcomas.[7,10] Patients undergoing limb-sparing surgery with wide resection of the compromised soft tissue followed by radiation have success rates ranging from 60% to 100% for all soft tissue sarcomas of the extremities.[10] Overall, margin of resection and adjunctive radiation and or chemotherapy are associated with survival outcome.

CASE PRESENTATION

A 52-year-old female was referred by her primary care physician for evaluation of a long-standing "bump" over the dorsum and plantar aspect of the first interspace of her left foot which increased in size rapidly over the last several months. She described mild tenderness over the site of the mass. Her past medical history was significant for hypertension. Lisinopril was her only medication. Past surgeries included a cholecystectomy and a cesarean section. Her only allergy is penicillin that causes her to break out in a rash. No family members have cancer history and the review of systems was unremarkable.

Physical exam revealed a 7 cm soft and tender mass extending between the first and second metatarsals palpable on both the dorsal and the plantar aspect of the forefoot (Figure 10). Vascular and neurological systems were intact. Inguinal adenopathy was not appreciated. Systemic examination was normal. Diagnostic studies consisting of radiographs, fine needle aspiration (FNA) and MRI were then preformed. The radiographs revealed a partially calcified plantar soft tissue mass with mild

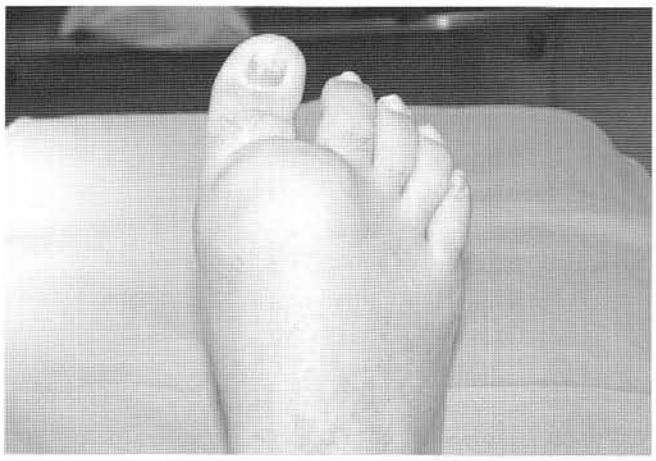

Figure 10. A 52-year old female with soft tissue mass in the first intermetatarsal space right foot.

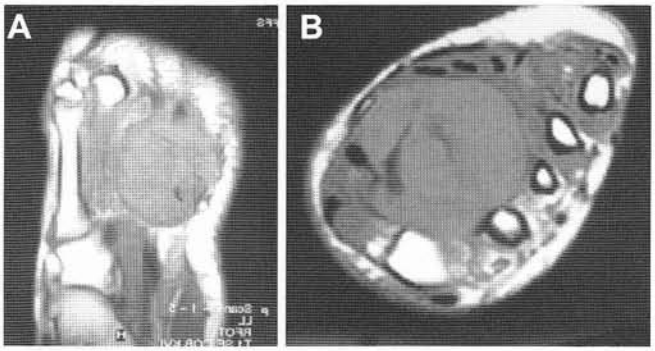

Figure 11A, B. MRI of the synovial sarcoma of the first intermetarsal space.

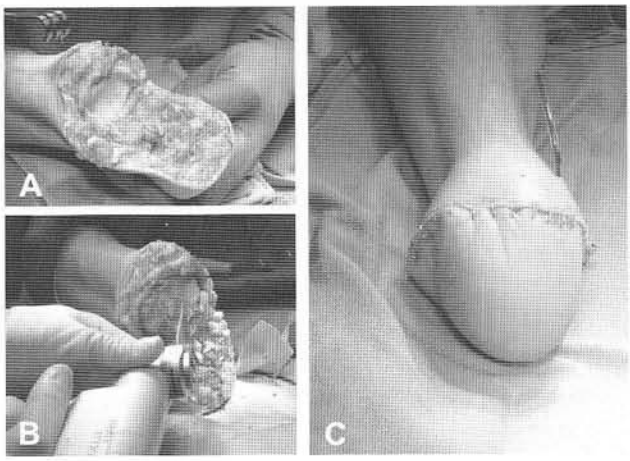

Figure 12A. Disarticulation of the foot at the ankle is the first step in the Symmes amputation. Figure 12B. Medial and lateral malleolli are removed along with the tibial cartilage. Figure 12C. The plantar flap of tissue is closed over the distal tibia.

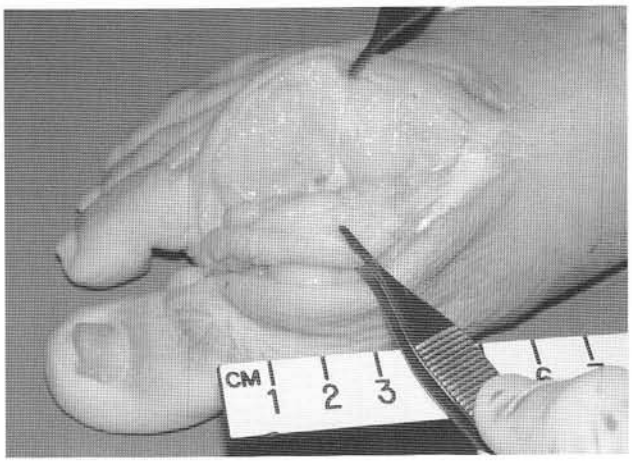

Figure 13. With the pathologist the lesion is exposed to reveal a solid lobulated rubbery type of material that has clearly crossed the local tissue planes. There is no encapsulation of the lesion.

erosion of the shaft of the second metatarsal. The MRI revealed a heterogeneous soft tissue mass with some calcifications (Figure 11). Multiple gray to pale elongated tissue fragments of tissue were visible from the gross FNA. The microscopic hematoxylin and eosin stain of the FNA displayed highly cellular spindle cells, S-shaped nuclei and brisk mitotic activity. The results of the FNA warranted a full body bone scan and a CT of the chest, abdomen, and pelvis, all which were negative. Pathology reported the tumor to be a monophasic synovial sarcoma.

A Symes amputation (disarticulation at the ankle joint) was performed because a wide excision would not allow for a functional foot due to the significant size of the tumor (Figure 12). The lesion was viewed with the pathologist and appeared to be solid and lobulated, and did cross tissue planes (Figure 13). The patient was then consulted to oncology and began radiation therapy. Postoperatively the patient was progressing well with a prosthesis (Figure 14).

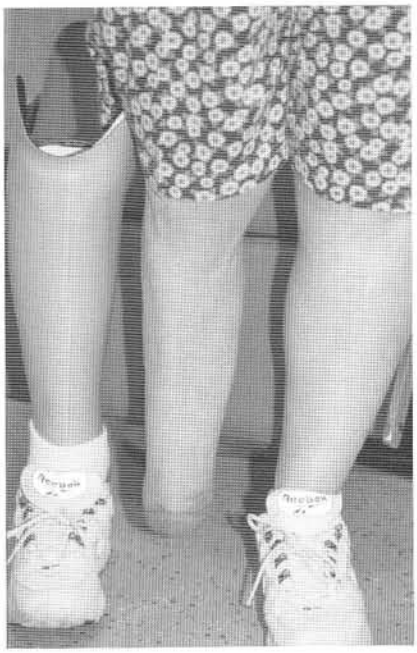

Figure 14. Good prostheses are available for the patients following a Symmes amputation.

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