Diagnosis and management of primary malignant tumors in the upper extremity

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Abstract

Bone and soft tissue sarcomas of the upper extremity are relatively uncommon. In many cases, they are discovered incidentally during evaluation of traumatic injuries or common ailments such as rotator cuff tendonitis or tennis elbow. Thus, it is important for all orthopedic surgeons to understand the differential diagnosis, workup, and treatment for upper extremity lesions. An appreciation of the clinical and radiographic features of primary malignant lesions aids in identifying patients that need referral to an orthopedic oncologist and a multidisciplinary team.

Introduction

Primary malignant tumors of the upper extremity are rare.[1] In patients <30 years of age, the number of benign and malignant tumors is relatively equal; in older patients, malignant tumors are more common, but their incidence is still lower than benign lesions. The most common malignant bone tumor in the upper extremity is osteosarcoma and the most common malignant soft tissue sarcoma is malignant fibrous histiocytoma (Table 1).[1-5] Bone and soft tissue sarcomas of the upper extremity can have high mortality rates, especially in later stages. The ten-year survival rate of soft tissue sarcoma is approximately 72% and the disease-free survival is 63%,[2,3] with similar survival rates among bone sarcomas.[4]

A PubMed search was performed to identify developments in diagnosis and treatment of these malignancies.

Diagnostic evaluation: Laboratory tests

Laboratory tests are often nonspecific. Complete blood cell counts can be affected in primary or secondary tumors, particularly in diseases that occupy bone marrow. Serum chemistry abnormalities can include elevated blood urea nitrogen, creatinine or hypercalcemia. Specific tumor markers including quantitative immunoglobulins, Serum Protein Electrophoresis (SPEP), Urine Protein Electrophoresis (UPEP), prostate-specific antigen can be elevated in multiple myeloma, metastatic disease, or prostate cancer, respectively. Serum alkaline phosphatase levels in primary osteosarcomas should be documented as levels correlate with prognosis.[6]

Diagnostic imaging

Radiographs

Lesions in the extremities are typically diagnosed earlier than axial tumors due to the fine trabecular detail visible on plain radiographs. The metaphysis is the most common location for bone tumors. The zone of transition between lesion and host bone can provide insight into the type of lesion. Well-demarcated lesions are usually benign, while poorly demarcated tumors are typically aggressive or denote an infectious process. Ossification is indicative of bone formation by the tumor. Calcification can indicate cartilaginous process. An expanded, thinned but intact cortex can be a manifestation of benign process. Cortical destruction or formation of new bone, as seen in Codman's triangle, can indicate an aggressive or malignant mass. Radiographic inspection can help identify non-oncologic conditions. Soft tissue masses can also present with calcification. It is commonly seen in tumoral calcinosis, myositis ossificans, synovial osteochondromatosis, and as juxta-articular calcification in synovial sarcomas.

Advanced imaging

Computed Tomography (CT) is preferred to evaluate margination, calcification, cortical disruption, and axial location. A thin-slice helical scanner (~1mm) allows for improved two-dimensional and three-dimensional reconstructions. Bone scintigraphy, although non-specific, may help detect active and aggressive primary lesions, as well as metastatic lesions. Positive Emission Tomography (PET) can be used and provides higher resolution images than bone scintigraphy. For soft tissue lesions, ultrasound can assist in characterization of size, depth, and composition, including assessment of vascularity with

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added Doppler imaging. Magnetic Resonance Imaging (MRI) is superior to CT in evaluation of intramedullary and soft-tissue extension of bone tumors and can assist in accurately diagnosing soft-tissue tumors. Intravenous contrast can help to evaluate vascularity and relationship to neurovascular structures.

For soft tissue tumors, MRI cannot completely distinguish malignant from benign masses. It can, however, distinguish tumors with high adipose tissue ratio (high T1, low T2 signal) from those without. Characteristics of fatty tumor suggestive of malignancy include patient age >60 years, lesion size >10 cm, thick septa (>2 mm), presence of non-adipose mass-like areas, and composition of less than 25% adipose tissue.[7] MRI with intravenous contrast is currently preferred for extremity soft-tissue sarcomas. Low signal intensity on T1-weighted images, high signal intensity on T2-weighted images, heterogeneous appearance, and contrast enhancements are features common to soft-tissue sarcomas.[8,9]

Biopsy

Biopsy should be performed as a final component of the workup. Indications for biopsy include size >5cm, subfascial or thigh location, and aggressive or malignant appearance on imaging.[10] Lymph node biopsy is seldom used due to rarity of lymph node metastases in primary malignant bone tumors and primary soft-tissue sarcomas. Exceptions requiring lymph node biopsy are childhood rhabdomyosarcoma, epithelioid sarcoma, synovial sarcoma, and clear cell sarcoma. [6]

Biopsy site selection

Incisions should be made longitudinally in an area that can be excised en-bloc during a subsequent operation. Biopsy at the margins is preferred as central portions of the tumor may be necrotic and less architecturally consistent. Soft tissue and bone sarcomas exhibit significant morphologic heterogeneity compared to relatively homogeneous carcinomas. For the humeral region, use anterior deltoid splitting approach. The deltopectoral interval is more prone to local recurrence after subsequent resection of the proximal humerus. Vacuum-assisted closure techniques must be avoided to prevent further dissemination of malignant cells.[11]

Surgical staging

The two most common staging systems are the Musculoskeletal Tumor Society (MSTS) (Enneking system), and the American Joint Committee on Cancer (AJCC) system. The MSTS is more popular amongst orthopaedic surgeons and has separate systems for malignant (Roman numerals) and benign lesions (Arabic numerals). The site is based on the tumor compartment, whether it is intraosseous (T1) or penetrates beyond the cortex (T2). The grade can be classified as low-grade (G1, low metastatic potential) or high grade (G2, high metastatic potential). G2 requires more radical surgical management and possible neo/adjuvant chemotherapy. Metastasis is classified as absent (M0) or present (M1), after radiographic evidence of lung, node, or intramedullary "skip" lesions.[12]

The AJCC has developed a system for primary bone tumors based on the topography of the primary Tumor (T), the histologic Grade (G), Nodal involvement (N), and absence or presence of Metastases (M) (Table 2). AJCC also has a staging system for soft tissue sarcomas based on similar criteria. However, the topography is further divided based on whether the tumor is deep or superficial to the muscular fascia, respectively (Table 3).

Principles of management

Surgical excision can be classified into four basic types (Table 4).[12] A wide resec-

Table 1. Prevalence of malignant bone tumors sarcoma.

	All ages	Age specific		
Type	Percent	0-20 years	20-50 years	> 50 years
Osteosarcoma	29	56	25	12
Primary chondrosarcoma	19	4	21	17
Myeloma	13		9	30
Malignant lymphoma	13	5	11	19
Ewing tumor	11	26		
Fibrosarcoma	3			
Other	12			

Table 2. Prevalence of soft tissue sarcoma.

	All ages	Age specific				
Type	Percent	0-5 years	6-15 years	16-25 years	26-45 years	> 46 years
Undifferentiated pleomorphic sarcoma (UPS)	37			14	25	53
Synovial sarcoma	8		15	23		
Malignant schwannoma	8			12		
Liposarcoma	8					10
Fibrosarcoma	6	29	9		11	
Leiomyosarcoma	5					8
Angiomatoid UPS	5	10	33			
Dermatofibrosarcoma protuberans	3					
Epithelioid sarcoma	3					
Other	11	Rhabdomyosarcoma (23)			Malignant peripheral nerve sheath tumor (12)	

tion with normal margins in all directions should be achieved. Bone should be resected 3-4 cm beyond the zone of abnormal uptake to avoid intraosseous tumor extension. The adjacent joint and capsule should also be resected. Although 1 cm margins have been recommended in the past, sarcomas grow along rather than traverse major fascial planes. In these cases, smaller tissue cuffs might be sufficient, particularly when combined with other treatment modalities.

Limb salvage

While historically treated with amputation, recent advances have made limb salvage the preferred treatment for upper extremity tumors. Careful patient selection is necessary, as significant expected loss of function, widely metastatic disease, or diminished life expectancy should preclude complex reconstructive procedures.[13]

Principles of limb salvage

In limb salvage, vascular reconstruction takes precedence, followed by skeletal stabilization and soft tissue reconstruction. Reconstruction to replace all functionally critical nerves and tendons should then be performed. Tendon transfers and functional muscle transfers should be considered when functionally significant major muscle compartments are resected or when minimal motor nerve recovery is anticipated.[13]

Amputation

From 1960-1980, approximately 30% of malignant upper extremity tumors were treated with amputation. Presently, the rate is approximately 5-10%. Severe functional impairment is the most common reason for amputation in the upper extremity. Prior unplanned excision resulting in widespread tissue contamination and a large (T>5cm), high-grade tumor that invades major neurovascular structures are also indications for amputation. Significant involvement of brachial plexus necessitates a forequarter or similar shoulder girdle amputation.

Outcomes

Limb salvage demonstrates increased rates of local recurrence (15-20%) compared to amputation. However, with appropriate treatment of recurrence, there is no difference in long-term survival.[14,15] The amputation rate following failed limb salvage has been reported from 3-30%. Limb salvage itself is not a predictor of increased rate of metastases or poor survival, as the five-year survival after limb salvage is 70-75%. High tumor grade and size >8cm are independent predictors of poor survival in upper extremity sarcoma patients.[15]

Adjuvant therapy

Chemotherapy is used to diminish the size of the primary tumor and eliminate micrometastases for osteosarcoma, Ewing sarcoma, and malignant fibrous histiocytoma. Neoadjuvant chemotherapy makes resection easier, safer, and improves long term survival in patients with non-metastatic extremity osteosarcoma.[16] Patients with a good response to chemotherapy (>90% tumor necrosis) have increased disease-free survival rates.[17] In conjunction, adjuvant chemotherapy is started 2-3 weeks after surgery. Additionally, external beam radiation can be used for definitive control of tumor for Ewing sarcoma and primary lymphoma of bone. In soft tissue sarcomas, wide resection with negative margins is acceptable for low-grade and high-grade sarcomas. Yet, wide resection and external beam radiation have been used in

Table 3. AJCC staging systems for primary bone tumors and soft tissue tumors.

Stage	Surgical site/ Topography	Nodal involvement	Metastasis	Histologic grade
A) Primary bone tumors				
IA	T1	N0	M0	low grade
IB	T2	N0	M0	low grade
IIA	T1	N0	M0	high grade
IIB	T2	N0	M0	high grade
III	T3	N0	M0	any grade
IVA	any T	N0	M1a	any grade
IVB	any T	N1	M1b	any grade
B) Soft tissue tumors				
IA	T1a/b	N0	M0	low grade
IB	T2a/b	N0	M0	low grade
IIA	T1a/b	N0	M0	high grade
IIB	T2a	N0	M0	high grade
III	T2b	N0	M0	any grade
IV	any T	N1	M0	any grade
IV	any T	any N	M1	any grade

Table 4. Surgical excision modalities and their indications.

Surgical excision	Descriptions and indications
Intralesional	Performed within the tumor and is seen in piecemeal debulking or curettage. Indicated only for benign lesions and is often combined with adjuvant local therapy.
Marginal	Occurs through the reactive zone. May leave microscopic disease that can manifest as satellite or skip lesions.
Wide/en bloc	Preferred for bone sarcomas. Indicated for stage IA and stage IB tumors.
Radical	Indicated for stage IIA and stage IIB tumors.

conjunction to minimize local recurrence. Preoperative radiotherapy has not been shown to increase postoperative wound complications in the upper extremity.[18,19]

Primary bone lesions

Osteosarcoma

Osteosarcoma is the most common primary bone malignancy. It occurs in the humerus in 10% of cases, most commonly in the proximal humerus.[20,21] It most often occurs in patients 20-30 years of age, but incidence rises again in patients >65 who have pre-existing Paget's disease or have undergone prior radiation therapy.[20,22] Common symptoms are pain and swelling, with or without a palpable soft tissue mass.[20,22] 5-12% of patients initially present with a pathologic fracture. Lung metastasis is a predictor of the pathologic fracture and poor patient prognosis.[23,24]

Radiographs should be obtained upon presentation. Among the intramedullary subtype, 90% of lesions are metaphyseal.[25] These lesions are destructive with cortical breach and exhibit radial ossification described as a "sunburst pattern". They can also display periosteal reaction with Codman's triangle and variable degrees of calcification.

Parosteal osteosarcoma typically exhibits radio-dense lesions with a broad, sessile base on the outer cortical surface. These typically do not have intramedullary involvement. Periosteal osteosarcoma appears as a radiolucent mass on the outer cortical surface with bony spicules, a thickened irregular underlying cortex, and usually does not involve the medullary canal.

Treatment modalities vary by subtype (Table 5).[26] Local recurrence is 4-6% for both limb salvage and amputation, with no difference in survival between the two.[25,27] Resection of metastases is recommended as it increases survival fivefold, specifically after solitary lung metastases.[28] Adjuvant chemotherapy is critical in these patients. Treatment with a Free Vascularized Fibular Autograft (FVFG) has demonstrated success to promote union post-resection (93.3%) and is unaffected by pre or post-operative chemotherapy.[29] However, the post-operative complication rate of FVFG requiring reoperation is 34%, which is significantly greater than the 10% of revision surgeries with a prosthetic implant during reconstruction.[30]

Greater than 90% tumor necrosis after neoadjuvant chemotherapy is a positive predictor of survival (>61% versus 37-52% with <90% tumor necrosis).[25,31] Poor prognostic factors include: metastatic disease at presentation, primary tumor in the axial skeleton, large tumor volume, and elevated alkaline phosphatase or lactate dehydrogenase levels. Other poor prognostic factors include: poor response to preoperative chemotherapy, skip metastases, and lymph node involvement. Long-term survival for localized disease is 60-78%.[25,32] Numerous studies have shown improved survival for surface subtypes,[33,34] including 5 and 10-year survival for parosteal at 91% and 83%, respectively. Survival with metastatic disease is 20-30%.[25,35]

Ewing's sarcoma

5-10% of Ewing's Sarcoma cases occur in the shoulder girdle.[35] It commonly presents in the second decade of life with a male predilection (1.3-1.5:1). Symptoms include pain, swelling, and presence of a mass. Approximately 20-28% of patients will be febrile at presentation.[36]

Radiographic features may include lytic, destructive lesions with ill-defined borders, cortical breach located in diaphysis or metadiaphysis, and periosteal reaction. Many cases will demonstrate significant soft tissue mass on MRI. This will appear as a large, unmineralized soft tissue mass with an associated osseous lesion.

Optimal treatment should include multidrug neoadjuvant chemotherapy, local control, and multidrug adjuvant chemotherapy. The preferred method of local control is surgical resection with or without reconstruction. Radiation has been used with some success for local control of unresectable lesions and lesions that show poor response to chemotherapy.[37,38]

The most important prognostic factor is presence of metastasis.[35,37,39] Five-year survival is 65-82% for local disease and 25-39% for metastatic disease. Ten-year survival is 63% for local disease and 32% for metastatic disease. Five and ten-year survival for isolated Ewing's of the forearm and hand are 84% and 74% respectively, in patients who received chemotherapy, surgery, and adjuvant radiation and chemotherapy.[38]

Chondrosarcoma

Chondrosarcoma most commonly occurs in the humeral metaphysis. Younger patients typically present with low-grade tumors, and older patients with high-grade lesions. At initial presentation, 60% of patients had night pain and 21% vague regional pain. Only 19% of chondrosarcomas were incidental findings. Approximately 3-8% of patients presented with a pathologic fracture.[40,41]

The six subtypes of chondrosarcoma include central conventional, secondary, mesenchymal, dedifferentiated, clear cell and periosteal (Table 6). Central conventional chondrosarcoma accounts for 75-90% of those diagnosed.[42-44]

Plain radiographs of low-grade tumors demonstrate stippled calcification, endosteal scalloping, and lysis.[45] Increased endosteal scalloping can be indicative of malignancy. Unlike low-grade tumors, high-grade tumors show cortical destruction with endosteal scalloping, cortical thickening, and soft tissue masses. They may also demonstrate amorphous calcification with large non-calcified regions. MRI may demonstrate low signal intensity of T1 images and high signal intensity of T2 images.[46] Medullary filling of greater than 90% is indicative of malignancy.

Low-grade tumors are treated with wide resection are associated with low local recurrence.[47] Intralesional curettage for benign to low-grade malignant chondrosarcomas has been beneficial but has not been proven superior to conservative treat-

Table 5. Treatment modalities organized by osteosarcoma subtype.

Osteosarcoma subtype	Grade	Treatment
Intramedullary	High	Chemotherapy and wide excision. Limb salvage or amputation.
Intramedullary	Low	Wide surgical excision. Limb salvage or amputation.
Periosteal	High	Chemotherapy and wide excision. Limb salvage or amputation.
Parosteal	Low	Wide surgical excision. Limb salvage or amputation.
Appendicular	High	Limb salvage (possible for 85%) or amputation.
Dedifferentiated	High	Wide surgical excision. Limb salvage or amputation.

ment.[40,41,47-49] Intermediate and high-grade tumors are best treated with wide resection. Chemotherapy is beneficial for mesenchymal and dedifferentiated subtypes.

Soft tissue lesions

Undifferentiated pleomorphic sarcoma

Undifferentiated Pleomorphic Sarcoma (UPS) is most often a primary soft tissue tumor, although it can also occur as a primary bone tumor. UPS demonstrates fibrous tissue in a storiform pattern. It is the most common soft tissue sarcoma of the upper extremity, most frequently involving the proximal humerus. It typically occurs in the 6-8th decade of life and presents with localized pain and swelling. Approximately 25% of all cases present with pathologic fracture.[44]

Initial radiographs show permeative, "moth-eaten", destructive lesions in the metaphyseal or metadiaphyseal region emerging from the original soft tissue mass. This lesion typically shows little or no periosteal reaction or calcification. MRI may show hemorrhagic components within the mass. UPS appears hypo-intense on all MRI sequences and demonstrates nodular peripheral gadolinium enhancement in solid, non-myxoid portions of the mass.[50]

Treatment is similar to osteosarcoma and can include neoadjuvant chemotherapy, wide excision, and adjuvant chemotherapy. Radiation may be beneficial for unresectable disease or questionable postoperative margins. Prognosis depends on tumor size, depth, and histology grade.[44,51] These factors correlate closely with both metastases and survival. Tumor necrosis >90% after neoadjuvant chemotherapy is associated with improved survival. Patients <40 at time of diagnosis have improved survival. Local recurrence rates range from 19-44%, and distant metastatic rates are between 23%-36%. Overall, rates are between 39%-74%. Nonmetastatic disease has five-year survival rates of 50-70% with multimodality treatment versus 0-20% without chemotherapy. UPS with metastases has a five-year survival rate of approximately 5%.[52]

Synovial sarcoma

Synovial sarcoma is the second most common soft-tissue sarcoma in the extremities in patients ages 16-25. In the shoulder, arm, elbow, and wrist the tumor arises in deep compartments, near joints, and in association with tendon sheaths, bursae, and joint capsules. Approximately 5% of these sarcomas arise in the shoulder region.[5] Typical anatomic presentations include the shoulder, arm, elbow and wrist. Synovial sarcoma typically occurs in young adults and children, but may arise in older patients. Presentation often includes history of a slow growing mass, often >5 cm at time of first visit and pain in 50% of patients.

Radiographs may demonstrate a soft tissue mass and calcification in up to 1/3 cases. Absence of calcification indicates a high-grade lesion and poor prognosis. Approximately 20% of cases show bony involvement including erosion, invasion, and periosteal reaction.[53] MRI typically reveals well defined masses with rounded or lobulated margins in deep tissues around the joint. The mass may displace surrounding soft tissue structures and appears isointense to skeletal muscle on T1 images but hyperintense on T2. Smaller sized tumors may appear more homogenous, while larger tumors are usually heterogeneous.[54] Often, synovial sarcoma will demonstrate fluid-fluid levels or appear septated on MRI. Use of gadolinium may show diffuse or heterogeneous enhancement.

Treatment includes wide resection with adjuvant chemotherapy and/or radiation. Risk factors for disease progression and poor outcome are age >25, tumor size >5 cm, tumor necrosis, invasion of bone or neurovascular structure, and metastatic disease.[55] Approximately 40% of synovial sarcoma lesions will metastasize to the lungs, bone or lymph nodes with a 50% post-operative recurrence rate.[56] The five-year survival rate for synovial sarcoma is 50-65%,[55] while ten-year survival rate is 25%.[44]

Liposarcoma

Approximately 11% of liposarcomas occur in the upper extremities.[57] They represent 16% of all soft tissue sarcomas of the shoulder and are the second most common in the shoulder region of patients >40 years old.[5] Most liposarcomas are diagnosed in the sixth decade, whereas myxoid and round cell tumors occur in younger patients. The five subtypes are: well-differentiated, myxoid, round cell, pleomorphic and dedif-

Table 6. Survival rates of various chondrosarcoma subtypes.

Chondrosarcoma subtype	Grade	Survival rate (percentages)
Central conventional	Various	Ten-year: 29-83*
Secondary	Low	--
Periosteal	Low	--
Clear cell	Low	Five-year: 100 Ten-year: 89
Mesenchymal	High	Ten-year: 28
Dedifferentiated	High	Five-year: 0-18

*Survival rates at ten years vary depending on tumor stage.

Table 7. Characteristics of various liposarcoma subtypes.

Liposarcoma subtype	Grade	Prevalence (%)	Metastatic rate (%)	Survival rate (%)
Well-differentiated	Low	>50		10-20 year – 100 Dedifferentiation rate – 2.0
Myxoid & round cell	Myxoid - low Round cell - high	40-50	33	5 year – 8.23 10 year – 0
Pleomorphic	High	<10		
Dedifferentiated	High	<10	15-20	5 year – 70

Most cases of round cell liposarcoma have a 10-year dss of 87% whereas myxoid has a poorer prognosis of 81%.

ferentiated (Table 7).[58,59]

MRI is preferred for diagnosis. Well-differentiated liposarcoma can be difficult to distinguish from benign lipomas on MRI. Features consistent with malignancy include size greater than 10 cm, enhancing thick septae, nodular, nonfatty components and a lesion compromised of 75% or less fat.[7] Myxoid subtype has heterogeneous high-low signal patterns, while dedifferentiated subtype has heterogeneous signal abnormality on T1 and T2 images.[50]

Treatment consists of wide excision and adjuvant radiation. Adjuvant chemotherapy has shown benefit in high-grade lesions and metastatic disease.

The dedifferentiated subtype has a local recurrence rate of 40%, metastatic potential of 15-20%, 5-year survival of approximately 70% and has shown survival decrease at 10-20 years.[44] Overall poor prognosis has been associated with patients >45 years old, male, and local recurrence.[59,60]

Malignant peripheral nerve sheath tumors

Malignant Peripheral Nerve Sheath Tumors (MPNST) compromise 10% of soft tissue sarcomas in the shoulder region and display a predilection for the flexor surfaces of forearms.[5] MPNST is associated with Neurofibromatosis Type 1(NF-1) in 25-70% of cases, while the remainder are idiopathic.[58] NF-1 associated tumors tend to occur approximately 10 years earlier than their idiopathic counterparts with a higher male predilection.

On MRI, it can be difficult to differentiate between benign and malignant lesions. The "target sign" on T2 weighted images and central enhancement with gadolinium are associated with benign lesions.[61,62] Enlarging size, invasive lesions, and gadolinium uptake are more indicative of malignant tumors.[58]

Treatment usually involves wide excision.

Fibrosarcoma

Fibrosarcoma often originates as a deep forearm mass. It is common in patients age 30-55. An infantile subtype of fibrosarcoma affects children <2 and is more common in males. They typically present as a slow-growing, painless mass. MRI is the most useful imaging in diagnosis.

Treatment for fibrosarcoma consists of wide resection and adjuvant radiation. Chemotherapy is controversial, but has been recommended for locally extensive disease, metastatic disease and high-grade tumors (50-60% of which have lung metastasis at the time of diagnosis).[44] The five-year disease-free survival in local disease treated with excision and radiation is approximately 80%.[63]

Dermatofibrosarcoma protuberans

Dermatofibrosarcoma Protuberans (DFSP) commonly occurs in the superficial forearm, but can also occur around the shoulder, where it accounts for 16% of soft tissue sarcomas in that region.[5] It occurs most commonly in the 3rd/4th decades of life, (median age at diagnosis 51) with a male predilection.[64] 10-20% of patients report antecedent trauma at time of presentation. Most patients provide a history of a painless nodule, and physical exam may reveal associated skin color changes.

Imaging can be difficult as the lesion is very superficial. Radiographs may show an unmineralized, superficial, nodular soft tissue mass. MRI may better define the lesion as isointense to muscle of T1 and hyperintense on Short-TI Inversion Recovery (STIR) images. Contrast will show moderate enhancement secondary to hypervascularity and may be iso or hyperintense to fat on T2.[65]

Treatment should involve wide excision with 3 cm margins (this is less clear and a little controversial), including deep fascia.[66] Radiation has been shown to improve local control as well.[67,68] Use of Imatinib, a PDGF receptor tyrosine kinase inhibitor, has been used in lesions with t(17;22) translocations and has shown promising early outcomes.[69] SU11248, a tyrosine kinase inhibitor, is also being studied for use in treatment of Imatinib resistant tumors.[70] DFSP is often a low grade sarcoma with high cure rates after wide excision. A 50% local recurrence rate is seen with excision of deep masses and poor margins.[66]

Epithelioid sarcoma

Epithelioid sarcoma constitutes less than 2% of all soft tissue sarcomas.[5] 60% of epithelioid sarcomas occur in the hand and forearm,[54] (most commonly dorsum of the forearm. Deeper masses spread along tendon sheaths, neurovascular bundles and fascial planes, and can involve lymph nodes. The tumor typically affects adolescents and young adults, but has been diagnosed in all age groups. Patients commonly report a slow growing mass with minimal pain. Superficial lesions can be multi-nodular and lead to ulceration.

Radiographs can reveal a soft tissue mass and rarely show calcification or bony reaction or destruction. MRI demonstrates varied appearances. The lesion has a broad range of sizes and may be subcutaneous or deep with ill-defined borders. The tumor is usually isointense to muscle on T1 but may have areas of varying signal. Appearance on T2 is related to the composition of the tumor and contrast enhancement may range from partial and non-uniform to homogenous.[54,71,72] Treatment should consist of wide surgical resection with local recurrence rates of approximately 35%.[71,72] Generally, larger proximal tumors display worse outcomes. Metastases to the lungs are most common, with lymph node involvement relating directly to tumor size.[54] Due to relatively common late recurrence and metastasis, long-term surveillance is recommended. The five and twenty-year survival is 55-70% and 10% respectively.

Rhabdomyosarcoma

Rhabdomyosarcoma is the most common soft tissue sarcoma of children and adolescents. 7% of all cases involve the upper extremity.[57] The embryonal subtype is most common in children, and alveolar type is most common in adolescents. Pleomorphic rhabdomyosarcoma is common in adults and has a propensity for the lower extremities but is not uncommon in the upper extremities. Patients often report history of a rapidly enlarging painful mass. Alveolar subtype is the most common in the upper extremity and carries the worst prognosis.[73] Metastases are present in approximately 20% of patients at presentation as this lesion commonly metastasizes to lung and lymph nodes.

MRI is the most helpful imaging modality. Treatment consists of wide resection and radiation for local disease. Multidrug chemotherapy and immunotherapy for unresectable or metastatic disease is beneficial.[74,75]

The five-year survival for surgically resected local disease is approximately 70%.[76,77] Metastatic disease demonstrates a 5-year survival rate of 30%.[75]

Leiomyosarcoma

Leiomyosarcoma comprises 5% of soft tissue sarcomas in the shoulder region, but can present in other locations as well.[5] It tends to occur in older patients. A history and exam finding of soft tissue mass may be the only notable feature.

Radiographs may reveal a "moth-eaten" appearance (ill-defined with cortical destruction in the metaphysis and a soft tissue mass shadow). The associated bone may have reactive sclerosis but no calcification of the lesion. MRI demonstrates a non-specific appearance with intermediate signal intensity on T1 and T2.[78]

Low-grade lesions are treated with wide excision, although successful treatment has been reported with only curettage and cryotherapy. High-grade lesions should be treated with neoadjuvant chemotherapy, wide excision, and postoperative chemotherapy. Despite limited radiosensitivity, radiation is still used to treat unre-

sectable disease or tumors with questionable margins.

Leiomyosarcoma has a high metastatic rate, approximately 50%, with most metastases occurring in the lungs. The five-year survival rate is >90% for low grade and 50%-70% for intermediate to high grade lesions.[79]

Conclusions

When encountering lesions of the upper extremity, one must remember the extensive list of pathology that can manifest. Tumors of the upper extremity can range from benign to high-grade malignancies with poor prognosis. Many symptoms for these lesions can be similar; therefore, obtaining proper imaging and tissue are crucial to making the correct diagnosis. Many of these pathologies, and all malignancies, should be treated with a multidisciplinary team. While many of the lesions reviewed have well agreed-upon standards of treatment, others are more nuanced. With advances in surgical options and adjunct medical therapies, we hope to see continued improved outcomes for patients with malignant upper extremity lesions.

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