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SCIENTIFIC ARTICLE

MRI, MDCT features, and clinical outcome of extremity leiomyosarcomas: experience in 47 patients

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Abstract
Objective To describe MRI, MDCT features, and clinical outcome of extremity leiomyosarcomas (LMS).
Materials and Methods In this IRB-approved, HIPAA-compliant retrospective study, we included 47 patients (23 women, 24 men; mean age: 55.3 years, range: 17–85 years) with pathologically confirmed extremity LMS seen at our adult tertiary cancer center between 2000 and 2012. MRI/MDCT of primary tumors in 23 patients and follow-up in all patients were reviewed by two radiologists in consensus. Clinical data were extracted from electronic medical records.
Results Primary tumors were distributed in bones (6 out of 47), deep soft tissues (24 out of 47), and superficial soft tissues (17 out of 47). On imaging (bone=4, deep soft tissue = 11, superficial soft tissue=8), compared with skeletal muscle, they were T1 iso-hypointense and T2 hyperintense. Bone LMS were metaphyseal tumors with cortical destruction (3 out of 4). Deep soft-tissue LMS were large with hemorrhage (7 out of 11) and necrosis (10 out of 11). Superficial soft-tissue LMS were relatively smaller, homogeneously enhancing (6 out of 8) tumors. Distant metastases developed in 32 out of 47 patients (bone LMS [6 out of 6], deep soft-tissue LMS [18 out of 24], superficial soft-tissue LMS [8 out of 17]), commonly to lung (29 out of 47) and bone (14 out of 47). At the time of writing, 22 out of 36 patients (bone LMS [4 out of 6], deep soft-tissue LMS [15 out of 24], superficial soft-tissue LMS [4 out of 17]) have died. There was no statistically significant correlation between metastatic disease and tumor size or grade.
Conclusion Extremity LMS arise in bones and in the deep and superficial soft tissues, frequently metastasize to the lungs, and have a poor prognosis. Superficial LMS tend to have a better prognosis than bone or deep soft-tissue LMS.

Keywords Extremity leiomyosarcoma · Bone sarcoma · Soft-tissue sarcoma · MRI · Metastases

Introduction

Leiomyosarcoma (LMS) is a rare malignant mesenchymal neoplasm showing smooth muscle differentiation with an incidence of 0.7/100,000, comprising approximately 10 % of all soft-tissue sarcomas and the fourth most common soft-tissue sarcoma [1, 2]. LMS most commonly occur in the uterus and retroperitoneum and less commonly in the viscera, bone, somatic soft tissue, and skin [3, 4]. Bone LMS is a distinct and rare entity, the prevalence of which is not known and not addressed in the most recent WHO edition of bone and soft-tissue tumors. LMS are characterized by positive immunohistochemical staining for smooth muscle markers, including smooth muscle actin, desmin, and caldesmon [3]. An important determinant of the biological behavior of sarcomas is the grade, which is based on differentiation, mitotic activity, and extent of necrosis [5, 6]. In addition to the grade, the outcome of LMS is also determined by the age of the patient, the size of the tumor, the stage, and the extent of neurovascular invasion [7–9]. The prognosis of LMS in general is poor with an overall 5-year survival rate of 33 % [8].

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Leiomyosarcomas are sub-classified into uterine LMS, soft-tissue LMS, which includes cutaneous, major vessel, and deep soft-tissue LMS, and bone LMS [4]. Deep soft-tissue LMS are divided into retroperitoneal and somatic (peripheral) LMS, which include LMS arising in the extremities and trunk [4]. LMS of the extremities and trunk including cutaneous LMS tend to have a better prognosis than uterine, retroperitoneal, and major vessel LMS [3, 4, 10].

The imaging features of LMS of the extremities have not been widely reported in the radiology literature. Most of the studies describe LMS of the extremities as a subset of LMS occurring in more common sites like the uterus, retroperitoneum, and IVC [11, 12]. Although there have been few studies focusing on bone LMS [2, 13–16], with respect to soft issue LMS, there has been no clear distinction between subcutaneous and deep soft-tissue LMS. The objective of this study was therefore to describe the imaging features of primary and metastatic extremity LMS, providing a correlation with the management and outcome.

Materials and methods

Subjects

This was a Health Insurance Portability and Accountability Act-compliant institutional review board-approved retrospective study with waiver for informed consent. We identified 47 consecutive patients with a diagnosis of primary LMS of the extremity who were referred to, or primarily treated at our institution between January 2000 and December 2012. Of the 47 patients, 17 (36.1 %) were referred for management of advanced or metastatic disease. The histopathology of all these patients was reviewed at our institute to confirm the diagnosis of LMS. LMS of other sites including uterine, retroperitoneal and vascular LMS were looked for in all patients, but not noted in any of them. One patient with a history of prior hysterectomy for leiomyomas had a slide review of the hysterectomy specimen after the diagnosis of extremity LMS to exclude metastatic LMS and was found to have no malignant features in the uterine leiomyoma, confirming the extremity LMS to be a new primary.

Imaging

Pretreatment imaging of the primary tumor was available in 23 of these 47 patients and included MRI examinations in 22 patients (21 with intravenous gadolinium) and CT in 8 patients (6 with intravenous contrast). Follow-up imaging in all the 46 patients was reviewed and included CT scans in 29 patients and MRI in 17 patients.

Image analysis

Two oncoradiology fellowship-trained radiologists with 7 and 15 years of experience respectively reviewed all the available imaging in consensus. The following imaging features of primary tumors were recorded: location, margins, largest dimension, attenuation on CT (compared with skeletal muscles), signal intensity on T1- and T2-weighted images compared with skeletal muscle, degree of enhancement on CT and MRI compared with skeletal muscle (less than, similar to or greater than skeletal muscles), homogeneity, presence of necrosis, hemorrhage, and infiltration of the adjacent structures. Evaluation of metastatic disease included the site of first metastasis and location of all metastases.

Clinical features, management, and outcomes

The electronic medical records for all patients were reviewed to obtain the following clinical data: sex, date of initial diagnosis, age at initial diagnosis, size of the primary tumor, date of initial treatment, treatment types (radical resection, chemotherapy, radiation therapy), dates of local recurrences or metastatic disease, site of first metastatic lesion, sites of all metastatic lesions. Final clinical outcomes were obtained using the electronic medical record.

Histopathology correlation

The electronic medical record for all patients was reviewed to obtain the following information regarding tumor pathology: size, tumor grade (as per the French Federation of Cancer Centers [FNCLCC] grading system), and surgical margins [5].

Results

The study population consisted of 24 women and 23 men with a mean age of 55.3 years (range, 17–85 years). The anatomical distribution of the primary tumors was as follows: 34 patients had tumors involving the thigh, 7 had tumors involving the lower leg, 4 had tumors involving the upper arm, 1 patient each had tumors involving the forearm and foot. The extremity LMS were seen involving primarily either the bone (6 out of 47 [12.8 %]), or the soft tissues (41 out of 47 [87.2 %]). Tumors arising from the soft tissues were either in the deep soft tissues (24 out of 41 [58.5 %]) or in the subcutaneous or superficial soft tissues (17 out of 41 [41.5 %]).

Imaging features of primary LMS of the extremities

Twenty-three of the 47 patients had imaging of the primary tumor available for review. Four of the 23 tumors were primary bone LMS while the remaining 19 out of 23 tumors were

primary soft-tissue LMSs (11 deep soft-tissue tumors and 8 superficial tissue tumors). The primary LMSs of the extremities were large tumors with a mean size of 10.77 cm (range, 2.4 cm to 19.5 cm). Tumors in the thigh (9.8 cm) were larger on average than tumors in other locations (6.2 cm).

Primary bone LMS of the extremities

The anatomical locations of the 4 bone LMS included 3 in the tibia and 1 in the femur. The mean length of the bone lesions was 10.4 cm (range 6.4–16.5 cm). On MRI (n=3), relative to the skeletal muscle, all the tumors were hypointense on T1-weighted imaging. On T2-weighted imaging, they were heterogeneous and appeared hyperintense compared with the skeletal muscle, but less intense than fluid (Fig. 1). On non-fat-suppressed fast spin-echo T2-weighted images, the tumors were iso- to hypointense compared with subcutaneous fat, while they were hyperintense to fat on fat-suppressed T2-weighted images. After the administration of gadolinium, all the tumors demonstrated heterogeneous enhancement greater than skeletal muscles. None of the lesions demonstrated hyperintense foci on fat-suppressed T1-weighted imaging to suggest hemorrhage and none of the lesions demonstrated necrosis. On CT (n=2), bone LMS were isodense to the skeletal muscles with a soft-tissue component and heterogeneous enhancement (n=2). Anatomically, all the tumors were located in the juxta-articular metaphysis extending into the adjacent diaphysis, involving both the medulla and cortex. None of them was subperiosteal in location or associated with periosteal reaction. Three tumors demonstrated cortical disruption with extension into the surrounding soft tissues. None of the lesions demonstrated intra-articular extension.

Extremity LMS of the deep soft tissues

The mean size of the deep soft-tissue tumors (n=11) was 14.8 cm (range 2.4–19.5 cm). On MRI (n=11), all of the soft-tissue tumors had well-circumscribed margins and were isointense compared with skeletal muscle on T1-weighted imaging (Fig. 2). On T2-weighted imaging with fat suppression, all the tumors were heterogeneously hyperintense relative to skeletal muscle and fat, but less intense than fluid. On fast spin-echo T2-weighted imaging (n=5), the deep soft-tissue tumors were hyperintense relative to skeletal muscle, but had areas that were iso- to hypointense compared with subcutaneous fat (Fig. 2). After the administration of gadolinium, 10 of the 11 tumors had heterogeneous enhancement with non-enhancing areas of necrosis and cystic changes.

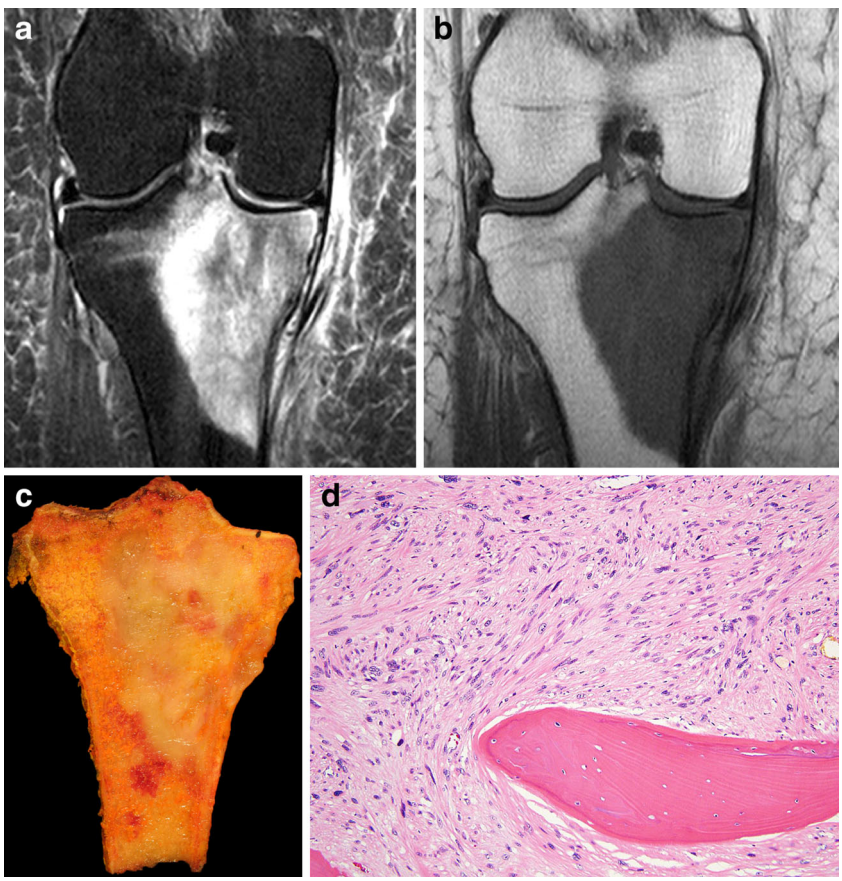

Fig. 1 A 66-year-old woman with primary bone leiomyosarcoma. **a**, **b** Coronal fat-suppressed T2-weighted and T1-weighted MR images of the leg demonstrate a T2 hyperintense and T1 hypointense lesion involving the juxta-articular metaphysis of the proximal tibia with no extension into the adjacent knee joint. **c** Similar to the MR findings, a coronal section of the resection specimen shows an irregular tumor in the metaphysis of the tibia with extension into the epiphysis. Note the white, fleshy appearance. **d** Histological examination shows typical features of leiomyosarcoma, including a fascicular architecture and elongated spindle cells with brightly eosinophilic cytoplasm surrounding native bony trabeculae

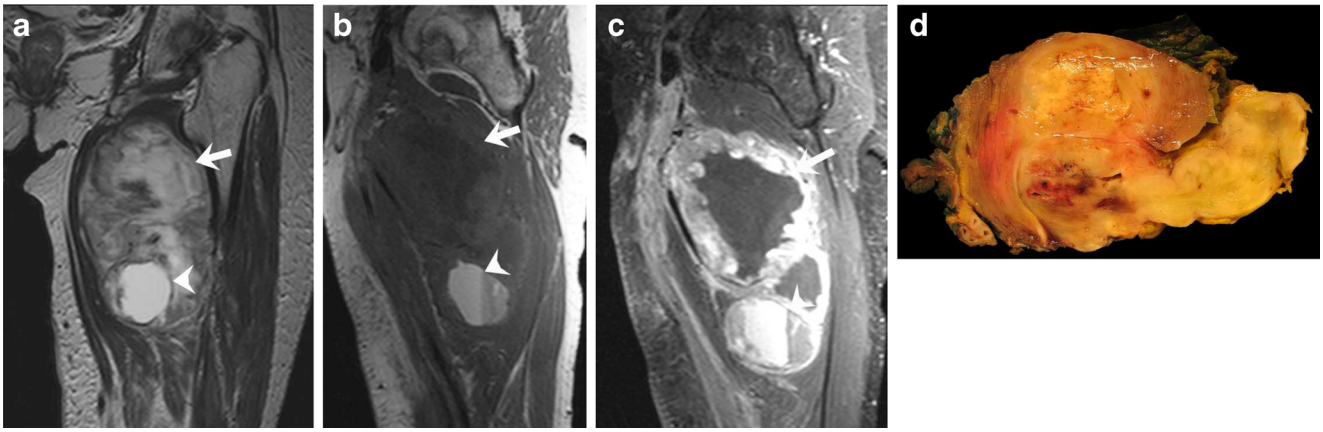

Fig. 2 A 76-year-old woman with deep soft-tissue leiomyosarcoma. **a**–**c** Coronal fast spin-echo T2-weighted, sagittal T1-weighted, and post-gadolinium fat-suppressed T1-weighted MR images of the thigh demonstrate a relatively well-circumscribed intramuscular mass in the thigh. The superior component of the mass (*arrow*) is heterogeneously T2 hyperintense and T1 hypointense compared with skeletal muscle, with peripheral thick enhancement consistent with central necrosis. The peripheral tumor has a low signal intensity compared with subcutaneous fat on T2-weighted images. The inferior component of the mass (*arrowhead*) has a T2 cystic appearance with dependent T1 hypointense layering consistent with hemorrhage. **d** Gross examination of the surgical resection specimen demonstrates a well-circumscribed, tan, fleshy mass with foci of hemorrhage (*lower field*) and a large, yellow, rounded focus of necrosis (*upper field*)

Hemorrhage in the form of T1 hyperintensity was noted in 7 of the 11 tumors. None of them had a suggestion of calcification, which was confirmed at histopathology. Three of the 11 tumors demonstrated local invasion into the surrounding neurovascular bundles, while one patient showed invasion of the adjacent bone. Anatomically, all the tumors were located distant from the joints except one tumor that was present close to the glenohumeral joint. On CT (n=6) the deep soft-tissue tumors were isodense to skeletal muscle and demonstrated heterogeneous enhancement (n=5). None of them demonstrated calcification on CT.

Extremity LMS of the superficial soft tissues

The mean size of the superficial soft-tissue LMS (n=8) was 6.9 cm (range 3.0–13.5 cm). On MRI (n=8), superficial soft-tissue LMS had well-circumscribed margins and compared with skeletal muscle were isointense on T1-weighted imaging. All the tumors were heterogeneous in signal intensity on T2-weighted imaging except one that was homogeneous in signal intensity. Compared with skeletal muscle and fat (n=7), they were hyperintense (less than fluid) on fat-suppressed T2-weighted imaging. There were iso- to hypointense areas compared with fat on fast spin-echo T2-weighted sequences (n=2; Fig. 3). On post-gadolinium images, 6 out of 8 tumors demonstrated homogeneous enhancement while 2 out of 8 tumors showed heterogeneous enhancement owing to necrosis. Hemorrhage was noted in 3 out of 8 tumors. There was no suggestion of calcification in any of the tumors at MRI, which was confirmed at histopathology. There was edema extending along the adjacent fascial lining in 6 out of 8 tumors, skin contact in 4 out of 8, and skin thickening in 2 out of 8 tumors. There was no deep fascial extension in any of the tumors.

Imaging of local recurrence and metastatic tumors (follow-up imaging)

Thirty-two of the 47 patients developed distant metastases over a median follow-up time of 36 months (range, 7–240 months), 6 of whom also developed local recurrence in addition to distant metastases. Four of these 6 patients with local recurrence had positive margins at primary surgical resection. Locally recurrent tumors were similar to the primary tumors on MRI (n=6) and compared with skeletal muscles, were isointense on T1-weighted imaging and heterogeneously hyperintense on T2-weighted imaging. After gadolinium administration, all the recurrent tumors were seen as heterogeneous, nodular enhancing masses in the surgical bed.

Of the 32 patients with distant metastases, 4 patients had metastases at presentation, while 12 developed metastases within the first year of their diagnosis. The most common sites of metastases were the lung (29, 61.7 %) and bone (14, 29.8 %). Table 1 presents the sites and frequency of metastatic lesions of primary LMS of the extremities. Pulmonary metastases (n=29) were seen as multiple bilateral pulmonary nodules and masses in all the patients except one, who had a solitary metastatic deposit. The mean size of the largest metastatic lesion was 3.0 cm (range: 0.5 cm–7.0 cm). None of the lesions showed cavitation. Skeletal metastases (n=14) were seen as lytic lesions in both the axial and appendicular skeleton except in one patient, who developed a new solitary sclerotic lesion in the iliac bone, presumed to be metastatic from the LMS (not biopsied). Liver metastases (n=11) were multiple in all patients except in one patient who had a solitary hepatic metastatic deposit. On contrast-enhanced CT, the hepatic metastases were hypodense, well-circumscribed intraparenchymal or subcapsular lesions with heterogeneous

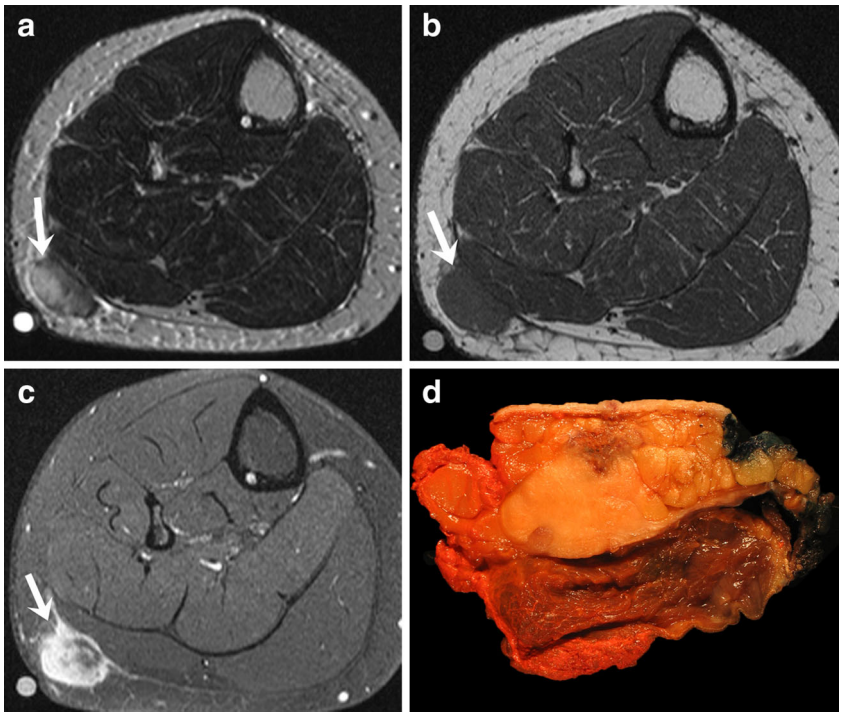

Fig. 3 A 58-year-old woman with superficial soft-tissue leiomyosarcoma. **a**–**c** Axial fast spin-echo T2-weighted, T1-weighted, and post-gadolinium fat-suppressed T1-weighted MR images of the calf demonstrate a well-circumscribed subcutaneous lesion (*arrow*), which is T2 hyperintense and T1 isointense compared with skeletal muscle. The posterior–lateral component of the tumor is low to similar in signal intensity compared with the subcutaneous fat on the T2 sequence. Post-gadolinium images show heterogeneous enhancement. Note the surface marker on the skin overlying the tumor. **d** Gross examination of the surgical resection specimen demonstrates a white mass replacing the subcutaneous adipose tissue, abutting the superficial fascia

enhancement. The mean size of the largest hepatic metastasis was 3.0 cm (range 1.0–5.0 cm). The lung was the first site of metastatic disease in 23 of the 32 patients (72 %). The remaining patients had their first metastases to the liver (n=2), scalp (n=2), peritoneum, bone, intramuscular, paraspinal, and sinonasal tissues (n=1).

All 6 patients (100 %) with primary bone LMS, 18 out of 24 patients (75 %) with deep soft-tissue LMS, and 8 out of 17 patients (47.1 %) with superficial soft-tissue LMS developed metastatic disease. With respect to lung metastases, 5 out of 6 patients with bone tumors, all of the patients with deep soft-tissue tumors, and 7 out of 8 patients with superficial soft-tissue tumors eventually developed lung metastases.

Table 1 Distribution of sites of metastases in extremity leiomyosarcoma (n=47)

Site	Number	Percentage
Lung	29	61.7
Bone	14	29.8
Liver	11	23.4
Muscle	10	21.3
Lymph nodes	9	19.2
Peritoneum	9	19.2
Subcutaneous	6	12.8
Bowel	4	8.5
Pancreas	3	6.4
Spleen	1	2.1
Brain	1	2.1
Scalp	1	2.1
Adrenal	1	2.1
Epidural space	1	2.1

Clinical management and outcome

Four out of 6 patients with primary bone LMS underwent radical excision of the primary tumor. One patient with bone LMS was treated with primary chemo-radiation without excision, while the remaining 1 patient chose not to undergo treatment. Twenty-two out of 24 patients with deep soft-tissue LMS underwent radical excision of the primary tumor, 16 of whom received neoadjuvant radiation therapy. One patient with deep soft-tissue LMS underwent a less extensive debulking palliative surgical procedure with concomitant chemo-radiotherapy, while 1 other patient received palliative chemotherapy for extensive metastatic disease. All 17 patients with subcutaneous lesions were managed with radical excision, 8 of whom received neoadjuvant radiation therapy.

Twenty-two out of 47 patients (46.8 %) had a final outcome of death at a median interval of 36 months (range, 6–228 months) from diagnosis to death. Four of the 6 patients (66.7 %) with primary bone LMS, 15 out of 24 patients (62.5 %) with deep soft-tissue LMS, and 4 out of 17 patients (23.5 %) with subcutaneous LMS had a final outcome of death, with a median time from diagnosis to death of 30 months (range, 18–48 months), 30 months (range, 6–96 months), and 126 months (range, 84–228 months) respectively. There was no statistically significant difference in the

outcome of the bone, deep soft-tissue, and subcutaneous LMS.

Histopathology analysis

Leiomyosarcoma of the extremities were large tumors at histopathology with a median tumor size of 6.0 cm (range, 2–23 cm). As per the FNCLCC grading system [5], 35 out of 47 had high-grade tumors (bone LMS=5; deep soft-tissue LMS=16; superficial LMS=14), 5 out of 47 had intermediate-grade tumors (deep soft-tissue LMS=3; superficial LMS =2), and 2 out of 47 had low-grade tumors (one each deep soft-tissue and superficial LMS). Grade was unavailable in 5 out of 47 patients. The mitotic count ranged between 1 and 79/10 high power fields (HPF; median, 16; mean 22). Overall, 17 tumors had positive margins after primary excision. Correlation of the eventual outcome of death with size showed that 10 out of 16 patients with primary tumors >10 cm (62.5 %) died during follow-up, while 12 out of 31 patients with primary tumors <10 cm (38.7 %) died during follow-up (p >0.05). Correlation of development of metastases with size showed that 11 out of 16 patients with primary tumors >10 cm (68.8 %) developed metastases during follow-up, while 20 out of 31 patients with primary tumors <10 cm (64.5 %) developed metastases during follow-up (p >0.05). There was no significant correlation between tumor grade and development of metastases or death.

Discussion

Leiomyosarcomas are usually reported in the 5th and 6th decade of life [2, 8]. Most of the patients in our study (41 out of 47, 87.2 %) were more than 40 years of age at presentation. Peripheral and extremity LMS, in contrast to uterine LMS, are reported to be common in men. However, there was no sex predilection in our study. The most common sarcomas of the extremities excluding the bone sarcomas are unclassified pleomorphic sarcoma (previously malignant fibrous histiocytoma), liposarcoma, synovial sarcoma, LMS and malignant peripheral nerve sheath tumors [17]. Imaging, especially MRI, and biopsy are often utilized to arrive at a diagnosis and to plan management in extremity soft-tissue sarcomas. We observed three types of LMS of the extremities in our study, namely bone, deep soft-tissue, and superficial soft-tissue LMS. Sundaram et al. found in their study [15] that bone LMS had areas with signal characteristics similar to those of lymphoma, i.e., iso- to hypointense compared with subcutaneous fat on fast spin-echo T2-weighted images. The low signal was attributed to the leiomyosarcomatous histology. The extremity LMS in our study including bone LMS shared this imaging feature, which is most likely attributable to similar histological correlation.

The imaging features of bone LMS in our study were consistent with those of earlier reports [15]. Similar to the study by Sundaram et al., bone LMS in our study were elongated lesions located in the juxta-articular metaphysis with extension into the diaphysis and had no intra-articular extension [15]. Cortical disruption with extension of tumor into the surrounding soft tissues was present in 75 % of cases (3 out of 4) in our series, findings that are similar to those of prior reports by Sundaram et al., who found soft-tissue extension in 66 % of patients with bone LMS [15]. Subperiosteal LMS has been described in the literature, but has not been encountered in any of the cases in our study [18]. The differential diagnoses for bone LMS include lymphoma and metastases. Bone LMS can be difficult to differentiate from lymphoma. In contrast to metastasis, bone LMS were elongated lesions in our study similar to the description by Sundaram et al. [15]. LMS from other sites can metastasize to the extremities; none of the patients in our study had a history of LMS of other sites.

Deep soft-tissue LMS were larger (average size 14.8 cm) than superficial soft-tissue LMS (average size 6.6 cm), heterogeneous in enhancement because of internal hemorrhage (63.6 % versus 37.5 % in superficial soft-tissue tumors) and necrosis (91 % versus 25 % in superficial soft-tissue tumors). Owing to their smaller size at presentation, the subcutaneous tumors were homogeneous in enhancement. The main differential diagnoses for extremity soft-tissue LMS include other sarcomas like liposarcoma, unclassified pleomorphic sarcoma (previously MFH), and synovial sarcoma. Rare extremity tumors like extraskeletal Ewing sarcoma, extraskeletal osteosarcoma, and extraskeletal chondrosarcoma can be considered in the differential diagnosis of extremity soft-tissue LMS [19, 20].

The differential diagnoses for superficial soft-tissue tumors are varied and can range from benign tumors like neurofibromas/schwannomas to malignant tumors like LMS, angiosarcoma, dermatofibrosarcoma, myxofibrosarcoma, and unclassified sarcoma. In the study of 367 patients with superficial soft-tissue sarcomas by Salas et al., LMS was the second most common sarcoma (22 %) following unclassified sarcoma (24 %) [21]. The differentiation between benign and malignant superficial soft-tissue tumors can be difficult. However, Calleja et al., in their study of 136 patients with superficial soft-tissue tumors (74 with malignant tumors [including 5 LMS] and 62 with benign tumors), found that malignant superficial soft-tissue masses were often <5 cm in size and were associated with fascial edema, skin thickening, skin contact, hemorrhage, and necrosis [22]. The mean size of the superficial LMS in our study was slightly larger than in this study (6.9 cm). Hemorrhage was seen in one third of the superficial tumors in our study. Similar to the observation of Calleja et al., most of the superficial LMS in our study were associated with fascial edema, although skin thickening and contact were not constantly seen.

Overall, 32 out of 47 patients (68.1 %) developed metastases, with the lung being the most common site (61.7 %). The next most common locations of metastases were bone (29.8 %), liver (23.4 %), and muscle (21.3 %). The distribution of metastatic sites in patients with LMS of the extremity in our study varied from prior reports of metastases in abdominopelvic LMS, where liver (53 %) and lung (47 %) were the most frequent [12]. This is most likely due to different venous drainage pathways of abdominopelvic and extremity tumors. We observed that the incidence of metastases was lower with the subcutaneous LMS compared with the bone and deep soft-tissue LMS, although this could not be statistically proven. This is consistent with a prior observation by Cany et al., who, in their study of 105 patients with superficial soft-tissue sarcoma (19 % of whom had LMS), concluded that superficial soft-tissue sarcomas carry a low risk of metastases [23]. The lower incidence of metastases was attributed by Salas et al. to the small size and lower grade of superficial soft-tissue sarcomas. Although the overall percentage of metastases was lower in the superficial soft-tissue LMS (49 %) in our study compared with the bone (100 %) and deep soft-tissue (75 %) LMS, this is much higher than that reported by Cany et al. (13.3 %) and Salas et al. (14.4 %) in superficial soft-tissue sarcomas in general, which can be explained by the higher grade and homogeneous population of only LMS (not other soft-tissue sarcomas) in our study [21, 23]. Local tumor recurrence was noted in 6 out of 47 patients in our study and all these patients also had distant metastases. An important risk factor for local tumor recurrence is the presence of positive resection margins, which was noted in 4 out of 6 patients with local recurrence in our study.

The prognosis for LMS is poor. The 2- and 5-year survival in the study by Massi et al. of 42 patients with extremity LMS was 42.3 % and 32.6 % respectively [8]. In our series 22 out of 47 patients (46.8 %) had a final outcome of death at a median interval of 36 months (range, 6–228 months). Patients with subcutaneous LMS had longer median survival in our study (126 months; range, 84–228 months) compared with bone (30 months; range, 18–48 months) and deep soft-tissue LMS (30 months; range, 6–96 months). Several prior studies have shown that tumor size has a significant correlation with decreased survival [8, 9]. Although not statistically significant, the findings in our study are in agreement with those of these prior studies in that there was a higher percentage of deaths (62.5 %) in patients with primary tumors >10.0 cm compared with patients with primary tumors <10.0 cm (38.7 %). There was no statistical significant correlation between metastatic disease and tumor grade or tumor size. Patients with superficial LMS had longer survival in our study, which is likely related to their small size and earlier diagnosis. A similar observation was made in several prior studies. The 5-year overall survival in the study of superficial sarcomas by Salas et al. was 80.9 % compared with 61.4 % for deep soft-tissue tumors in the study by Coindre et al. [21, 24]. In a comparison of the various subtypes of superficial sarcomas, Salas et al. found similar metastasis-free survival and overall survival for patients with LMS, myxofibrosarcoma, and unclassified sarcoma [21]. Angiosarcoma, on the other hand, had worst survival [21].

The major limitation of our study is the retrospective study design. Another limitation was the availability of imaging of the primary tumor prior to treatment in only 23 of the 47 patients. Most of the patients in our series were referred to our tertiary cancer center after the resection of the primary tumor for management of metastatic disease and thus may not be representative of the general spectrum. However, we believe that our study adds to the existing knowledge about the clinical and imaging features of an uncommon malignancy like extremity LMS.

To summarize, we present an imaging series of extremity LMS, highlighting both imaging and clinical features. LMS of the extremities can have low signal areas compared with fat on fast spin-echo T2 sequences, which can be attributed to their leiomyosarcomatous histology. LMS of bone tend to be elongated juxta-articular metaphyseal tumors with a propensity toward cortical destruction. Deep soft-tissue LMS of the extremities tend to be large, well-circumscribed, heterogeneously enhancing tumors, often with hemorrhage and necrosis. Superficial soft-tissue LMS of the extremities are well-circumscribed, relatively small, homogeneously enhancing masses, often associated with fascial edema. The most common sites of metastases in our study were the lung and bone, most commonly from bone and deep soft-tissue extremity LMS. Superficial soft-tissue LMS tend to have better outcome with a lower metastatic rate and longer survival compared with bone or deep soft-tissue LMS.

Conflicts of interest No conflicts of interest.

References

1. Ducimetiere F, Lurkin A, Ranchere-Vince D, et al. Incidence of sarcoma histotypes and molecular subtypes in a prospective epidemiological study with central pathology review and molecular testing. PLoS One. 2011;6:e20294.
2. Kransdorf MJ. Malignant soft-tissue tumors in a large referral population: distribution of diagnoses by age, sex, and location. AJR Am J Roentgenol. 1995;164:129–34.
3. Grossmann AH, Layfield LJ, Randall RL. Classification, molecular characterization, and the significance of pten alteration in leiomyosarcoma. Sarcoma 2012; 2012:380896.
4. Weiss SW. Smooth muscle tumors of soft tissue. Adv Anat Pathol. 2002;9:351–9.
5. Fletcher CD, Hogendoorn P, Mertens F, Bridge J. World Health Organization classification of tumours of soft tissue and bone. World Health Organization; 2013.

6. Hornick JL, Fletcher CD. Criteria for malignancy in nonvisceral smooth muscle tumors. Ann Diagn Pathol. 2003;7:60–6.
7. Coindre JM, Terrier P, Guillou L, et al. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group. Cancer. 2001;91:1914–26.
8. Massi D, Beltrami G, Mela MM, Pertici M, Capanna R, Franchi A. Prognostic factors in soft tissue leiomyosarcoma of the extremities: a retrospective analysis of 42 cases. Eur J Surg Oncol J. 2004;30:565–72.
9. Miyajima K, Oda Y, Oshiro Y, et al. Clinicopathological prognostic factors in soft tissue leiomyosarcoma: a multivariate analysis. Histopathology. 2002;40:353–9.
10. Miettinen M, Fetsch JF. Evaluation of biological potential of smooth muscle tumours. Histopathology. 2006;48:97–105.
11. Colleran G, Madewell J, Foran P, Shelly M, O'Sullivan PJ. Imaging of soft tissue and osseous sarcomas of the extremities. Semin Ultrasound CT MR. 2011;32:442–55.
12. O'Sullivan PJ, Harris AC, Munk PL. Radiological imaging features of non-uterine leiomyosarcoma. Br J Radiol. 2008;81:73–81.
13. Brewer P, Sumathi V, Grimer RJ, et al. Primary leiomyosarcoma of bone: analysis of prognosis. Sarcoma. 2012;2012:636849.
14. Jundt G, Moll C, Nidecker A, Schilt R, Remagen W. Primary leiomyosarcoma of bone: report of eight cases. Hum Pathol. 1994;25:1205–12.
15. Sundaram M, Akduman I, White LM, McDonald DJ, Kandel R, Janney C. Primary leiomyosarcoma of bone. AJR Am J Roentgenol. 1999;172:771–6.
16. Tewfik JN, Greene GS. Fluorine-18-deoxyglucose-positron emission tomography imaging with magnetic resonance and computed tomographic correlation in the evaluation of bone and soft-tissue sarcomas: a pictorial essay. Curr Probl Diagn Radiol. 2008;37:178–88.
17. Tirumani SH, Jagannathan JP, O'Regan K, et al. Molecular targeted therapies in non-GIST soft tissue sarcomas: what the radiologist needs to know. Cancer Imaging. 2013;13:197–211.
18. Narvaez JA, De Lama E, Portabella F, Ortega R, Condom E. Subperiosteal leiomyosarcoma of the tibia. Skeletal Radiol. 2005;34:42–6.
19. Javery O, Krajewski K, O'Regan K, et al. A to Z of extraskeletal Ewing sarcoma family of tumors in adults: imaging features of primary disease, metastatic patterns, and treatment responses. AJR Am J Roentgenol. 2011;197:W1015–1022.
20. McAuley G, Jagannathan J, O'Regan K, et al. Extraskeletal osteosarcoma: spectrum of imaging findings. AJR Am J Roentgenol. 2012;198:W31–37.
21. Salas S, Stoeckle E, Collin F, et al. Superficial soft tissue sarcomas (S-STS): a study of 367 patients from the French Sarcoma Group (FSG) database. Eur J Cancer. 2009;45:2091–102.
22. Calleja M, Dimigen M, Saifuddin A. MRI of superficial soft tissue masses: analysis of features useful in distinguishing between benign and malignant lesions. Skeletal Radiol. 2012;41:1517–24.
23. Cany L, Stoeckle E, Coindre J-M, Kantor G, Bonichon F, Bui BN. Prognostic factors in superficial adult soft tissue sarcomas: analysis of a series of 105 patients. J Surg Oncol. 1999;71:4–9.
24. Coindre JM, Terrier P, Bui NB, et al. Prognostic factors in adult patients with locally controlled soft tissue sarcoma. A study of 546 patients from the French Federation of Cancer Centers Sarcoma Group. J Clin Oncol. 1996;14:869–77.