




Staging and Surveillance of Myxoid Liposarcoma: Follow-up Assessment and the Metastatic Pattern of 169 Patients Suggests Inadequacy of Current Practice Standards

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ABSTRACT

Background. Unlike other sarcoma subtypes, myxoid liposarcoma (MLS) has a propensity for extra-pulmonary metastases. Computed tomography (CT) scan of the chest, abdomen, and pelvis has become an accepted practice for surveillance. However, recent literature suggests that this may be inadequate. This study aimed to assess the ability of current imaging methods to detect metastases adequately in this population.

Methods. The study identified 169 patients with MLS diagnosed between 2000 and 2016. The timing and location of metastases, the reasons leading to the MLS diagnosis, and the imaging methods were recorded. The locations of metastases were classified into the following categories: pulmonary, soft tissue, bone, retroperitoneal, intraperitoneal, solid organ, and lymph node.

Results. An initial diagnosis of metastasis was made at presentation with staging CT scan for 3 (10 %) of 31 patients, with a follow-up surveillance CT scan for 15 (48 %) of the patients or with subsequent imaging obtained in response to patient-reported symptoms for 13 (42 %) of the patients. The proportions of patients who had metastases in each location were as follows: soft tissue (84 %),

pulmonary (68 %), intraabdominal (48 %), solid organ (48 %), bone (45 %), lymph node (32 %), and retroperitoneal (29 %). Although 14 patients had bone metastases, only 1 patient had a sclerotic/blastic presentation visualized on CT scan, and the diagnosis for the remaining 13 patients was determined by magnetic resonance imaging (MRI).

Conclusion. Due to metastatic disease identified outside surveillance imaging for 58 % of the patients, the diversity of locations, and the significant failure of CT and bone scan to identify bone metastases, this study questioned the adequacy of CT scan for surveillance of MLS. Consideration should be given to the use of whole-body MRI for detection of metastasis in MLS.

Soft tissue sarcomas (STSs) are a heterogeneous group of malignant tumors featuring more than 50 different histologic subtypes. Despite the histologic variability between these subtypes, they generally exhibit a similar presentation and pattern of metastasis. Therefore, staging and surveillance practices are similar for most soft tissue sarcomas. Given the propensity of most STSs to metastasize to the lungs, current recommendations include a chest computed tomography (CT) scan at diagnosis for staging and either low-dose CT scan or plain radiographs of the chest for surveillance. The first site of metastasis is the lung in 73% of STS patients,¹ with 52 % of patients having isolated pulmonary lesions.²

Liposarcomas make up 17–25% of all STSs, with four additional sub-classifications defined by the World Health Organization.^{3,4} Myxoid liposarcoma (MLS) represents the

second most common type of liposarcoma,⁵ with a 14–32% risk of metastasis.^{5–7} Unlike most other STSs, MLS is known to have a higher risk of extra-pulmonary metastases, with 14–45% of metastatic disease reported to occur in the lungs, whereas up to 94% are reported to occur in extra-pulmonary sites.^{6–9}

Previous studies have reported the retroperitoneum as the most common location for extrapulmonary metastasis, but other common locations cited include osseous sites (spine), soft tissue (abdominal or chest wall), lymph nodes, and intraabdominal sites.^{5,6,9–11}

The findings of these initial studies have supported using CT of the chest, abdomen, and pelvis for staging and surveillance of patients with myxoid liposarcoma. Although other studies describe a preponderance of spinal metastases in MLS,¹¹ several studies report failure of bone scan, CT scan, and even positron emission tomography (PET)-CT to identify them.^{11–15} Thus, clinical practice guidelines have included consideration of total spine magnetic resonance imaging (MRI) as part of the staging workup for MLS.¹⁶

The variability in location and incidence of metastatic MLS reported throughout the literature highlights the diagnostic challenge of detecting and defining these lesions, suggesting that our current standards of investigation lack accuracy and reliability. The current recommendations for staging and surveillance of MLS remain unclear with regard to the frequency and method of imaging. Furthermore, it is plausible that our current beliefs about the pattern of metastasis in MLS are biased by the imaging methods previously used, with the true behavior of this disease under- or misrepresented.

Although the detection of metastatic disease itself is important for prognosis, understanding the full extent of the disease is imperative when management decisions are being made. For example, in the setting of oligometastatic disease, surgical resection may be considered, and in the setting of vertebral metastatic disease, radiotherapy may be performed to prevent catastrophic neurologic compromise with disease progression. On the contrary, systemic chemotherapy may be recommended instead of aggressive local surgical treatment in the setting of multifocal metastatic disease.

More recently, the use of whole-body MRI (WBMRI) has been proposed for metastatic evaluation in MLS to evaluate appendicular locations of soft tissue and osseous involvement. However, previous studies are small, and to date, neither national nor international cancer protocols have adopted this as standard.^{6,9,17,18} Where insurance/payor approvals are necessary, cost and inefficiency have limited the adoptability of WBMRI in the absence of data providing unequivocal evidence of benefit. Early limitations of WBMRI, including prolonged acquisition

time (longer than 1 h) and five separate scanning levels, have more recently been ameliorated by advances in techniques (addition of turbo spin echo sequences) and modified protocols (rolling platforms in the Z direction).¹⁹ Yet guidelines on the use of the MRI imaging method in surveillance protocols remains ill-defined given the existing literature and limited understanding of metastatic pattern and disease progression in these patients.

This report presents a series of patients with metastatic myxoid liposarcoma from a single institution, highlighting the patterns of metastasis and the imaging methods used for detection. The reported study aimed to assess the ability of current practices for the staging and surveillance of MLS to detect metastatic disease adequately.

METHODS

Using our institution's prospective registry, we identified 169 patients with a diagnosis of myxoid liposarcoma in the extremity or trunk between 2000 and 2016. Institutional review board approval was obtained (#18-0103-C) before commencement of the study.

We included all patients with documented metastasis, and no minimum follow-up time was required. The study identified 32 patients with either metastatic disease at presentation or development of metastatic disease after initial presentation. Only one patient identified from our registry was excluded, due to lack of access to medical records. We then performed a detailed retrospective review of the 31 remaining patients, including both medical notes and imaging reports. Timing, number, and anatomic region of metastatic lesions; reasons leading to diagnosis of metastasis (i.e., routine surveillance, patient-reported symptoms, or incidental finding), and imaging methods used to diagnose the metastasis all were documented.

For the purpose of this analysis, the anatomic regions of metastatic disease were classified into the following categories: pulmonary, soft tissue, bone, retroperitoneal, intraperitoneal, solid organ, and lymph node. Intraperitoneal lesions included masses within the abdominal cavity not arising from an organ or lymph node (LN) and located within the peritoneal cavity, as opposed to in the retroperitoneal space. The individual number of metastatic lesions in each patient was not calculated, and it should be noted that a patient may have had multiple lesions within one given anatomic region (e.g., multiple lesions may have existed within the bone, soft tissue, lungs, and the like). Statistical analysis of metastatic parameters based on round cell classification was performed using Student's *t* test comparison of means and chi-square comparison of percentages.

The imaging methods used for staging and surveillance varied throughout the study and reflected changes in practice over time. All the patients received an initial CT scan of either the chest or the chest, abdomen, and pelvis. Surveillance monitoring typically involved a chest x-ray every 3 months for 2 years, every 6 months for 3 years, and then annually for 10 years. However, some patients underwent CT scanning of the chest or the chest, abdomen, and pelvis for surveillance, again reflecting changes in practice over time.

RESULTS

In our cohort of patients with myxoid liposarcoma, the overall metastatic rate was 20 % (32/169). The average final follow-up period was 73 months from the initial diagnosis (range, 2–182 months). Of the 31 patients in our final cohort, 3 (10 %) had metastases diagnosed at their initial presentation with staging of the CT chest or the CT chest, abdomen, and pelvis, 15 (48 %) had their diagnosis determined on routine imaging at a surveillance follow-up evaluation, and 13 (42 %) had their diagnosis determined outside surveillance from imaging obtained in response to patient-reported symptoms.

The median disease-free survival for the 28 patients with delayed onset of metastases was 44 months (range, 2–143 months). Whereas 17 patients (55 %) had a single anatomic region (as defined in the Methods section) of metastatic disease at initial presentation, 14 (45 %) had multiple anatomic locations of metastatic involvement. At the final follow-up visit, 84 % of the patients had development of disease in multiple anatomic regions, averaging 3.5 regions of disease per patient (range, 1–7).

The proportions of patients with development of metastases in each anatomic region were as follows: soft tissue (84%), pulmonary (68%), intraabdominal (48%), solid organ (48%), bone (45%), lymph node (32%), and retroperitoneal (29%) (Table 1). We saw no significant difference in the presentation of metastasis in tumors with a round cell component, but we did see a trend toward increased metastatic spread to the retroperitoneum and lymph nodes (Table 2). Of the 31 patients with metastases, only 5 (16%) initially presented with pulmonary-only disease. Only two (6%) of the patients remained with pulmonary metastasis alone at the final follow-up evaluation.

Of the 17 patients presenting with one anatomic site of disease, soft tissue was the most common first site of disease spread, observed in 7 (41%) of the 17 patients. Six of these patients (35%) did not have their diagnosis determined on routine imaging. One lymph node metastasis, one bone metastasis, and three soft tissue metastases were

diagnosed with MRI, and one soft tissue metastasis was diagnosed with a neck CT as a result of patient-reported symptoms. When all sites of metastases in all the patients were considered, the most common location of metastasis from self-reported symptoms was soft tissue (67 %).

On further investigation, only 10 patients had true oligometastatic disease. Of these 10 patients, 5 (50%) presented with tumors in the soft tissues, making it the most common anatomic region for true oligometastatic presentation compared with 30% (3/10) of the patients presenting with pulmonary oligometastatic disease. Of the 10 patients with oligometastasis at presentation, 8 underwent resection. A second metastasis was noted in six patients (75%) an average of 8.8 months after surgery. Five patients died of their disease an average of 33 months after resection. The remaining three patients were alive at the most recent follow-up visit respectively 30, 42, and 60 months after metastatic presentation.

The most common location of metastasis diagnosed incidentally (asymptomatic and outside staging/surveillance imaging) was bone (92%). The study had 14 patients with bone metastases, but only 1 of these patients with a sclerotic/blastic presentation was identified on CT scan. The bone metastases of the remaining 13 patients were diagnosed on MRI. Of particular interest, 12 of these 13 patients had a CT scan, and 7 also had a bone scan within 1 month after the diagnostic MRI (average, 13 days for CT and 11 days for bone scan), all of which reported “no evidence of bone metastasis.” One patient had no prior imaging of the affected location for comparison. Furthermore, all subsequent CT scans performed after diagnosis of bone metastases failed to demonstrate bone involvement. This indicates the futility of CT and bone scan in terms of their ability to diagnose bone metastases in myxoid liposarcoma. The disease was noted in 9 (64%) of the 14 patients with bone metastasis at the time of the initial metastatic diagnosis, and in the remaining 5 patients an average of 5.5 months after the initial metastatic diagnosis. This suggests early involvement of the skeleton when myxoid liposarcoma metastasizes, but given the inability of the staging/surveillance CT scans to diagnose these lesions at initial occurrence, further conclusions on this are limited.

In a close review of the imaging of patients for whom both CT scan and MRI were obtained, we identified many lesions initially reported as soft tissue masses on CT scan that subsequent MRI identified as primarily a bone metastasis with soft tissue extension. Examples include paravertebral and mediastinal soft tissue masses reported on CT that later were demonstrated to be vertebral bone lesions with soft tissue extension into the paravertebral or mediastinal spaces, pelvic retroperitoneal soft tissue masses later described as iliac bone lesion with soft tissue retroperitoneal extension, and chest wall soft tissue mass

TABLE 1 Classification of metastatic locations in myxoid liposarcoma displayed as number of patients with metastatic deposit in a given anatomic location^a

Location of metastasis	No. of patients (<i>n</i> = 31) <i>n</i> (%)	Description
Soft tissue (ST)	26 (84)	Abdominal/chest wall (15) Pelvis (11) Lower extremity (8) Back/paraspinal (6) Mediastinal (6) Upper extremity (2)
Pulmonary	21 (68)	
Intraabdominal	15 (48)	
Solid organ	15 (48)	Liver (6) Heart (4) Pancreas (4) Brain (1) Adrenal (1) Colon (1)
Bone	14 (45)	Spine (13) Pelvis/sacrum (10) Long bone (7) Other (3)
Lymph node	10 (32)	
Retroperitoneal	9 (29)	

^aMost of the patients had multiple sites of metastasis

TABLE 2 Distribution of metastasis by round cell classification

	Round cell (<i>n</i> = 12) <i>n</i> (%)	Non-round cell (<i>n</i> = 19) <i>n</i> (%)	<i>p</i> value
Average DFS (months)	38	54	0.3052
Average no. of metastases locations	3.41	3.45	0.7585
<i>Location of metastasis</i>			
Soft tissue	8/12 (67)	16/19 (84)	0.2780
Pulmonary	8/12 (67)	13/19 (65)	0.9105
Intraabdominal	8/12 (67)	10/19 (53)	0.4486
Solid organ	8/12 (67)	9/19 (47)	0.2837
Bone	6/12 (50)	8/19 (42)	0.6680
LN	8/12 (67)	7/19 (37)	0.1093
Retroperitoneal	8/12 (67)	6/19 (32)	0.0608

DFS disease-free survival, LN lymph node

later described as a rib bone lesion with soft tissue extension into the chest wall. Four of the patients with vertebral bone metastasis required urgent decompression upon identification due to cord compression from epidural extension.

Case Examples

Case 1. This case involved the status of a 46-year-old man after resection of a right popliteal fossa myxoid

liposarcoma. Initial staging with CT chest showed no evidence of metastatic disease. The man presented 5 years later with pain and a palpable mass in the right groin. An MRI was obtained, which confirmed a soft tissue mass in the groin consistent with metastatic disease. The MRI also showed multiple sites of bony metastatic disease (pelvis, femur, spine with epidural soft tissue extension) that were asymptomatic. A CT scan of the chest, abdomen, and pelvis and a whole-body bone scan, performed within 3 and

7 days, respectively, were reported without evidence of bony metastasis (Fig. 1a–c).

Case 2. This case involved the status of a 51-year-old man after resection of a left thigh myxoid liposarcoma. Initial staging with CT scan of the chest, abdomen, and pelvis showed no evidence of metastatic disease. As part of routine surveillance 2 years later, a CT scan of the chest was ordered, which showed paravertebral and mediastinal soft tissue masses without evidence of bony metastatic disease. A whole-body bone scan was additionally performed, which also was reported without evidence of skeletal metastasis. An MRI 10 days later showed diffuse evidence of bony metastatic disease throughout the vertebral column, with epidural extension and spinal cord compression. Mediastinal and paravertebral masses identified on the CT scan were now noted to be soft tissue extensions from vertebral bone metastases (Fig. 2a–d).

DISCUSSION

Myxoid liposarcoma is a common subtype of a rare malignancy. Treatment generally involves surgical excision in cases of localized disease. Because this tumor is highly radiosensitive, preoperative radiation frequently is used to shrink the tumor and facilitate surgical resection. With combined treatment, local recurrence is extremely rare, and most patients are cured.²⁰

The vast majority of metastases in most soft tissue sarcomas occur in the lung. Our results further demonstrate that myxoid liposarcoma has a significant propensity for extra-pulmonary metastases. Previous studies have suggested the retroperitoneum and spinal vertebra as other locations of extra-pleural metastasis. As a result, CT scan

of the chest, abdomen, and pelvis and MRI of the spine have been recommended for staging and surveillance by the National Comprehensive Cancer Network.¹⁶ Yet, no standard of care exists for the timing and type of imaging surveillance in MLS, and concerns remain regarding the adequacy of current protocols and lack of extremity imaging. Although some centers specializing in soft tissue sarcoma care are using WBMRI for staging and surveillance for some patients, the ability to adopt these protocols generally for this disease group is limited by the paucity of data in the literature to support the need. As a result, national and international cancer guidelines have not recognized WBMRI as a standard of care, and thus support for insurance/payor approval continues to be a significant barrier. This report presents the largest cohort of patients with myxoid liposarcoma published to date, providing granular detail on the presentation of their metastatic disease.

The results of our study provide a detailed description of the location and timing of metastasis in myxoid liposarcoma and challenge current surveillance protocols. First, the pattern of metastases we see in this cohort is highly variable, supporting the need for staging and surveillance imaging with high sensitivity and a wide field of view. Many of the patients in our cohort (48%) displayed multiple different locations of metastatic disease at initial presentation, and two patients had pulmonary-only metastases, suggesting that our current protocols of chest-only imaging or chest, abdomen, and pelvis CT result in inadequate surveillance of metastatic disease. Additionally, 42% of the patients in this study had their metastatic disease diagnosed outside of routine surveillance, again suggesting that our current protocols are inadequate.

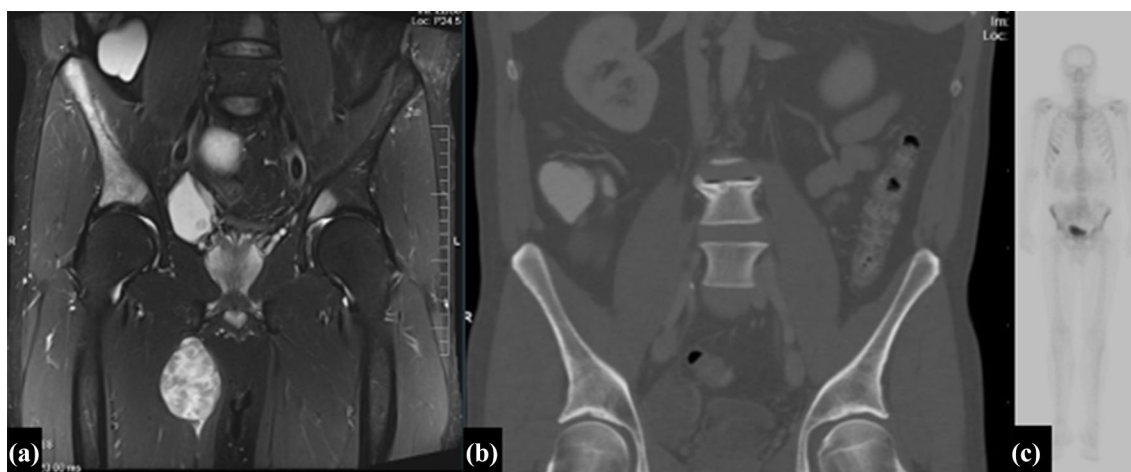


FIG. 1 Representative images from case 1. **a** Coronal T2-weighted magnetic resonance imaging (MRI) of the pelvis showing multiple areas of metastatic disease including the inciting soft tissue mass in the groin and multiple soft tissue and intraosseous lesions in the

pelvis. **b** Coronal computed tomography (CT) scan of the abdomen/pelvis and **c** whole-body bone scan without evidence of bony metastatic disease

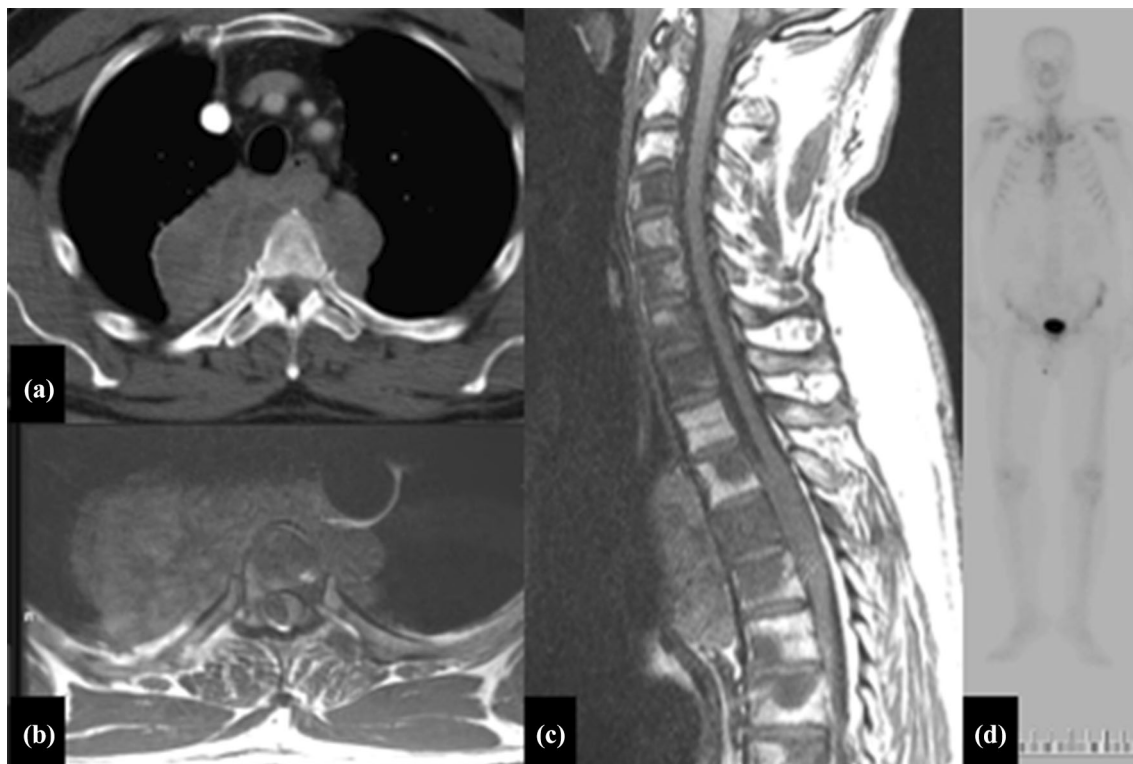


FIG. 2 Representative images from case 2. **a** Axial computed tomography (CT) scan of the chest showing a large mediastinal mass concerning for soft tissue metastasis without evidence of intraosseous metastasis. **b, c** Axial and sagittal T1-weighted images from spine

magnetic resonance imaging (MRI) showing diffuse intraosseous vertebral metastasis with epidural and mediastinal soft tissue extension. **d** Whole-body bone scan unable to detect intraosseous metastasis reported with no evidence of bony metastatic disease

When the study focused on the location of metastasis, it highlighted many important things. First, although 68% of the patients had evidence of pulmonary metastasis, only 16% (5/31) of the patients had pulmonary-only involvement at the initial metastatic discovery. Furthermore, even this is likely an overestimation because two of the five patients were found to have soft tissue metastasis outside the initial imaging field only 2 and 5 months after diagnosis of pulmonary metastasis. Thus, it is unlikely that these patients truly had isolated pulmonary metastasis at discovery. These findings suggest that pulmonary metastasis actually occurs later in the disease process than metastasis at other sites.

Second, the most common location of metastasis was within the soft tissues. However, the true incidence of soft tissue metastasis is unclear because many of the lesions identified on CT actually may be soft tissue extensions of bony metastasis, and extremity soft tissue metastases are likely underreported because the extremities were imaged only in the setting of symptomatic lesions.

Third, intraosseous metastasis was seen in 45% of the patients. It also is likely underrepresented in this cohort and underdiagnosed in the entire myxoid liposarcoma population. The majority of bone metastases (93%) were missed

on surveillance CT imaging. Only one patient presented with a sclerotic pattern of bone metastasis that was identified on CT scan. The remainder of the intraosseous lesions had preserved cortical and intramedullary trabecular patterns of bone, even in the common setting of significant associated soft tissue extension. This absence of bone destruction and turnover explains the inability of bone scan to identify these lesions. Of particular note, 71% of the patients with osseous metastasis were identified incidentally, and 50% of the patients were noted to have long bone involvement. This suggests a delay in diagnosis and under-estimation of bone metastasis in patients with myxoid liposarcoma. Additionally, intraabdominal and various solid organ sites of metastasis were observed in nearly half of the patients. Lymph node metastasis was identified in 32% of the patients, which was not restricted to the sentinel extremity location, but rather included many distant locations.

Finally, contrary to expectations, retroperitoneal metastasis represented the least frequent location of metastatic spread.

Although it is well known that unlike other sarcomas, myxoid liposarcoma has a propensity for extra-pulmonary metastases, our results suggest that routine CT scan of the

chest, abdomen, and pelvis is not sufficient for evaluation of metastatic disease in this population. Additionally, given the high rates of extremity osseous and soft tissue involvement (which again still likely is underreported given the lack of routine extremity imaging), adding an MRI of the spine alone likely remains insufficient.

With 58% of patients having metastatic disease identified outside surveillance imaging, with the diversity of metastatic locations, and with the significant failure of CT and bone scan to identify bone metastases, this study calls into question the adequacy of the current protocols. Furthermore, the heterogeneity and paucity of extremity imaging performed for patients with myxoid liposarcoma also may contribute to a delay in diagnosis for many patients. Our results support a recent report by Stevenson et al.¹⁴ showing the inadequacy of axial CT scans in identifying metastatic MLS lesions. Additionally, the results show that 43% (3/7) of patients had metastatic disease found exclusively on MRI, with direct effects on management.

Various methods of imaging have been used and compared for their ability to detect metastatic bone lesions. Findings have shown that MRI can identify intramedullary osseous metastasis in advance of the cortical matrix destruction or pathologic osteoblastic process visualized on nuclear medicine bone scan.²¹ The MRI procedure exploits the atomic differences between fat composition and water due to the relatively long coherence time of protons in water. In the setting of tumorigenic edema, increased interstitial fluid present in the bone marrow space manifests as hyperintense signal on T2-weighted images. Additionally, the infiltration of the normal fatty marrow content by neoplastic disease results in a hypointense signal in the bone marrow on T1-weighted images. The ability of MRI to visualize alterations in fat composition and interstitial fluid within bone marrow is singular among current imaging methods.¹⁹

The propensity of myxoid liposarcoma to metastasize to bone¹⁷ coupled with the multiple case reports of occult metastatic MLS bone lesions subsequently diagnosed on MR^{12,22-26} is troubling. One prospective study of patients with myxoid liposarcoma found that CT scan was able to detect only 14% of the patients with osseous metastatic disease diagnosed on MRI, with radiographs and bone scintigraphy also far less sensitive.²⁷

Additional studies have supported this concern, demonstrating low or no avidity of MLS bone metastases on nuclear medicine bone scan or fluorodeoxyglucose (FDG)-PET scan,^{15,21,22,27-30} resulting in false-negative results.³¹ Some of these findings may be explained by the low glucose uptake of myxoid liposarcoma,²⁹ with this liposarcoma subtype having a low standard uptake value (SUV) maximum of 2.3 ± 1.7 .²⁸

Additionally, as evidenced in this study, the bony metastasis of myxoid liposarcoma tends to replace the marrow space and develop extra-osseous soft tissue extension without osteolytic destruction of the bony architecture or induced reactive osteoblastic sclerosis as would be evidenced on CT or bone scan. The preponderance of data in addition to this report outlining the common occurrence of soft tissue and osseous metastatic involvement suggests that MRI is the more appropriate imaging method when clinicians are evaluating for myxoid liposarcoma osseous metastatic disease.

The number of patients with oligometastatic disease in the current cohort was small, and given the inadequacies highlighted by this study of current surveillance protocols to detect early disease, it is possible that even the initial classification of patients in this study as oligometastatic may have been inaccurate. However, these data certainly suggest that pulmonary and retroperitoneal locations, as previously thought, are not the most common sites of disease nor the most common initial locations of metastatic presentation. Although one third of the oligometastatic disease in this study was noted to be in the lungs, a soft tissue location was more common as the initial presentation of metastatic disease in half of the patients. Moreover, soft tissue also was the most common anatomic region for metastasis in the patients overall, suggesting the early occurrence of soft tissue metastases in the course of systemic spread of myxoid liposarcoma.

Defining the occurrence and extent of metastatic disease in sarcoma patients is paramount. Standard treatment for myxoid liposarcoma is neoadjuvant radiation followed by wide local resection. However, in the setting of metastatic disease, surgery of the primary tumor, especially if there is significant surgical risks or associated morbidity, may be deferred given the disseminated nature of the disease at presentation. Due to the significant effectiveness of radiotherapy in myxoid liposarcoma (in contrast to most other sarcoma subtypes), this may serve as an attractive alternative option for local control in such a patient. Additionally, defining the presence of metastasis at any point in the disease course (at presentation or postoperative surveillance) is important from both a prognostic and therapeutic perspective. In the setting of oligometastatic disease, aggressive management with metastasectomy may be performed. It is difficult to determine which individual patients will have survival benefit from this, but confirming the absence of other disease sites and defining the disease-free interval are an important part of this decision-making. For a patient with multifocal metastatic disease, systemic chemotherapy would likely be considered, and thorough imaging of disease sites would be necessary for monitoring of the therapeutic response. Furthermore, early identification of lesions with the potential to cause morbidity,

especially in the spine and long bones, allows treatment with radiotherapy to avoid catastrophic complications. Thus, adequate staging and surveillance protocols are of utmost importance to determine the most appropriate treatment plan for the patient, and ability to study how the type and timing of various interventions may improve morbidity and mortality.

Of the patients undergoing presumed oligometastectomy in this study, 75% had further disease progression. For 83% of these patients, the progression occurred within 1 year, and 50% experienced progression within 6 months after surgery. The remaining three patients were alive respectively 2.5, 3.5, and 5 years later.

Drawing conclusions on the survival benefit of resecting oligometastases, however, is challenged by the small numbers of patients studied and the potential that some patients undergoing resection may have been misclassified as oligometastatic given inadequate staging protocols. Additionally, the study may have included other patients who could have benefited from early diagnosis and aggressive management with metastasectomy if our protocols had been sensitive enough to define these patients at oligometastatic presentation. This further supports the importance of improved imaging and surveillance protocols to understand the true extent of disease in a given patient, avoiding surgery for patients with multiple sites of disease and identifying the oligometastasis at earlier time points when they occur. Only with such improvements will we be able to reach evidence-based conclusions regarding the true outcomes from resection of oligometastatic disease.

This study had some limitations, particularly the small sample given the rarity of this disease. We were unable to detect statistical differences in the metastatic patterns of tumors with and without the round cell component or to compare survival outcomes after oligometastectomy. Given that we were reviewing patients with existing metastatic disease, we did not require a minimum follow-up period, and thus the conclusions regarding overall rates of metastasis and survival outcomes are limited. Additionally, because many patients in this cohort were identified with multiple sites of disease at their initial presentation of metastasis, we are unable to define the true sequence of metastases development. However, this does highlight that we are diagnosing metastasis in our patients at a later stage in the disease process and likely underestimating the true extent of their disease earlier in its course. This is crucial when metastasectomy is considered in the setting of presumed oligometastatic disease, and catastrophic neurologic complications are prevented, as seen in our cohort with spinal metastases, especially considering the significant radiosensitivity of MLS.¹¹

These findings support the need for further research to determine the ideal imaging method and schedule for staging and surveillance of myxoid liposarcoma, with consideration of whole-body MRI for screening of bone and extremity soft tissue metastases.¹⁷ As a result of this study and consistent emerging data from others, we have adopted a limited-sequence, T2-weighted, whole-body MRI screening protocol at our institution. However, further information is needed to determine the most appropriate surveillance schedule.

DISCLOSURE There are no conflicts of interest.

REFERENCES

1. Billingsley KG, et al. Multifactorial analysis of the survival of patients with distant metastasis arising from primary extremity sarcoma. *Cancer*. 1999;85:389–95.
2. Potter DA, et al. Patterns of recurrence in patients with high-grade soft tissue sarcomas. *J Clin Oncol*. 1985;3:353–66.
3. Dodd LG. Update on liposarcoma: a review for cytopathologists. *Diagn Cytopathol*. 2012;40:1122–31.
4. Jo VY, Fletcher CD. WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition. *Pathology*. 2014;46:95–104.
5. Lemeur M, et al. Prognostic factors for the recurrence of myxoid liposarcoma: 20 cases with up to 8 years follow-up. *Orthop Traumatol Surg Res*. 2015;101:103–7.
6. Muratori F, et al. Myxoid liposarcoma: prognostic factors and metastatic pattern in a series of 148 patients treated at a single institution. *Int J Surg Oncol*. 2018;2018:8928706.
7. Haniball J, et al. Prognostic factors and metastatic patterns in primary myxoid/round-cell liposarcoma. *Sarcoma*. 2011;2011:538085–538085.
8. Pearlstone DB, et al. Patterns of recurrence in extremity liposarcoma: implications for staging and follow-up. *Cancer*. 1999;85:85–92.
9. Fuglo HM, et al. Metastatic pattern, local relapse, and survival of patients with myxoid liposarcoma: a retrospective study of 45 patients. *Sarcoma*. 2013;2013:548628.
10. Schwab JH, et al. Skeletal metastases in myxoid liposarcoma: an unusual pattern of distant spread. *Ann Surg Oncol*. 2007;14:1507–14.
11. Schwab JH, et al. Spinal metastases from myxoid liposarcoma warrant screening with magnetic resonance imaging. *Cancer*. 2007;110:1815–22.
12. Conill C, et al. Diagnostic efficacy of bone scintigraphy, magnetic resonance imaging, and positron emission tomography in bone metastases of myxoid liposarcoma. *J Magn Reson Imaging*. 2008;27:625–8.
13. Durr HR, et al. Myxoid liposarcoma: local relapse and metastatic pattern in 43 patients. *BMC Cancer*. 2018;18:304.
14. Stevenson JD, et al. Whole-body magnetic resonance imaging in myxoid liposarcoma: a useful adjunct for the detection of extrapulmonary metastatic disease. *Eur J Surg Oncol*. 2016;42:574–80.
15. Sheah K, et al. Metastatic myxoid liposarcomas: imaging and histopathologic findings. *Skeletal Radiol*. 2008;37:251–8.
16. von Mehren M, et al. Soft tissue sarcoma, version 2.2018, NCCN clinical practice guidelines in oncology. *J Natl Compr Cancer Neww*. 2018;16:536–63.

17. Gorelik N, et al. Early detection of metastases using whole-body MRI for initial staging and routine follow-up of myxoid liposarcoma. *Skeletal Radiol.* 2018;47:369–79.
18. Seo SW, et al. Feasibility of whole-body MRI for detecting metastatic myxoid liposarcoma: a case series. *Orthopedics.* 2011;34:e748–54.
19. Hynes JP, et al. Whole-body MRI of bone marrow: a review. *J Magn Reson Imaging.* 2019;50:1687–701.
20. Chung PWM, et al. Radiosensitivity translates into excellent local control in extremity myxoid liposarcoma: a comparison with other soft tissue sarcomas. *Cancer.* 2009;115:3254–61.
21. Papageorgiou I, et al. Whole-body MRI: a powerful alternative to bone scan for bone marrow staging without radiation and gadolinium enhancer. *Clin Transl Oncol.* 2020;22:1321–8.
22. Ishii T, et al. Unusual skeletal metastases from myxoid liposarcoma only detectable by MR imaging. *Eur Radiol.* 2003;13(Suppl 4):L185–91.
23. Lin S, et al. Metastasis of myxoid liposarcoma to fat-bearing areas: a case report of unusual metastatic sites and a hypothesis. *Oncol Lett.* 2015;10:2543–6.
24. Schwab JH, Healey JH. FDG-PET lacks sufficient sensitivity to detect myxoid liposarcoma spinal metastases detected by MRI. *Sarcoma.* 2007;2007:36785.
25. Sakamoto A, et al. Myxoid liposarcoma with negative features on bone scan and [18F]-2-fluoro-2-deoxy-D-glucose-positron emission tomography. *World J Surg Oncol.* 2012;10:214.
26. Lee SY, et al. Myxoid liposarcoma involving the liver, subcutaneous tissue, and epidural space in a polycystic disease patient. *Clin Nucl Med.* 2008;33:507–9.
27. Noble JL, et al. Imaging of skeletal metastases in myxoid liposarcoma. *Sarcoma.* 2010;2010:262361.
28. Brenner W, et al. Risk assessment in liposarcoma patients based on FDG PET imaging. *Eur J Nucl Med Mol Imaging.* 2006;33:1290–5.
29. Sambri A, et al. The role of 18F-FDG PET/CT in soft tissue sarcoma. *Nucl Med Commun.* 2019;40:626–31.
30. Eustace S, et al. A comparison of whole-body turboSTIR MR imaging and planar 99mTc-methylene diphosphonate scintigraphy in the examination of patients with suspected skeletal metastases. *AJR Am J Roentgenol.* 1997;169:1655–61.
31. Schwarzbach MH, et al. Assessment of soft tissue lesions suspicious for liposarcoma by F18-deoxyglucose (FDG) positron emission tomography (PET). *Anticancer Res.* 2001;21:3609–14.

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