Surgical Management of Metastatic Disease

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KEYWORDS

• Soft tissue sarcoma • Metastatic sarcoma • Liver metastasis
• Pulmonary metastasis • Metastasectomy

KEY POINTS

- The lung and liver are the most common sites of metastasis in sarcoma.
- First-line treatment of metastatic sarcoma is chemotherapy. In appropriate patients, sarcoma metastasectomy may be considered and may prolong survival in those with good performance status, longer disease-free interval between resection of primary tumor and appearance of metastatic disease, and oligometastasis, and when complete resection can be achieved.
- There is an extensive body of retrospective data on the surgical management of pulmonary sarcoma metastases. There are sparse retrospective data on the surgical management of hepatic sarcoma metastases and there is no consensus on the role of surgery.
- Additional local treatment modalities include radiation therapy and ablative techniques.
- Patients with soft tissue and bone sarcomas should be referred to specialty sarcoma centers and treatment decisions made in conjunction with a multidisciplinary team of medical, radiation, and surgical oncologists who specialize in the care of such patients.

INTRODUCTION

Sarcomas, including soft tissue sarcomas (STSs) and bone sarcomas, are rare cancers of mesenchymal cell origin that include more than 50 histologic subtypes and many more molecularly distinct entities.[1–3] After gastrointestinal stromal tumors (GISTs), (the management and survival outcomes of which have improved greatly following the introduction of targeted tyrosine kinase inhibitor [TKI] therapies), the next most common subtypes of STS are liposarcoma and leiomyosarcoma. The annual incidence of STS ranges from 2.4 to 3.6 new cases per 100,000 in population-based studies.[4] The American Cancer Society estimates that 12,310

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Surg Clin N Am 96 (2016) 1175–1192
http://dx.doi.org/10.1016/j.suc.2016.05.010 surgical.theclinics.com
0039-6109/16/$ – see front matter

new cases of STS will be diagnosed and 4990 patients will die in 2016 in the United States alone.[5] Despite treatment, approximately 50% of patients with STS are diagnosed with or develop distant metastatic STS (mSTS), reducing their 5-year overall survival (OS) to less than 10% and their median OS to approximately 8 to 15 months.[2,6]

For primary resectable STS, surgery is the mainstay of treatment. However, for patients with mSTS, systemic therapy with conventional chemotherapy remains the primary treatment modality. Increased OS has been achieved in some patients who receive multimodality therapy, including surgery, for their metastatic disease. Thus, patients with mSTS should be evaluated and managed by a multidisciplinary team of medical, radiation, surgical, thoracic, and orthopedic oncologists specializing in the treatment of STS.

This article provides an overview of the multimodality therapies for metastatic sarcoma, including chemotherapy, radiation therapy, and ablative techniques, with an emphasis on surgical metastasectomy for mSTS.

DIAGNOSIS AND PATTERN OF METASTATIC SOFT TISSUE SARCOMA

The probability of distant metastases from STS depends on primary tumor grade, size, depth of location, and whether it is recurrent disease or not. High-grade STS tends to metastasize more frequently than low-grade tumors and earlier in the clinical course.[2]

The lungs and liver are by far the most common sites of distant mSTS, with primary STS site influencing the pattern of metastasis.[7] Jaques and colleagues[7] reported that the proportion of lung/liver as a site of distant spread from a primary extremity sarcoma is 75:1, in contrast to primary retroperitoneal sarcoma, in which the ratio is 1:1.5, and visceral sarcomas in which the ratio is 1:10.

Leiomyosarcomas tend to show a higher rate of metastasis to the lungs, liver, and soft tissues. Metastases to bone are more often detected in myxoid round cell and metastatic dedifferentiated liposarcoma. Lymph node metastases are rare events, present in only 2.6% to 16% of all patients with STS.[6] Clear cell sarcoma, epithelioid sarcoma, and synovial sarcoma metastasize to lymph nodes in up to 10% of cases. Soft tissue metastasis usually presents as a late event associated with widely disseminated disease.[6] Brain metastases are uncommon in adult STS (1%); however, children with Ewing sarcoma or osteosarcoma are more often affected.[2]

Thus, distant staging of STS should include high-resolution contrast-enhanced chest computed tomography (CT) for moderate and high-grade tumors to evaluate for pulmonary metastases, and abdominal CT to evaluate for intra-abdominal metastases. Paraspinal MRI may be necessary in cases of myxoid liposarcoma because of its tendency to develop extrapulmonary metastases in this area.[8] PET imaging may be considered to identify additional sites of metastasis outside the lung in specific circumstances.

THE ROLE OF METASTASECTOMY FOR SARCOMA

In select patients with limited metastatic disease, multimodality treatment including surgical metastasectomy has been shown in some retrospective series to offer longer median OS after diagnosis of mSTS (33–39 months) and 5-year OS (30%–50%) compared with historical controls.[1,3,4,9–12] However, there are no randomized trials or prospective data available to establish standards of care for treatment sequencing in patients with potentially resectable mSTS.[13] Most studies evaluating the role of metastasectomy in patients with mSTS have focused on pulmonary metastasectomies with limited studies on hepatic resection.