CASE REPORT

Cerebellar, Pancreatic, and Paraspinal Metastases in Soft Tissue Sarcomas: Unusual Sites or Changing Patterns?

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ABSTRACT

Context Soft tissue sarcomas generally first metastasize to the lungs followed by the involvement of other sites such as lymph nodes and bones as part of the disseminated disease. Cerebellar and pancreatic metastases from tumors of mesenchymal origin such as soft tissue sarcomas are exceptional, more so in the absence of pulmonary metastases.

Case report A previously treated case of chest wall sarcoma presented with the sudden onset of neurological symptoms. An MRI brain scan was suggestive of a solitary cerebellar metastasis. A CT scan of the thorax and abdomen showed no evidence of disease. A metastasectomy of the solitary brain lesion confirmed a deposit from a previously treated sarcoma. Within two months he presented with central abdominal pain and low backache radiating down both lower limbs. FDG-PET and CT scans revealed a large pancreatic and left paraspinal mass with intense tracer uptake suggestive of metastatic involvement. There was no evidence of pulmonary metastases. A CT-guided biopsy was suggestive of high-grade sarcoma. He was treated with palliative radiotherapy with good symptomatic relief.

Conclusion Cerebellar, pancreatic, and paraspinal metastases from soft tissue sarcomas are rare, especially in the absence of pulmonary metastases. A high index of suspicion is necessary, and appropriate imaging should be considered for symptomatic patients.

INTRODUCTION

Soft tissue sarcomas (STSs) are relatively rare neoplasms, comprising less than 1% of all adult solid tumors. Approximately 60% of STSs occur in the extremities, mainly the lower limb. Primary STSs of the chest wall are even rarer and are usually classified as truncal sarcomas. Distant metastases occur in almost 25-30% of patients with STSs, with the vast majority preferentially metastasizing to the lungs which is the first site of recurrence in 80% of patients [1, 2]. Cerebellar, pancreatic and paraspinal metastases in the absence of pulmonary metastases are exceptional events in the natural history of mesenchymal neoplasms. The increasing use of systemic chemotherapy in the initial management of high-grade STSs may have led to an improvement in survival which could potentially provide an opportunity for metastatic involvement of unusual sites [3]. This is a report on a patient with a previously treated chest wall sarcoma who presented with a cerebellar metastasis as first site of recurrence followed by pancreatic and paraspinal metastases, without any evidence of pulmonary metastases. The purpose of this report is to increase awareness amongst clinicians regarding the possibility of unusual and changing patterns of metastatic involvement in soft tissue sarcomas.
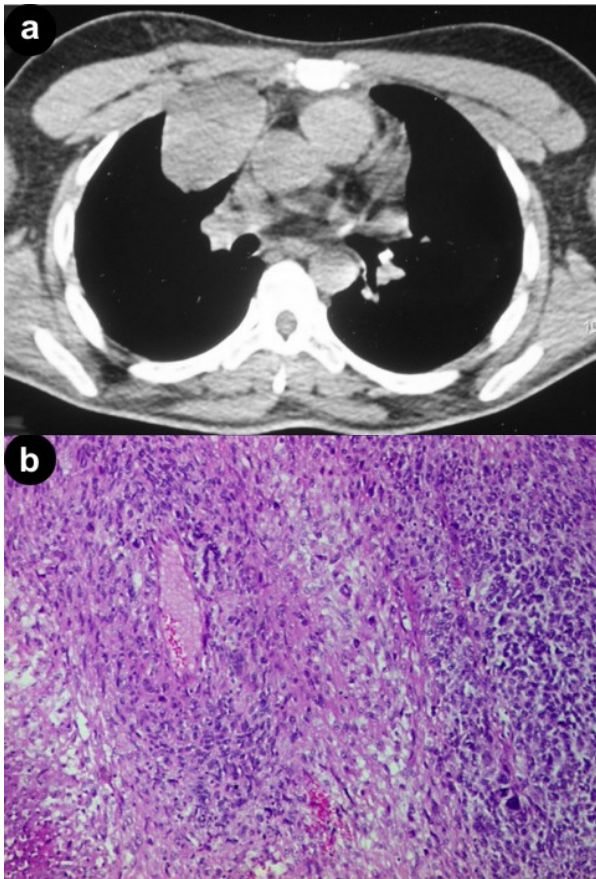
Figure 1. A CT scan of the thorax (**a.**) showing the chest wall primary lesion, and microphotograph (**b.**) of CT-guided biopsy from the lesion showing high-grade spindle cell sarcoma (H&E stain, 10x).

CASE REPORT

A 37-year-old man presented with a swelling of the right-side of the chest wall of three-month duration. A CT scan of the thorax revealed a large, well-defined soft tissue mass measuring 5x4x3 cm arising from the muscles of the second intercostal space but not breaching the pleura (Figure 1a). A CT-guided biopsy showed high-grade spindle cell sarcoma (Figure 1b). His metastatic work-up was negative. He subsequently underwent wide local excision of the tumour with negative surgical margins. The final surgical pathology was suggestive of a pleomorphic high-grade spindle cell sarcoma of uncertain histogenesis. It stained positive for smooth muscle antigen, vimentin, and Wilm's tumor 1 on immunohistochemistry. The patient received post-operative adjuvant radiotherapy of the tumor bed and remained locally controlled on regular follow-up. Two years

later, he presented with sudden onset headache, vomiting, blurred vision and diplopia. An MRI of the brain showed a large cystic lesion in the left cerebellar hemisphere with perifocal edema, mass effect and rim enhancement suggestive of a solitary brain metastasis (Figure 2a). At that time, a CT scan of the thorax and abdomen showed no evidence of either a local recurrence or any other site of distant metastasis. The patient was initially treated with whole brain radiotherapy at a dose of 30 Gy in 10 fractions, which was followed by a metastasectomy of the cerebellar lesion. This was reported as a poorly differentiated high-
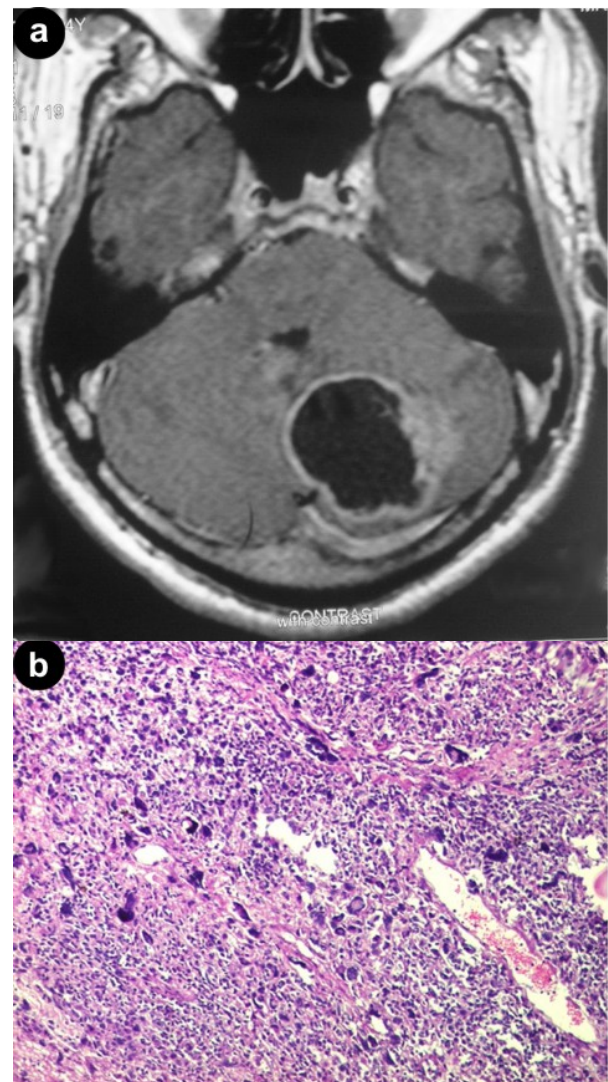

Figure 2. Axial view of T1-weighted post-gadolinium MRI (**a.**) showing cerebellar metastasis and microphotograph (**b.**) of the cerebellar metastasis showing spindle cells consistent with deposits from sarcomas.
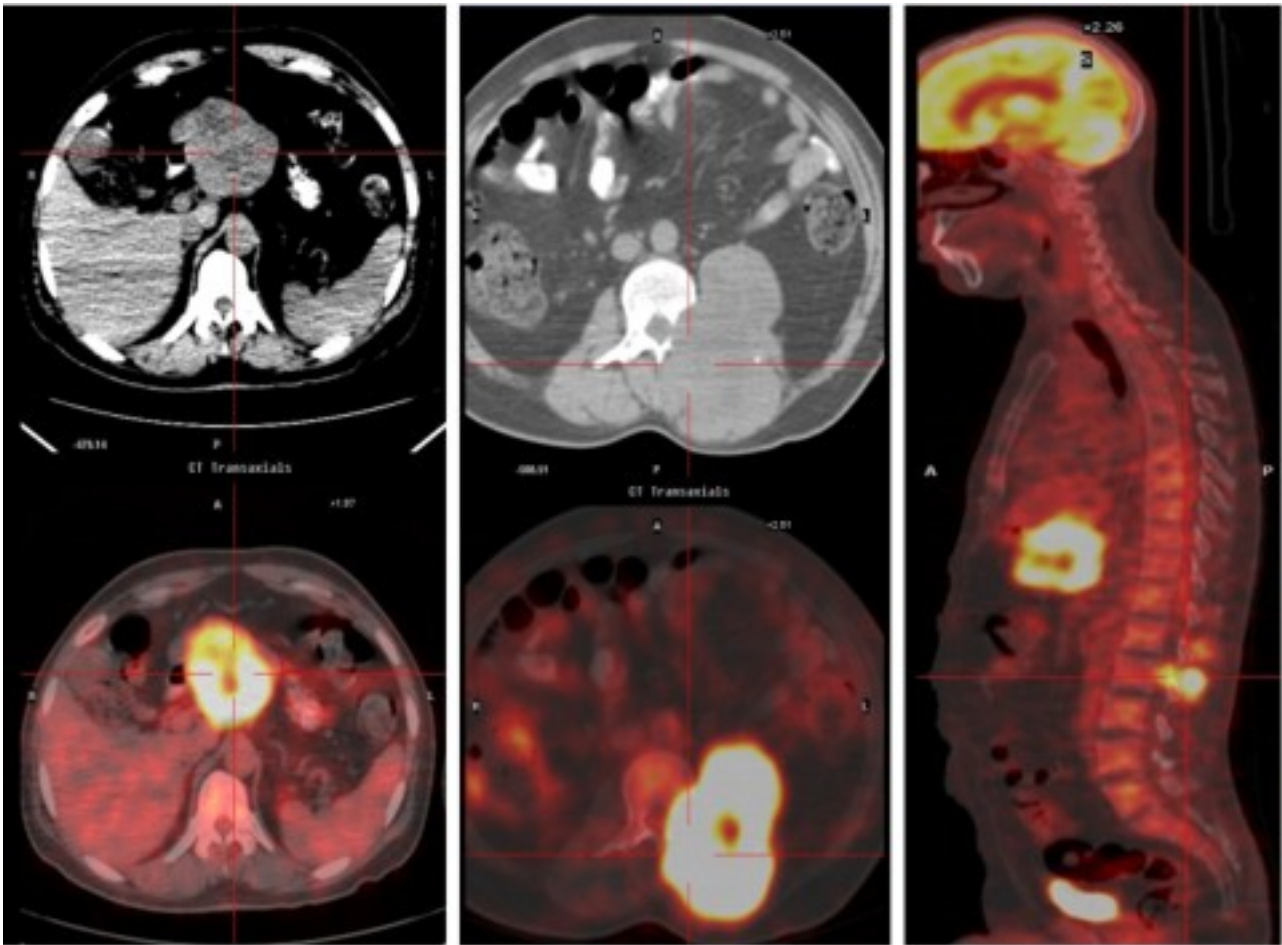
Figure 3. FDG-PET with attenuation CT showing significantly increased tracer uptake in the pancreatic and paraspinal metastatic masses.

grade metastatic tumour consistent with a previously treated sarcoma (Figure 2b). Within two months of surgery for the presumed solitary brain metastasis, he complained of low backache radiating to the left lower limb. A whole body FDG-PET scan and a CT scan of the thorax and abdomen revealed large pancreatic and left paraspinal masses with intense tracer uptake on PET scan; very high standardized uptake values were suggestive of metastatic involvement (Figure 3). The paraspinal mass extended from D12 to L4 eroding the transverse process, body and pedicle of the L2 vertebra without causing thecal sac compression. There was no evidence of pulmonary metastases. A CT-guided biopsy of the paraspinal mass was suggestive of high-grade sarcoma consistent with a known primary lesion (Figure 4). Immunohistochemistry was entirely non-contributory (negative for cytokeratin, desmin, smooth muscle antigen, leucocyte common antigen, CD20, and S-100). He was treated with palliative radiotherapy with good symptomatic relief. In
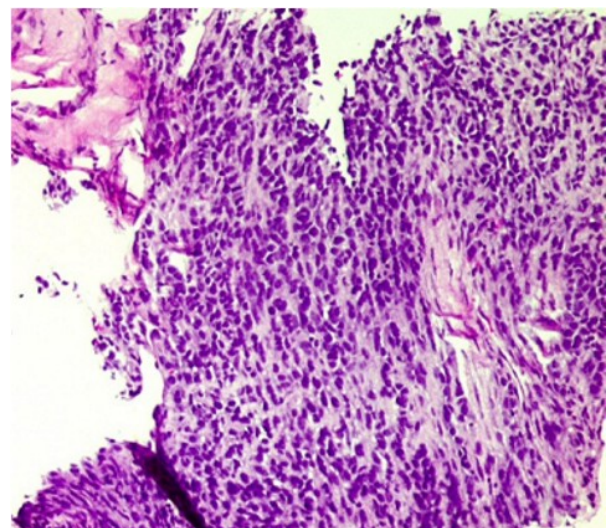
Figure 4. Section of the biopsy from a paraspinal mass showing metastases of a high-grade sarcoma (H&E stain, 10x).

view of the expected poor prognosis due to disseminated disease, he declined palliative systemic chemotherapy.

DISCUSSION

Primary STSs of the chest wall are much rarer and are usually classified as truncal sarcomas. In a retrospective analysis of sarcomas treated over a period of 40 years, there were only 189 patients with chest wall sarcoma. A large majority (60%) of them were high-grade, with desmoid tumours (21%) and liposarcomas (15%) being the most common histopathological subtypes [4]. Sarcomas preferentially spread by means of the hematogenous route and metastasize to the lungs which are the first site of distant relapse in almost 80% of cases [1, 2]. Metastases to the lymph nodes, bones, skin and soft tissues can occur later generally as part of widespread dissemination. Brain, pancreas and paraspinal metastases in the absence of pulmonary metastases are exceptional events in the natural history of tumors of mesenchymal origin.

In a large co-operative database of 1,240 patients with non-metastatic STSs, histologic grade was the most important independent predictor of metastasis development in the main histologic subtypes of STS, including unclassifiable sarcomas [5]. The 5-year metastasis-free survival rate was 90.8%, 70.4%, and 43.5% for grades 1, 2, and 3, respectively (P<0.01). On multivariate analysis, the relative risk of developing distant metastases was 3.1 and 7.8 times higher in grade 2 and 3 tumors, respectively, as compared to grade 1 tumors with highly significant P values. Tumor size and depth were also independent and significant predictors of outcome. Histologic subtype, although predicting outcome on univariate analysis, lost its significance on multivariate analysis. In a surgical series of 55 patients with primary chest wall STSs, a tumor size of less than 5 cm, wide surgical resection and low histologic grade were determinants of better disease-free survival. Multivariate analysis revealed histologic grade as the only independent predictor for the risk of death [6].

The true incidence of cerebellar metastases from STS is not clearly known. Brain metastases, including cerebellar metastasis, occur in a small minority of patients with STSs [3]. However, the majority of the series published combine all types of sarcomas including skeletal, extra-skeletal and round cell sarcomas. The largest prospective database on STSs has reported a very low incidence of STS brain metastases [7]. Out of a total of 3,829 patients with STSs seen over a 20-year period, only 40 (1%) were detected to have brain metastases, the majority of which were supratentorial in origin. Of the 19 patients who developed brain metastases metachronously, 18 had pulmonary metastases as the immediate prior site of disease. Yoshida *et al.* [8], analyzed 279 patients with STSs treated over a period of 24 years, and detected 20 (7.2%) patients with brain metastasis, 14 of which had lung metastases as well.

Intra-abdominal metastases are known to be associated with tumors of epithelial origin and occur in carcinoma of the lung, breast, thyroid, kidney and melanoma. There is very limited information on the occurrence of such abdominal metastases in tumors of mesenchymal origin. In a large retrospective review, only 19 (0.9%) out of 2,127 patients with primary non-visceral STSs were found to have intra-abdominal metastases [9]. The most common STSs metastasizing intra-abdominally were myxoid liposarcoma, leiomyosarcoma, and epitheloid sarcoma. A significantly higher association was seen with tumor size (greater than 5 cm), grade and deep location.

Pancreatic metastases are even rarer and are seldom detectable clinically although the reported incidence in autopsy series varies from 1.6 to 11% [10]. A significant number of patients do not have organ-specific complaints when the metastasis is detected incidentally on surveillance imaging. Symptomatic pancreatic metastases usually develop late, and are frequently accompanied by concurrent extrapancreatic deposits representing terminal stage disease as part of widespread dissemination. Metastatic

involvement of the pancreas may occur as a single localized mass, diffuse pancreatic enlargement or multiple pancreatic nodules. The differential diagnosis between pancreatic metastasis and primary pancreatic neoplasms may be difficult and challenging as their clinical presentation, signs, symptoms and imaging characteristics are very similar. Multinodularity, hypervascularity, the presence of extrapancreatic deposits and a previous history of cancer may be indicators of metastatic involvement rather than a primary pancreatic neoplasm. On CT scan, large metastatic lesions appear hypodense, but smaller deposits may be isodense and show peripheral rim enhancement [11]. They are usually hypointense on T1-weighted and hyperintense on T2-weighted MRI. Endoscopic ultrasound (EUS) is a very sensitive technique for characterizing pancreatic metastases, most of which appear solid and hypoechoic with well-defined borders. EUS guided biopsy is a safe and non-invasive procedure with high accuracy and low morbidity in experienced hands [12].

Although there are several large series dealing with the surgical management of pancreatic metastases mostly from epithelial cancers [10, 13, 14], only sporadic reports of pancreatic metastases in tumors of mesenchymal origin exist. Recently, an increasing number of such reports has been seen [15, 16, 17 ,18, 19, 20] in the medical literature. Whether this represents changing patterns of metastases in soft tissue sarcomas or is a result of widespread surveillance imaging or both is speculative. This patient had a high-grade pleomorphic spindle cell sarcoma (unclassifiable sarcoma), making him susceptible to the development of distant metastases. This is only the second reported case of pancreatic metastases from a sarcoma detected on FDG-PET. In this context, FDG-PET can be a highly sensitive whole-body staging procedure in the metastatic work-up for such patients. Oligometastases to the lung, liver and brain from several solid tumors including STSs are amenable to surgical resection which is known to improve survival and the quality of life in the absence of widespread disease. The effectiveness of radical surgical resection even in patients with limited pancreatic metastases remains to be conclusively established. However, with considerable improvements in the operative morbidity and mortality of pancreatic resections, there is accumulating evidence that patients with isolated solitary pancreatic metastasis with a long disease-free interval could benefit from aggressive local therapy [13, 14, 17]. The prognosis for patients with pancreatic metastases and concurrent extra-pancreatic disease continues to remain poor with a median survival of 4-6 months with palliative systemic chemotherapy and the best supportive care.

CONCLUSION

Cerebellar, pancreatic and paraspinal metastases from soft tissue sarcomas are rare, especially in the absence of pulmonary metastases. A high index of suspicion is necessary, and appropriate imaging should be considered for symptomatic patients.

Conflict of interest The authors have no potential conflicts of interest

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