Case Report

Malignant peripheral nerve sheath tumor of thigh with sphenoid and brain metastases: Extremely rare occurrence with dismal prognosis despite significant response to palliative chemoradiotherapy

ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST) is a neurogenic tumor arising from peripheral nerves or nerve sheaths. MPNSTs are highly aggressive sarcomas mainly associated with neurofibromatosis type-1 (NF-1) with high rates of local recurrence and distant metastasis carrying a dismal prognosis. Lung is the most common metastatic site. Bone metastasis although documented in the literature is still very rare, while dissemination to brain without the involvement of lungs and that too in a non-NF-1 case is extremely unusual. A 48-year-old female was diagnosed with a case of non-NF-1 MPNST left thigh with bone metastases including sphenoid. Despite showing complete resolution of skeletal and primary lesions postpalliative chemoradiotherapy, she developed brain metastases and succumbed to her disease. This case is discussed to highlight an unusual scenario we encountered, the clinical course of the disease with its management, and overall poor prognosis. To the best of our knowledge, this may be the earliest case of MPNST with sphenoid metastases detected by 18-fluorodeoxyglucose positron-emission computed tomography scan and a sporadic case of brain metastases reported in the world literature.

Keywords: 18-Fluorodeoxyglucose positron-emission computed tomography scan, brain, chemoradiotherapy, malignant peripheral nerve sheath tumor, metastases, sphenoid

INTRODUCTION

Malignant peripheral nerve sheath tumor (MPNST) is the most common mediastinal or truncal neurogenic sarcoma[1] with one-third of patients being metastatic on presentation[1] and carries the worst prognosis.[2] MPNSTs are mostly associated with neurofibromatosis type-1 (NF-1) demonstrating higher rates of distant dissemination[3] and an incidence of 4.6% compared to only 0.001% in general population.[4] MPNST metastasizes mainly to lungs while brain metastases are extremely rare,[5] and sphenoid involvement has scarcely been reported in the literature. Metastatic MPNST often shows poor chemoresponse,[6] while radiotherapy (RT) remains the cornerstone of treatment for local control and pain palliation.[6]

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CASE REPORT

A 48-year-old female with no known comorbidities presented with painful swelling of the left lower thigh and low-back pain

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for 2 months. Magnetic resonance imaging (MRI) showed an ill-defined lesion involving flexor and lateral compartments of the distal third of the left femur causing cortical breach. An excision biopsy was done which showed partially encapsulated tumor with extensive necrosis with tumor cells arranged in sheets and cords separated by hyalinized stroma with eosinophilic cytoplasm, high nuclear: cytoplasmic ratio, and large pleomorphic nuclei showing prominent nucleoli with perivascular accentuation. Immunohistochemistry (IHC) stained positive for vimentin, epithelial membrane antigen, and S100 [Figure 1] whereas it stained negative for cytokeratin, smooth muscle actin, desmin, leukocyte common antigen, calponin, CD 34, CD 31, and human melanoma black-45 which confirmed the diagnosis of MPNST. Clinically, there was no evidence of café-au-lait spots or neurofibromas with a negative family history. A whole-body 18-fluorodeoxyglucose positron-emission computed tomography (^{18}FDG-PET/CT) scan was done which showed a 5.3 cm × 6.8 cm × 12.2 cm soft-tissue lesion distal third left thigh with a standard uptake value (SUV) of 18.22 [Figure 2], multiple skeletal lesions involving sacrum (SUV = 11.74), left acetabular roof (SUV = 9.15), pelvic bones, dorsolumbar spine [Figure 3], and sphenoid bone (SUV = 10.75) [Figure 4].

Sphenoid lesion biopsy revealed metastases of MPNST with IHC positive for vimentin and S100 [Figure 5]. She was treated with palliative RT to pelvis to a dose of 30 Gy in 10 fractions followed by six cycles of 3-weekly palliative chemotherapy ifosfamide 2.5 g/m^2, mesna 600 mg/m^2, and doxorubicin 30 mg/m^2. Response assessment postchemotherapy with 18-FDG-PET/CT revealed marked regression in size and metabolic activity of thigh lesion (SUV 1.27) [Figure 6], complete metabolic resolution of all skeletal [Figure 7], and sphenoid lesion [Figure 8]. Due to persistent pain left thigh, she received local RT to a dose of 50 Gy in 25 fractions which resulted in a significant symptomatic and functional improvement. She was sent home for convalescence, but she again presented within a month with severe headache and vomiting. MRI brain was done which showed multiple intracranial metastases [Figure 9] for which palliative whole-brain RT 20 Gy in five fractions was given. However, despite all supportive measures, her condition kept on deteriorating, and she finally succumbed to her illness.

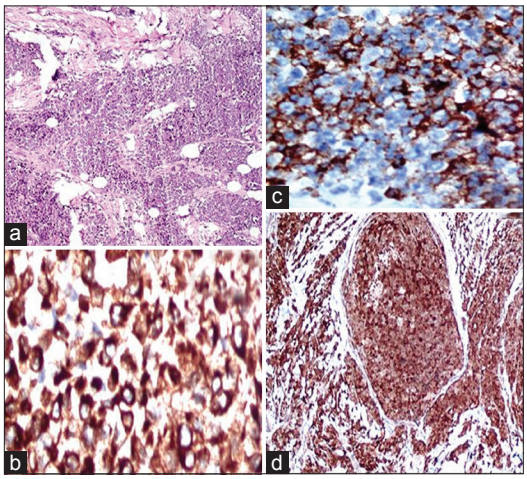

Figure 1: Excision biopsy of the left thigh lesion showing (a) extensive necrosis with tumor cells arranged in sheets and cords separated by hyalinized stroma with eosinophilic cytoplasm, high nuclear as follows: cytoplasmic ratio, large pleomorphic nucleus showing prominent nucleoli with perivascular accentuation (H and E, ×10). Immunohistochemistry positive for (b) vimentin (×40); (c) epithelial membrane antigen (×40); and (d) S100 (×10) confirming the diagnosis of malignant peripheral nerve sheath tumor

DISCUSSION

MPNST accounts for 5%–10% of all soft-tissue sarcomas.[7] Half the cases of MPNST are associated with NF-1, an autosomal dominant neurocutaneous disorder associated with poor prognosis, and a higher incidence of distant metastases compared to non-NF-1 cases.[3] Lung has been described as the most common site of distant metastases from MPNST[1-10] followed by bone,[2,10] liver,[2,8] LNs,[8] pleura,[10] retroperitoneum,[10] and heart,[3] although this remains a topic of debate and further research.[10] Although bone metastases have been described often in the literature,[2,6,10] the extensive research in Pubmed and Medline revealed no literature on biopsy-proven metastases to sphenoid from MPNST as reported by us. Brain as a site of distant dissemination is extremely rare, and only 21 cases all over the world were reported until 2016.[5] Very few cases of non-NF-1 type[10] and sporadic cases without concomitant lung involvement[9] have been reported till date.

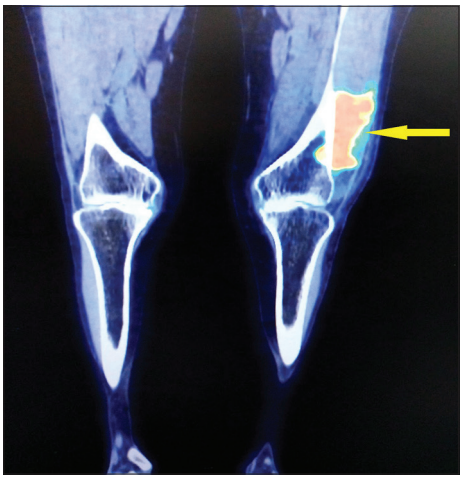

Figure 2: 18-Fluorodeoxyglucose positron-emission computed tomography scan (fused image) showing a metabolically active soft-tissue lesion distal third left thigh (yellow arrow)

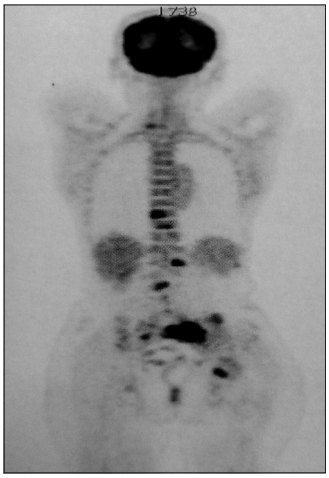

Figure 3: 18-Fluorodeoxyglucose positron-emission computed tomography scan (maximum intensity projection image) showing metabolically active multiple skeletal lesions involving sacrum, left acetabular roof, pelvic bones, and dorsolumbar spine

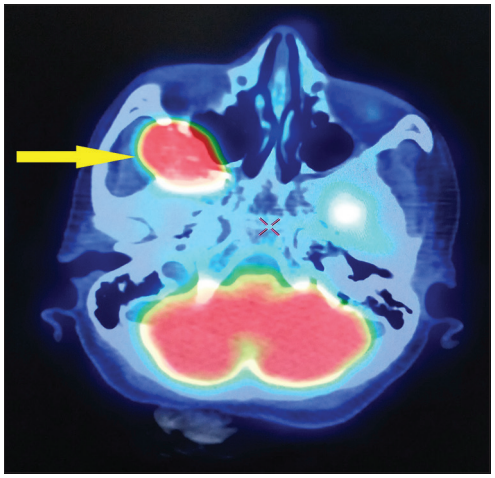

Figure 4: 18-Fluorodeoxyglucose positron-emission computed tomography scan (fused image) showing metabolically active skeletal lesion involving sphenoid bone (yellow arrow)

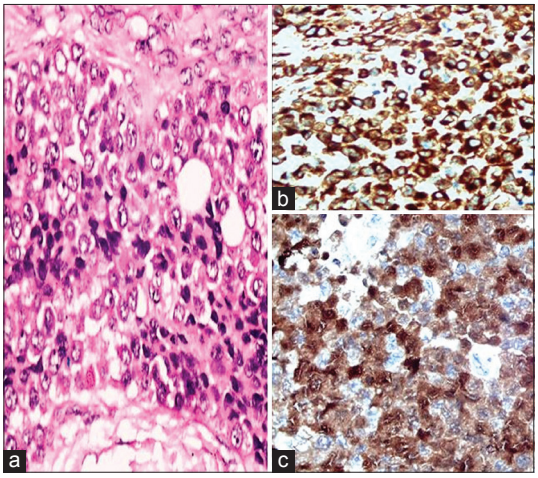

Figure 5: Biopsy from sphenoid lesion showing (a) metastases of malignant peripheral nerve sheath tumor (H and E, ×40); with immunohistochemistry positive for (b) vimentin (×40); and (c) S100 (×40)

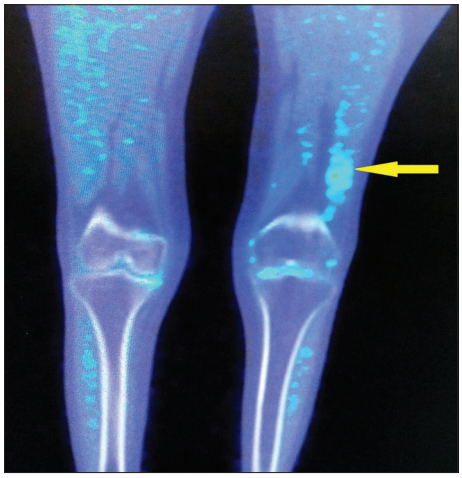

Figure 6: Response assessment postchemotherapy with 18-fluorodeoxyglucose positron-emission computed tomography scan (fused image) showing marked regression in size and metabolic activity of thigh lesion (yellow arrow)

MPNSTs arise mainly from peripheral nerves, from preexisting peripheral nerve sheath tumor, or from plexiform neurofibromas.[6] They are commonly located in the extremities followed by trunk or mediastinum and head and neck.[2] Mediastinal primaries carry the worst prognosis with higher rates of local recurrence and distant metastases as they are asymptomatic compared to the extremity MPNSTs which generally present with pain and an enlarging mass lesion.[2,6] CT scan and MRI may help in determining the anatomical extent of the lesion but noncontributory in detecting metastatic or secondary lesions for which 18-FDG-PET/CT has a high accuracy and specificity[2,6] apart from differentiating between benign neurofibromas and MPNSTs.[6] Definitive diagnosis of MPNST can be inferred with immunohistopathology showing nuclear atypia and tumor necrosis with IHC positive for S100 and negative for smooth muscle markers.[1]

Tumor size ≥10 cm, recurrent tumor, mediastinal location, and association with NF-1 are the documented risk factors for distant metastases.[2] Surgery is the treatment of choice for localized nonmetastatic disease. Disseminated cases due to their heterogeneous nature and poor response to conventional chemotherapy such as ifosfamide and doxorubicin[6] pose a therapeutic challenge. The addition of etoposide and carboplatin has shown significant clinical response,[6] while targeted therapy with sunitinib, erlotinib, sorafenib, tipifarnib, everolimus, and bevacizumab may result in an added survival advantage.[6] RT either in adjuvant or in palliative settings remains the mainstay of therapy to prevent local recurrence and pain alleviation. Ifosfamide and doxorubicin resulted in complete resolution of all primary bone metastases including the sphenoid lesion while palliative RT provided excellent pain relief. However, she developed

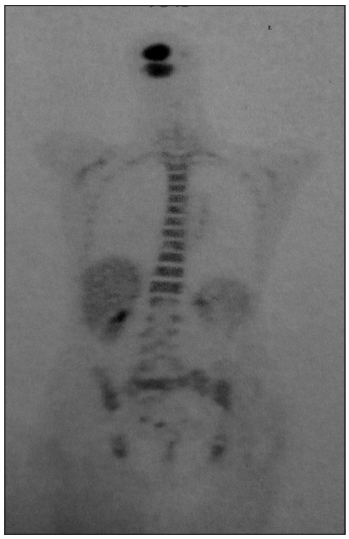

Figure 7: Postchemotherapy 18-fluorodeoxyglucose positron-emission computed tomography scan (maximum intensity projection image) showing complete metabolic resolution of all skeletal lesions

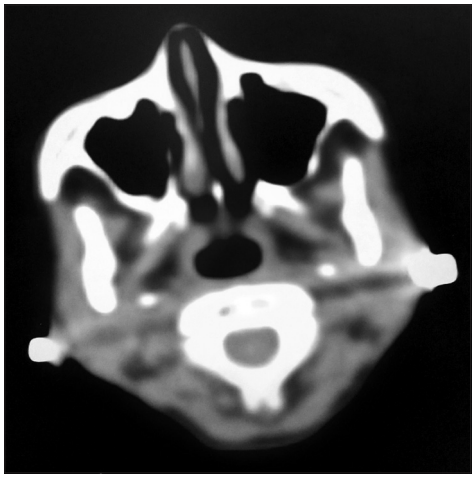

Figure 8: Postchemotherapy 18-fluorodeoxyglucose positron-emission computed tomography scan (fused image) showing complete metabolic resolution of the sphenoid lesion

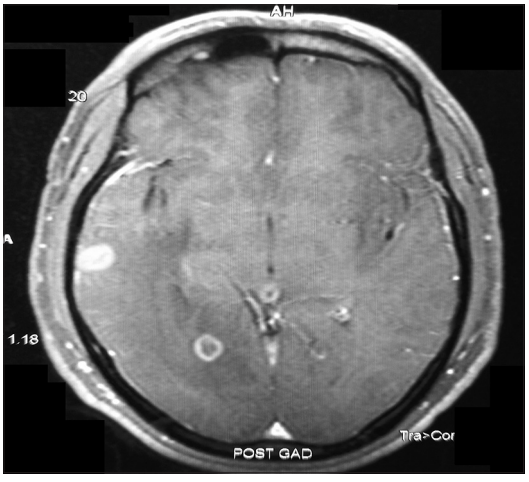

Figure 9: Magnetic resonance imaging brain (axial section) showing multiple intracranial metastases

brain metastases within a month postchemotherapy which showcased the highly aggressive behavior of this disease.

CONCLUSION

MPNST metastasizing to sphenoid and brain without involving lung is extremely rare, heralding ominous sign for the patient, thus indicating the lethal nature of this entity with a survival of mere 10 months' postdetection[5] irrespective of location and NF-1 association. This case highlights the pivotal role of 18-FDG-PET/CT in postchemotherapy response assessment and detecting rare metastatic sites compared to conventional imaging. This case emphasizes the fact that although conventional chemotherapy regimens may provide radiological and symptomatic relief but have poor outcome on overall and disease-free survival. Further exploring the plethora of molecular pathways expressed in MPNSTs may open avenues for novel targeted therapies which may benefit prognosis and final survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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