



## ORBITAL METASTASIS IN EWING'S SARCOMA: A RARE CAUSE OF PROPTOSIS

### Oncology

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### ABSTRACT

Ewing's sarcoma is the second most common primary malignant bone tumor that typically affects diaphysis of long bones during the second decade of life. Diagnosis is often delayed due to nonspecific presentation and is frequently misdiagnosed as osteomyelitis. Metastatic disease is present in approximately 25% of patients at diagnosis. Usual sites of metastasis are lung, bone, liver and other organs (<5%) but orbital metastasis presenting as unilateral proptosis is extremely rare. We hereby present three cases of Ewing's sarcoma with unilateral proptosis due to orbital metastasis. The first patient is 8 year old female with Ewing's sarcoma of shaft of left femur, received neoadjuvant chemotherapy followed by radiotherapy, but developed right eye proptosis during the course of treatment. The second patient is 5 year old female with Ewing's sarcoma of left ulnar shaft with multiple bone and lung metastasis along with orbital metastasis leading to left eye proptosis. The third patient is 22 year old male with Ewing's sarcoma of right thigh with multiple bone and lung metastasis along with orbital metastasis leading to left eye proptosis.

### KEYWORDS

Ewing's Sarcoma, Proptosis, Orbital Metastasis

### INTRODUCTION

Ewing's sarcoma is the malignant small round cell tumor of bone occurring in childhood and adolescence.<sup>[1]</sup> Skeletal Ewing's sarcoma primarily arises from diaphysis of long bone. Metastatic disease is present in approximately 25% of patients at diagnosis.<sup>[2]</sup> Usual sites of metastasis are lung, bone, liver and other organs (<5%) but orbital metastasis presenting as unilateral proptosis is extremely rare.<sup>[3]</sup> Herein, we report three cases of orbital metastasis from primary skeletal Ewing's sarcoma.

#### Case 1:

An eight year old female patient presented in our department with complaints of pain followed by swelling in left thigh since 3 months duration in March 2016. On local examination large firm lump of size approximately 10x10 cm was noticed at left upper thigh with restricted hip joint movement. All baseline investigations were within normal limits while MRI left femur was suggestive of lytic bony lesion of size 14x9.2x6.8cm (CC, ML, AP respectively) with skip lesions and invasion of the neurovascular bundle involving upper, middle third femoral shaft, neck and head. Histopathology of lesion showed sheets of round blue cells. Immuno-histochemistry (IHC) was MIC 2 positive. (Figure- 1a, 1b).

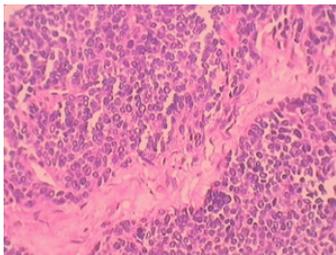


Figure-1a

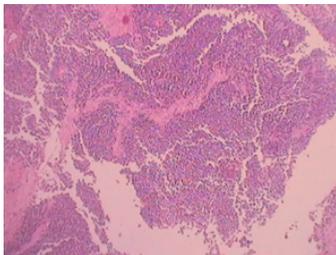


Figure-1b

The pathological and radiological reports strongly favored the diagnosis of Ewing's sarcoma. After confirmation of diagnosis patient initially received 3 cycles of chemotherapy VACA regimen (inj. Vincristine, Actinomycin-D, Cyclophosphamide, and Adriamycin) and showed good response. After 2 more cycles of same chemotherapy patient defaulted treatment for 3 months and then presented in OPD with complaints of dyspnea and proptosis of right eye associated with excruciating pain and loss of vision since past 15 days (figure-2)



Figure-2

On workup, chest X-ray revealed multiple lung metastases. SPECT-CT showed abnormal intense tracer uptake in proximal end and middle third of shaft of femur with right sided retro-bulbar lesion. (figure-3)



Figure-3

Patient received a cycle of palliative chemotherapy VACA regimen followed by palliative external beam radiotherapy (EBRT) to right upper femur for pain (3000c Gy in 10#). Unfortunately patient could not be salvaged.

#### Case 2:

This case refers to a 5 year old female who presented at our OPD with 6 months history of post traumatic swelling in left forearm. Patient was then evaluated and biopsy from swelling was suggestive of round cell

tumor and IHC showed diffuse MIC-2 positivity, favoring diagnosis of Ewing's sarcoma. MRI revealed lytic lesion in mid/distal metadiaphysis of ulna, with hyper-intense soft tissue density on T2w images and hypo intense in T1w images, measuring approximately 13.6x5.3x4.9cm. Chest x-ray revealed bilateral multiple lung metastases. Bone scan showed tracer uptake in skull, left ulna and left femur. Patient received 4 cycles of chemotherapy (inj. Etoposide and inj. Ifosphamide alternating with VAC regime). On reassessment after 4 cycles of chemotherapy, poor response and radiological progression of disease was seen so, patient further received two cycles of second line chemotherapy (inj. Gemcitabine and inj. Docetaxel) followed by palliative EBRT of 3000cGy in 10# via Cobalt 60 to the left upper ulna and to upper end of left femur. During RT patient developed pain and redness in left eye and gradually developed proptosis within 10 days. MRI brain showed hyper-dense lesion in occipital and left frontal region extending into left orbital region suggesting metastases. Patient was planned for palliative chemotherapy but unfortunately patient could not be saved.

### Case 3:

A 23 year old male presented with 3 months history of gradual pain and swelling in right anterior mid-thigh. Locally the swelling was at anterior mid-thigh of size 7cmx7cm, fixed to underlying structure, range of motion of adjacent joint was normal. Baseline investigations were normal. MRI revealed hyper intense signal on T2w images and hypo intense signal on T1w images involving upper and middle part of shaft of femur with focal cortical destruction and antero-medial soft tissue density lesion 9.8x3.9x5.1 cm in size. Incisional biopsy of the lesion was performed and microscopy revealed sheets of atypical cells with round cell morphology. The IHC was positive for Vimentin, MIC-2 and LCA, strongly in favor of round cell tumor of Ewing's family. Patient then received 6 cycles of chemotherapy (inj. Vincristine, Actinomycin D, Cyclophosphamide, Adriamycin) followed by EBRT 6000cGy in 30# by Cobalt 60. Patient was on regular follow up. After 6 months patient presented with one month history of left eye proptosis associated with diplopia and gradual diminution of vision. CECT brain was done in view of metastases, revealing hyperdense multiple soft tissue lesions largest in left frontal region with extension into left orbit in both extra and intraconal compartments, showing sunray calcification. Further metastatic workup with chest x-ray and bone scan revealed multiple lung and bone metastases. Patient is currently on palliative chemotherapy (inj. Ifosphamide and Etoposide alternating with VACA regime). (Figure- 4)



Figure-4

### DISCUSSION

Ewing's sarcoma is the second most common primary tumor of bone in children, after osteosarcoma. Its peak incidence usually occurs during second decade of life typically arising from the diaphysis of long bone. The most common site of involvement is pelvis followed by in order femur, below knee, ribs, spine, and humerus.<sup>[4]</sup> These tumors are highly invasive that 25% of new cases are metastatic at presentation. Approximately 95% of Ewing's sarcoma have translocation between the EWS gene on chromosome 22 and the FLI1 gene on chromosome 11 (t [11; 22] [q24; q12]) or the ERG gene on chromosome 21 (t [21; 22] [q22; q12]). Metastases to orbit are extremely rare in Ewing's sarcoma.<sup>[5]</sup>

Orbital metastasis are an infrequent etiology of proptosis approximately demonstrated in 3 to 7% of orbital biopsies.<sup>[6]</sup> Usually orbital metastases are unilateral but eventually as the metastasis grows it may involve the other orbit too. Most orbital metastases are from the

breast followed by lungs but the prevalence varies in different series.<sup>[7]</sup> In a large series estimating the causes of proptosis in children, only two patients out of a total of 585 had Ewing's sarcoma.<sup>[8]</sup> Mohan and Sen have reported two cases of metastatic Ewing's sarcoma in their series of 91 cases of unilateral proptosis of neoplastic origin.<sup>[9,10]</sup> Ewing's sarcoma tumor being known for the longest lag time and highly invasive nature tends to metastasize early. Above mentioned three cases had developed lung metastasis before developing orbital metastases consistent with the previously reported cases. Atypically Ewing's sarcoma may first time present with only orbital metastasis rendering the establishment of diagnosis difficult for clinician. MRI brain is the best investigation modality to diagnose orbital metastasis.

There are no specific guidelines for the management of orbital metastases. In our setting palliative chemotherapy was given but two out of three did not respond well and could not be salvaged. This could be attributed to aggressive nature of disease and noncompliance to the treatment. However the 23 year old case showed regression in the metastatic site with improved vision after receiving palliative chemotherapy and is currently responding well to the palliative care.

### CONCLUSION

The above three cases are reported here for the rarity of their presentation and metastasis to soft tissue in orbit. Proptosis due to metastases from Ewing's sarcoma can occur early and may even be the first presenting sign. Therefore, all cases with proptosis in Ewing's sarcoma should be considered for orbital metastatic workup and considered for early treatment in order to improve quality of life.

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