

Case Report

Rare Case of Sellar and Suprasellar Metastasis from Ewing's Sarcoma of Tibia

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ABSTRACT

We hereby report a case of metastatic Ewing's sarcoma presenting with rapid-onset total ophthalmoplegia, optic atrophy, and right temporal hemianopia. Comprehensive ophthalmic and neurological evaluation with targeted radioimaging revealed a tumor mass centered over the sella, compressing optic chiasma, extending to involve the left cavernous sinus and the left orbital apex. Whole-body imaging revealed the evidence of multifocal lung and mediastinal metastasis with focal lytic defect in the left femoral head. Histopathological evaluation of transnasal punch biopsy from the nasopharyngeal extension of the tumor revealed small round-cell tumor with strong CD99 positivity, supporting the diagnosis of Ewing's sarcoma. Rapid, aggressive extensions of the metastatic tumor into vital structures despite the initiation of chemoradiation of the extensive intracranial tumor led to unexpected demise of the patient. Our case is an unusual case of Ewing's sarcoma metastasis manifesting as a sellar mass and mimicking a pituitary adenoma radiologically, with a rapid progression within 2 weeks to cause massive extension of tumor into suprasellar, infrasellar, and left parasellar area, indicative of highly malignant nature of the tumor.

KEYWORDS: *Multimodal approach, sellar and suprasellar metastasis of Ewing's sarcoma, strong CD99 positivity, subclinical metastasis, total ophthalmoplegia*

INTRODUCTION

Ewing's sarcoma, primarily a bone lesion, occurs between the first and second decades of life in 80% of cases.^[1,2] It generally occurs in the lower extremities and pelvic girdle and rarely in the orbit. Central nervous system (CNS) involvement in case of bone or soft-tissue sarcomas is rare.^[3-7] There is heterogeneity in reported rates of CNS metastases in Ewing's sarcoma. Weins and Hattab^[3] reported CNS metastases in 2% of cases of Ewing's sarcomas/primitive neuroectodermal tumors (PNET). Bekiesinska-Figatowska *et al.*^[4] reported brain metastasis in 1% of cases of Ewing's sarcoma. Porto *et al.*^[5] reported an overall incidence of hematogenous brain metastasis in 0.9% of children with solid tumors in which none was from a case of Ewing's sarcoma.

Since the outcomes of metastatic Ewing's sarcoma are poor, early diagnosis is crucial with a multimodal approach^[8] for the treatment of primary tumor.

Herein, we report a case of Ewing's sarcoma of the extremity metastasizing to the sellar and suprasellar region involving the left orbital apex along with bilateral lung, abdominal, and left femoral head metastases.

CASE REPORT

A 13-year-old female with a history of below the knee amputation 3 months prior for Ewing's sarcoma [Figure 1], presented to her primary care physician, with left hemicranial headache and rapidly progressive diminution of vision in the left eye along with drooping of eyelid, binocular diplopia, and difficulty in moving the eye for 2 weeks. She also gave a history of single episode of projectile vomiting associated

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with nasal bleed for which a noncontrast computed tomography (NCCT) of the head was performed. This NCCT revealed a large heterogeneously enhancing mass lesion approximately 34 mm × 26 mm in the sellar and suprasellar region compressing optic chiasma suggestive of pituitary macroadenoma. The patient was referred to our institution for neurosurgical intervention of this pituitary macroadenoma diagnosed at the outside institution. However, the patient did not present until 2 weeks later.

Clinical evaluation at this time revealed no additional ocular or neurological complaints. Her family history and previous history for any genetic disorders were also unremarkable. In the right eye, best-corrected Snellen's visual acuity was 6/6 with no obvious ocular abnormality. In the left eye, there was no light perception, and there was axial proptosis (2 mm), total ptosis, total ophthalmoplegia [Figure 2a and b], total afferent pupillary defect with total optic atrophy, and loss of corneal reflex. Visual-field examination revealed right temporal hemianopia. The remainder of the neurologic examination was normal.

Otorhinolaryngologic evaluation revealed an irregular mass in the right nasopharynx arising from its posterosuperior wall, and an irregular mass in the left sphenoid recess extending into the left nasopharynx. The patient's blood analysis revealed slightly low levels of pituitary hormones (Prolactin 2.7 ng/ml [normal 2.8–29.2 ng/ml], thyroid stimulating hormone 0.27 μ IU/mL [normal 0.35–0.50 μ IU/mL]) with increased lactate dehydrogenase (884.54 U/L [normal < 247 U/L]) and alkaline phosphatase (456.3 U/L [normal 50–162 U/L]). Magnetic resonance imaging brain at this time [Figure 3a] demonstrated an extensive hyperintense mass lesion centered over sella, engulfing the pituitary gland, compressing the optic chiasma and completely occupying the left cavernous sinus, attenuating the left internal carotid artery (ICA), and abutting the right cavernous sinus and right ICA. The mass was further extending to the sphenoid and posterior ethmoid sinuses, with a small extension to the left orbital apex partially encasing the left optic nerve. The mass had destroyed the clivus and had extended inferiorly into the left nasopharynx and posteriorly into the prepontine cistern. The left Meckel's cave was also involved. Whole-body imaging revealed multifocal irregular heterogeneously enhancing soft-tissue lesions of variable size suggestive of lung and mediastinal metastases [Figure 3b and c]. We also found a lesion with similar enhancement (32 mm × 28 mm × 26 mm) in the right cardiophrenic angle encasing and displacing

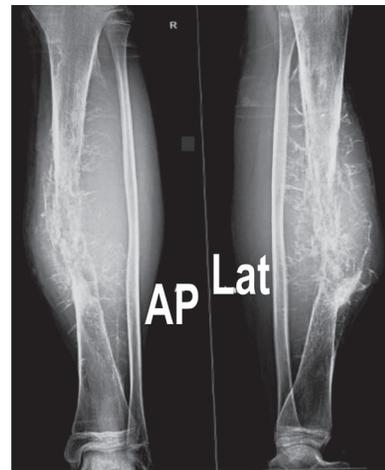


Figure 1: Anteroposterior and lateral radiograph of the right leg showing lytic lesion with large soft-tissue component and hair-on-end periosteal reaction in mid-diaphysis of tibia



Figure 2: Left eye. (a) Total ptosis, (b) total ophthalmoplegia

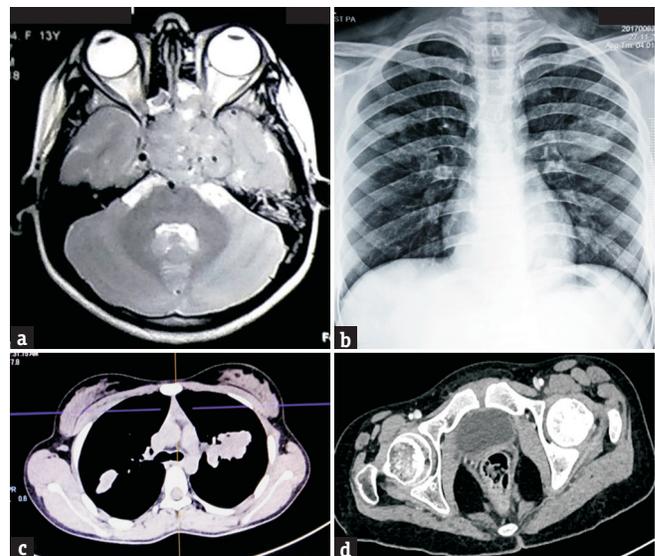


Figure 3: (a) Magnetic resonance imaging brain showing large mass based on sellar/suprasellar region extending to the left orbital apex, ethmoidal air cells, and cavernous sinus. (b) Chest X-ray showing well-defined opacities in bilateral mid-zones. (c) Computed tomography chest showing irregular soft-tissue lesions in lungs and mediastinum. (d) Computed tomography pelvis showing lytic lesion in the left femoral head

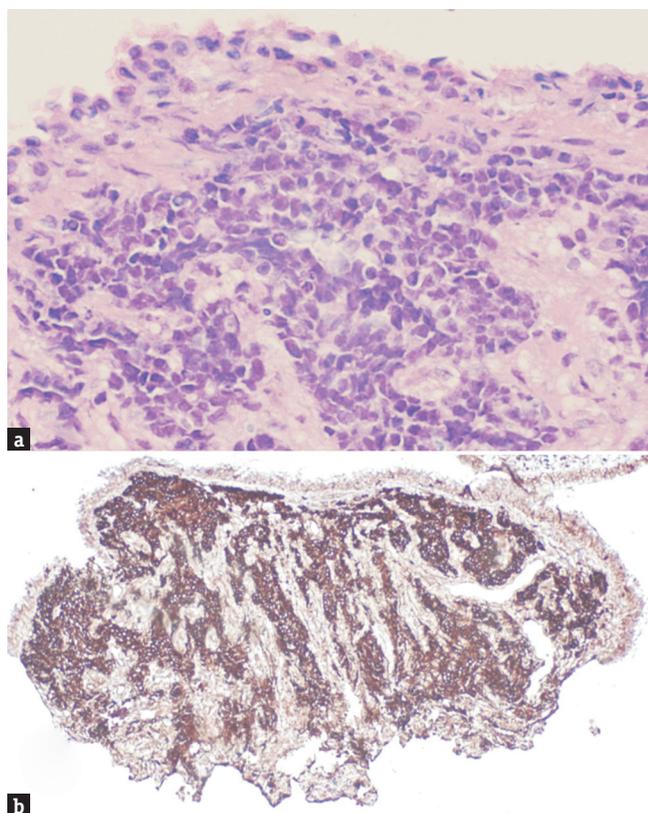


Figure 4: (a) H and E-stained section of nasopharyngeal punch biopsy specimen showing nests of small round blue cells, (b) Strong CD99 immunoreactivity

the posthepatic inferior vena cava anteriorly, abutting the right atrium and distal thoracic esophagus. A few enhancing lymph nodes in both axillae and in the mesentery and a focal lytic defect of the left femoral head was also found [Figure 3d].

Histopathology of punch biopsy from the nasopharyngeal extension of the tumor revealed nests of small round blue cells in the subepithelium suggestive of a small round-cell carcinoma. Strong CD99 positivity, borderline synaptophysin immunoreactivity, and chromogranin nonreactivity supported the diagnosis of Ewing's Sarcoma [Figure 4a and b].

As per discussion in our Institutional tumor board, we planned neoadjuvant chemoreduction followed by surgery for this Stage IVb tumor (T3N1M1b) which was classified as unfavorable intermediate risk group of metastatic Ewing's sarcoma as per Ladenstein *et al.*^[9-11] On subsequent follow-up after two cycles of chemotherapy with vincristine, doxorubicin, cyclophosphamide intervened with ifosfamide, and etoposide, the patient developed loss of vision in the right eye and dysphagia, due to expansion of the CNS and mediastinal masses. In view of this, emergency decompression was planned; however,

patients relatives refused surgery due to expected poor prognosis. The patient finally died of cardiorespiratory failure.

DISCUSSION

In pediatric patients, majority of brain tumors including sellar masses are primary, metastatic involvement accounting for only 1%–10%.^[3] Sites of primary for the CNS metastatic tumors in children when compared to adults, are vastly different, with kidney, adrenals, bone, and soft tissue being the most common.^[3,12]

Ewing's sarcomas, rare neoplasia of childhood, typically presenting with an osseous primary, mostly metastasize to lung, bone, and bone marrow^[13,14] and have a low incidence of CNS metastasis. In the majority of cases, CNS metastasis is the result of direct extension of bony metastasis in proximity to the brain tissue, while hematogenous brain metastases occur in less than 1.8% of the cases.^[4,7,15] Up to 80%–90% have subclinical metastasis at the time of presentation; however, the upfront metastatic disease is found in <25% of patients at the time of diagnosis.^[10,16]

Deopujari *et al.*^[17] in their review of different pediatric suprasellar tumors have remarked that sellar and suprasellar tumors form a separate entity as far as incidence, histology, and responsiveness to therapy is concerned and metastatic tumors such as Ewing's/PNET are rare to this region.^[3,17-20] Ewing's presenting as a sellar mass is a diagnostic and therapeutic challenge as in our case.^[18] In our patient, with a history of resected Ewing's sarcoma of tibia, NCCT head at the initial presentation of the patient to her primary physician revealed an intracranial sellar lesion without any apparent osseous involvement of the calvarium mimicking a pituitary adenoma. However, repeat neuroimaging was done at her presentation to our institution 2 weeks later, which showed significant interval growth with differentials shifting towards a metastatic Ewing's sarcoma, and this was supported by immunohistochemical studies on the biopsy specimen. This corroborates with the findings of Weins and Hattab,^[3] who in their retrospective review of 20 years of pathological spectrum of CNS metastases in 1135 cases in pediatric population, found only a single case of metastatic sellar/suprasellar involvement of Ewing's sarcoma.

Among the factors altering the prognosis significantly in Ewing's sarcoma, serum LDH levels have been defined as an effective biomarker with high serum levels having low overall survival.^[21] In addition, a high

probability of subclinical metastasis and a decrease in survival independent of the site of primary tumor has been documented in cases with gross soft-tissue extensions at the primary site of tumor.^[22] Our patient had an aggressive primary tumor which led to multiple distant metastases and a poor response to therapy and survival. This may have been due to the large soft-tissue component at the primary site (tibia) as evident on her initial radiograph of the right leg, and her high LDH levels.^[21,22]

Our case is hence unusual in its presentation as a rare case of sellar metastasis of Ewing's sarcoma in pediatric age group which was initially indistinguishable radiologically from pituitary macroadenoma^[20,23] and highlights the need of appropriate medical oncological workup at the time of initial presentation/surgery. This also emphasizes that by the time CNS involvement is diagnosed in these patients, they have had multiple metastasis and a poor prognosis for survival despite aggressive therapy.^[10,16] Thus, a multimodal approach with chemotherapy, surgery, and radiotherapy is recommended for all primaries irrespective of their extent and site to enhance the life expectancy in this young patient population of Ewing's Sarcoma.

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Conflicts of interest

There are no conflicts of interest.

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