



Case Report

# Primary Ewing's sarcoma of the petroclival bone: A case report and literature review

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## ABSTRACT

**Background:** Primary Ewing's sarcoma (ES) is typically seen within the long bones, vertebrae, or pelvis. Uncommonly, it can be found within the cranium among the rarest locations for primary ES are the skull base, in particular, the petroclival bone.

**Case Description:** The patient is a 68-year-old female with past medical history of Stage III breast cancer who presented with severe retro-orbital headache and diplopia due to a cranial nerve VI palsy. Magnetic resonance imaging (MRI) revealed a mass at the left petroclival bone with extension into the adjacent left petrous apex and into the posterior aspect of the left cavernous sinus proximal to the carotid artery. The patient subsequently underwent an endoscopic transsphenoidal biopsy. Pathological and molecular analysis supported a diagnosis of ES. The patient then underwent neoadjuvant chemotherapy and radiotherapy. At 12 month-follow-up, her petroclival ES demonstrated significant interval decrease in size on MRI surveillance imaging.

**Conclusions:** This is the third case of primary ES of the petroclival bone to be reported in the literature. In this patient, management consisted of surgical incisional biopsy followed by adjuvant radiation and chemotherapy. Knowledge and awareness of this type of tumor is important for the skull base surgeon.

**Keywords:** Cranial Ewing's sarcoma, Petroclival bone, Skull base

## INTRODUCTION

Ewing's sarcoma (ES) is a bone malignancy that is usually seen in the pediatric population, but it may also present in adults. ES is commonly found in the pelvis, femur, tibia, vertebrae, and humerus, and pathologically manifests as small, round, and blue cells with a poor prognosis.<sup>[1]</sup> Primary cranial ES is uncommon and constitutes 1% of all cases of ES.<sup>[2]</sup> It is typically seen in the calvarium while skull base lesions are an infrequent site of primary occurrence.<sup>[3]</sup> Clinical presentation of these skull base tumors may include headache, nausea, vomiting, cranial nerve (CN) palsies, or trigeminal nerve involvement.<sup>[3,4]</sup> A particularly rare location of primary skull base ES is the petroclival bone; only two prior cases have been reported in the literature.<sup>[4,5]</sup> In this report, we present a third patient with this rare entity.

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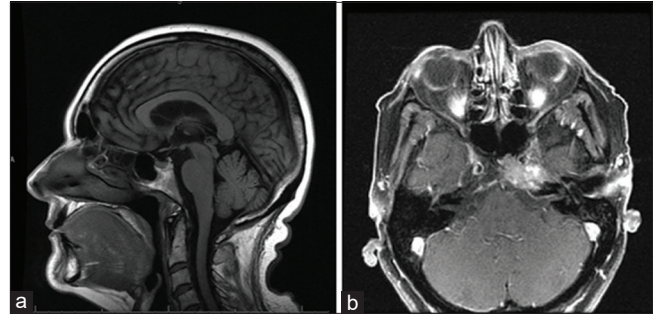
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## CASE REPORT

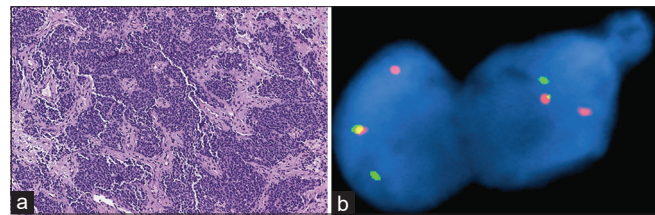
A 68-year-old female with past medical history of Stage III breast cancer treated in 2011 presented in 2017 with severe retro-orbital headache primarily on the left side around her temple and posterior neck. The headache lasted a few days and resolved; however, soon after, she developed associated symptoms of diplopia. She denied any concurrent adenopathy, trismus, numbness, nasal congestion, recent epistaxis, or any prior diplopia symptoms. Her physical exam was notable for leftward gaze restriction suggestive of a left-sided CN VI palsy. She initially presented to her primary care provider with these symptoms and underwent magnetic resonance imaging (MRI) which revealed a mass at the left petroclival bone with extension into the adjacent left petrous apex and the posterior aspect of the left cavernous sinus concerning for recurrence/metastatic disease of her previously treated breast cancer [Figure 1a and b]. Follow-up positron emission tomography/computed tomography scan showed a destructive left skull base lesion and a hypermetabolic right cervical lymph node. MRI orbit and brain were unremarkable. The patient subsequently underwent an endoscopic transsphenoidal biopsy and right open neck lymph node biopsy.

Frozen section pathology demonstrated small round blue cell tumor consistent with primitive neuroectodermal tumor (PNET)/ES [Figure 2a]. Fluorescence *in situ* hybridization (FISH) analysis is positive for rearrangement of the ES breakpoint region 1 (EWSR1) (22q12) locus supporting the diagnosis [Figure 2b]. The mass was positive for EWSR1/friend leukemia integration 1 (FLI1) fusion transcript which was detected by reverse transcription (RT)-DNA amplification with the size of the amplification product consistent with a Type 1 fusion transcript. The tumor also showed membranous diffuse positivity for CD99 and nuclear positivity for FLI-1 by immunohistochemistry. Bone marrow biopsy demonstrated no evidence of bone marrow involvement by tumor supported by CD99 (MIC2) immunostaining which only stained a subset of lymphocytes and precursor cells but did not highlight abnormal cell populations. Lumbar puncture also did not demonstrate any overtly cytologically malignant cells. Together, the molecular findings supported the diagnosis of ES.

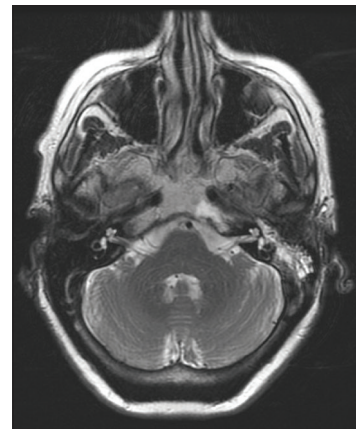
At her postoperative follow-up visit, the patient's CN symptoms had improved with ocular movements closer to baseline and reduction in headache severity. The patient was then treated with induction chemotherapy consisting of dactinomycin/cyclophosphamide alternating with ifosfamide/etoposide for four cycles. This was followed by radiotherapy and seventeen cycles of consolidative chemotherapy for cure. One month after completion of her chemotherapy and radiotherapy, MRI surveillance imaging



**Figure 1:** Magnetic resonance imaging demonstrating mass at the left petroclival bone with extension into the left petrous apex and left cavernous sinus. (a) Sagittal view of lesion. (b) Axial view of lesion.



**Figure 2:** Pathological analysis of tumor biopsy reveals findings consistent with Ewing's sarcoma. (a) Hematoxylin and eosin staining showing small, round, blue cells ( $\times 10$  magnification) (b) fluorescent *in situ* hybridization showing Ewing's sarcoma breakpoint region 1 (22q12) gene rearrangement.



**Figure 3:** Axial view of lesion postchemoradiation therapy.

demonstrated a significant interval decrease in enhancement and size of the mass [Figure 3].

## DISCUSSION

Approximately 90% of cases of primary ES occur in patients younger than 20-years-old and it most commonly involves the long bone shafts, pelvic bones, or within ribs or vertebrae.<sup>[1,6]</sup> Primary cranial ES is rare with an estimated incidence of 1–2% of all cases of ES.<sup>[7]</sup> The most common

area of cranial involvement is the parieto-occipital region, while skull base involvement is less frequently observed.<sup>[7]</sup> Although metastasis of ES is relatively common, metastasis from primary cranial ES is exceptionally rare with only one case seen in the literature.<sup>[4]</sup> As a result, the prognosis is better for primary cranial lesions compared to primary lesions elsewhere in the body.<sup>[8]</sup>

Histopathologic analysis of the lesion biopsy demonstrated small, malignant, round blue cells consistent with ES or PNET [Figure 2b]. However, the World Health Organization recently retitled PNET into a new pathological group called embryonal tumor with multilayer rosettes,<sup>[9]</sup> in concordance with a molecular signature of an amplification of the *C19MC* locus on chromosome 19. ES is the primary member of the family of tumors called ES family of tumors, which includes PNET, and as a result, most of the literature refers to both entities as equivalent within a molecular spectrum.<sup>[10]</sup> Moreover, the lesion was immunohistochemically positive for CD99, which is highly sensitive and specific for ES.<sup>[11,12]</sup> FISH analysis revealed an *EWSR1* (22q12) gene rearrangement and *EWSR1/FLI1* fusion transcript which was detected by RT-DNA amplification, which is also specific and sensitive for ES [Figure 2].<sup>[13]</sup> Together, the histopathological, molecular, and immunohistological evidence strongly supported the diagnosis of primary ES.

On literature review, only two prior cases have been documented of primary petroclival ES.<sup>[5,4]</sup> In both cases, management consisted of initial surgical debulking or partial tumor resection with adjuvant radiotherapy and chemotherapy. The first case, reported by Balasubramaniam *et al.* in 2008, was a 17-year-old male who presented with headache, hearing impairment, and ataxic gait with imaging pertinent for a calcified heterogeneous mass consistent with ES involving the right petrous temporal and clival bone resulting in compression of the right cerebellum. The tumor was treated with surgical debulking a right retrosigmoid craniectomy and adjuvant chemoradiation with 12-month follow-up demonstrating marked tumor regression. The second case, reported by Thakar *et al.* in 2012, was a 29-year-old male who presented with a week history of intermittent headaches and progressive restriction of right eye movement. Imaging demonstrated a destructive clival bone lesion consistent with ES with sellar and parasellar involvement. Decompression of the lesion was completed through a transnasal-transsphenoidal approach and adjuvant radiation and chemotherapy were planned postoperatively. However, 2 weeks after initiation of radiotherapy, the patient developed spastic paraparesis secondary to metastatic lesions throughout his spine and died a week later.

In our case, transsphenoidal biopsy worked to functionally debulk the lesion as the patient's diplopia and headache improved postoperatively even before the initiation of

chemotherapy and radiotherapy. Aggressive initial surgical resection was deferred due to the tumor's extension into the cavernous sinus and involvement of the carotid artery. Postchemoradiation, the patient's symptoms have not returned and the most recent imaging has not demonstrated disease progression or recurrence. Therefore, we did not pursue additional surgical resection due to the patient's tumor stability and risk of surgical morbidity due to surrounding vascular structures. However, prior studies have shown that radical tumor excision, if surgically appropriate, is recommended to reduce tumor mass and increase adjuvant therapy effectiveness.<sup>[14]</sup>

## CONCLUSIONS

Primary ES of the petroclival bone is a rare entity. However, awareness and knowledge of management of this lesion is important for the skull base surgeon. Successful treatment can be facilitated by resection or debulking, which can be successfully done transsphenoidally followed by adjuvant radiotherapy and chemotherapy.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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