Case Report

# A rare case of extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor developing in maxillary sinus of an old patient

Maithili Mandar Kulkarni, Siddhi Gaurish Sinai Khandeparkar, Avinash R Joshi, Chitrangi Barpande

Department of Pathology, Shrimati Kashibai Navale Medical College and General Hospital, Narhe, Pune, Maharashtra, India

**Abstract**

Ewing's sarcoma/primitive neuroectodermal tumor (ES/PNET) family of tumors is an uncommon group of malignant neoplasms that may present in both skeletal and extraskeletal sites. PNET outside the central nervous system is called peripheral PNET (pPNET) developing from migrating embryonal cells of the neural crest. Very few cases of pPNET of the maxilla are reported in English literature. These tumors may be difficult to diagnose due to their primitive morphology. These tumors occur predominantly in infancy or early childhood. The occurrence of extraskeletal ES/PNET in the maxillary sinus in an old age is very rare. We report a case of extraskeletal ES/PNET developing in maxillary sinus in a 60-year-old woman. The ES/PNET should be included in the differential diagnosis of a small round cell tumor and immunohistochemical analysis with a panel of immunomarkers should be done for correct diagnosis and proper treatment.

**Key Words:** Ewing's sarcoma, primitive neuroectodermal tumor, maxillary sinus, neural crest cells

**Address for correspondence:**
Dr. Maithili Mandar Kulkarni, Shrimati Kashibai Navale Medical College and General Hospital, Narhe, Pune - 411 041, Maharashtra, India.
E-mail: drmaithili@rediffmail.com
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## INTRODUCTION

Ewing's sarcoma/primitive neuroectodermal tumor (ES/PNET) family of tumors is an uncommon group of malignant neoplasm that may present in both skeletal and extraskeletal sites. Extraskeletal ES/PNET is quite rare and typically involves the trunk and the extremities.[1,2] PNET outside the central nervous system is called peripheral PNET (pPNET) developing from migrating embryonal cells of the neural crest.[3] pPNETs are less common with varying incidence of occurrence in head and neck region.[4] These tumors occur predominantly in infancy or early childhood. Very few cases of pPNET of the maxilla are reported in English literature.[5] These tumors may be difficult to diagnose due to their primitive morphology. Ancillary laboratory techniques including immunohistochemistry, cytogenetic analysis, reverse transcriptase polymerase chain reaction and fluorescent in-situ hybridization have become invaluable in helping to differentiate ES/PNET from other small round cell neoplasm.[6]

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## CASE REPORT

A seventy-year-old female presented to the ENT Outpatient Department with a history of epistaxis from the left nostril since 6 days. She had a headache in the area of left frontal and maxillary sinus. The patient was a known case of hypertension. There was no other significant family or past history. Anterior rhinoscopy showed blood clots in middle meatus, with maxillary fullness. Computed tomography (CT) scan paranasal sinus (PNS) view was done



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which showed expansile soft tissue mass lesion measuring 4.3 cm × 4.3 cm × 4.4 cm [anterioposterior (AP) × transverse (TR) × cranio-caudal (CC)] involving maxillary sinus with the destruction of all the walls of the maxillary sinus and mild postcontrast enhancement [Figure 1a]. The lesion extended to the left nasal cavity. Erosion of the floor of the left orbit was seen. The findings were suggestive of a neoplastic lesion. Biopsy of the mass was done from the nasal cavity and send for histopathological examination.

Single tissue bit measuring 1 cm × 1 cm × 0.4 cm, grayish brown and firm in consistency was received. Section studied showed tissue lined by pseudostratified columnar epithelium. The subepithelial tissue showed a tumor composed of tumor cells arranged in sheets and at places forming nesting pattern. The tumor cells showed high N:C ratio, stippled nuclear chromatin and scanty cytoplasm [Figure 1b]. Few abnormal mitotic figures were noted [Figure 2a]. At places, rosette formation with fibrillary processes was noted [Figure 1c, 2b]. The possibility of small round blue cell tumor was considered with a differential diagnosis of lymphoma, PNET, rhabdomyosarcoma and poorly differentiated carcinoma. Immunohistochemical study with following panel of markers was done such as CD20 (L26, Dako), CD3 (Dako), Pan CK (AE1/AE3, Dako), CK7 (OV-TL12/30, Dako), myogenin, desmin (D33, Dako), chromogranin (Dako), S100 (Dako), CD99 (12E7 (Dako), Ki67 (MM1, Novac) and p53 (Do-7, Dako). Immunomarkers CD20, CD3, PanCK, CK7, myogenin, desmin, chromogranin and S100 were negative. CD99 showed strong membranous immunoreactivity [Figure 1d]. Ki67 labeling index was 70% confirming its malignant nature and p53 immunoreactivity was markedly increased (20%) [Figure 1e]. Based on the meticulous immunohistomorphological analysis, diagnosis of PNET/extraskeletal Ewing's sarcoma was offered. Translocation *t*(11,21) was advised. The patient was lost to follow-up.

## DISCUSSION

With the advent of immunohistochemical, cytogenetic and molecular genetic techniques, PNET, Askin tumor and skeletal-extraskeletal ES are considered to be ends of morphologic spectrum known as ES/PNET family of tumors. The ES/PNET family of tumors is characterized by the presence of nonrandom translocations leading to the fusion of EWS gene on 22q12 with one of the several members of the ETS family of transcription factors. The most frequent of these translocations is *t* (11;22)(q24;12), detected in approximately 90% of cases. PNET end of the spectrum shows sheets or lobules of small round cells containing darkly staining round or oval nuclei. The cytoplasm is indistinct except in areas where the cells are more mature and the elongated hair-like cytoplasmic extensions coalesce to form rosettes.[7] Our case showed few rosette-like structures with fibrillary processes.

ES/PNET occurs mainly in children and young adults. PNET has a wider range of age group. Our patient was a 70-year-old female. Radiological workup includes standard radiograph, CT, MRI and bone scintigraphy. The radiological appearance of these tumors is not specific for differentiation of pPNETs

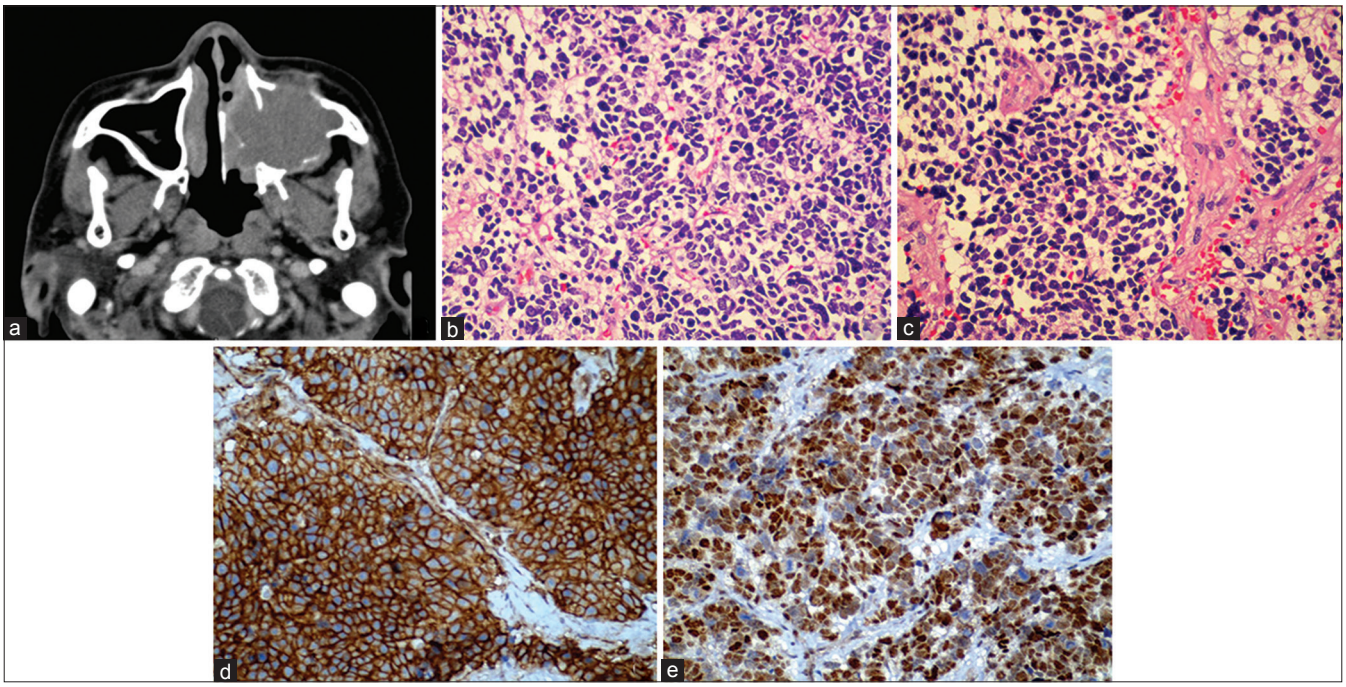


**Figure 1:** (a) Computed tomography scan showing expansile lesion in the left maxillary sinus. (b) Photomicrograph showing tumor composed of round blue cells arranged in sheets (H&E stain, ×100). (c) Photomicrograph showing rosette formation with fibrillary processes. (H&E stain, ×100). (d) Tumor cells showing CD99 membrane positivity (IHC stain, ×100). (e) Tumor cells showing >20% nuclear p53 expression (IHC stain, ×100)

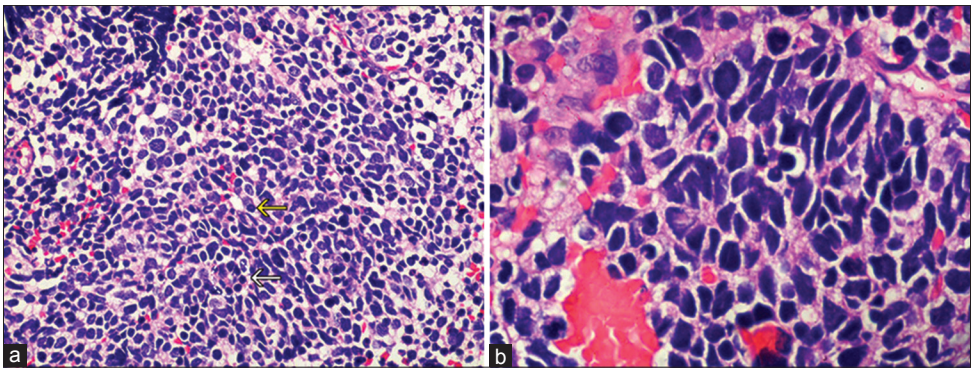


**Figure 2:** (a) Photomicrograph showing an abnormal mitotic figure (yellow arrow) and rosette formation with fibrillary processes (round circle with white arrow) (H&E stain, ×400). (b) Photomicrograph showing rosette formation with fibrillary processes (H&E stain, ×1000)

from other types of bone and soft tissue tumors.[8] Hence, histopathology is of utmost importance for the diagnosis. These tumors occur rarely in head and neck and are mainly found to arise in mandible or skull. Tumors arising in maxillary sinus are extremely rare and <15 cases have been reported in literature.[9-11]

Of the 13 cases studied, seven were males and six were females. There is no sex predilection. Nine cases were of age <30 years, while only four cases were more than 40-year-old. Rosette formation was seen in only one case.[5,10,11] Immunohistochemical analysis was done in eight cases of which CD99 was done in seven cases. All seven cases showed immunoreactivity for CD99. Other case showed immunoreactivity for neuron-specific enolase and S100. EWS-FLI1 was done in two cases and the diagnosis was confirmed.

The differential diagnosis includes other small round cell tumors like lymphoma, poorly differentiated carcinoma, desmoplastic small round cell tumor and rhabdomyosarcoma. The tumor cells of ES/PNET show membranous immunoexpression for CD99/MIC2. CD99 can be positive in other tumors such as mesenchymal chondrosarcoma, poorly differentiated synovial sarcoma and lymphoma. Thus, although immunostains for CD99 are highly sensitive for recognizing the ES/PNET, this marker should be used as a part of a panel of immunostains. The molecular technique should be done for definitive diagnosis. The prognosis for patients with ES/PNET has steadily improved. The combination of surgery and/or radiotherapy and systemic chemotherapy results in a cure rate close to 75% in this group.[7] Raised p53 expression is seen in EWS-FLI1-expressing cells. By univariate analysis, cases with p53 of more than 20% have significantly poorer overall survival among patients with localized disease and in multivariate analysis, p53 > 20% is one of the strongest negative prognostic factors.[12] In our case, p53 immunoexpression was increased (>20%) indicating a poor prognosis. Ki67 expression constitutes a valuable indicator of poor prognosis in localized Ewing's sarcoma family of tumors.[13]

Our case highlights that though the development of ES/PNET in the maxilla of an old patient is a rare occurrence, it should be included in the differential diagnosis of a small round cell tumor and a panel of immunohistochemical markers should be done to arrive at a correct diagnosis and proper treatment.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Angervall L, Enzinger FM. Extraskeletal neoplasm resembling Ewing's sarcoma. Cancer 1975;36:240-51.
2. Rud NP, Reiman HM, Pritchard DJ, Frassica FJ, Smithson WA. Extraosseous Ewing's sarcoma. A study of 42 cases. Cancer 1989;64:1548-53.
3. Coffin CM, Dehner LP. Peripheral neurogenic tumors of the soft tissues in children and adolescents: A clinicopathologic study of 139 cases. Pediatr Pathol 1989;9:387-407.
4. Mohindra P, Zade B, Basu A, Patil N, Viswanathan S, Bakshi A, *et al*. Primary PNET of maxilla: An unusual presentation. J Pediatr Hematol Oncol 2008;30:474-7.
5. Hormozi AK, Ghazisaidi MR, Hosseini SN. Unusual presentation of peripheral primitive neuroectodermal tumor of the maxilla. J Craniofac Surg 2010;21:1761-3.
6. Manduch M, Dexter DF, Ellis PM, Reid K, Isotalo PA. Extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor of the posterior mediastinum with t(11;22)(q24;q12). Tumori 2008;94:888-91.
7. Weiss SW, Goldblum JR. Ewing's sarcoma/PNET tumor family and related lesions. In: Weiss SW, Goldblum JR, editors. Enzinger and Weiss's Soft Tissue Tumors. 2nd ed. Philadelphia: Mosby; 1998. p. 945-87.
8. Ibarburen C, Haberman JJ, Zerhouni EA. Peripheral primitive neuroectodermal tumors. CT and MRI evaluation. Eur J Radiol 1996;21:225-32.
9. Sun G, Li Z, Li J, Wang C. Peripheral primitive neuroectodermal tumour of the maxilla. Br J Oral Maxillofac Surg 2007;45:226-7.
10. Wang C, Qiu TT, Yu XF, Xuan M, Gu QQ, Qian W, *et al*. Rare presentation of peripheral primitive neuroectodermal tumor in the maxilla and mandible: A report of two cases. Oncol Lett 2014;8:615-9.
11. Shah S, Huh KH, Yi WJ, Heo MS, Lee SS, Choi SC. Primitive neuroectodermal tumor of the maxillary sinus in an elderly male: A case report and literature review. Imaging Sci Dent 2014;44:307-14.
12. de Alava E, Antonescu CR, Panizo A, Leung D, Meyers PA, Huvos AG, *et al*. Prognostic impact of P53 status in Ewing sarcoma. Cancer 2000 15;89:783-92.
13. López-Guerrero JA, Machado I, Scotlandi K, Noguera R, Pellín A, Navarro S, *et al*. Clinicopathological significance of cell cycle regulation markers in a large series of genetically confirmed Ewing's sarcoma family of tumors. Int J Cancer 2011 1;128:1139-50.