EWING’S SARCOMA / PNET OF SINO-NASAL REGION: A RARE CASE REPORT

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ABSTRACT
Ewing sarcoma (ES) and primitive neuroectodermal tumor (PNET) are closely related, round cell tumors belonging to of Ewing’s family of tumors (EFT). EFT is highly malignant neoplasm affecting children and young adults, which very rarely involves the head and neck region. Only few cases have been reported in the sinonasal region. In this article, we report a 13 years old female patient with ES/PNET in sinonasal region for its rarity. The patient presented with protruding mass on right side of nasal cavity with obstruction and epistaxis of 1 month duration. The patient underwent for endoscopic nasal surgery under general anesthesia, the mass was excised completely. The biopsy specimen histopathology revealed undifferentiated round cell malignant neoplasm, and the definitive diagnosis of ES/PNET was made with immunohistochemistry. The patient was treated with adjuvant chemotherapy. This article analyses the rarity, clinical, pathological, immunohistochemical, molecular aspects of ES/PNET and discusses the recent update on this entity in sinonasal region, so as to differentiate from other small round tumors of the region for their appropriate therapeutic implications.

KEYWORDS: Ewing’s sarcoma, Peripheral Neuroectodermal tumor, Sino-nasal region, Small round cell tumor.

INTRODUCTION
In 1918, Arthur Stout described a small round cell tumor as primitive neuroectodermal tumor (PNET) in the ulnar nerve. Later, in 1921 James Ewing described a tumor of undifferentiated cells in long bones as Ewing's sarcoma. Over the years, these two tumors were described as two distinct entities, since both share similar immunohistochemical, cytogenetic, and molecular features, are now considered to be the ends of a histological spectrum of “Ewing’s family of tumors” (Desai and Nirmala, 2010).

The incidence of these tumors occurring in the head and neck region is just 2-7%. Mandible and maxilla are the most common sites, whereas involvement of the sinonasal region is very rare (Thompson, 2007), and only few case reports have been published in world literature (Sunil, et al., 2012). Small round cell tumor of the sinonasal region may pose diagnostic difficulties, but their correct classification by means of histology, immunohistochemistry or molecular biology can ascertain their diagnosis, prognosis and an appropriate targeted therapy.

MATERIALS AND METHODS
The excised mass immersed in 10% formalin was received in the department of Pathology. The specimen was grossed, further fixed, processed for dehydration, clearing, impregnation, embedding, block making and section cutting using rotary microtome. The sections were routinely stained with hematoxyllin and Eosin (H&E) for histopathology study, which revealed undifferentiated round cell malignant neoplasm. Separate blocks were prepared and sent to pathologist of “The human protein Atlas” Lab Surgpath Mumbai for Immunohistochemistry (IHC) staining and studies, which clearly differentiated the round cell malignant neoplasm as ES/PNET. The patient was treated with adjuvant chemotherapy for ES/PNET.

RESULTS AND DISCUSSION
Case history
A 13 years old female presented with nasal block on right side with epistaxis since 3 month. It was a recurrent antrochonal polyp. Local examination of the nostril revealed soft fleshy mass protruding and obstructing the right nostril. Left nostril was patent. Oral cavity and oropharynx were normal. Laboratory Investigations were within normal limits. Epstein Barr Virus (EBV) IgG and IgM antibodies were negative. Computerized Tomography (CT) scan on plain coronal section showed (Figure 1 a and b) soft tissue lesion originating from right inferior turbinate and filling the entire right nasal cavity with widening of right osteomeatal complex with a diagnosis of Polyp. The patient underwent complete excision of the mass with endoscopic nasal surgery under general anesthesia. Grossly, the mass was measuring 2 x 2 cms. The cut section was solid white in color with areas of hemorrhage and necrosis. Histopathology revealed sub-epithelial tumor (Figure 2a) composed of groups and sheets of uniform small to medium sized round cells arranged in lobular and trabecular patterns. The nuclei were round having fine chromatin and prominent nucleoli and the cytoplasm was scant clear with indistinct cell borders. Mitotic figures with moderate pleomorphism were seen.
2 b) Invasion into surrounding tissue was noticed. Foci of hemorrhage and necrosis seen. Immunohistochemistry was performed, which was strongly positive for CD 99 (Figure 2c) and vimentin (Figure 2d). It was negative for CD45, CD56, CD57, Desmin, HMB45, Myogenin, Pan CK, Synaptophysin. A final diagnosis of Extraskeletal Ewing’s sarcoma / Peripheral neuroectodermal tumor of sino-nasal tract was made. Patient was treated with adjuvant chemotherapy. Clinically and radiologically no recurrence of disease was noted during a follow-up period of 1 year.

Figure 1: (a) Computerized tomography-coronal view and (b) showing heterogeneously enhancing soft tissue lesion involving the right maxillary, ethmoidal, frontal and right nasal cavity with destruction of medial wall of right maxillary sinus.

DISCUSSION
ES/PNET is high-grade, round-cell tumors with a neuroectodermal phenotype of childhood and adolescence with slight male predilection (Thompson, 2007). Clinically the tumor may simulate osteomyelitis. It is highly malignant neoplasm having both skeletal and extraskeletal forms. The skeletal forms are more frequent and occur in long bones of the extremities. The extraskeletal form usually occurs in the soft tissue of lower extremities, paravertebral tissues, chest wall, retroperitonium and rarely in the head and neck region (Sunil, et al., 2012). Only 2-3% of them are found in the head and neck area primarily involving mandible and the skull base. It is extremely rare in the sinonasal region.

Grossly, it is white, fleshy polypoid and multilobulated neoplasm that rarely exceeds 10 cm in diameter. The cut surface is gray-yellow, soft, and friable with necrosis. Histologically, it is marked by densely packed sheets of uniform, small round cells, arranged in lobular pattern. The nuclei are round, with a distinct nuclear membrane, fine powdery chromatin and one to two small nucleoli. The cytoplasm is ill-defined, scanty, and pale to vacuolated as a result of intracellular deposits of glycogen. Coagulative necrosis is frequently identified. Vascular structures with degenerated “ghost” cells arranged in organoid pattern is a common feature known as “filigree” pattern.

The differential diagnosis of ES/PNET includes all other ‘small round blue-cell tumors, particularly lymphoblastic lymphoma, desmoplastic small cell tumor, and embryonal/alveolar rhabdomyosarcoma, olfactory neuroblastoma and sinonasal undifferentiated carcinoma, which requires the application of special studies to confirm the diagnosis. The tumor cells contain glycogen, which is highlighted with a periodic acid-Schiff (PAS) stain (Meis-Kindblom et al., 1996).

Immunohistochemically, there is consistent positivity for vimentin. CD99 (013; HBA71; p30/32; MIC2) is a cell surface glycoprotein consistently expressed by the cells of ES/PNET (Scotlandi et al., 1996). Further, positivity has been described for neuron-specific enolase, protein gene product 9.5, Leu7 (CD57), secretogranin II, and neurofilaments, suggesting neuroepithelial differentiation and are expressed less often (Carter et al., 1990). Cytogenetic
and molecular genetic techniques (fluorescence in situ hybridization [FISH] and reverse transcriptasepolymerase chain reaction [RT-PCR]) using, paraffin-embedded tissues has greatly facilitated the diagnosis of these tumors. About 95% of cases of ES/PNET show reciprocal translocation t(11;22) (q24;q12) or t(21;22) (q22;q12), which results in the fusion of the EWS (Ewing sarcoma) gene at 22q12 with the FLI1 or ERG gene, respectively. In the remaining cases, EWS is fused with other genes, such as FEV, ETV1, and E1AF (Barr and Womer, 2007).

The metastatic spread of ES/PNET is to the lungs and pleura, other bones and central nervous system. About 25% of the patients have multiple bone and/or visceral lesions at the time of presentation. The treatment of ES/PNET represents one of the success stories of medical oncology and is based on multiagent systemic chemotherapy, combined with surgical removal of the tumor and/or radiation. Local control is achieved in over 85% of the cases, and the actuarial 5-year disease-free survival is 75%. Prognostically, direct soft tissue extension, metastasis, filigree microscopic pattern are associated with poor prognosis whereas tumors with EWS–FLI1-type fusion with better prognosis.

![Figure 2](image)

Conclusions
The diagnosis and analysis of ES/PNET amalgamates the usual or classical tolls such as histology and immunohistochemistry with newer molecular techniques like FISH and PCR may allow us not only to understand the biology of these lesions better but also to develop better techniques for their diagnosis and potential treatment.
REFERENCES


