CASE REPORT

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Primitive neuroectodermal tumor (PNET) of nasal cavity

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ABSTRACT

This is case where an elderly woman referred to our clinic with history of recurrent epistaxis from right nostril for one year duration associated with persistent right nasal blockage, hyposmia, loss of weight and loss of appetite.
On examination noted polypoidal mass at right sphenoethmoidal recess with evidence of previous surgery. Patient underwent endoscopic removal of the mass and histopathologic examination was reported as malignant small round blue cells tumors from right olfactory cleft and right ethmoidal air cells. Based on immunohistochemical examination, it was consistent with primitive neuroectodermal tumour (PNET).

Key Words: Primitive neuroectodermal tumor, PNET, nasal cavity, small round cell tumor

Introduction

Primitive neuroectodermal tumors (PNETs) are highly malignant small round cell tumors of neuroectodermal origin which affect soft tissues and bone. Their clinical manifestation exhibit great diversity and pathologic similarities with other small round cell tumors. Betsakis et al. (1) in 1996 divided these tumors in three group based on tissue of origin which is

- Central nervous system (CNS) PNETs which derived from CNS.
- Neuroblastoma which derived from autonomic nervous system (ANS)
- Peripheral PNETs derived from tissues outside the CNS and ANS

The incidence of PNETs in the head and neck region is around 2-7% where mandible and skull base are the two most common site. Its incidence in sinonasal region can be considered as rare (2,3) and very limited cases been reported due to its rareness.

In this case report we discuss a case of PNET originating from olfactory cleft in the nasal cavity.

Case report

A 72 years old lady with background history of Diabetes mellitus and hypertension complained of recurrent epistaxis from right nostril for one year duration, which occured on blowing her nose. Each time the epistaxis was moderate amount and stopped spontaneously. The above symptoms were associated with persistent right nasal blockage, hyposmia, loss of weight and loss of appetite. However she denied other nasal symptoms including facial pain or swelling, blurring of vision or diplopia, headache or ear symptoms.

She initially presented elsewhere and was noted to have multiple polypoidal mass in the right nasal cavity involving right maxillary sinus, middle meatus and ethmoids. The mass was noted to be arising from right posterior superior nasal septum. She underwent endoscopic endonasal excision of tumour. The histopatological examination (HPE) was reported as neuroendocrine carcinoma (Intermediate grade) and eventually referred to us for further management.

On nasoendoscopy in clinic, we noted there was evidence of previous nasal surgery and polypoidal mass at right sphenoethmoidal recess. We proceed with computed tomography scan (CT Scan) and magnetic resonance imaging (MRI) of paranasal sinus and brain which was reported as:

- Irregular soft tissue lesion noted in the right ethmoid sinus extending anteriorly to the ostium of the frontoethmoidal recess and right frontal

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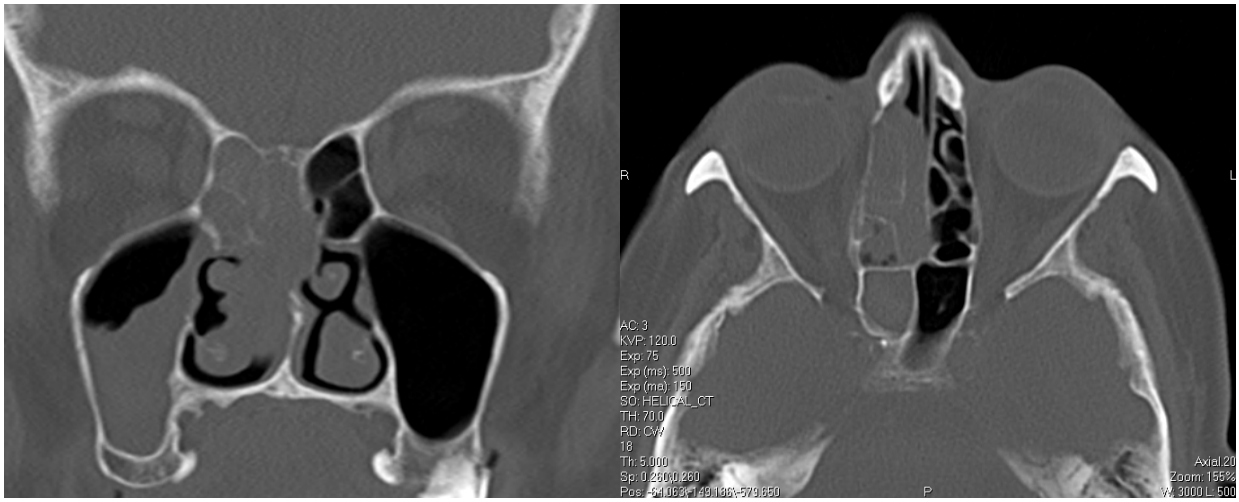

Fig. 1. CT paranasal sinus shows irregular soft tissue mass in the right ethmoid sinus extending anteriorly to frontoethmoidal recess, frontal sinus and posteriorly to ipsilateral sphenoethmoidal recess. (Left: Coronal cut, right: Axial cut).

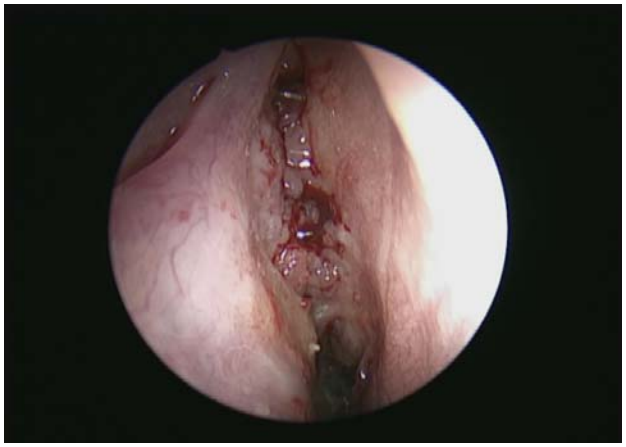

Fig. 2. Polypoidal tumor seen arising from the olfactory cleft.

- sinus and extending posteriorly to the ipsilateral sphenoethmoidal recess. (figure 1)
- The lesion showed enhancement on post contrast.
- There was evidence of extension of the lesion beyond the duramater at right frontal region.

Endoscopic transnasal excision of tumor was performed in which the intra operative findings were:

- Polypoidal tumor seen arising from the olfactory cleft (figure 2)
- Dehiscent of right cribriform plate where the tumor extend intracranially
- There was normal healthy brain tissue with no evidence of duramater in between.
- Cerebrospinal fluid (CSF) leak was noted post removal of tumor and was repaired intraoperatively with nasoseptal flap.

HPE was reported as malignant small round blue cells tumors from right olfactory cleft and right ethmoidal air cells. Based on immunohistochemical examination it was consistent with primitive neuroectodermal tumour (PNET).

Discussion

PNET was first described by Stout in 1918, which was thought to arise from nerves at the time (3). However in 1973 Hart and Earle applied the term primitive neuroectodermal tumour which they described as a group of small round cell tumors of the central and peripheral nervous system that was derived from fetal neuroectodermal precursor cells (4). The origin of PNETs are from outside the autonomic nervous system. They are also known as peripheral neuroepithelioma and peripheral neuroblastoma (5). It usually occurs in the soft tissue of lower extremities, chest wall, paravertebral tissues, retroperitoneum and rarely in the head and neck region.

The incidence of these tumors is very rare and can occur at any age with peak incidence during adolescence (4). Literature review revealed that PNETS are usually present in the second decade of life with slight male preponderance. Further advances in immunohistochemical analysis has helped further to distinguish PNETs from other small round cell tumors such as rhabdomyosarcoma, neuroblastoma and lymphoma. The clinical behavior of PNET is usually aggressive with worse outcome compared to other small round cell tumors. Thus it is important to make a correct diagnosis of PNET for its effective management.

The clinical symptoms depend on the site of the tumor, which includes pain and swelling of the surrounding structures due to mass effect. The nasal cavity symptoms will be progressive unilateral nasal

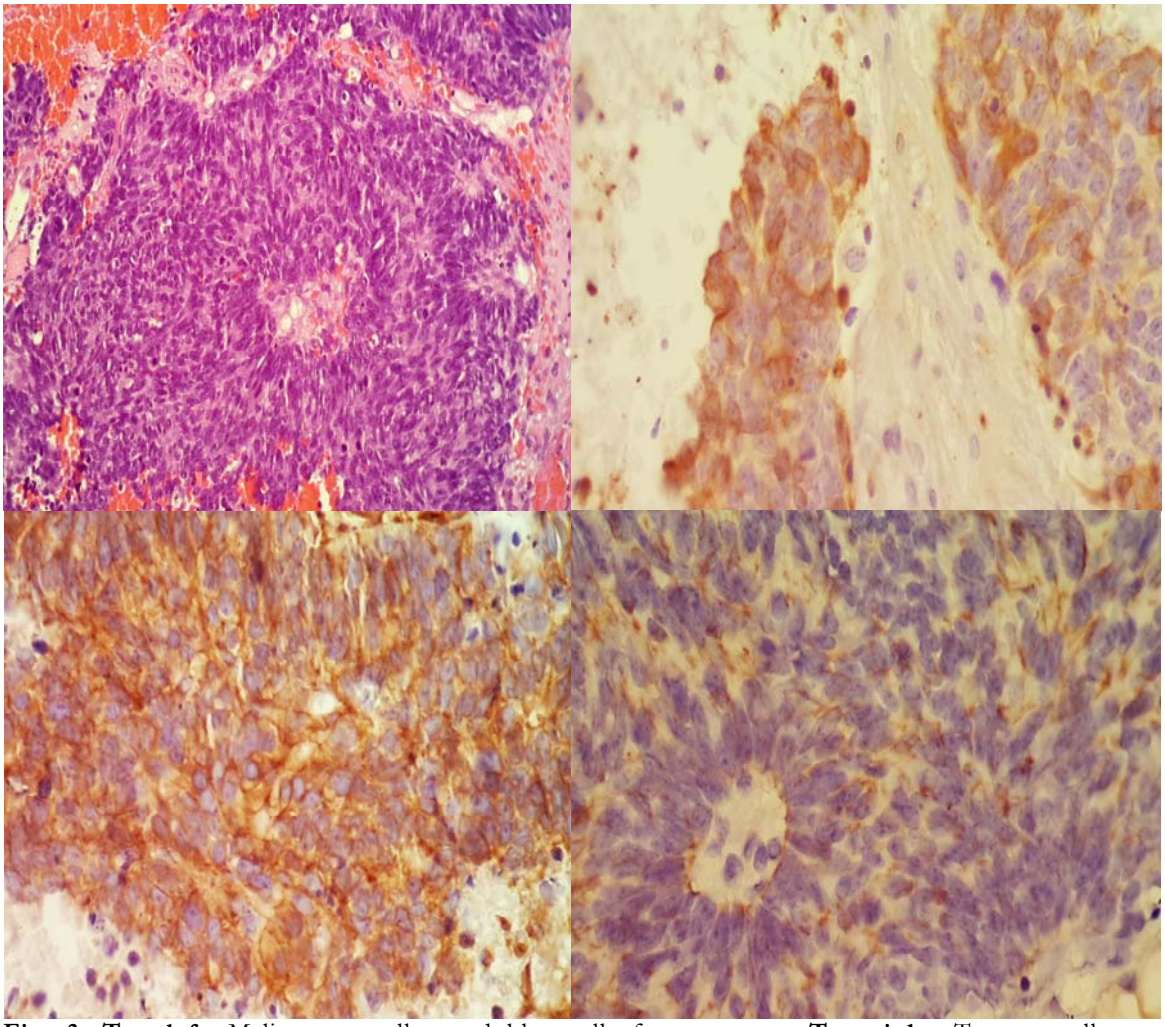

Fig. 3. Top left: Malignant small round blue cells form rosettes, **Top right:** Tumour cells are immunoreactive toward CD99, **Bottom left:** Tumour cells are immunoreactive toward neuron specific enolase, **Bottom right:** Tumour cells show focal reactivity toward cytokeratin.

blockage, pain with swelling when the tumor is big and invasive.

Macroscopically it is multilobulated and polypoidal tumor, rarely exceed 10cm in diameter. The cut surface is gray-yellow, soft and friable with necrosis, (3) which is consistent with our histological appearance.

Microscopically PNETs appear as small round cell sheets or lobules (figure 3) with the presence of Homer-wright rosette (6). There was some vague rosettes seen microscopically with evidence of small round cells. The ultrastructural characteristic of the tumor are neurosecretory granules with microtubules and microfilament with short dendritic processes between cells which are consistent with PNETs.

Immunohistochemically, PNETs demonstrates a polyphenotypic profile, as might be expected of a primitive tumor. Specifically, there is consistent positivity for vimentin and variable expression for desmin, neurofilaments, neuron-specific enolase (NSE), Leu-7 (CD57), and S-100 protein. In 50% of cases PNETs is immunopositive for cytokeratin with diffuse or focal reactivity. These tumors are negative for HMB-45, leukocyte common antigen (CD45), myogenin, and MyoD1. Greater than 95% of PNETs are positive for MIC2 (CD99) (7). In our case the tumor were positive for CD99, vimentin, NSE and cytokeratine and focally positive for EMA, S100 and chromogranin and negative for synaptophysin.

Cytogenetic and molecular genetic technique such as fluorescence *in situ* hybridization (FISH) and reverse transcriptase polymerase chain reaction (RT-PCR) using paraffin-embedded tissue has a major role in diagnosing PNETs (2). More than 95% of cases of ES/PNET on cytogenetic examination show the reciprocal translocation 11;22 (q24;q12), which results in the fusion of the EWS gene with the FLI or ERG genes (7). In our case the cytogenetic analysis revealed that there was

- Deletion of one (Ewing sarcoma breakpoint region 1 (EWSR1) at locus 22q12
- Aneuplody of chromosome 22

- Negative for rearrangement involving the SS18 gene which are common for synovial sarcoma soft tissue tumors

Tissue biopsy together with cytogenetic and immunohistochemical studies is essential in making the diagnosis of PNETs. Computed tomography scan (CT Scan) and magnetic resonance imaging (MRI) are to determine the extension of tumor and metastasis. There is high incidence of metastasis in PNETs at presentation, so full examination to determine metastasis is indicated in a suspected case of PNET which includes chest x-rays, CT scan of chest and a bone marrow biopsy. The metastatic spread is usually to the lungs, pleura, other bones and CNS. In our case there is absence of distant metastasis.

Due to aggressiveness and poor prognosis of PNETs a combine modality of treatment is advocated which is surgery with post operation radio or chemotherapy. Multimodality treatment is advocated to prevent metastatic disease, recurrent disease and to treat residual tumor after resection. The prognosis is still poor even with radical surgery combined with chemo and radiation therapy. In our case patient underwent radical tumor resection and is waiting for post-operative chemo and radiotherapy.

There is marked difference between outcomes of patient who underwent radical and non-radical surgery, the outcome is poorer in the latter. Radiotherapy is advocated to primary site and local nodes. The recommended chemotherapeutic regimens in the treatment of PNETs includes vincristine, doxorubicin and cyclophosphamide with ifosfamide and etoposide (IE) (8).

Radical surgical removal of tumor and early treatment are the important factors that increase the survival rate. Complete remission after initial treatment is common but long term disease-free survival has been discouraging. Two year survival rate is less than 65% (9) and it reduces to 25% if tumor is greater than 5 cm (10). Literature review suggest that patients with metastatic disease uniformly have poor outcome ranging from 0-25%, 5-yr survival rates compared to 40-79% for those with localized disease. In our case it is too early to determine the disease-free survival rate as our patient just underwent initial treatment.

As a conclusion, primitive neuroectodermal tumors are a group of aggressive malignancies that occur very rarely in the head and neck. The most significant prognostic factor is the presence of metastatic disease, where the prognosis is poor. Significant advances in the neoadjuvant and adjuvant chemotherapeutic regimens, as well as improved facility in diagnosing these tumors through cytogenetic and immunohistochemical analysis, is vital in early diagnosing and treatment which should improve the long term disease-free survival.

References

1. Batsakis JG, Mackay B, el-Naggar AK. Ewing's sarcoma and peripheral primitive neuroectodermal tumor: an interim report. Ann Otol Rhinol Laryngol 1996; 105: 838-843.
2. Patil AM, Yendigeri SM, sajjanar BB, Kudadi SS. Ewing sarcoma/ PNET of sinonasal region: a rare case report. www.sciencejournal.in. 2013; 2(2).
3. Stout AP. A tumor of the ulnar nerve. Proc NY Pat Soc 1918; 18: 2-11.
4. Heung ML, Seung HH, Jeong SW, et al. Primitive neuroectodermal tumor of nasal cavity: case report. J Rhinol. 1997; 4: 57-60.
5. Jurgens H, Bier V, Harma D, et al. Malignant peripheral neuroectodermal tumors: a retrospective analysis of 42 patients. Cancer 1988; 61: 349-357.
6. Chowdhury K, Manoukian JJ, Rochon L, Begin LR. Extracranial primitive neuroectodermal tumor of the head and neck. Arch Oto- laryngol Head Neck Surg 1990; 116: 475-478.
7. Iezzoni JC, Mills SE. "Undifferentiated" small round cell tumors of the sinonasal tract: Differential diagnosis update. Am J clin Pathol 2005; 124: 110-121.
8. Carvajal R, Meyer P. Ewing's sarcoma and primitive neuroectodermal family of tumor. Hematol Oncol Clin North Am. June 2005; 19: 501-525.
9. Jones JE, McGill T. Peripheral primitive neuroectodermal tumors of the head and neck. Arch Otolaryngol Head Neck Surg 1995; 121: 1392-1395.
10. Kushner BH, Haydu S, Gulati SC. Extracranial primitive neur- oectodermal tumors. Cancer 1991; 67: 1825-1826.