Case report

Peripheral Primitive Neuroectodermal Tumor (pPNET) of the Parotid: Report of a Rare Case

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Abstract

Primitive neuroectodermal tumors (PNETs) are a family of highly malignant soft tissue neoplasms mostly occurring in children and young adults. PNETs usually develop in the thoracopulmonary region, abdomen, pelvis, and rarely in the head and neck region. Here, a case of PNET located in the parotid gland is reported.

Key words: Head and neck cancer, parotid gland, primitive neuroectodermal tumor

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Introduction

Primitive neuroectodermal tumors (PNETs) are a category of highly malignant tumors that belong to Ewing's sarcoma family of tumors.[1] They are composed of small round cells of neuroectodermal origin and mainly affect the central nervous system (CNS). PNETs outside the CNS and the autonomic nervous system are exceedingly rare and are called peripheral PNETs (pPNETs). They most commonly occur in the thoracopulmonary region (Askin's tumor), abdomen, pelvis, extremities and rarely in the head and neck.[2,3,4] PNETs have been reported more frequently in the second decade of life with a slight male predominance.[5]A review of the scientific literature describes only a few cases of pPNET affecting the parotid gland. Here, we report a case of pPNET of parotid in a 26-year-old man.

Case report

A 26-year-old man presented with complaint of a progressively enlarging right facial swelling for 15 months. On physical examination, there was a firm non-tender swelling with ill-defined margins and no local rise of temperature. Intraoral examination revealed an ulcerative mass occupying the whole buccal vestibule of the right maxilla. There was no evidence of dental caries or periodontal disease in that area. The patient reported a history of an incisional biopsy with the histopathological diagnosis of lymphoepithelial cyst 12 months before. Laboratory findings were within normal limits.

Contrast enhanced axial and coronal computed tomography (CT) revealed a well-defined homogeneous soft tissue mass extending from the zygomatic arch to the mandibular ridge involving the right parotid gland. The mass caused mild erosion in the medial aspect of ramus and pushed the airway tract inside (Figure 1).

Incisional biopsy was performed under local anesthesia and, on histopathological examination, solid sheets and islands of uniform, small round cells with round nuclei, scanty clear cytoplasm, and indistinct cell outlines were revealed. There were neither obvious mitotic figures nor rosette formation (Figure 2). Due to these findings, a small round cell tumor with a differential diagnosis of malignant lymphoma, rhabdomyosarcoma, PNET, metastatic neuroblastoma and poorly differentiated carcinoma was suggested. For definitive diagnosis, immunohistochemical study was done. The immunohistochemistry showed negativity for cytokeratin, leukocyte common antigen (LCA) and actin, and strong positivity for vimentin, MIC2 (CD99) and S-100. Hence, a final diagnosis of pPNET was established (Figure 3).

To evaluate any distant metastasis and tumor staging, CT scan of the lungs and abdomen and whole body bone scan with TC-99m were performed and no distant metastasis was detected. Because of the proximity of vital structures and tumor extensiveness, surgical excision could not be performed; therefore, the patient underwent 17 cycles of chemotherapy (including vincristine, actinomycin D, and ifosfamide) and radiotherapy. The patient is under follow-up for 32 months and no recurrence has been seen up to now.

Discussion

PNET was first described by Hart and Earle in 1973 as a group of small round cell tumors occurring in children and originating from the primitive neural crest cells.[6,7] Based on the originating tissue, Batsakis, *et al*. divided the PNET family into three groups: 1) Central PNETs (cPNETs) such as medulloblastoma, which originates from the central nervous system; 2) Tumors arising from the autonomic nervous system such as neuroblastoma; and 3) Peripheral PNETs (pPNETs) encompassing tumors derived from tissues outside the central and autonomic nervous system.[8]

pPNET was first introduced by Stout in 1918.[9] The pPNETs also belong to the Ewing family of tumors which include osseous and extraosseous Ewing's sarcoma and pPNET. This family of tumors show a characteristic chromosomal translocation in molecular cy-

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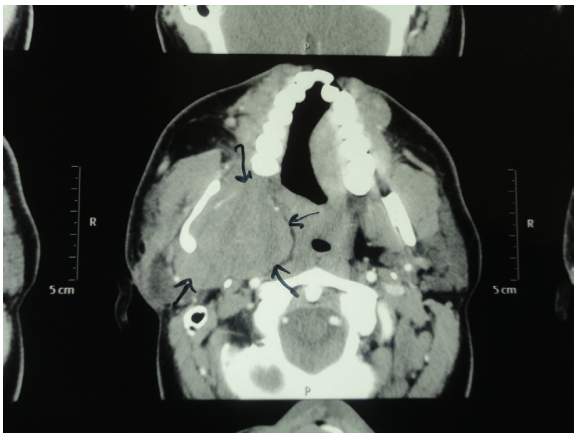

Figure 1. Contrast enhanced axial CT showing a well-defined homogeneous soft tissue mass involving the right parotid gland.

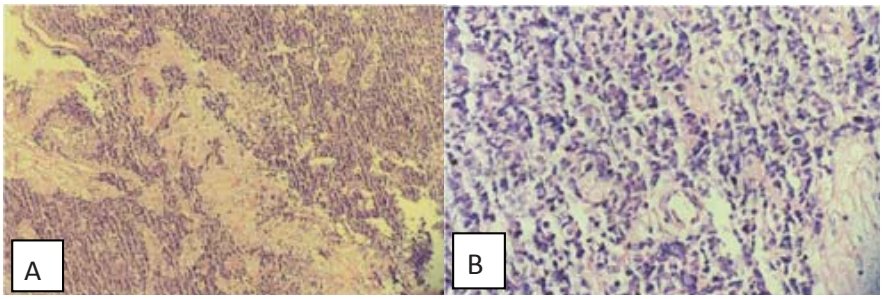

Figure 2. (A) Micros c copic examination revealing a tumoral tissue composed of sheets and islands of proliferating uniform, small round ells.(H & E staining; ×100) **(B)** Higher magnification showing small round nuclei, scanty clear cytoplasm, and indistinct cell borders. (H & E staining; ×200).

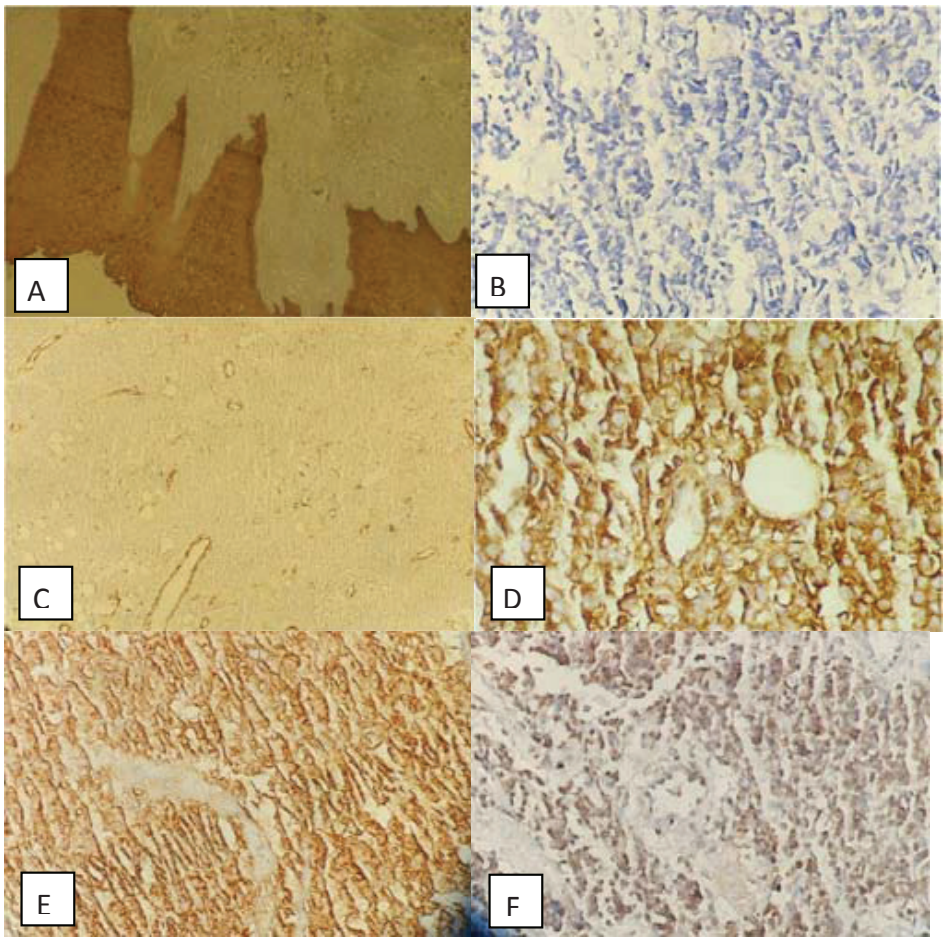

Figure 3. (A) Immunohistochemical staining showing negativity for cytokeratin, **(B)** leukocyte common antigen (LCA), **(C)** and actin, **(D)** and strong positivity for vimentin, **(E)** MIC2 (CD99) **(F)** and S-100. (IHC staining X400)

togenic analysis t(11; 22) (q24; q12) leading to the EWS gene mutation, resulting in EWS- FLI1 fusion protein formation.[10,11]

pPNETs represent 1% of all sarcomas and are most common in the thoracopulmonary region (Askin's tumor), pelvis, abdomen and extremities. Most studies have reported that the head and neck region is a rare site of involvement.[2,12] In a retrospective analysis of 42 patients with pPNETs, Jurgens, *et al*. reported that only 4 involved the head and neck region.[13] However, two case series reported by Jones and Kimber, *et al*., showed that head and neck localizations were second after thoracopulmonary involvement.[14,15] In the head and neck, the most common location of occurrence is the orbit, followed by neck and the parotid gland.[2]

PNETs have a tendency to affect young adults with a slight male predominance.[3,12] In a review by Nikitakis, *et al*. on 43 patients with pPNETs localized in the head and neck region, a predilection for children and adolescents with a mean age of 21 years was observed.[1]

The diagnosis of PNET is based on histological, immunohistochemical and ultrastructural findings. Microscopically, PNET is a member of the "small round cell tumors" group including lymphoma, neuroblastoma, rhabdomyosarcoma and Ewing's sarcoma. It is composed of small, uniform round to oval cells with round nuclei, scanty clear or eosinophilic cytoplasm and indistinct cell outlines. The differentiation of PNET from Ewing's sarcoma is based on the presence of neural differentiation which is indicated by histological evidence of Homer-Wright rosettes. The immunohistochemistry is positive for CD99 (MIC2), neural differentiation markers like neuron-specific enolase (NSE), S-100, synaptophysin and chromogranin. Although immunoreactivity with CD99 is very sensitive for PNET, it is not confined to this tumor as it can be detected in acute lymphoblastic lymphoma, T-cell lymphoblastic leukemia, synovial sarcoma, and rhabdomyosarcoma. Ultrastructurally, PNETs reveal primitive cells with long cytoplasmic processes with glial filaments, microtubules, and neurosecretory granules. Finally, polymerase chain reaction (PCR) and fluorescence *in situ* hybridization (FISH) are also helpful to assay the chromosomal translocation.[2,10,16]

Because of the tendency for recurrence and early distant metastasis to lung, liver, and bone marrow, the overall prognosis of PNET is poor. Its disease -free survival rate is less than 50% in 3 years and 30%–45% in 5 years. It seems that primary tumor location is an important prognostic factor. Tumors originating from the paraspinal and scapular areas have the most favorable response to treatment, while abdominal and pelvic tumors are unresponsive. Head and neck tumors have an intermediate outcome and orbital tumors seem to have a better prognosis.[3,10,17]

Successful treatment requires using a combination of therapeutic modalities including surgery, followed by radiotherapy with doses ranging from 45 to 60 Gy for local control, and chemotherapy. Adequate surgical excision with negative margins is effective for local control. In cases with proximity of vital structures, preoperative chemotherapy and radiotherapy can be used. In inoperable tumors, concomitant chemoradiotherapy protocols are used. Chemotherapeutic agents including dactinomycin, vincristine, alkylating agents such as cyclos, phophamide and ifosfamide and anthracyclines such as doxorubicin have proved to be helpful in PNET. Because of its propensity for local recurrence and distant metastasis, a full metastatic work-up including a chest X-ray, CT scan of the lungs, a bone scan, and bone marrow aspiration should be performed.[10,16,18]

In conclusion, although pPNET is rare in the head and neck, it should be considered in the differential diagnosis of small round cell tumors. Due to its poor prognosis, accurate diagnosis and aggressive treatment including surgery, chemotherapy and radiation radiotherapy should be performed for the patient.

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