Case Report

A Rare Case of Peripheral Primitive Neuroectodermal Tumor Arising from the Minor Salivary Gland in a Young Woman

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Abstract: We report here a case of peripheral primitive neuroectodermal tumor (PNET) arising from the minor salivary gland. A 22-year-old woman was admitted to our hospital for surgical excision of a small painless cheek tumor with a 7-month history. Macroscopically, the tumor measured 10 × 5 × 6 mm and was located in the minor salivary gland. Microscopically, the tumor comprised proliferating, small, round cells with scant cytoplasm and high nuclear cytoplasmic ratios. The tumor cells showed some mitotic figures and Homer-Wright-type rosettes. Immunohistochemically, the tumor cells were immunopositive for CD99, synaptophysin, CD56, S-100 protein, and vimentin. Based on these findings, the patient was diagnosed as having PNET arising from the minor salivary gland. There are very few case reports of PNET in the head and neck region, and to the best of our knowledge, this is the first case report of PNET arising from the minor salivary gland.

Key words: peripheral primitive neuroectodermal tumor (PNET), minor salivary gland, CD99, Homer-Wright-type rosette formation

Introduction

Peripheral primitive neuroectodermal tumor (PNET) is a member of the Ewing’s sarcoma family of malignancies1,2). Although PNET can arise from various sites3), very few case reports of such tumors in the head and neck region exist4-6), and there have been no cases reported of PNET originating in the minor salivary gland. We report here, to the best of our knowledge, the first case of PNET arising from the minor salivary gland in the right cheek.

Case Report

A 22-year-old woman was admitted to our hospital for a detailed examination of a small oral tumor, first noted by her family dentist. She was aware of the tumor in the right cheek for 7 months. She was otherwise well and had no prior medical history of note. Physical examination revealed a small, painless, oval, firm mass measuring 1 cm in diameter located in the right upper cheek. There were no palpable lymph nodes in the neck. The patient had no symptoms related to the tumor.

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cheek 7 months before, but there were no clinical symptoms such as pain or bleeding. She had been healthy until this admission, and the other members of her family appeared free of such a hereditary disease. On physical examination, a solitary elastic hard tumor mass was felt in the right cheek, and the tumor was successfully surgically excised. No preoperative image diagnosis or blood examination was carried out.

**Gross findings**

Macroscopically, the tumor was solitary and $10 \times 5 \times 6$ mm in size. The cut surface was solitary, whitish, and well delineated from the normal surrounding tissues (Figs. 1A, 1B). There was no necrosis, hemorrhage, or cystic areas in the tumor.

**Histopathological findings**

Microscopically, the tumor consisted of proliferating, small, round cells with scant cytoplasm and high nuclear cytoplasmic ratios, arranged in sheets (Fig. 2A). The minor salivary glands were involved in the tumor (Fig. 2B), which had invaded the adjacent muscles. The tumor cells showed some mitotic figures and Homer-Wright-type rosette formations. Periodic acid-Schiff (PAS) staining was positive in the cytoplasm, indicating that the tumor cells contained glycogen (Fig. 3A). Mitotic figures were frequently seen, with a ratio of $>10$ figures per 10 high power fields.

**Immunohistochemical findings** (Table 1)

The tumor cells were immunopositive for CD99 (Fig. 4A), synaptophysin (Fig. 4B), chromogranin A, CD56, S-100 protein, and vimentin, but immunonegative for cytokeratin (CK AE1/3), epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), leukocyte common antigen (LCA), desmin, and alpha-smooth muscle actin ($\alpha$-SMA).

![Fig. 1. Macroscopic examination of tumor](image)

The tumor was $10 \times 5 \times 6$ mm in size, and appeared solitary, whitish, and well delineated from the surrounding normal tissue.
MIB1 was not tested due to the markedly high mitotic activity detectable by hematoxylin eosin staining. In the absence of any molecular characterization, the patient was diagnosed as having PNET arising from the minor salivary gland, based on the histopathological and immunohistochemical findings.
Outcome

The patient was well without evidence of disease recurrence 5 months after the surgical excision. Postoperative imaging diagnosis, including both positron emission tomography-computed tomography (PET-CT) with 18F-fluorodeoxyglucose (18F-FDG) and magnetic resonance imaging (MRI), revealed no abnormalities elsewhere in the whole body. Laboratory findings, including blood counts and blood chemistry, were within normal limits.

Discussion

PNET is a neoplasm characterized by neural epithelial differentiation that is difficult to
distinguish on the basis of cytology and histology alone \(^3\). Light microscopy of PNET often reveals small round cells that may form a lobular or pseudorosette pattern, called Homer–Wright-type rosette formation \(^{1-4,6}\). Histopathologically, the differential diagnosis includes other small round cell tumors such as rhabdomyosarcoma, neuroblastoma, and lymphomas \(^7\).

There are several immunohistochemical antibodies available as neural markers that specifically label PNET cells, including those against S-100, chromogranin A, synaptophysin, and CD56. However, immunopositivity for vimentin and CD99 (MIC-2 gene) is of particular diagnostic value for differentiating PNET from other small round cell tumors \(^4,5,7\).

The present case was initially thought to be a poorly differentiated salivary gland epithelial tumor based on its origin from the minor salivary gland. However, the small round tumor cells were immunohistochemically negative for epithelial markers, such as keratin and EMA, or myoepithelial markers, such as \(\alpha\)-SMA and GFAP, which are the predominant histological components of epithelial salivary gland tumors. On the other hand, the tumor cells were immunopositive for neuroendocrine markers such as synaptophysin, chromogranin A, and CD56, as well as diffusely immunopositive for CD99 (MIC-2 gene). These immunohistochemical findings and the histopathological finding of Homer-Wright-type rosette formation led to the final diagnosis of PNET.

Definitive categorization of PNET and other small round cell tumors in the head and neck region usually requires biopsy, frozen-section diagnosis, and surgical excision. According to Helsel \textit{et al} \(^3\), the findings of single noncohesive cells and loosely cohesive clusters composed of small to medium-sized cells with scanty cytoplasm, unipolar cytoplasmic processes, round to oval nuclei with smooth nuclear membranes, and glycogen immunopositivity are suggestive of PNET. Therefore, the finding of such a small round cell tumor on initial examination should be followed by a careful search for rosette formations and immunohistochemical examination for CD99 expression to reach an accurate final diagnosis.

Votta \textit{et al} \(^2\) reported that CD99 immunopositivity characterizes expression of the t(11:22) (q24:12) gene product, and that this genetic anomaly is a highly sensitive marker for PNET. Recently, Makary \textit{et al} \(^8\) reported an unusual histological variant of Ewing’s sarcoma that was confirmed by fluorescence in situ hybridization to show a diagnostic translocation rearrangement in the EWR1 gene at 22q12. Thus, such molecular techniques are essential in determining an unusual histological type of PNET.

PNET has been detected at various sites including the thoracopulmonary region (Askin’s tumor), pelvis, kidney, uterus, ovary, urinary bladder, and pancreas \(^1\). This tumor rarely occurs in the head and neck region, with few reported sites such as the orbit and the parotid gland \(^3\). Moreover, only a few case reports are available for PNET in the oral region, namely the tongue \(^6\), parotid gland \(^1,3\), maxillary gingiva \(^9\), and anterior mandible \(^2\) (Table 2). However, there are no previous reports of PNET arising from the minor salivary gland.

A report by Pereira \textit{et al} \(^9\) of oral PNET metastasizing from the chest highlights the
necessity to determine whether any such tumor is primary or metastatic, because in the latter case prognosis is very poor. In the case of their patient, a rapidly growing painful mass measuring 35 mm in diameter on the right lower gingiva was observed 5 months after chest PNET was detected, and the patient died 3 weeks later. However, in our patient, the absence of abnormal uptake elsewhere in the whole body determined by PET-CT and the absence of a history of malignancy indicated that the tumor arising from the minor salivary gland was a primary tumor.

In the few reported cases of PNET in the oral region, tumor size was 25 mm in diameter in one case in the tongue \(^6\), 30 to 75 mm in three cases of parotid gland tumors \(^3\), 20 mm in the one case in the maxillary gingiva \(^4\), and 50 mm in the anterior mandible \(^2\); the size of the tumor in our patient was the smallest oral PNET thus far reported at 10 mm. Among the reported six cases, the patients with PNET in the tongue \(^6\) or maxillary gingiva \(^4\) died of the tumor, and one patient each with PNET in the parotid gland \(^1\) and the anterior mandible \(^2\) remained alive; the outcome in two of the patients with a parotid tumor was not reported \(^3\). Our patient remains alive without evidence of disease recurrence. It is clearly necessary to study more cases of PNET to determine whether tumors arising from the minor or major salivary gland carry a similarly favorable prognosis to those arising from the orbit \(^7\).

In conclusion, a rare case of small PNET arising from the small salivary gland was reported. Because PNET frequently has a poor prognosis, an accurate diagnosis that differentiates it from other primary salivary gland tumors based on immunohistochemical investigation is necessary.

References


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