

# Malignant peripheral primitive neuroectodermal (pPNET) of tongue

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## Abstract

Primitive neuroectodermal tumors (PNETs) are relatively rare tumors. Tumors that once would have been diagnosed as Ewing's sarcoma are now often designated as peripheral neuroepithelioma or synonymously PNET. This paper reports a case of PNET located orally on the tongue, which is, to our knowledge, the first case reported in medical literature. The patient was treated with postoperative radiotherapy and chemotherapy. Multiple liver metastases occurred 5 months after the initial diagnosis and following extensive chemotherapy the patient was only able to survive for a further 10 months.

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## 1. Introduction

Malignant pPNET (peripheral neuroepithelioma) is a rare tumor, which most commonly affects the thoracopulmonary region (Askin's tumor), pelvis, abdominal region and extremities [2,3].

Most studies have reported this tumor much less frequently located in the head and neck region [4–7]. However, in the two large series of pPNET reported by Jones and Kimber et al., head and neck localizations were 42% (11 of 26) and 23% (6 of 26), respectively, second only to tumors of the thoracopulmonary region [3,8]. Overall, the incidence of pPNET in the head and neck seems to be rare, reflecting the general low incidence of these tumors. This paper reports a case of head and neck malignant pPNET located at the oral tongue and review the related literature.

## 2. Case report

A 20-year-old male was admitted to the hospital with a 4-month history of pain, a progressively enlarging an oral tongue mass and a neck lymphadenopathy. Head and neck examinations and magnetic resonance imaging (MRI) revealed a 2.5 cm × 2.5 cm non-tender and a fixed mass on the tongue located posterolaterally (Fig. 1) and a 4 cm × 4 cm right jugulodigastric lymphadenopathy.

Laboratory findings were within normal limits. Cranium, thorax, whole abdomen computed tomographies (CT) and whole body bone scan were performed to determine the tumoral extent and the presence of metastasis however all were found to be normal.

A partial glossectomy and bilateral modified radical neck dissection were performed.

On close examination the tumor measured 2.5 cm in diameter and was white-gray and fleshy with multiple areas of haemorrhage and necrosis. Histopathological examination revealed uniform small round cells with scant cytoplasm and high nuclear cytoplasmic ratios (Fig. 2). The

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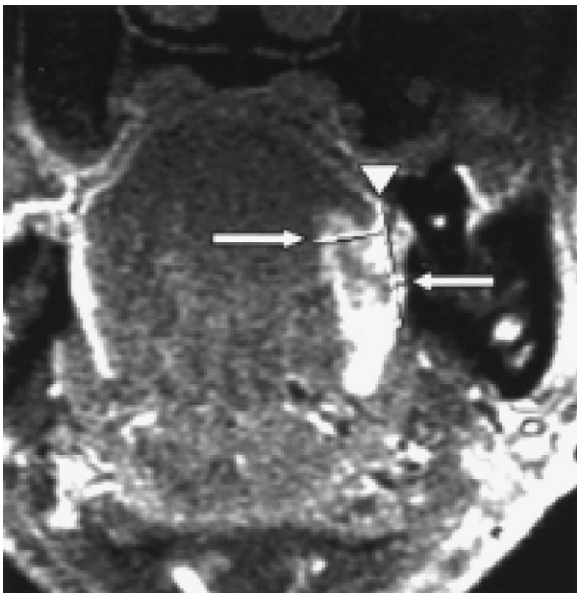


Fig. 1. MRG findings of the lesion located posterolaterally on the tongue.

immunohistochemical reaction for MIC2 showed positive diffusion while there was no staining with pancytokeratin, epithelial membrane antigen, desmin, vimentin, smooth muscle actin or leukocyte common antigen (Fig. 3).

Three of the 10 lymph nodes in the right neck region showed metastatic tumoral deposits.

The histopathological findings were consistent with malignant peripheral primitive neuroectodermal tumor (pPNET) of the oral tongue.

The patient received 50 Gy postoperative radiotherapy to the oral cavity and right neck region beginning 3 weeks after surgery.

He received four cycles of chemotherapy, every 21 days following radiotherapy, which consisted of etoposide, vinblastine, adriamycin, ifosfamide and mesna. Just after the completion of the fourth cycle, multiple liver metastases were observed. The patient received etoposide,

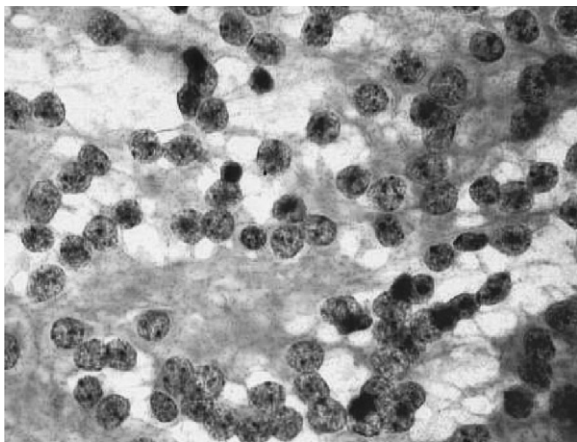


Fig. 2. Small round cells with round or oval nuclei and Homer–Wright type pseudorosettes formations. Hematoxylin–eosin–safran (100×).

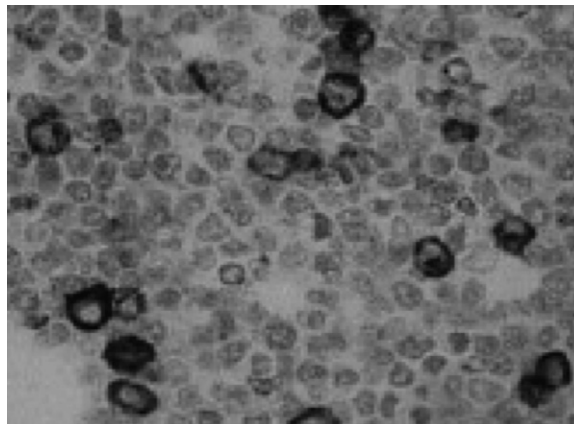


Fig. 3. Tumoral cells diffuse positively staining for MIC2 at immunohistochemical examination (100×).

ifosfamide and cisplatin (VIP regimen) as second line salvage therapy. The patient died due to the progression of distant metastases, having survived for an additional 10 months.

### 3. Discussion

Primitive neuroectodermal tumors are members of the Ewing's sarcoma family composed of small round cells. Due to their rare occurrence, optimal therapy is challenging, particularly when they occur in the head and neck region. Furthermore, the prognosis is generally poor because of the high incidence of metastasis at the time of initial diagnosis.

Primitive neuroectodermal tumor (PNET) is a term that has been used to describe a family of tumors of common neuroectodermal origin. This broad family can be subdivided into three major groups: the first group is central PNET (cPNET), encompassing tumors arising from the central nervous system such as medulloblastoma; second group, neuroblastoma, includes tumors arising from the autonomic nervous system; and the third group, peripheral PNET (pPNET), refers to PNET arising outside the central and autonomic nervous systems [1].

pPNET accounts for 1% of all sarcomas [2,9]. They are usually observed as a rapidly enlarging, often painful mass and are most frequently located in the thoracopulmonary region (Askin's tumor), pelvis, abdominal region and limbs, especially the lower limbs. There is additionally a rare occurrence in the head and neck region and the most common location is the orbit, neck and the parotid gland.

Histologically, the most helpful diagnostic feature is the presence of rosettes, usually of the Homer–Wright type, which indicate neural differentiation. Immunohistochemically, MIC-2 (CD99) positivity is very useful, because in most cases it is identified as malignant pPNET–peripheral neuroepithelioma and Ewing's sarcoma. Neuron-specific

enolase, synaptophysin, chromogranin, neurofilament, and S-100 are also useful in differential diagnosis [15].

In our case, Homer–Wright type pseudorosettes formations were present and tumoral cells diffuse positively stained for MIC2 at immunohistochemical examination.

In a recent review by Nikitakis et al. an observation of reveal 43 patients with pPNET in the head and neck region, revealed a predilection for children and adolescents was also present. The mean age was 21-year [15].

Our case was also 21-year-old and his lesion was located in the oral tongue is the first case in research literature which referred to a malignant primitive neuroectodermal tumor in this localization according to this review and our search in the literature [15].

pPNET were reported by Jurgens et al. (four cases), Kushner et al. (one case), Lattes (one case), Kimber et al. (six cases), and Cavazzana et al. (six cases) as the parts of larger series because of the lack of sufficient clinical information pertinent to the specific cases [4,5,6,8,10].

The prognosis of pPNET is generally very poor, with a disease—free survival rate of approximately 50% in 3 years and 30–45% in 5 years [4,12]. There is a propensity for rapid metastatic spread to the distant sites, especially the lung, liver and bone [2,12]. In the study of Jones and McGill; only 38% of patients with metastatic disease were alive within 2 years following diagnosis and there was a propensity for rapid metastatic spread to distant sites especially the lung, liver, and bone [2,3,12].

The site of origin of the tumor seems to be another important factor for prognosis. In the series of Kimber et al. 12 tumors arising from the head and neck region and the chest had an intermediate prognosis compared with tumors from the paraspinal and scapular areas and abdominal tumors which did not respond to treatment [8].

The orbita located pPNET is found to be less aggressive and none of the tumors in the other locations of the eight reported cases exhibited systemic metastatic spread and only one patient died of the disease [3].

In our patient, multiple liver metastases occurred 5 months after the initial diagnosis and overall survival was only 10 months due to distant spread.

Aggressive treatment strategies, using a combination of different therapeutic modalities, offer the best results. Surgery followed by radiation therapy for ablation of residual microscopic disease and chemotherapy seems to be the appropriate treatment for the patients with localized disease. Effective local control requires negative surgical margins. Preoperative chemotherapy and radiotherapy can be used in selected patients especially with the presence of the proximity or involvement of vital structures. In inoperable patients radiotherapy and chemotherapy are the only therapeutic options [3,4,8,11,15].

Recommendation for radiation is dependent on the primary site and the size of the tumour, histology, the patient's age and the extent of disease before and after surgical resection [13]. In most cases postoperative

radiotherapy with doses ranging from 45 to 60 Gy is used and reported to provides good local control [3].

Dactinomycins, vincristine, alkylating agents such as cyclophosphamide and ifosfamide, as well as anthracyclines such as doxorubicin (adriamycin) and epi-doxorubicin have been proven to be useful in PNET. Zimmermann et al. reported complete or partial remission in all patients treated with preoperative chemotherapy, including etoposide, vincristine, adriablastin, ifosfamide, and actinomycin D [14]. KIMBER et al. achieved complete remission in 52% of their patients treated with Ewing's sarcoma protocol, which consists of ifosfamide, actinomycin D, vincristine, and doxorubicin [8].

In conclusion; pPNET should be included in the differential diagnosis of small, round, blue cell tumors in the head and neck. A combination of multiple diagnostic modalities, surgery, radiation therapy and chemotherapy are the treatment options and this multimodality treatment offers the best outcome.

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