CASE REPORT

Imaging findings in mandibular primitive neuroectodermal tumour: a report of a rare case and review of the literature

CH Yeh¹, KM Yeow¹, SY Chu¹, KT Pan¹, CF Hung¹, S Hsueh² and IH Su^{*1}

¹Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taiwan; ²Department of Pathology, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taiwan

Primitive neuroectodermal tumours (PNETs) are aggressive undifferentiated tumours that occur mainly in the central nervous system (CNS). Reviewing the literature, only six cases of primary PNET of the mandible have been reported. These rare tumours are usually overlooked in clinical practice. An 18-year-old woman who presented with dental caries and left cheek swelling was initially diagnosed with facial cellulitis, but the swelling persisted despite adequate intravenous antibiotic therapy. Subsequent ultrasound and MR examinations revealed a tumour originating from the left mandibular ramus. The ultrasonography-guided percutaneous core needle biopsy confirmed the diagnosis of peripheral PNET. The radiographic features of mandibular PNETs are similar to those of PNETs in other regions, except for haemorrhage, necrosis and calcification. In addition, this is the first reported case with sonographic and MR images of this rare tumour, and the first case that was diagnosed based on the ultrasonography-guided percutaneous core needle biopsy. Using these image characteristics, mandibular PNETs can be diagnosed more accurately.

Dentomaxillofacial Radiology (2011) **40**, 451–456. doi: 10.1259/dmfr/92169329

Keywords: mandible; neoplasm; PNET; computed tomography; magnetic resonance imaging; sonography; needle biopsy

Case report

An 18-year-old woman was transferred to the emergency department at the Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taiwan, with progressive painless swelling of the left lower face, with a sensation of numbness and difficulty opening the mouth for 1 month. She had no fever, cough, sore throat, dysphagia, odynophagia or tinnitus. On physical examination, an 8 × 8 cm firm fixed mass with local warmth was noted at the left lateral aspect of her chin. Since she had a prolonged problem with dental caries and left chin swelling, she was admitted with the initial impression of facial cellulitis. However, the facial swelling persisted despite adequate empirical intravenous antibiotic treatment for a presumed infection of dental origin. In addition, the atypical symptoms (gradual painless swelling and sensation of

numbness) also increased the risk of neoplastic disease. Therefore, further imaging evaluation of the head and neck was obtained. High-resolution ultrasonography showed a well-defined heterogeneous hypoechoic mass, suggesting a neoplastic lesion, at the left masseter region (Figure 1). MRI of the head and neck revealed a soft-tissue mass arising from the left mandibular ramus and occupying the left masseter compartment. The tumour was isointense to normal muscle on T_1 weighted (T1W) images and hyperintense on T_2 weighted (T2W) images. It enhanced heterogeneously after the intravenous administration of gadolinium (Figure 2). Bony cortex erosion and involvement of left mandibular canal were also evident, as well as bone marrow replacement, which was seen with isointense signal change on T1W and T2W images. Although facial cellulitis of dental origin was still possible, a neoplasm of the left mandibular ramus was considered the most likely diagnosis.

An ultrasonography-guided percutaneous core needle biopsy with an 18 G coaxial cutting needle was performed (Figure 1).

*Correspondence to: I-Hao Su, Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital at Linkou, Chang Gung University, No 5, Fu Hsing Street, Kueishan, Taoyuan 333, Taiwan, R.O.C. E-mail: foliatu@adm.cgmh.org.tw

Received 28 December 2009; revised 8 April 2010; accepted 26 April 2010

Figure 1 Ultrasonography (a) and Doppler scan (b) of the left chin revealed a well-defined heterogeneous hypoechoic mass at masseter region. Subsequently, an ultrasonography-guided percutaneous core needle biopsy with an 18 G coaxial cutting needle was performed (c)

Enhanced CT of the head and neck, including chest and abdomen, was performed for further evaluation and tumour staging after the ultrasonography-guided percutaneous core needle biopsy for the left mandibular tumour. It showed the tumour had caused cortical destruction and a sunburst periosteal reaction of the left ramus of the mandible and focal widening of the proximal portion of the left mandibular canal, indicating canal involvement.

On histopathological examination, the biopsy specimen showed poorly differentiated tumour cells with small blue round or oval nuclei and scant cytoplasm. The tumour cells were mildly positive for desmin, diffusely positive for CD99, and negative for S-100, calponin, HMB-45, CK5/6, AE1/AE3, GFAP (6 F 2) and HHF-35 (Figure 3). Based on these histopathological features and the immunohistochemical pattern, the tumour was diagnosed as a primitive neuroectodermal tumour (PNET). The tumour was a solitary tumour in the left ramus of the mandible with no other primary tumours or distant metastasis and was diagnosed as a primary peripheral PNET arising in the mandible. Oral surgeons were consulted for *en bloc* resection. However, the tumour was unresectable because of the unacceptable extensive cosmetic and functional destruction that would be caused after resecting the involved portion of the left mandibular ramus. The patient was therefore referred to the haematology department for concurrent chemotherapy and radiotherapy.

Discussion

The PNET, a subtype of the family of small round cell malignancies, was first described in 1918 by Stout.¹ These rare tumours are found mostly in the central nervous system (CNS) and, based on their histological features, PNETs are presumed to be aggressive, undifferentiated tumours arising from multipotent embryonic neuroepithelial cells. Rarely, PNETs may be found outside the CNS. These peripheral PNETs are most common in the thoracopulmonary region, kidneys and retroperitoneal area.² Given their insidious clinical symptoms, variable locations and rarity, the accurate diagnosis of peripheral PNETs poses a challenge for clinicians and radiologists.

The actual incidence of peripheral PNET is difficult to estimate owing to its rarity and because clear diagnostic criteria were established only recently. Although peripheral PNETs can affect any age group, they tend to affect adolescents and young adults more often.³ Some studies have reported a slight male predominance.⁴ Generally, the prognosis of peripheral PNETs is unfavourable. A combination of adequate surgical resection, effective multi-agent chemotherapy and concurrent radiotherapy if possible is necessary to improve survival. The overall 5-year survival rates for localized and metastatic tumours range from 65% to 74% and 25% to 45%, respectively.^{5,6} Tumours arising from the paraspinal region and scapular areas respond better to treatment, while abdominal and pelvic PNETs respond poorly.⁷

Figure 2 MRI of the head and neck showed a soft-tissue tumour arising from the left ramus of the mandible occupying the left masticator space. The tumour was isointense to normal muscle on coronal T1W images (a) and hyperintense on axial T2W images (b), and it had heterogeneous enhancement after intravenous administration of gadolinium (c). Bone marrow involvement was also shown on MRI. Enhanced CT of the head and neck in the soft-tissue (d) and bone (e) windows showed cortical destruction and sunburst-like periosteal reaction of left mandibular ramus

Several reviews on the CT and MR features of peripheral PNETs have been published. On CT, PNETs are usually isodense or slightly hypodense compared with normal muscle.^{2,7,8} Both coarse and fine calcifications are uncommon. Central hypodense areas consistent with tumour necrosis and cystic change are found in large tumours, and sometimes hyperdensities consistent with haemorrhage can be seen. Almost all of these tumours show heterogeneous enhancement after the intravenous administration of an iodine-containing contrast medium. On T1W MRI, most peripheral PNETs are isointense or slightly hyperintense compared with normal muscle. Typical T2W signals are heterogeneous, but are generally hyperintense compared with adjacent normal muscle. A cystic necrotic component and haemorrhagic change are usually obvious on MRI if present. In addition, PNETs tend to displace adjacent structures, instead of invading them directly. Encasement of vessels or trachea is rare. Extension along neural foramina is common in retroperitoneal or paraspinal PNETs.

The first case of mandibular PNET was reported in 2002 as a painless, progressively enlarging lower jaw

mass in a 6-year-old girl.⁹ In the literature, only six cases of primary peripheral PNET arising in the mandible have ever been reported.^{10–14} The patient age and gender, tumour location, treatment modalities and outcomes are summarised in Table 1. The patients were 4 females and 2 males with ages ranging from 6 to 38 years. The tumours were located around the mandibular symphysis in three cases and in the ramus of the mandible in the other three cases. As in our case, the six reported patients initially presented with a painless swelling of the chin or cheek.

The radiographic features of mandibular PNETs in these cases are compared in Table 2. Ultrasonography of the mandibular PNET was not available in the six reported cases, while a well-defined heterogeneous hypoechoic mass was seen in our patient. On CT, the tumours were isodense to the adjacent muscles in two cases and hypodense in four. MRI was reported only in one previous case. The signal of the tumours was isointense to adjacent muscles on T1W images and hyperintense on T2W images. Heterogeneous peripheral enhancement after the intravenous administration of

Figure 3 Poorly differentiated tumour cells with small blue round-to-oval nuclei and scant cytoplasm (a) were seen histologically ($\times 200$). The specimen was mildly positive for desmin (b), diffusely positive for CD99 (c), and negative for calponin (d), AE1/AE3 (e) and HHF-35 (f)

gadolinium-containing contrast medium was seen in both cases. Moreover, some common features of peripheral PNET, including haemorrhage, necrosis and calcification, were not found in any of the seven cases. This may be because these characters are related to size of tumour, and the location and symptom of the mandibular PNET make it easier to be detected earlier in clinical practice.

The most common sonographical differential diagnosis for a focal mass in the masseter region is haemangioma or abscess after a dental procedure. The haemangiomas commonly appear as ill-defined hypoechoic heterogeneous masses containing sinusoidal vascular spaces and phleboliths as well as slow blood flow inside. The abscess in the masseter muscle usually appears as a well-defined

hypoechoic heterogeneous mass with peripheral thick wall and containing debris. These sonographical findings of the above differential diagnoses were not revealed on our case, so the suspicion of neoplasm was increased, resulting in the ongoing needle biopsy.

The appearance of the soft-tissue mass wrapping the mandible narrows the radiological differential diagnosis made on CT and MRI and through our consideration, including osteomyelitis, non-Hodgkin lymphoma, osteosarcoma, ameloblastoma and metastasis. Nevertheless, the radiological findings of our presented case lack the presence of sequestrum or abscess formations, large bubbly osteolytic lesions, extensive bony destruction or cervical nodal metastasis. So the possibility that

Table 1 General data and clinical course in the seven reported cases

Case	Age (years)/gender	Location in the mandible	Treatment modalities	Follow-up (months)	Recurrence/metastasis	Status
Ozer ⁹	6/female	Mental and parasymphiseal	<i>En bloc</i> resection, post-operative chemotherapy	10	Local recurrence, re-operated, tumour free	Alive
Sundine ¹⁰	38/female	Mandibular ramus, right	Surgical resection, post-operative chemotherapy, palliative radiation therapy	18	Spinal and lung metastases	Dead
Alrawi ¹¹	18/female	Mental and parasymphiseal	Pre-operative chemotherapy, <i>en bloc</i> resection	14	No local recurrence or distant metastasis	Alive
Votta ¹²	18/female	Mental and parasymphiseal	Pre-operative chemotherapy, <i>en bloc</i> resection	14	No local recurrence or distant metastasis	Alive
Kanaya ¹³	38/male	Mandibular ramus, right	<i>En bloc</i> resection, selective neck dissection, post-operative radiation therapy	36	No local recurrence or distant metastasis	Alive
Anonymous ¹⁴	11/male	Mandibular ramus, left	Chemotherapy, radiotherapy	36	No local recurrence or distant metastasis	Alive
Our case	18/female	Mandibular ramus, left	Chemotherapy, radiotherapy	14	No distant metastasis	Alive

Table 2 Summary of the image findings in the seven reported cases

Case	Size (cm)	Ultrasonography	Density on CT	MRI signal	Haemorrhage/ necrosis/ calcification	Enhancement	Neural foramen invasion
Ozer ⁹	10 × 12	N/A	Hypodense	N/A	(-)/(-)/(-)	N/A	(-)
Sundine ¹⁰	N/A	N/A	Isodense	N/A	(-)/(-)/(-)	N/A	Obliteration of the right inferior alveolar canal
Alrawi ¹¹	N/A	N/A	Isodense to mild hypodense	N/A	(-)/(-)/(-)	N/A	Obliteration of the right mental foramen and inferior alveolar canal
Votta ¹²	N/A	N/A	Hypodense	N/A	(-)/(-)/(-)	N/A	(-)
Kanaya ¹³	N/A	N/A	Isodense	N/A	(-)/(-)/(-)	N/A	(-)
Anonymous ¹⁴	N/A	N/A	Hypodense	T1WI isointense, T2WI slightly hyperintense	(-)/(-)/(-)	Peripheral enhancement	(-)
Our case	3.9 × 2.5 × 6.7	Well-defined margin, heterogeneous hypoechoic content	Hypodense	T1WI isointense, T2WI hyperintense	(-)/(-)/(-)	Heterogeneous enhancement	Invasion of the left inferior alveolar canal

N/A, not applicable; T1WI, *T*₁ weighted image; T2WI, *T*₂ weighted image

this lesion represented the above differential diagnoses was considered unlikely.

Because of the infection-like clinical findings and superficial location of mandibular PNETs, sonography and ultrasonography-guided percutaneous core needle biopsy are considered the appropriate imaging modality and procedure to confirm this diagnosis, although they were not applied on previously reported cases.

Open surgical biopsy is more invasive with higher morbidity when compared with minimally invasive ultrasonography-guided percutaneous core needle biopsy. Real-time ultrasonographical guidance allows precise needle position, excludes vascular lesions to avoid any interventional complication and provides flexible patient positioning so that needle biopsy can be performed quickly and safely on soft-tissue masses around superficial bone lesions.^{15–17} Several reports have been

published on the usefulness and accuracy of needle biopsy specimens for histopathological diagnosis of superficial soft-tissues neoplasms.^{15–18}

In conclusion, all seven cases of mandibular PNET initially presented with a gradually growing painless facial swelling and were misdiagnosed as infectious disease. The radiographic features of mandibular PNETs on CT and MRI are summarised. Although intratumoral haemorrhage, necrosis and calcification are usually seen in other peripheral PNETs, they are not found in the peripheral PNETs arising in the mandible. Sonographically, the mandibular PNETs appear as well-defined heterogeneous hypoechoic masses, and they can be accurately diagnosed based on the ultrasonography-guided percutaneous core needle biopsy. These image findings and procedures of mandibular PNET can alert the physicians to this rare maxillofacial tumour and facilitate precise diagnosis and proper treatment strategies.

References

1. Stout AP. A tumor of the ulnar nerve. *Proc NY Pathol Soc* 1918; **12**: 2–12.
2. Khong PL, Chan GC, Shek TW, Tam PK, Chan FL. Imaging of peripheral PNET: common and uncommon locations. *Clin Radiol* 2002; **57**: 272–277.
3. Kushner BH, Hajdu SI, Gulati SC, Erlandson RA, Exelby PR, Lieberman PH. Extracranial primitive neuroectodermal tumors. The Memorial Sloan-Kettering Cancer Center experience. *Cancer* 1991; **67**: 1825–1829.
4. Schmidt D, Herrmann C, Jurgens H, Harms D. Malignant peripheral neuroectodermal tumor and its necessary distinction from Ewing's sarcoma. A report from the Kiel Pediatric Tumor Registry. *Cancer* 1991; **68**: 2251–2259.
5. Parham DM, Hijazi Y, Steinberg SM, Meyer WH, Horowitz M, Tzen CY, et al. Neuroectodermal differentiation in Ewing's sarcoma family of tumors does not predict tumor behavior. *Hum Pathol* 1999; **30**: 911–918.
6. Kimber C, Michalski A, Spitz L, Pierro A. Primitive neuroectodermal tumours: anatomic location, extent of surgery, and outcome. *J Pediatr Surg* 1998; **33**: 39–41.
7. Dick EA, McHugh K, Kimber C, Michalski A. Imaging of non-central nervous system primitive neuroectodermal tumours: diagnostic features and correlation with outcome. *Clin Radiol* 2001; **56**: 206–215.
8. Kim MS, Kim B, Park CS, Song SY, Lee EJ, Park NH, et al. Radiologic findings of peripheral primitive neuroectodermal tumor arising in the retroperitoneum. *Am J Roentgenol* 2006; **186**: 1125–1132.
9. Ozer E, Kanlikama M, Karakurum G, Sirikci A, Erkilic S, Aydin A. Primitive neuroectodermal tumour of the mandible. *Int J Pediatr Otorhinolaryngol* 2002; **65**: 257–261.
10. Sundine MJ, Bumpous JM. Primitive neuroectodermal tumor of the mandible: Report of a rare case. *Ear Nose Throat J* 2003; **82**: 211–214.
11. Alrawi SJ, Tan D, Sullivan M, Winston J, Laree T, Hicks W, et al. Peripheral primitive neuroectodermal tumor of the mandible with cytogenetic and molecular biology aberrations. *J Oral Maxillofac Surg* 2005; **63**: 1216–1221.
12. Votta TJ, Fantuzzo JJ, Boyd BC. Peripheral primitive neuroectodermal tumor associated with the anterior mandible: A case

- report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; **100**: 592–597.
13. Kanaya H, Hirabayashi H, Tanigaito Y, Baba K. Ewing's sarcoma/primitive neuroectodermal tumour of the mandible: report of a rare case and review of the literature. *J Otolaryngol-Head Neck Surg* 2007; **36**: E15–18.
 14. Anonymous. Primary peripheral primitive neuroectodermal tumor of mandible. *J Pediatr Hematol Oncol* 2008; **30**: 258–260.
 15. Yeow KM, Tan CF, Chen JS, Hsueh C. Diagnostic sensitivity of ultrasound-guided needle biopsy in soft tissue masses about superficial bone lesions. *J Ultrasound Med* 2000; **19**: 849.
 16. Torriani M, Etchebehere M, Amstalden E. Sonographically guided core needle biopsy of bone and soft tissue tumors. *J Ultrasound Med* 2002; **21**: 275–281.
 17. Soudack M, Nachtigal A, Vladovski E, Brook O, Gaitini D. Sonographically guided percutaneous needle biopsy of soft tissue masses with histopathologic correlation. *J Ultrasound Med* 2006; **25**: 1271–1277.
 18. Ray-Coquard I, Ranche're-Vince D, Thiesse P, Ghesquière H, Biron P, Sunyach MP, et al. Evaluation of core needle biopsy as a substitute to open biopsy in the diagnosis of soft-tissue masses. *Eur J Cancer* 2003; **39**: 2021–2025.