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Primary spinal peripheral primitive neuroectodermal tumour: a report of 3 cases and review of the literature

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Abstract

Peripheral primitive neuroectodermal tumours (PNETs) are rare and highly malignant tumours in the spine, with a predilection for young adults. There are no standard guidelines for treating these tumours. Surgical resection combined with postoperative radiotherapy and chemotherapy is a common and effective treatment at present. Even so, survival time of patients with these tumours is still very short. In this study, we present three rare cases of thoracic epidural PNETs and review the literature.

Key words: *primary spinal peripheral, primitive neuroectodermal tumour (PNET), thoracic epidural PNET, case report, review of the literature.*

Introduction

Primitive neuroectodermal tumour (PNET) is a kind of malignant tumour derived from neuroectoderm and composed of undifferentiated small round cells. It was first proposed by Hart and Earle in 1973 [11]. It has the characteristics of low differentiation, high invasiveness, and pleomorphism, often involving the central nervous system and mesenchymal tissues such as the bone, cartilage, and muscle, and most of them have a poor prognosis. It usually occurs in childhood and early adulthood, 10 to 20 years old is the highest incidence of the age [25]. It is more common among males with the incidence twice as high as among females [8].

According to the tumour location, PNET can be divided into central PNET and peripheral PNET or Ewing's sarcoma/PNET. They originate from the neural tube and neural crest respectively [4], but have similar cellular morphological and genetic characteristics. Peripheral PNET (pPNET) occurs outside the central nervous system, involving the chest wall, trunk, limbs and other locations. Clinically, pPNET is rarely involved in the spine, and many authors describe spinal pPNET as "extremely rare". The most commonly involved sites are the lumbar spine, followed by the thoracic and cervical vertebrae [2]. Due to its low incidence, most of the related literature consists of case reports [19]. This paper reports 3 cases of primary thoracic epidural pPNET in our hospital and reviews the literature.

Case reports

Case 1

Presentation

A 10-year-old female presented with paroxysmal burning back pain that occurred 20 days ago and radiated to the costal arch without any obvi-

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ous cause. It often occurred at night and lasted for 20 minutes each time. Four days ago, the child had a sudden onset of weakness in both legs accompanied by numbness. Physical examination on admission revealed tenderness in the T7 spinous processes and subcostal hypoesthesia. Muscle strength was 5/5 in both upper limbs and 3/5 in both lower limbs. Both knee reflexes were hyperactive with bilateral positive Babinski sign. Magnetic resonance imaging (MRI) revealed a 2.3 × 1.1 × 4.5 cm mass shadows in the spinal canal at the level of T5-7 and bilateral foramina in T5-6, which appeared hypointense on T1-weighted image and hyperintense on T2-weighted image (Fig. 1). The boundary with adjacent tissues was clear, and the spinal cord was compressed. Lymphoma was considered in the differential diagnosis of this disease.

Operation

Considering the rapid progression of symptoms, surgical treatment was performed on the first day after hospitalization. A posterior midline incision was selected for the operation. The spinous process and lamina of T5-T7 were completely removed while preserving facet joints, and the tumour was exposed to the epidural. Microscopically, the tumour was well defined with the spinal cord, the capsule is intact, tough and soft, dark red in colour, easy to haemorrhage, and the spinal cord is compressed to the ventral side. After complete excision of the tumour,

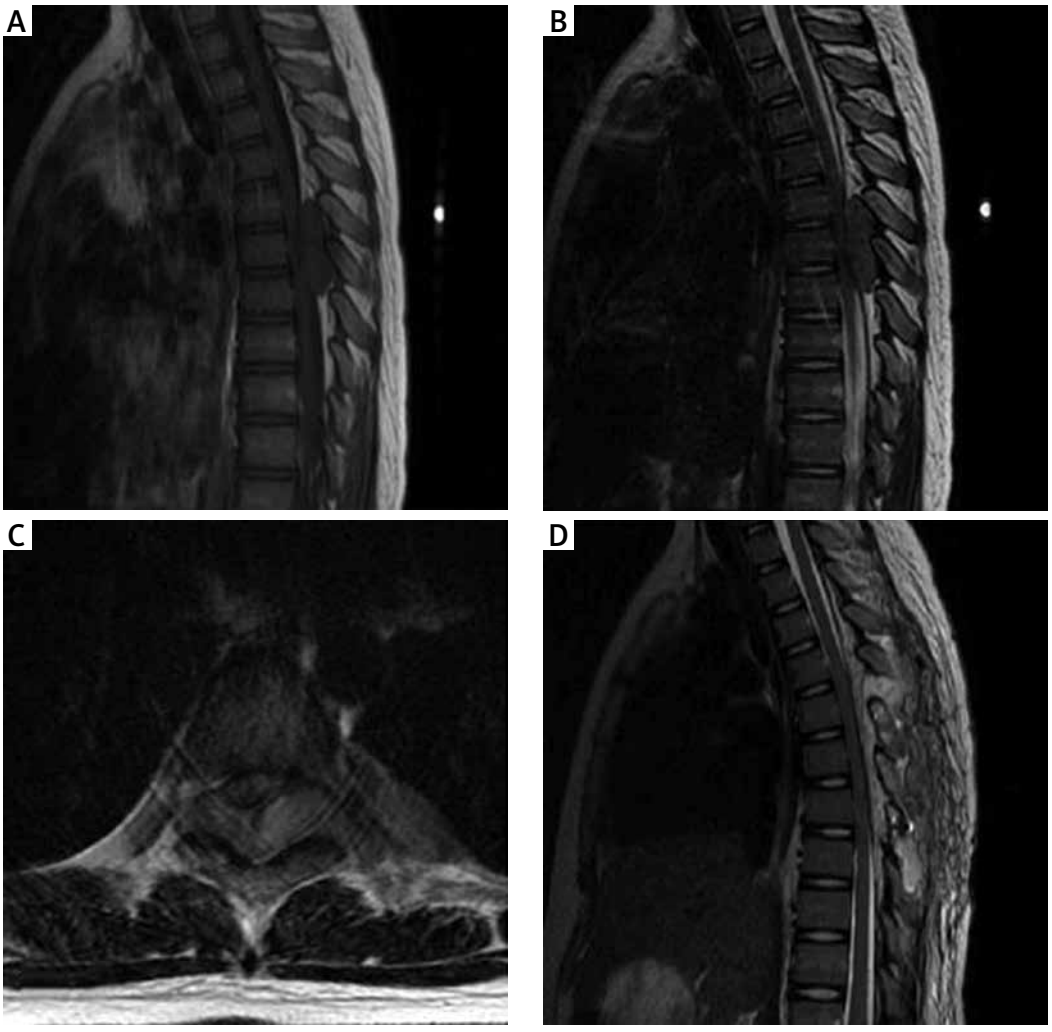

Fig. 1. Preoperative MR imaging. **A**) Sagittal T1-weighted MRI; **B**) Sagittal T2-weighted MRI; and **C**) Axial T2-weighted MRI shows a space-occupying lesion at the T5-T7 level. **D**) Post-operative sagittal T2-weighted MRI.

the spinal cord pulsed well, replanted the spinous process and lamina, and the specimen was sent to pathology.

Pathology

Histopathological analysis: The tumor cells were uniform in size and arranged in sheets with a focal papillary structure. Immunohistochemical: CD45 (–), NSE (+), GFAP (–), Syn (–), CgA (–), Ki-67 (+ 50%), CK (–), Vimentin (+), CD99 (+). Pathological diagnosis: Primitive neuroectodermal tumor (PNET).

Postoperative course

Postoperatively, the patient reported significant relief of back pain, the muscle strength of both lower extremities returned to grade IV, and Babinski sign turned negative. Subsequently, the patient received the local radiotherapy with a dose of 36 Gy/20 f, but no regular chemotherapy followed. Six months later, the patient was re-examined in our hospital. Imaging examination showed a 1.6 × 1.0 × 3.1 cm mass in the spinal canal at the T9-T10 level, with significant enhancement and suspected tumor recurrence. The patient underwent surgical treatment in our department again, and the postoperative pathological results were confirmed as PNET. Subsequently, she was treated with four cycles of cyclophosphamide, pirarubicin, and vincristine. However, before the fifth chemotherapy, MRI suggested tumor recurrence again. The patient's family decided to forego further treatment, after which she was lost to follow-up.

Case 2

Presentation

A previously healthy 35-year-old woman suffered from back discomfort for one month. Five days ago, the patient developed numbness and weakness in both lower limbs, with occasional needling sensation. A few hours before admission, the patient had a sudden immobility of the lower extremities, accompanied by incontinence. Neurological examination indicated tenderness in the spinous process at the T3-T5 level. Lower limb power was 0/5 bilaterally associated with truncal weakness while the upper limb power was normal. Both deep tendon reflexes were present and Babinski signs were equivocal. All sensations below T5 were absent. An enhanced MRI revealed a 4.8 × 3.9 × 5.4 cm irregular mass observed inside and outside the spinal canal at the T3-T5 levels, and the boundary was not clear (Fig. 4). The tumour was hypointense on T1 images and hyperintense on T2 images, and enhancement was inhomogeneous after contrast injection. The corresponding spinal cord was compressed and moved to the right with oedema. She began receiving methylprednisolone and was preparing for emergency surgery.

Operation

Laminectomies of the T2-T4 vertebrae were performed with preservation of the facet joints, to fully expose the tumour. The lesion was dorsal to the dura at the T3-T4 level, showing a greyish-white fish-like shape and filling the spinal canal. The lesion grew into the thoracic cavity along the left intervertebral

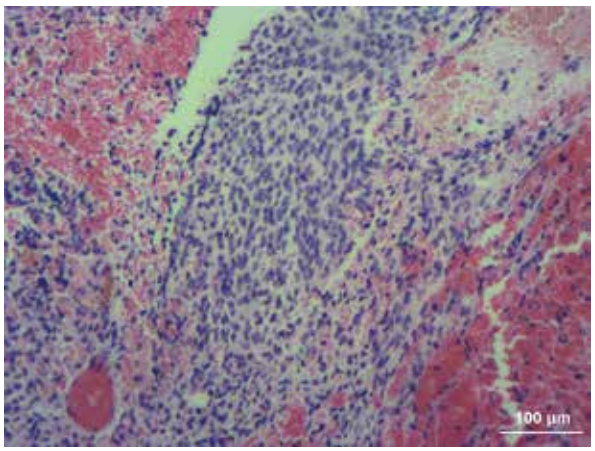

Fig. 2. Histopathological images. Diffuse sheets of small round blue cells (HE).

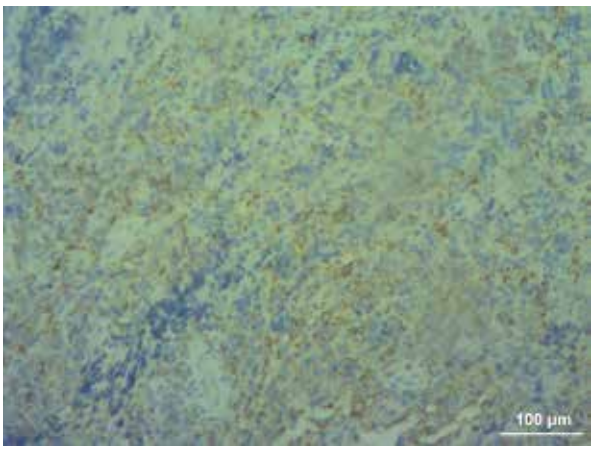

Fig. 3. Immunohistochemical staining images of positive CD99.

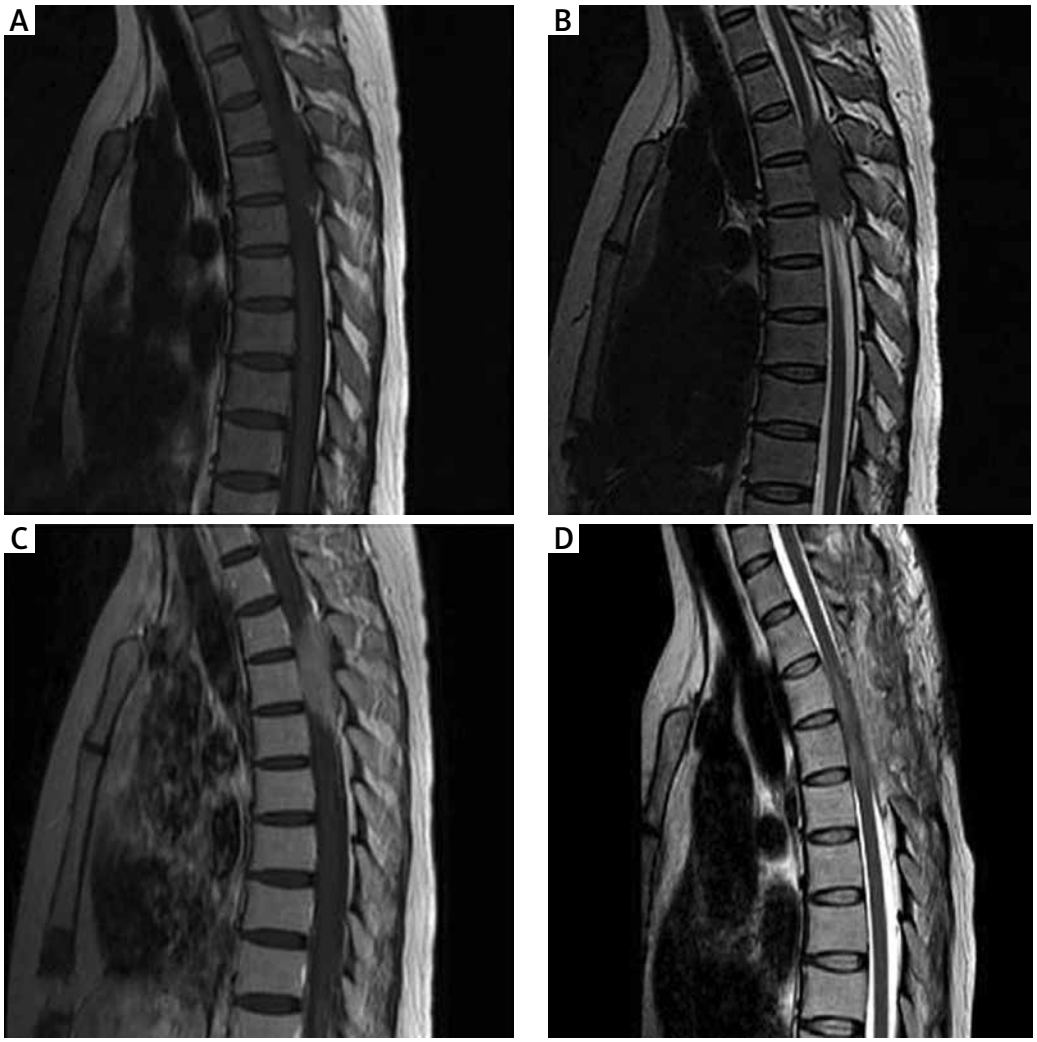

Fig. 4. Preoperative MR imaging. **A**) Sagittal T1-weighted MRI; **B**) Sagittal T2-weighted MRI; and **C**) Sagittal enhanced T1-weighted MRI show a space-occupying lesion at the T3-T5 level. **D**) Post-operative sagittal T2-weighted MRI.

foramen. Using microsurgical techniques, the lesion was carefully separated from the normal tissue and resected. Since the extraspinal tumour could not be safely resected, only the dorsal dural and intervertebral foramen lesions were removed in this operation. To ensure that there was no residual tumour in the spinal canal, the excised tissue was sent to pathology.

Pathology

Histopathological analysis: The tumour cells were diffused and arranged in sheets, the cells were small, uniform in size and less plasmid (Fig. 5). Immunohistochemical findings: CK (–), EMA (–), Vimentin (–), CD99 (+), Ki-67 (30% +), NSE (–), Syn (–), Smur100 (–), CD3 (–), CD20 (–), Desmin (–), CD56 (–), LCA (–), CD38 (–), CD138 (–), GFAP (–), TTF-1 (–) (Fig. 6). Pathological diagnosis: Small round cell malignant tumour, inclined to primitive neuroectodermal tumour.

Postoperative course

Her preoperative back discomfort was relieved but the numbness below the T5 level was the same as before. The muscle strength of both lower limbs was 1/5, and there was no significant improvement until discharge. We recommended a combination of radiotherapy and chemotherapy to the patient, but she refused chemotherapy after receiving two rounds of radiotherapy (30 Gy/15 f and 16 Gy/18 f).

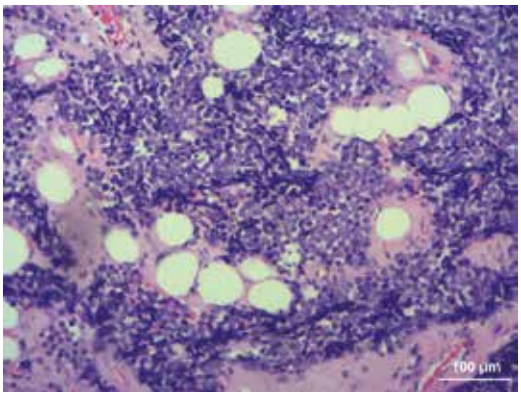

Fig. 5. Histopathological images show diffuse sheets of primitive cells with round nuclei and scanty cytoplasm.

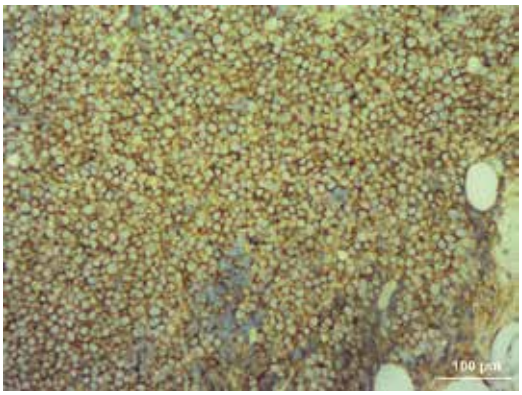

Fig. 6. Immunohistochemical staining images of positive CD99.

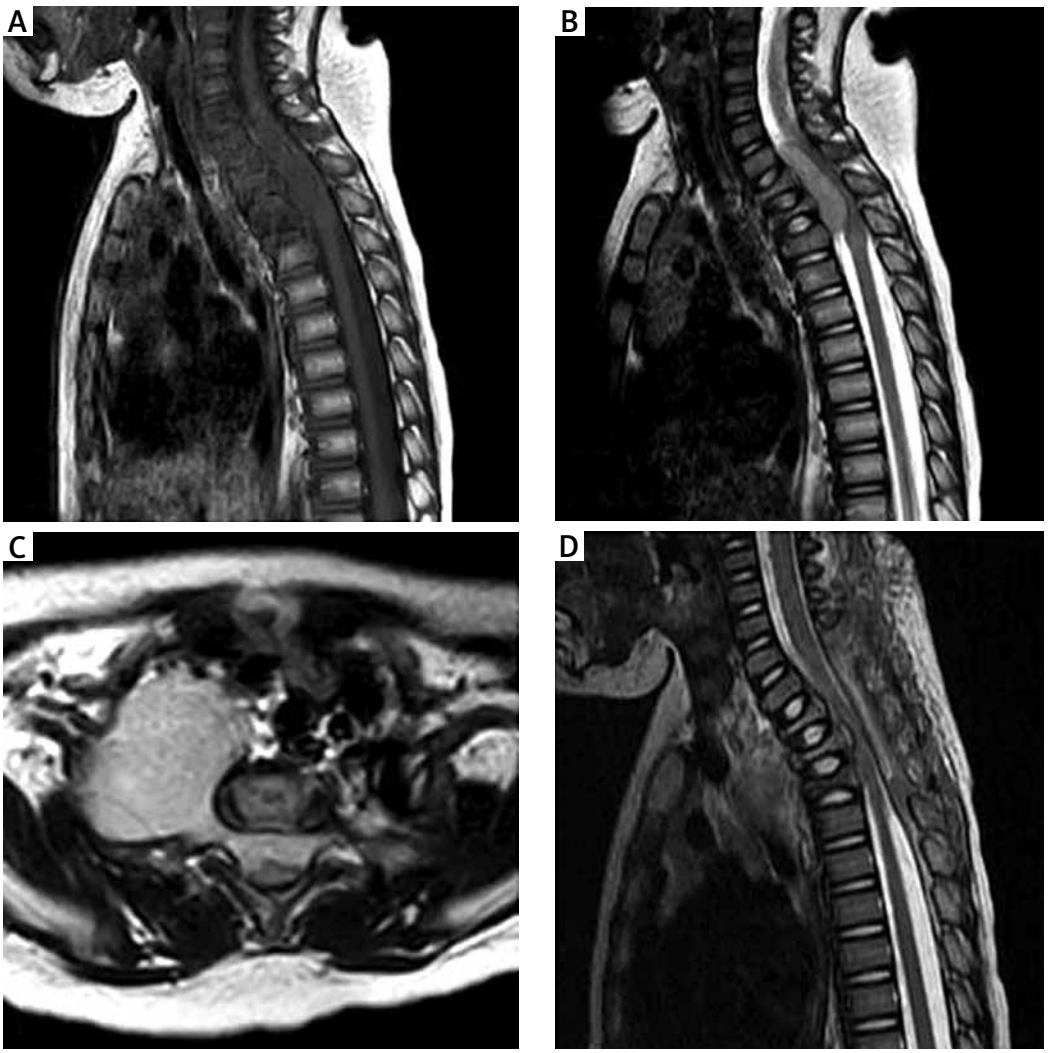

Fig. 7. Preoperative MR imaging. **A**) Sagittal T1-weighted MRI; and **B**) Sagittal T2-weighted MRI shows a space-occupying lesion at the T1-T3 level. **C**) Axial T2-weighted MRI shows the extraspinal extension of the tumour through the neural foramen, forming a dumbbell-shaped mass. **D**) Post-operative sagittal T2-weighted MRI shows the resection of the intraspinal tumour part.

Three months later, a postoperative MRI showed that the tumour outside the spinal canal was significantly larger than before. Unfortunately, the patient did not continue the treatment in our hospital and was lost to follow-up.

Case 3

Presentation

A 10-month-old male child presented with weakness in lower limbs 4 days before admission. At first, the patient was unable to stand on his own, but immediately progressed to being unable to crawl and sit alone, and he was unable to turn over when he was admitted to the hospital. The muscle strength of both lower limbs was grade 3/5 and the tendon reflex was hyperactive. MRI revealed that there was a long T1 and long T2 mass signal shadow inside and outside the spinal canal at the level of the T1-3 vertebral body. The lesion size in the spinal canal was about 3.1 × 0.6 × 1.4 cm, and the lesion size in the right thoracic cavity was about 4.5 × 3.3 × 4.8 cm, the adjacent spinal cord was compressed (Fig. 7).

Operation

A midline posterior incision was performed, and the C7-T3 spinous process, lamina, and the outer margin of the transverse process were exposed. The spinous process and lamina were removed to expose the dura. The tumour was located ventral to the epidural of the spinal cord. The tumour was greyish-red, soft, and adhered to nerve roots, compressing the spinal cord. The adhesions between the tumour and peripheral nerves were carefully separated under the microscope, and the tumour was completely removed in sections and all specimens were sent to pathology. After the operation, the patient was successfully extubated and returned to the ward.

Pathology

Histopathological analysis: Diffuse sheets of small round cells with increased mitosis. Immunohistochemical findings: CK (–), Vimentin (+), Syn (–), NF (–), CD34 (–), NeuN (–), GFAP (–), NSE (–), EMA (–), Smur100 (–), Ki-67 (80% +), LCA (–), MP0 (–), CD117 (+), CD43 (–), CD99 (+). Pathological diagnosis: Small round cell malignant tumour, considering primitive neuroectodermal tumour (PNET) (Fig. 8).

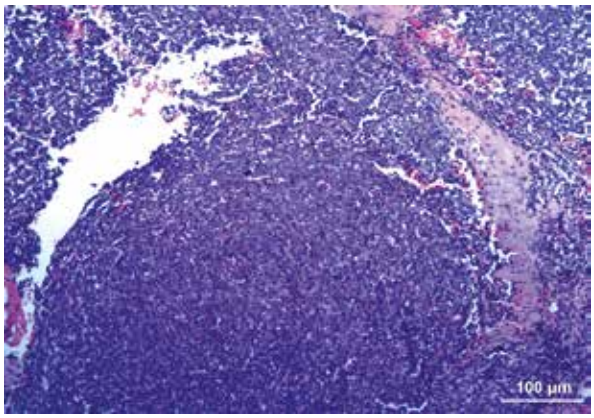

Fig. 8. Histopathological images. Diffuse sheets of small round cells with increased mitosis.

Postoperative course

Post-operatively, the patient had an uneventful recovery, with muscle strength returning to grade 4/5 and can turn over by himself. After the patient's physical conditions permitted and with parental consent, he received chemotherapy immediately. He was treated with 4 cycles of VDC (vincristine, doxorubicin, cyclophosphamide) and IE (ifosfamide, etoposide). At a follow-up visit 5 months after surgery, the patient's condition remains stable and there was no tumour recurrence [3].

Discussion

Classification

The nomenclature and diagnostics of PNET were first proposed by Hart and Earle in 1973 [11]. It was originally used to describe undifferentiated tumours originating from primitive neuroectoderm in the brain, which is very rare and highly malignant. In general, PNET can be further divided into two types according to the location of tumour: central PNET (cPNET) and peripheral PNET (pPNET). Although both have similar cellular morphological and genetic characteristics, more and more studies have shown that there are differences between them in genetics, pathology, metastasis pathway, and treatment regimen [5].

pPNET, which originates from the neural crest, is a small round cell tumour of peripheral soft tissue. Under light microscopy, pPNET and Ewing's sarcoma have similar small round blue cells, and both have the same chromosomal translocation t(11; 22)(q24; q12). Therefore, it is generally believed that pPNET belongs to the EWS family. In 2002, the World Health Organi-

zation (WHO) classified Ewing's sarcoma and pPNET under the same category in the classification of soft tissue tumours, collectively referred to as ESFT/pPNET (Ewing's sarcoma family tumours/peripheral PNET) [9]. However, it is very difficult to distinguish pPNET from Ewing's sarcoma, which largely depends on the presence of neural differentiation in immunohistochemistry or ultrastructure [30]. In immunohistochemistry, Ewing's sarcoma has almost no expression of neural markers, and the tumour cells are more primitive. However, pPNET expressed at least two neural markers, and there was evidence of differentiation [23]. At present, in the latest WHO classification of soft tissue and bone tumours in 2013, PNET is no longer used as a synonym for Ewing's sarcoma [6].

Clinical manifestations

The clinical manifestations of intraspinal pPNET usually have no obvious specificity, so it is difficult to distinguish them from other tumours in the spinal canal by their clinical manifestations. The clinical symptoms of primary intraspinal pPNET are mainly determined by tumour growth location, degree of invasion and structure involved [27], which can be manifested as local pain, limb weakness, hypoesthesia and urination and defecation dysfunction. Due to the high degree of malignancy, pPNET usually progresses rapidly, showing a progressive worsening trend in a short time. In this paper, all 3 patients showed a progressive decrease in the muscle strength of both lower limbs in a short period of time, and one of them developed acute incontinence symptoms.

MRI characteristics

MRI is a crucial imaging modality for the evaluation of spinal tumour, and is usually the first choice for the diagnosis of pPNET. The location of pPNET in the spinal cord is intramedullary, extramedullary intradural, or extradural with a paraspinal component [28,30]. It can occur at all levels of the spine, mainly in the lumbar vertebrae, and accounts for about half of all reported cases [22]. In our cases, all 3 lesions occurred in the thoracic epidural region, and 2 of them had extraspinal tissue invasion.

However, the radiological manifestations of pPNET in the spinal canal are not specific, and it is difficult to distinguish it from other tumours. In most reports, pPNET shows hypointense or isointense on T1-weighted imaging and hyperintense on T2-weighted imaging, with heterogeneous enhancement [30], which is consistent with our report. In addition, the epidural pPNET is irregular, which can grow out of the spinal canal through the intervertebral foramen, invading the vertebral body or paraspinal soft tissue and involving both inside and outside of the spinal canal at the same time. The extraspinal part of the lesion is usually larger than the intraspinal part [7]. Previous studies [8,26] have found that based on preoperative MRI findings, pPNET is often misdiagnosed as schwannoma, meningioma, neurofibroma, lymphoma, metastasis, etc. Although it is impossible to distinguish PNET from other primary spinal lesions by MRI results, it can help doctors understand the location of the tumour and the degree of nerve compression, which is still a necessary examination method.

Molecular mechanism

Approximately 85% of tumours diagnosed as PNET have translocations t(11;22)(q24;q12). At the molecular genetic level, the chromosome 22q12 breakpoint is clustered within a single gene called EWS, and the chromosome 11q24 breakpoint is located in a gene called FLI1 [1,29]. The consistent presence of EWS-FLI1 molecules in PNET suggests a critical role in tumour biology. In experiments assessing the ability of fusion proteins to induce tumour transformation, chimeric proteins have been shown to affect the growth characteristics of certain cell lines. Transfection of EWS-FLI1 or EWS-ERG can induce the transform mouse NIH3T3 fibroblasts, allowing them to acquire tumour-like properties. The conversion activity requires both EWS and FLI1 domains [15,16]. Transfection of wild-type FLI1 does not lead to cellular transformation, suggesting that EWS-FLI1 is functionally distinct. EWS-FLI1 may also exert tumorigenic effects via deregulation of programmed cell death. Some paper reported that antisense inhibition of EWS-FLI1 leads to increased susceptibility of PNET cell lines to chemotherapy-induced apoptosis [31]. These indicated EWS-FLI1 affected the cell death and played an important role in tumour progression.

Pathology

The diagnosis of pPNET can only be determined by pathological examination, and histopathological analysis alone is not enough, but also needs to be combined with immunohistochemistry [12]. In gross pathology, pPNET is usually a fish-like greyish-red mass. Under the microscope, small and round undifferentiated cells can

be seen, with uniform in size, compact arrangement, hyperchromatic nucleoli, scanty cytoplasm, eosinophilic, tumour necrosis, and Homer-Wright rosette structure [3]. In immunohistochemical analysis, CD99 was diffusely expressed on almost all pPNET cell membrane. CD99 is the product of the MIC2 gene in pPNET tissues, and is almost not expressed in cPNET. In addition, positive expressions of other immunohistochemical markers such as neuron-specific enolase (NSE), S-100, glial fibrillary acidic protein (GFAP), Vimentin and nestin, etc., often indicate the presence of neuroectodermal differentiation in tumour and support the diagnosis of pPNET [13]. In this paper, the postoperative pathology of 3 cases showed CD99 positive, and the expression of neural differentiation antigen was found in all cases, which was consistent with the pPNET diagnosis.

Treatment

Due to the low incidence of primary spinal pPNETs, there are no standard treatment guidelines currently. Most scholars believe that surgery is the first choice for the treatment of pPNET. One study showed that total tumour resection can improve the 2-year survival rate and prolong the median survival time of patients with pPNET [21]. The principle of surgical treatment is the same as most spinal tumours: decompression is the primary goal to prevent further decline of neurological function; resect as much tumour as is safe; obtain sufficient samples for pathological examination [8]. The three patients in our report all developed symptoms of nerve compression with rapid progressive course. In order to relieve the symptoms and avoid irreversible nerve damage, surgical treatment was performed as soon as possible after admission, and their symptoms were improved after surgery. Laminectomy with preservation of the facet joint was selected in all operations. In case, we replanted the spinous process and lamina to ensure spinal stability and improve the prognosis and quality of life of the patient.

However, surgery alone cannot prolong the long-term survival rate of patients with pPNET, and the recurrence rate is high. Most reports have chosen surgery combined with radiotherapy and chemotherapy [24]. Most studies have shown that postoperative adjuvant radiotherapy is an important method for the treatment of spinal pPNET, and its therapeutic effect is superior to that of postoperative adjuvant chemotherapy [21,31]. Currently, the optimal radiotherapy regimen for pPNET is controversial. In the literature, the total dose of radiotherapy is 30-60 Gy [8]. However, for children, radiotherapy should be used with caution or not for the time being in consideration of the impact on the central nervous system and endocrine system [14]. In recent years, chemotherapy has had a good effect on the treatment of pPNET. At present, the standard chemotherapy regimens of pPNET are alternately VDC (vincristine, doxorubicin and cyclophosphamide) and IE (ifosfamide and etoposide). The total course of treatment is 6-9 months, and there is no difference in chemotherapy regimens between adults and children [10]. According to existing reports, the overall prognosis of spinal pPNET patients is still not ideal even if treated with surgery, radiotherapy and chemotherapy [17]. The metastasis or infiltration of pPNET to organs outside the central nervous system is more common, and it is easy to metastasize to lung tissue and bone tissue [18,20]. Perry ***et al***. reported that the average survival time of primary intraspinal pPNET was only 22 months [20]. In case 1 and case 2, two patients only received radiotherapy without chemotherapy after surgery, and their tumours recurred several months later. In case 3, the patient was actively treated with chemotherapy after the operation. At present, there were no obvious signs of tumour recurrence during the 3-month follow-up, the patient's condition was stable.

Conclusions

In summary, primary spinal pPNET is a rare malignant tumour, but with increasing reports of pPNET, doctors should pay attention to this disease as one of the possible diagnoses. The symptoms and imaging results of the patients are usually not specific, and diagnosis requires histopathological examination and immunocytochemical analysis. At present, there is still no standard treatment guideline for spinal pPNET. Surgical resection, individualized radiotherapy and chemotherapy are still the mainstream treatment methods. The prognosis of patients with this disease is poor and further research is needed in the future.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our hospital, and informed consent was obtained from all participants and legal guardians.

Disclosure

The authors report no conflict of interest.

References

1. Aurias A, Rimbaut C, Buffe D. Chromosomal translocations in Ewing's sarcoma. N Engl J Med 1983; 309: 496-498.
2. Bachchan A, Roy K, Saha SK, Pathak D, Nadkarni A. Primary spinal peripheral primitive neuroectodermal tumor with acute presentation: A case report and review of literature. Asian J Med Sci 2019; 10: 59-61.
3. Cabral Gustavo APS, Nunes CF, Melo Jr JO, Guimarães RD, Gonçalves MB, Rodrigues RS, Correa JLA, Teixeira Jr OM, Klescoski Jr J, Lapenta MA, Landeiro JA. Peripheral primitive neuroectodermal tumor of the cervical spine. Surg Neurol Int 2012; 3: 91.
4. Cambruzzi E, Guerra EE, Hilgert HC, Schmitz HJ, Silva VL, Milani DM, Cruz RP, Pruinelli R. Primitive neuroectodermal tumor of the liver: a case report. Case Rep Med 2011; 2011: 748194.
5. Chen JY, Song JN, Meng H, Feng H. Intraspinal primitive neuroectodermal tumors: Report of four cases and review of the literature. Neurol India 2009; 57: 661-668.
6. Doyle LA. Sarcoma classification: an update based on the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone. Cancer 2014; 120: 1763-1774.
7. Duan XH, Ban XH, Liu B, Zhong XM, Guo RM, Zhang F, Liang BL, Shen J. Intraspinal primitive neuroectodermal tumor: Imaging findings in six cases. Eur J Radiol 2010; 80: 426-431.
8. Ellis JA, Rothrock RJ, Moise G, McCormick PC, Tanji K, Canoll P, Kaiser MG, McCormick PC. Primitive neuroectodermal tumors of the spine: a comprehensive review with illustrative clinical cases. Neurosurg Focus 2011; 30: E1.
9. Fletcher CDM, Unni KK, Mertens F. World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Soft Tissue and Bone. IARC Press, Lyon 2002.
10. Grier HE, Krailo MD, Tarbell NJ, Link MP, Fryer CJH, Pritchard DJ, Gebhardt MC, Dickman PS, Perlman EJ, Meyers PA, Donaldson SS, Moore S, Rausen AR, Vietti TJ, Miser JS. Addition of ifosfamide and etoposide to standard chemotherapy for ewing's sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med 2003; 348: 694-701.
11. Hart MN, Earle KM. Primitive neuroectodermal tumors of the brain in children. Cancer 1973; 32: 890-897.
12. Khmou M, Malihy A, Lamalmi N, Rouas L, Alhamany Z. Peripheral primitive neuroectodermal tumors of the spine: a case report and review of the literature. BMC Res Notes 2016; 9: 438.
13. Kumar R, Reddy SJ, Wani AA, Pal L. Primary spinal primitive neuroectodermal tumor: case series and review of the literature. Pediatr Neurosurg 2007; 43: 1-6.
14. Mascarin M, Drigo A, Dassie A, Gigante M, Franchin G, Sartor G, Trovò MG. Optimizing craniospinal radiotherapy delivery in a pediatric patient affected by supratentorial PNET: a case report. Tumori 2010; 96: 316-321.
15. May WA, Gishizky ML, Lessnick SL, Lunsford LB, Lewis BC, Delattre O, Zucman J, Thomas G, Denny CT. Ewing sarcoma 11;22 translocation produces a chimeric transcription factor that requires the DNA-binding domain encoded by FLI1 for transformation. Proc Natl Acad Sci USA 1993; 90: 5752-5756.
16. May WA, Lessnick SL, Braun BS, Klemsz M, Lewis BC, Lunsford LB, Hromas R, Denny CT. The Ewing's sarcoma EWS/FLI-1 fusion gene encodes a more potent transcriptional activator and is a more powerful transforming gene than FLI-1. Mol Cell Biol 1993; 13: 7393-7398.
17. Meng XT, He SS. Primitive neuroectodermal tumor in the spinal canal: A case report. Oncol Lett 2015; 9: 1934-1936.
18. Mhawech-Fauceglia P, Herrmann F, Penetrante R, Beck A, Sait S, Block AM, Odunsi K, Fisher J, Balos L, Cheney RT. Diagnostic utility of FLI-1 monoclonal antibody and dual-colour, break-apart probe fluorescence in situ (FISH) analysis in Ewing's sarcoma/primitive neuroectodermal tumour (EWS/PNET). A comparative study with CD99 and FLI-1 polyclonal antibodies. Histopathology 2006; 49: 569-575.
19. Patil AS, Gupta PP, Iratwar SW. Primary spinal extradural extraosseous primitive neuroectodermal tumor/Ewing's sarcoma: a critical analysis and review. Asian J Neurosurg 2021; 16: 276-280.
20. Perry R, Gonzales I, Finlay J, Zacharoulis S. Primary peripheral primitive neuroectodermal tumors of the spinal cord: report of two cases and review of the literature. J Neurooncol 2007; 81: 259-264.
21. Qi W, Deng X, Liu T, Hou Y, Yang C, Wu L, Fang J, Tong X, Yang J, Xu Y. Comparison of primary spinal central and peripheral primitive neuroectodermal tumors in clinical and imaging characteristics and long-term outcome. World Neurosurg 2016; 88: 359-369.
22. Saeedinia S, Nouri M, Alimohammadi M, Moradi H, Amirjamshidi A. Primary spinal extradural Ewing's sarcoma (primitive neuroectodermal tumor): Report of a case and meta-analysis of the reported cases in the literature. Surg Neurol Int 2012; 3: 55.
23. Sanati S, Lu DW, Schmidt E, Perry A, Dehner LP, Pfeifer JD. Cytologic diagnosis of Ewing sarcoma/peripheral neuroectodermal tumor with paired prospective molecular genetic analysis. Cancer 2007; 111: 192-199.
24. Shah JP, Jelsema J, Bryant CS, Ali-Fehmi R, Malone Jr JM. Carboplatin and paclitaxel adjuvant chemotherapy in primitive neuroectodermal tumor of the uterine corpus. Am J Obstet Gynecol 2009; 200: e6-9.
25. Shoubash L, Nowak S, Vogelgesang S, Schroeder HWS, Müller JU. Surgical management of an adult manifestation of Ewing sarcoma of the spine – a case report. AME Case Rep 2018; 2: 34.
26. Tong X, Deng X, Yang T, Yang C, Wu L, Wu J, Yao Y, Fu Z, Wang S, Xu Y. Clinical presentation and long-term outcome of primary spinal peripheral primitive neuroectodermal tumors. J Neurooncol 2015; 124: 455-463.
27. Wang GQ, Guo FY. Primary intramedullary primitive neuroectodermal tumor: A case report and review of the literature. Medicine 2017; 96: e9001.
28. Wei X, Zhang X, Song Z, Wang F. Analysis of clinical, imaging, and pathologic features of 36 patients with primary intraspinal primitive neuroectodermal tumors: a case series and literature review. J Neurol Surg A Cent Eur Neurosurg 2021; 82: 526-537.
29. Whang-Peng J, Triche TJ, Knutsen T, Miser J, Douglass EC, Israel MA. Chromosome translocation in peripheral neuroepithelioma. N Engl J Med 1984; 311: 584-585.
30. Wu GY, Ghimire P, Zhu L, Baral A, Su JJ. Magnetic resonance imaging characteristics of primary intraspinal peripheral primitive neuroectodermal tumour. Can Assoc Radiol J 2013; 64: 240-245.
31. Yi H, Fujimura Y, Ouchida M, Prasad DD, Rao VN, Reddy ES. Inhibition of apoptosis by normal and aberrant Fli-1 and erg proteins involved in human solid tumors and leukemias. Oncogene 1997; 14: 1259-1268.