Primary spinal primitive neuroectodermal tumour: report of two cases mimicking neurofibroma and review of the literature

Pierwotny prymitywny guz neuroektodermalny kanału kręgowego naśladujący nerwiakowłókniaka – opis dwóch przypadków i przegląd piśmiennictwa

Ashis Patnaik, Sudhansu Mishra, Sanjib Mishra, Rama Deo

SCB Medical College, Cuttack, India

Neurologia i Neurochirurgia Polska 2012; 46, 5: 480-488
DOI: 10.5114/ninp.2012.31360

Abstract

Primary spinal primitive neuroectodermal tumours (PNETs) are a rare entity. Most of them occur in children and young adults. To date, 47 cases of primary spinal PNET have been reported in the literature. We present two cases of primary spinal PNET. In both cases, the tumours were thoracic extradural ones with intrathoracic extension through intervertebral foramina resembling neurofibroma. These tumours are highly aggressive with rapid growth as evidenced by the short history in both of our cases. Both cases underwent gross total removal of the intraspinal and thoracic components. Postoperatively, both patients underwent cranio-spinal radiotherapy.

A review of the literature shows that the overall prognosis of PNETs of the spinal cord is very poor even with adequate surgery, radiotherapy and chemotherapy. One patient died after 4 months and the other one is still alive 8 months after surgery, radiotherapy and chemotherapy.

Key words: primitive neuroectodermal tumour, primary, spinal, neurofibroma.

Streszczenie

Prymitywne guzy neuroektodermalne (*primitive neuroectodermal tumours* – PNET) umiejscowione pierwotnie w kanale kręgowym należą do rzadkości. Większość z nich występuje u dzieci lub młodych osób dorosłych. Do tej pory opisano 47 przypadków PNET w tej lokalizacji. W niniejszej pracy prezentujemy dwa takie przypadki. U obu chorych guzy były umiejscowione zewnątrztwardówkowo w odcinku piersiowym kanału kręgowego i szerzyły się poprzez otwory międzykręgowe do wnętrza klatki piersiowej w sposób przypominający nerwiakowłókniaka. Opisywane guzy mają bardzo agresywny przebieg i rosną szybko, na co wskazuje krótki wywiad w obu opisywanych przypadkach. Obie pacjentki poddano makroskopowo doszczętnemu wycięciu wewnątrzkanałowej i znajdującej się we wnętrzu klatki piersiowej części guza. Po operacji obie chore poddano radioterapii czaszki i kanału kręgowego.

Przegląd piśmiennictwa wskazuje, że ogólne rokowanie w PNET rdzenia kręgowego jest złe nawet mimo właściwego leczenia chirurgicznego połączonego z radio- i chemioterapią. Jedna z opisywanych pacjentek zmarła po 4 miesiącach od operacji, druga przeżyła dotąd 8 miesięcy po leczeniu chirurgicznym, radio- i chemioterapii.

Słowa kluczowe: prymitywny guz neuroektodermalny, pierwotny, rdzeniowy, nerwiakowłókniak.

Correspondence address: Mch, Ashis Patnaik, SCB Medical College, Manglabag 753007, Cuttack, India, e-mail: dr_ash@yahoo.co.in
Received: 5.12.2011; accepted: 25.01.2012

Introduction

The term 'primitive neuroectodermal tumour' (PNET) was coined by Hart and Earle in 1973 [1]. These tumours are more common in children. There is considerable confusion and controversy in the classi - fication of PNETs [2]. As for the World Health Organization (WHO) classification of brain tumours [3], all undifferentiated (primitive) tumours are derived from common neuroepithelial cells and are therefore classified as PNETs. They have been classified as central PNET (cPNET) or peripheral PNET (pPNET). They differ from each other in natural history, clinicohistological features and spread. However, both have the same poor clinical outcome [4]. To date, 47 cases of PNETs have been reported. Our two cases are exclusive in that both were extradural ones with extension into the thoracic cavity resembling neurofibroma with the exception that both had a very short history of progression. Few such presentations have been reported previously [5,6].

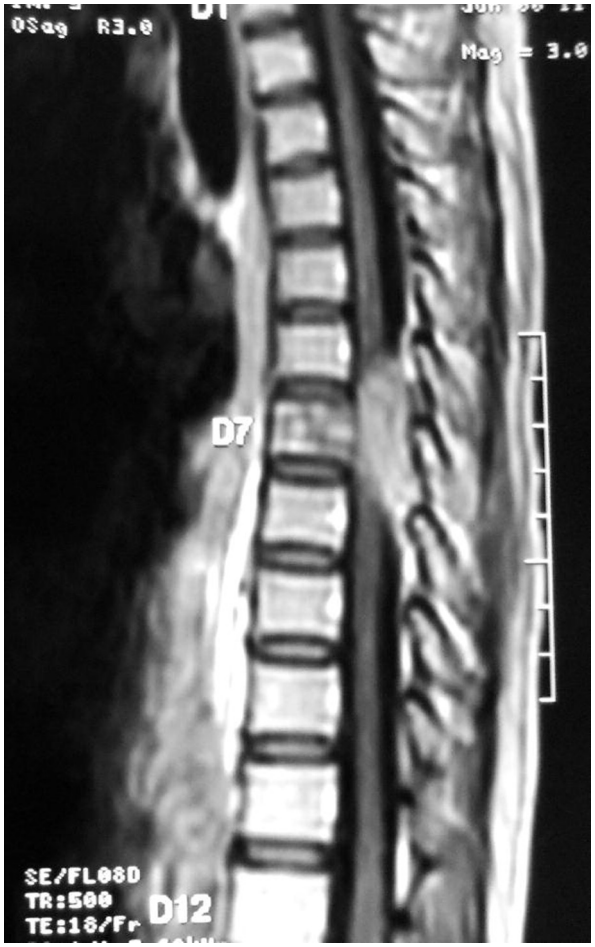

Fig. 1. Case 1: T1-weighted sagittal MR image after contrast injection showing the well-enhanced tumour

Case reports

Case 1

A 25-year-old woman presented with numbness, tingling and weakness of both feet which started 10 days before admission and progressed upwards, leading to paralysis of both legs for six days and urinary incontinence for one day. On neurological examination, motor power was grade 1/5 in the lower limbs, tendon reflexes were brisk and plantar responses were extensor bilaterally. She had hypoaesthesia below the T7 level. Magnetic resonance imaging (MRI) of the thoracic spine showed an extradural tumour at the T7 level compressing the cord and enhancing well after contrast injection (Figs. 1-3). The lesion extended into the left-side thoracic cavity, giving a picture of neurofibroma. A laminectomy was performed at the T6-T8 level. On exploration, the mass was extradural, soft, reddish-brown, vascular, adherent to the spinal cord and encasing the nerve roots. A total excision was achieved. The thoracic component was removed completely by left posterolateral thoracotomy. Histopathological examination and immunohistochemical staining confirmed the diagnosis of PNET. Postoperative computed tomography (CT) of the head (Fig. 4), thorax and abdomen was negative for any tumour pathology, indicating the primary nature of spinal pathology. By the third postoperative week, the patient was ambulatory with support. She had six cycles of chemotherapy consisting of cyclophosphamide followed by cranio-spinal radiation therapy spread over eight weeks. She was alive at 8-month follow-up postoperatively.

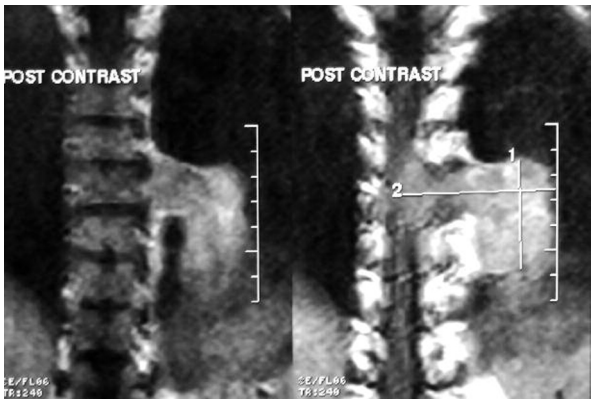

Fig. 2. Case 1: T1-weighted coronal MR image after contrast injection showing extension of the tumour into the left side of the thoracic cavity

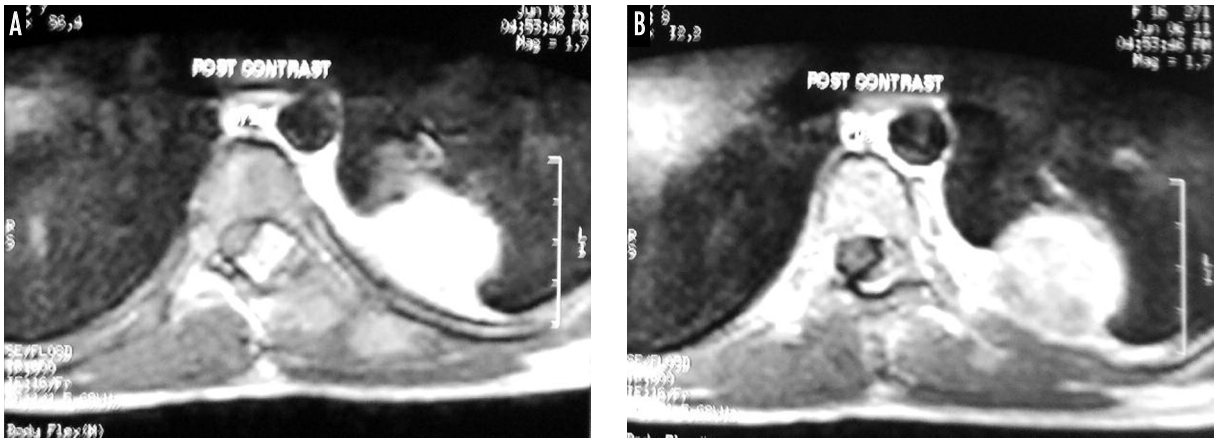

Fig. 3. Case 1: T1-weighted axial MR image after contrast injection showing the tumour compressing the cord to the right and extending through the intervertebral foramen into the left side of the thoracic cavity

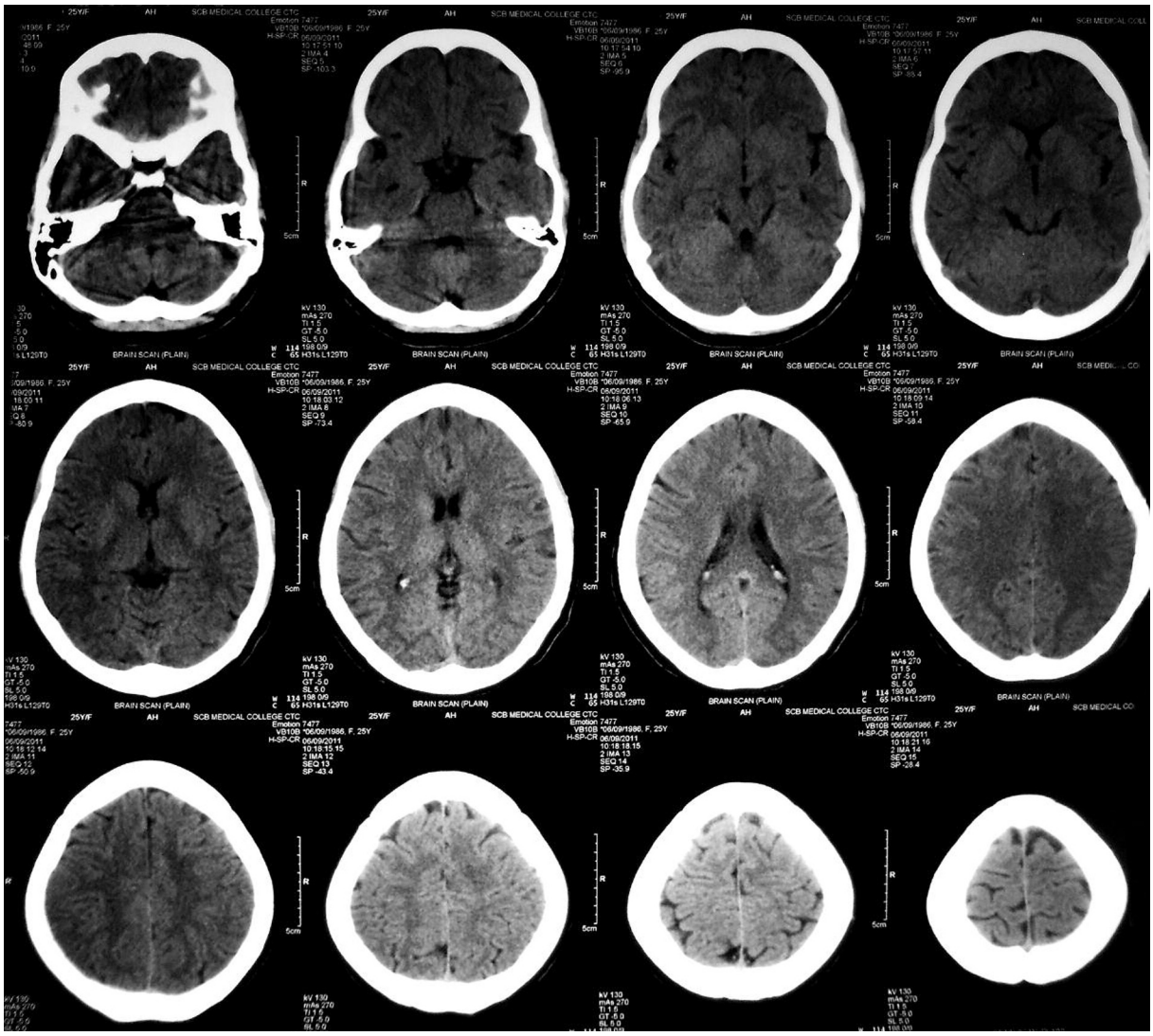

Fig. 4. Case 1: Postoperative cranial computed tomography showing no primary tumour in the brain

Case 2

A 36-year-old woman presented with weakness of both lower limbs followed by complete paralysis within a period of 30 days. She was bedridden for seven days before admission. On examination, the motor power was grade 0/5 in both lower limbs. There were signs of myelopathy in lower limbs with exaggerated knee and ankle jerks, ankle clonus, and bilateral Babinski sign. MRI of the cervical spine revealed a lesion extending from T8 to T11. The lesion extended into the left-side thoracic cavity through the dilated intervertebral foramen. The lesion was isointense on T1-weighted image and iso- to hyperintense on T2-weighted image (Figs. 5-7). A provisional diagnosis of spinal neurofibroma was made. A gross total excision of the lesion was achieved with T8-T11 laminectomy. The tumour was soft, friable, highly vascular and completely extradural in location, encasing the nerve root. The thoracic component could be removed partially by left posterolateral thoracotomy. Postoperatively, the patient showed partial improvement in the deficits, with power improving to 2/5. Histopathology and immunohistochemistry of the lesion revealed PNET (Figs. 8 and 9). She received focal radiation therapy spread over a period of six weeks, but declined to take chemotherapy. The patient died after 4 months of post-operative follow-up due to distant metastases.

Discussion

The concept of PNETs has been controversial for more than a decade. In the recently updated WHO classification, PNET is defined as an embryonal tumour composed of undifferentiated or poorly differentiated neuroepithelial cells which have the capacity for or display divergent differentiation along neuronal astrocytic, ependymal, muscular, or melanotic lines. Peripheral PNETs and Ewing's sarcoma (ES) are closely related malignant, small, and round-cell tumours of soft tissue and bones. Both pPNETs and ES strongly express the glycoprotein p30/32 (CD99), which is encoded by the microneme protein 2 (*MIC2*) gene. Because of immunohistochemical, ultrastructural and molecular bio-

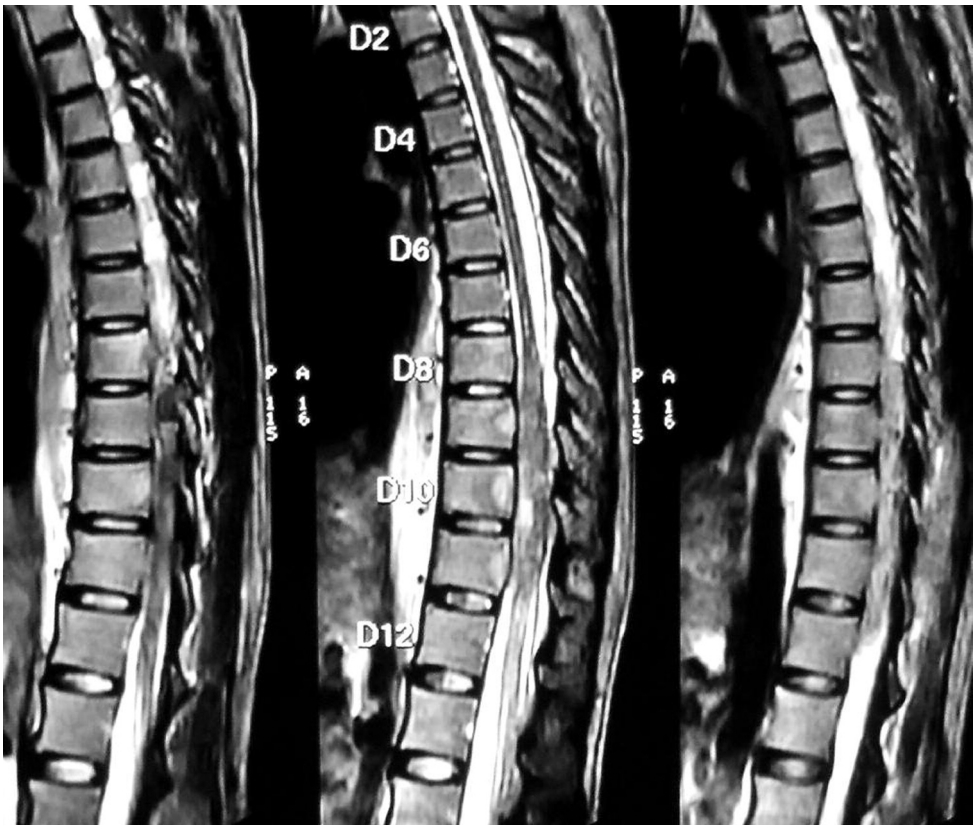

Fig. 5. Case 2: T2-weighted sagittal MR image showing isointense tumour extending from T8 to T11

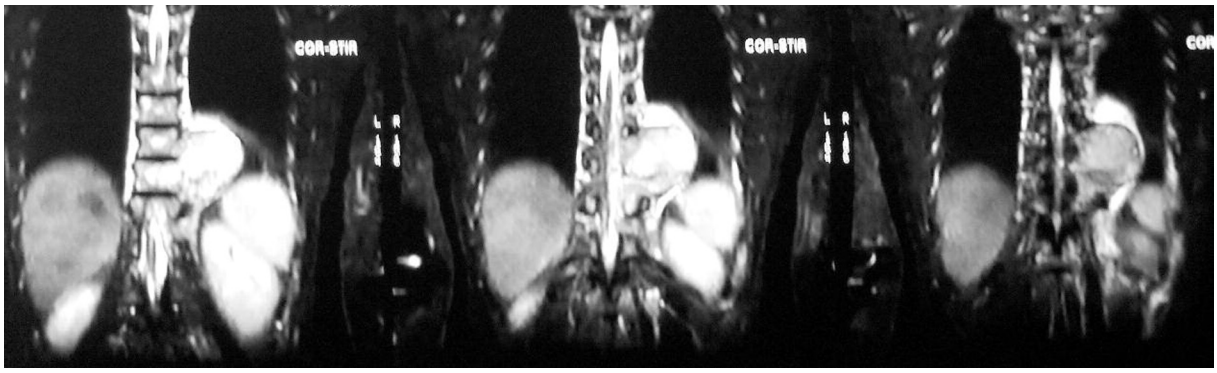

Fig. 6. Case 2: Coronal MR image showing the tumour extension into the left side of the thoracic cavity

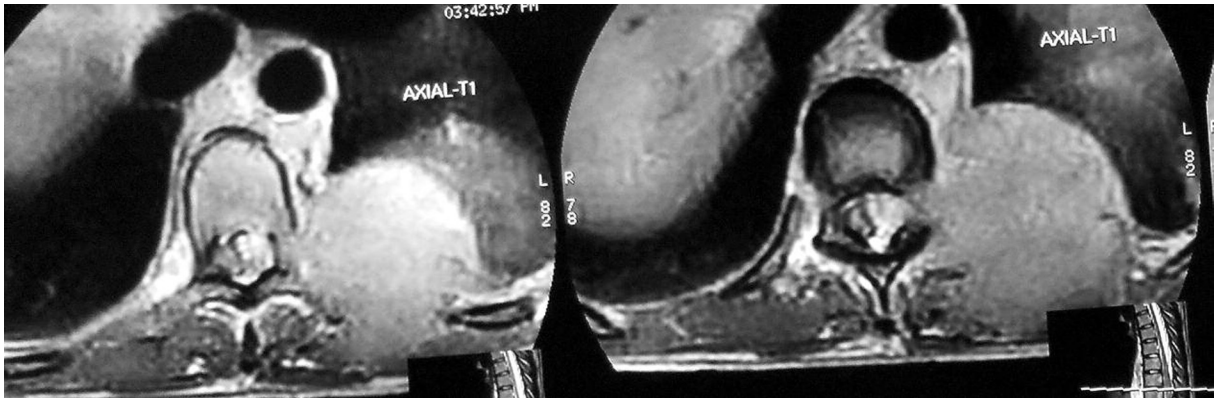

Fig. 7. Case 2: T1-weighted axial MR image showing the tumour

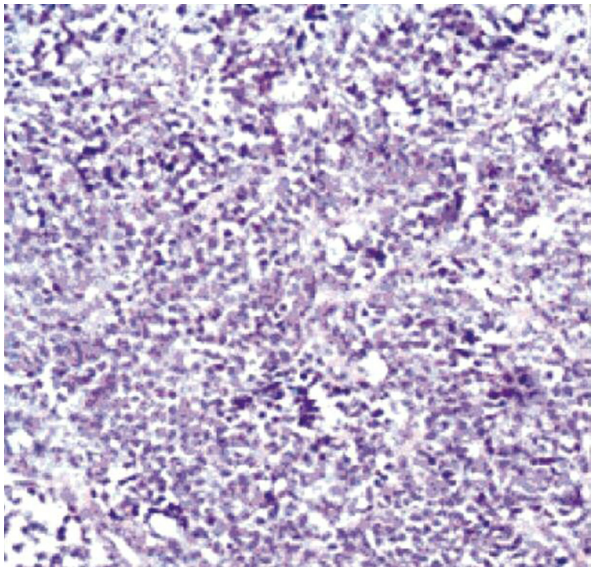

Fig. 8. Case 2: Light microscopy: The tumour cells were small and round morphologically, arranged in groups, with hyperchromatic nuclei and scanty cytoplasm (H&E, ×100).

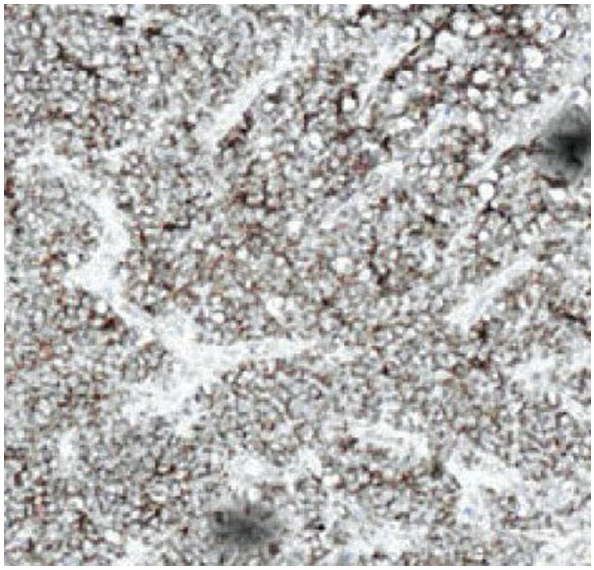

Fig. 9. Case 2: Immunohistochemistry showing CD99 (+) reactivity

Table 1. Demographic and clinical data of intraspinal primitive neuroectodermal tumours

Authors [Reference]	Age [years]/sex	Level	Location	Metastases	Survival [months]
Smith *et al.* [13]	24/M	Lumbar	Cauda equina	Lung	10
Kosnik *et al.* [14]	NA	Cervical	Unknown	None	NA
Kosnik *et al.* [14]	NA	Cervical	Unknown	None	NA
Kosnik *et al.* [14]	NA	Thoraco-lumbar	Unknown	Lung, bone, lymph node	NA
Rodriguez *et al.* [15]	16/M	–	–	–	–
Kepes *et al.* [16]	24/M	Lumbar	Cauda equina	None	18
Kepes *et al.* [16]	56/M	Lumbar	Cauda equina	None	Alive at 36
Kepes *et al.* [16]	39/M	Lumbar	Cauda equina	None	42
Liu *et al.* [17]	26/F	Lumbo-sacral	Extradural	None	Alive at 6
Sevick *et al.* [18]	26/M	Cervical	Intradural and extramedullary	Pleura, bone	36
Jaksche *et al.* [19]	15/F	Thoraco-lumbar	Intradural and extramedullary	None	18
Jaksche *et al.* [19]	26/M	Thoraco-lumbar	Intradural and extramedullary	None	36
Freyer *et al.* [20]	7/F	Thoraco-lumbar	Intramedullary	None	20
Ogasawara *et al.* [11]	16/M	Lumbar	Intramedullary	Intracranial	29
McDermott *et al.* [21]	47/M	Lumbar	Cauda equina	None	16
Kwon *et al.* [10]	3/F	Thoracic	Intramedullary	Intracranial	<1
Deme *et al.* [22]	22/F	Thoraco-lumbar	Intramedullary	None	Alive at 15
Koot *et al.* [23]	2/F	Cervical	Extramedullary	None	12
Papadatos *et al.* [24]	23	Thoracic	Intradural and extramedullary	None	12
Virani & Jain [6]*	4/M	Thoracic	Extradural	None	Alive at 18
Mawrin *et al.* [8]	69/M	Thoracic	Intramedullary	None	–
Yavuz *et al.* [25]	18/F	Lumbar	Extramedullary	None	Alive at 25
Albrecht *et al.* [26]	19/F	Lumbar	Intradural, intramedullary	Local recurrence	23
Mawrin *et al.* [8]	22/F	Thoracic	Intradural and extramedullary	Local recurrence	Alive at 9
Izycka-Swieszewska *et al.* [27]	26/M	Cervical	Extraspinal, intrameningeal	Local recurrence	3
Aydin *et al.* [28]	14/M	Thoracic	Extradural	None	–
Kampman *et al.* [4]	2/M	Cervical	Intramedullary	Local recurrence	7 days
Kumar *et al.* [7]	9/F	Thoracic	Extramedullary	None	Alive at 24
Kumar *et al.* [7]	8/M	Cervical	Extradural	Local recurrence	Recurred at 6
Kumar *et al.* [7]	18/M	Holocord	Intramedullary	None	Alive at 6 weeks
Nutman *et al.* [29]	19/F	Thoraco-lumbar	Intradural and extramedullary	None	Alive at 24
Musahl *et al.* [30]	27/M	Sacral	Extradural	–	Alive at 24
Dorfmüller *et al.* [31]	32/M	Sacral	–	Local recurrence	Alive at 29
Dorfmüller *et al.* [31]*	17/M	Lumbar	Extradural and paraspinal	Hemispheres	Alive at 23
Isotalo *et al.* [32]	52/M	Lumbo-sacral	Intradural	None	Alive at 12
Albrecht *et al.* [26]	29/F	Thoracic	Intradural	Local recurrence	Alive at 17

Table 1. Cont.

Authors [Reference]	Age [years]/sex	Level	Location	Metastases	Survival [months]
Akyüz *et al.* [9]	31/M	Lumbar	Intradural and extramedullary	Local recurrence	Alive at 24
Weber *et al.* [33]	26/M	Lumbar	–	Local recurrence	–
Kim *et al.* [34]	17/M	Thoraco-lumbar	Intramedullary	None	Alive at 24
Perry *et al.* [35]	27/M	Lumbar	Extradural	None	–
Perry *et al.* [35]	16/F	Lumbar	Extradural	None	Alive at 5
Jingyu *et al.* [36]	19/F	Cervical	Intradural and extramedullary	None	Alive at 10
Jingyu *et al.* [36]	46/M	Thoracic	Intradural and extramedullary	None	Alive at 14
Jingyu *et al.* [36]	58/M	Thoracic	Extradural	Vertebrae	Alive at 25
Jingyu *et al.* [36]	14/M	Thoracic	Intradural and extramedullary	None	Alive at 6
Gurkanlar *et al.* [37]	40 days/M	Thoraco-lumbar	Intradural and extramedullary	None	6
Nayak *et al.* [5]*	18/F	Thoracic	Extradural and paraspinal	–	–
Case 1* presented here	25/F	Thoracic	Extradural and paraspinal	None	Alive at 8
Case 2* presented here	36/F	Thoracic	Extradural and paraspinal	Lung	4

**Primary intraspinal primitive neuroectodermal tumour cases presenting with paraspinal mass*
F – female; M – male; NA – not available

logical similarities, pPNETs and ES have recently been categorized into the Ewing family of tumours [7,8].

These tumours commonly occur in the cerebellum but can arise in the pineal gland, cerebrum, spinal cord, brain stem, and peripheral nerves. Primary spinal PNETs come under the group of pPNET and most cases involving the spinal cord are drop metastases from primary intracranial tumours by cerebrospinal fluid. Intracranial seeding has also been reported in the literature [9-11]. Primary intraspinal PNETs are rare but so far 47 cases have been well described in the literature. We have summarized the clinical characteristics of the 49 cases, including our two cases, of intraspinal PNET reported to date (Table 1). However, the occurrence of exclusive extradural intraspinal PNET mimicking neurofibroma due to its intrathoracic component is extremely rare and five such cases (marked with asterisks in Table 1) have been reported thus far including our two cases.

Spinal PNET is characterized by adult onset and male predominance. The average age at presentation for patients with intraspinal PNET is much higher than the average age for intracranial PNET [12]. The duration of illness is often short, less than four months, and it can be as short as 10 days, as seen in one of our patients (Case 1). These tumours can occur at any level of the spine and the location can be intramedullary, intradural-extramedullary or extradural. Primary intraspinal PNETs show positive immunostaining for CD99 due to their biological similarity with Ewing's sarcoma group of tumours and they are included under the term pPNET. Both our cases were positive for CD99.

Cranial symptoms are not a feature of primary intraspinal PNET. This is a feature that distinguishes primary intraspinal PNET from primary intracranial PNET with spinal metastasis.

The prognosis of these tumours is very poor and treatment is far from satisfactory. Radical resection combined with radiation therapy and chemotherapy is the preferred treatment and leads to better outcomes. One of our patients, who is still alive 8 months postoperatively, underwent radical excision of both spinal and thoracic components with both radio- and chemotherapy. The other patient, who died 4 months postoperatively, had partial excision of the thoracic component due to adhesion to thoracic vascular structures and declined to undergo chemotherapy. This emphasizes the role of both radical resection along with adjuvant therapy in extending as well as improving the quality of life after surgery. Adjunctive immunotherapy is currently being investigated as a possible therapy [6]. The causes of death include metastatic disease, aggressive local spread, and progressive spinal cord involvement.

Primary spinal PNETs are now more frequently diagnosed as a result of improved histological techniques including immunohistochemistry. Previously, these cases were diagnosed as astrocytoma, ependymoma, or neurofibroma, depending on the location of the tumour in relation to the dura. Both our cases were strongly suspected as cases of neurofibroma due to their well-defined dumb-bell extension coming out into the thoracic cavity through the intervertebral foramina. Neurofibromas have a good prognosis, once they are fully excised. On the other hand, the PNETs present with a short history of symptoms in comparison to neurofibromas, as evidenced in both our cases. They tend to infiltrate into surrounding tissues and erode the dura. However, these findings were absent in our cases.

Conclusions

Our cases illustrate the adult age distribution and clinico-radiological features suggesting neurofibroma as the first diagnosis. However, the final diagnosis based on intraoperative finding and histological features was primary intraspinal PNET. Only three such cases of spinal PNET resembling neurofibroma have been reported in the literature. This is an excellent illustration of presentation of these rare tumours; they should be considered in differential diagnosis of short duration paraparesis.

These tumours are rarely diagnosed preoperatively with certainty, based on clinico-radiological features only. Good histological diagnosis supported with immunohistochemistry should be done in every suspected case so as to diagnose these relatively rare tumours. Due to their poor prognosis in spite of good surgical excision combined with aggressive adjuvant therapy, studies on molecular pathogenesis of these tumours and their application through immunotherapy are the key to future advances in treatment, which are currently lacking.

Disclosure

Authors report no conflict of interest.

References

1. Hart M.N., Earle K.M. Primitive neuroectodermal tumors of the brain in children. *Cancer* 1973; 32: 890-897.
2. Nishio S., Morioka T., Fukui M. Primitive neuroectodermal tumors. *Crit Rev Neurosurg* 1998; 8: 261-268.
3. Brat D.J., Parisi J.E., Kleinschmidt-DeMasters B.K., et al. Surgical neuropathology update: A review of changes introduced by the WHO classification of tumours of the central nervous system, 4th ed. *Arch Pathol Lab Med* 2008; 132: 993-1007.
4. Kampman W.A., Kros J.M., De Jong T.H., et al. Primitive neuroectodermal tumours (PNETs) located in the spinal canal; the relevance of classification as central or peripheral PNET: Case report of a primary spinal PNET occurrence with a critical literature review. *J Neurooncol* 2006; 77: 65-72.
5. Nayak P.K., Rao K.M., Sahoo G.C., et al. Primary thoracic primitive neuroectodermal tumor mimicking as neurofibroma. *Neurol India* 2011; 59: 648-649.
6. Virani M.J., Jain S. Primary Intraspinal primitive neuroectodermal tumor (PNET): a rare occurrence. *Neurol India* 2002; 50: 75-80.
7. Kumar R., Reddy S.J., Wani A.A., et al. Primary spinal primitive neuroectodermal tumor: case series and review of the literature. *Pediatr Neurosurg* 2007; 43: 1-6.
8. Mawrin C., Synowitz H.J., Kirches E., et al. Primary primitive neuroectodermal tumor of the spinal cord: case report and review of the literature. *Clin Neurol Neurosurg* 2002; 104: 36-40.
9. Akyüz M., Demiral A.N., Gürer I.E., et al. Primary primitive neuro-ectodermal tumor of cauda equina with intracranial seeding. *Acta Neurochir* (*Wien*) 2004; 146: 525-528.
10. Kwon O.K., Wang K.C., Kim C.J., et al. Primary intramedullary spinal cord primitive neuroectodermal tumor with intracranial seeding in an infant. *Childs Nerv Syst* 1996; 12: 633-636.
11. Ogasawara H., Kiya K., Kurisu K., et al. Intracranial metastasis from a spinal cord primitive neuroectodermal tumor: case report. *Surg Neurol* 1992; 37: 307-312.
12. Hargrave D.R., Zacharoulis S. Pediatric CNS tumors: current treatment and future directions. *Expert Rev Neurother* 2007; 7: 1029-1042.
13. Smith D.R., Hardman J.M., Earle K.M. Metastasizing neuroectodermal tumors of the central nervous system. *J Neurosurg* 1969; 31: 50-58.
14. Kosnik E.J., Boesel C.P., Bay J., et al. Primitive neuroectodermal tumors of the central nervous system in children. *J Neurosurg* 1978; 48: 741-746.
15. Rodriguez M., Dinapoli R.P. Spinal cord compression: with special reference to metastatic epidural tumors. *Mayo Clin Proc* 1980; 55: 442-448.
16. Kepes J.J., Belton K., Roessmann U., et al. Primitive neuroectodermal tumors of the cauda equina in adults with no detectable primary intracranial neoplasm-three case studies. *Clin Neuropathol* 1985; 4: 1-11.
17. Liu H.M., Yang W.C., Garcia R.L., et al. Intraspinal primitive neuroectodermal tumor arising from the sacral spinal nerve root. *J Comput Tomogr* 1987; 11: 350-354.
18. Sevick R.J., Johns R.D., Curry B.J. Primary spinal primitive neuroectodermal tumor with extraneural metastases. *AJNR Am J Neuroradiol* 1987; 8: 1151-1152.
19. Jaksche H., Wöckel W., Wernert N. Primary spinal medulloblastomas? *Neurosurg Rev* 1988; 11: 259-265.
20. Freyer D.R., Hutchinson R.J., McKeever P.E. Primary primitive neuroectodermal tumor of the spinal cord associated with neural tube defect. *Pediatr Neurosci* 1989; 15: 181-187.
21. McDermott V.G., el-Jabbour J.N., Sellar R.J., et al. Primitive neuroectodermal tumour of the cauda equina. *Neuroradiology* 1994; 36: 228-230.

22. Deme S., Ang L.C., Skaf G., et al. Primary intramedullary primitive neuroectodermal tumor of the spinal cord: case report and review of the literature. *Neurosurgery* 1997; 41: 1417-1420.
23. Koot R.W., Henneveld H.T., Albrecht K.W. Two children with unusual causes of torticollis: Primitive neuroectodermal tumor and Grisel's syndrome. *Ned Tijdschr Geneeskd* 1998; 142: 1030-1033.
24. Papadatos D., Albrecht S., Mohr G., et al. Exophytic primitive neuroectodermal tumor of the spinal cord. *Am J Neuroradiol* 1998; 19: 787-789.
25. Yavuz A.A., Yaris N., Yavuz M.N., et al. Primary intraspinal primitive neuroectodermal tumor: Case report of a tumor arising from the sacral spinal nerve root and review of the literature. *Am J Clin Oncol* 2002; 25: 135-139.
26. Albrecht C.F., Weiss E., Schulz-Schaeffer W.J., et al. Primary intraspinal primitive neuroectodermal tumor: Report of two cases and review of the literature. *J Neurooncol* 2003; 61: 113-120.
27. Izycka-Swieszewska E., Debiec-Rychter M., Wasag B., et al. A unique occurrence of a cerebral atypical teratoid/rhabdoid tumor in an infant and a spinal canal primitive neuroectodermal tumor in her father. *J Neurooncol* 2003; 61: 219-225.
28. Aydin M.V., Sen O., Ozel S., et al. Primary primitive neuroectodermal tumor within the spinal epidural space: report of a case and review of the literature. *Neurol Res* 2004; 26: 774-777.
29. Nutman A., Postovsky S., Zaidman I., et al. Primary intraspinal primitive neuroectodermal tumor treated with autologous stem cell transplantation: case report and review of the literature. *Pediatr Hematol Oncol* 2007; 24: 53-61.
30. Musahl V., Rihn J.A., Fumich F.E., et al. Sacral intraspinal extradural primitive neuroectodermal tumor: A case report. *Spine J* 2008; 8: 1024-1029.
31. Dorfmüller G., Würtz F.G., Umschaden H.W., et al. Intraspinal primitive neuroectodermal tumour: Report of two cases and review of the literature. *Acta Neurochir* (*Wien*) 1999; 141: 1169-1175.
32. Isotalo P.A., Agbi C., Davidson B., et al. Primary primitive neuroectodermal tumor of the cauda equina. *Hum Pathol* 2000; 31: 999-1001.
33. Weber D.C., Rutz H.P., Lomax A.J., et al. First spinal axis segment irradiation with spot-scanning proton beam delivered in the treatment of a lumbar primitive neuroectodermal tumour. Case report and review of the literature. *Clin Oncol (R Coll Radiol)* 2004; 16: 326-331.
34. Kim Y.W., Jin B.H., Kim T.S., et al. Primary intraspinal primitive neuroectodermal tumor at conus medullaris. *Yonsei Med J* 2004; 45: 533-538.
35. Perry R., Gonzales I., Finlay J., et al. Primary peripheral primitive neuroectodermal tumors of the spinal cord: report of two cases and review of the literature. *J Neurooncol* 2007; 81: 259-264.
36. Jingyu C., Jinning S., Hui M., et al. Intraspinal primitive neu - roectodermal tumors: report of four cases and review of the literature. *Neurol India* 2009; 57: 661-668.
37. Gurkanlar D., Korkmaz E., Gurler I.E., et al. Multilevel primary intraspinal PNETs in an infant associated with hydrocephalus. *Turk Neurosurg* 2010; 20: 82-85.