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Primary Primitive Neuroectodermal Tumor of the Conus Medullaris in an Elderly Patient: A Case Report and Review of the Literature

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Key Words
Primitive neuroectodermal tumor · Ewing's sarcoma family of tumors · Conus medullaris · Elderly patient

Abstract
Primary spinal primitive neuroectodermal tumors (PNETs) are very rare conditions. Most of these tumors occur in children and young adults. A 63-year-old man with a primary spinal PNET in the conus medullaris from the L1 to L2 level is presented in this report. The optimal treatment of primary spinal PNETs is yet unknown. Surgical resection, radiation therapy, and chemotherapy have been advocated for the treatment of spinal PNET based on PNETs at other sites. However, the outcome is very poor. There are a few reports of cases with long-term survival and no recurrence. In these patients, en bloc resections were performed.

Introduction

Primitive neuroectodermal tumors (PNETs) are rare malignant neoplasms which occur predominantly in children and young adults. PNETs belong to the Ewing's sarcoma family of tumors and are associated with the same reciprocal chromosomal translocation as the Ewing's sarcoma.

PNETs usually develop in the cerebellum; however, they can also arise from other sites of the central nervous system (CNS) such as the cerebral hemispheres, cortex, pineal gland and brain stem. Primary spinal PNETs are very rare conditions, and up to now,

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only 38 cases have been reported in the literature [1–26]. In this article, we report a rare case of a primary PNET of the conus medullaris in an elderly patient. The clinical, radiological and histological findings are presented and the relevant literature is reviewed.

Case Report

A previously healthy 63-year-old man was admitted to hospital with a 3 months' history of lower back pain projecting into the right leg. Spinal magnetic resonance imaging (MRI) demonstrated a disc hernia at the L2-L3 level and an intradural tumor from the L1 to L2 level (**fig. 1**a–c). After resection of the disc hernia, an intradural tumor resection was performed. The tumor was resected intralesionally because it was adhered to the spinal cord and nerve roots. Histopathological examination of the tumor specimen revealed a highly cellular, poorly differentiated neoplasm. The tumor was composed of small round cells with scanty cytoplasm and hyperchromatic nuclei. No well-defined Homer Wright and only a few ependymal rosettes were found (**fig. 2**a). Immunohistochemical staining for neuron-specific enolase (NSE) was strongly positive, as was staining for CD99 (MIC2) (fig. 2b). On the other hand, there was no evidence of significant epithelial differentiation.

Two months after the operation, the patient complained of progressive paresthesia and weakness of the right leg and was referred to our hospital. Spinal MRI demonstrated an intraspinal tumor extending from the Th12 to L2 level. The tumor showed high intensity on both T1- (**fig. 3**a) and T2-weighted images (fig. 3b). The patient underwent chemotherapy with a protocol for Ewing's sarcoma family of tumors, because the results of the histopathological examination of the tumor led us to reject the diagnoses of lymphoma and poorly differentiated carcinoma and confirmed the diagnosis of PNET (**fig. 4**). Additionally, he received radiation therapy consisting of 16 Gy to the spinal cord and 14 Gy to the whole brain and spinal cord. After these treatments, his neurologic symptoms completely resolved and the tumor disappeared on MRI (**fig. 5**a–c).

The patient continued low-dose chemotherapy with etoposide; however, 21 months after the operation, he again experienced paresthesia and weakness of the right leg because of recurrence of the tumor. He was then treated with a multidrug chemotherapy again, but his symptoms did not improve. He died due to progressive paresis 25 months after the operation.

Discussion

Primary spinal PNETs are rare lesions. The majority of spinal PNETs are the result of subarachnoidal spread of tumors in the neuraxis. In 1973, the term PNET was first introduced by Hart and Earle [27] to describe undifferentiated cerebral tumors. Reviewing this term, in 1983, Rorke [28] defined PNETs as 'central nervous system tumors predominantly composed of undifferentiated neuroepithelial cells'. At the same time, they subclassified these tumors on the basis of their cellular differentiation. Finally, in 1993, the World Health Organization (WHO) classification grouped these tumors into the category of embryonal tumors composed of undifferentiated or less differentiated neuroepithelial cells which have the capacity of differentiation to astrocytes, ependymal cells, melanocytes or muscle cells [25].

Histopathologically, PNETs are undifferentiated, small, round-cell tumors with hyperchromatic nuclei and features of neural differentiation, which typically form Homer Wright rosettes. The amount and quality of rosette formation vary substantially; some tumors may only show abortive rosette formation. On immunohistochemical examination, the most useful antibody for the diagnosis of PNET is the monoclonal antibody CD99, directed against the cell surface protein MIC2 whose gene is located on the pseudoautosomal region of the X and Y chromosomes. PNETs often have the same

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reciprocal chromosomal translocation, i.e. t(11;22)(q24;q12), which is the other key to the diagnosis of PNET [20].

PNETs involving the spinal cord are most commonly drop metastases from primary intracranial tumors, which disseminate via the cerebrospinal fluid. Therefore, primary intraspinal PNETs are extremely rare, and to our knowledge, only 38 cases have been reported in the literature so far (**table 1**) [1–26]. The age of the disease manifestation, including our case, ranged from 0 to 69 years, with an average age of 25.1 years. Our patient is the second oldest of all reported cases so far. In addition, there seems to be a male predominance for these tumors.

The optimal treatment of primary spinal PNETs is unknown because the tumors are very rare. Surgical resection, radiotherapy, and chemotherapy have been advocated for the treatment of spinal PNET based on PNETs at other sites. However, there is no agreement on the radiotherapy schedule, irradiance, and region (spine, brain, or both of them), as well as on the use and regimen of chemotherapy for PNETs. Successful results were reported using combinations of vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide in Ewing's sarcoma. Despite multimodal treatment combining surgery, radiotherapy, and chemotherapy, the outcome is very poor. However, there are a few reports of cases with long-term survival and no recurrence. In these patients, en bloc resection was performed [20].

In conclusion, primary spinal PNETs are very rare tumors seldom affecting elderly patients. Therefore, their treatment is not established. In spite of surgery, radiation therapy, and chemotherapy, the outcome is very poor. It seems that the key for long-term survival is early detection and en bloc resection.

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Table 1. Summary of patients with a primary spinal PNET

Patient [ref.]	Age	Sex	Site	Survival period	Recurrence and metastasis
1 [1]	24 years	M	lumbar, cauda equina	10 months	lung
2 [2]	6 months to 10 years	NA	cervical	NA	NA
3 [2]	6 months to 10 years	NA	cervical	NA	NA
4 [2]	6 months to 10 years	NA	thoracic-lumbar	NA	NA
5 [3]	24 years	M	lumbar, intradural, cauda equina	18 months	local recurrence
6 [3]	56 years	M	lumbar, intradural, cauda equina	alive at 36 month	none
7 [3]	39 years	M	lumbar, intradural, cauda equina	30 months	local recurrence
8 [4]	26 years	M	cervical, intradural, extramedullary	10 days	spinal canal, diffuse bone
9 [5]	26 years	F	lumbar-sacral, extradural	alive at 6 months	none
10 [6]	26 years	M	thoracic-lumbar, intramedullary	36 months	between two frontal horns, roof 4th ventricle
11 [6]	15 years	F	thoracic-lumbar, intra- and extramedullary	18 months	local recurrence
12 [7]	7 years	M	thoracic-sacral, intramedullary	20 months	local progression to cervical
13 [8]	16 years	F	lumbar, intramedullary	29 months	brain
14 [9]	47 years	M	lumbar-sacral, cauda equina, intra- and extramedullary	16 months	local progression
15 [10]	3 months	F	thoracic-lumbar, intramedullary	15 days	brain
16 [11]	22 years	F	thoracic-lumbar, intramedullary	alive at 15 months	local recurrence
17 [12]	23 years	F	thoracic, intradural extramedullary	alive at 12 months	none
18 [13]	32 years	M	sacral, cauda equina	29 months	local progression, brain
19 [13]	17 years	M	lumbar, cauda equina	alive at 23 months	none
20 [14]	52 years	M	lumbar-sacral, cauda equina	alive at 12 months	none
21 [15]	5 years	M	thoracic, extradural	alive at 8 months	none
22 [16]	69 years	M	cervical-thoracic, intra- and extramedullary	3 months	none
23 [17]	22 years	F	thoracic, extramedullary	alive at 9 months	local recurrence, brain
24 [18]	49 years	F	lumbar, cauda equina	23 months	diffuse intraspinal progression
25 [18]	29 years	F	thoracic, intramedullary	17 months	multiple intraspinal
26 [19]	26 years	M	cervical, intrameningeal	3 months	local recurrence, diffuse intraspinal
27 [20]	12 years	F	cervical-thoracic, extradural	32 months	local recurrence
28 [20]	10 years	M	cervical-thoracic, extradural	22 months	multiple lung
29 [20]	30 years	F	cervical, extramedullary	14 months	local recurrence
30 [20]	14 years	M	lumbar, extramedullary	alive at 67 months	none
31 [21]	31 years	F	lumbar-sacral, cauda equina	2 months	local recurrence, left frontoparietal
32 [22]	3 years	M	cervical, intramedullary	several days	local progression to brainstem
33 [23]	38 years	M	thoracic, intramedullary	18 months	brain, multiple spinal cord
34 [24]	54 years	F	cervical, intramedullary	NA	none
35 [25]	9 years	F	thoracic-lumbar, extramedullary	alive at 18 months	none
36 [25]	8 years	M	cervical, extradural	alive at 8 months	local recurrence
37 [25]	18 years	M	cervical, intramedullary	alive at 6 months	none
38 [26]	17 years	M	thoracic, intramedullary	alive at 6 months	none

NA = Not available.

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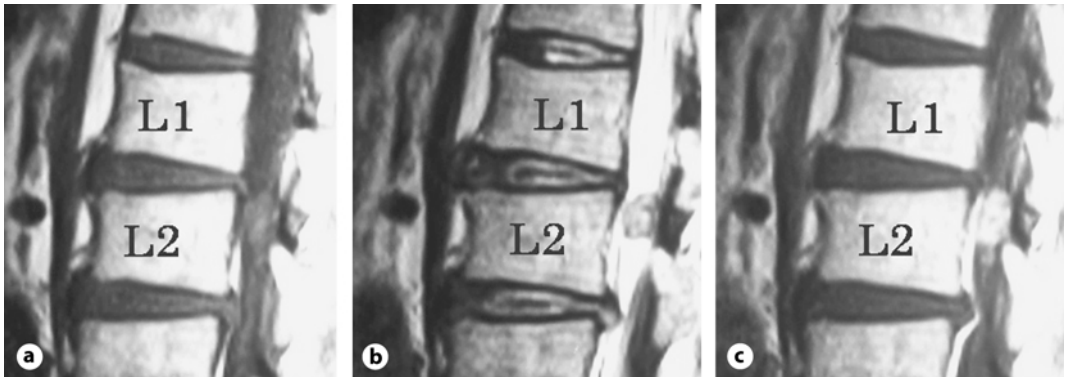

Fig. 1. Spinal MRI showed a disc hernia at the L2-L3 level and a generally isointense intradural tumor with focal high-intensity T1-weighted images at the level of L1-L2 (**a**). On T2-weighted MRI, the tumor demonstrated high intensity with focal low intensity (**b**). The tumor is homogenously enhanced by gadolinium (**c**).

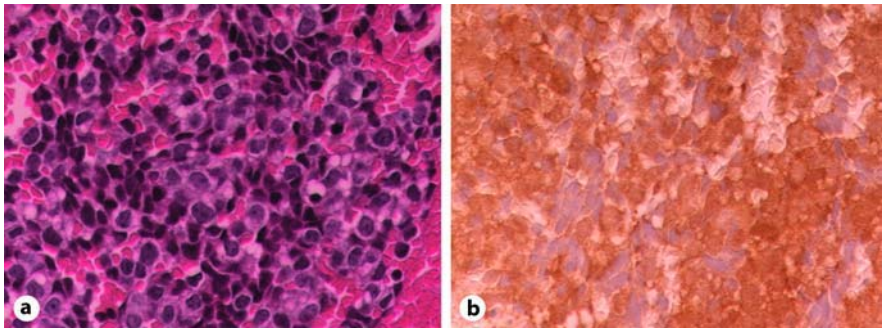

Fig. 2. Histopathological examination of the tumor specimen revealed a highly cellular, poorly differentiated neoplasm. The tumor was composed of small round cells with scanty cytoplasm and hyperchromatic nuclei. No well-defined Homer Wright and only a few ependymal rosettes were found (**a**). Immunohistochemical staining for NSE was strongly positive (pictures not shown), as was staining for CD99 (MIC2) (**b**).

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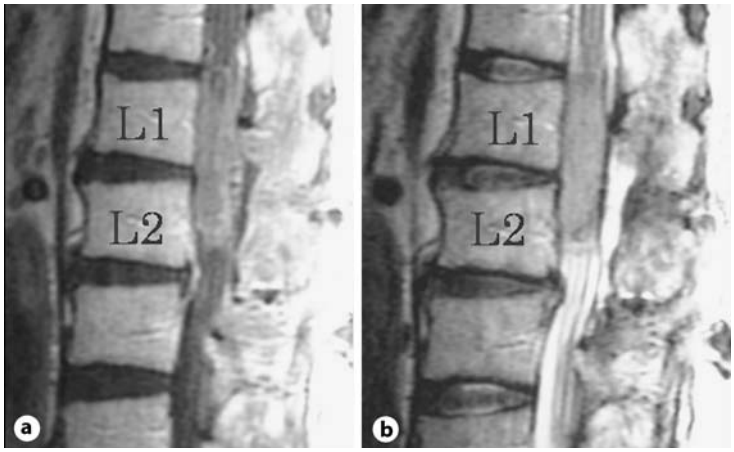

Fig. 3. Spinal MRI demonstrated an intraspinal tumor extending from the Th12 to L2 level. The tumor showed high intensity on T1-weighted image (**a**) as well as on T2-weighted image (**b**).

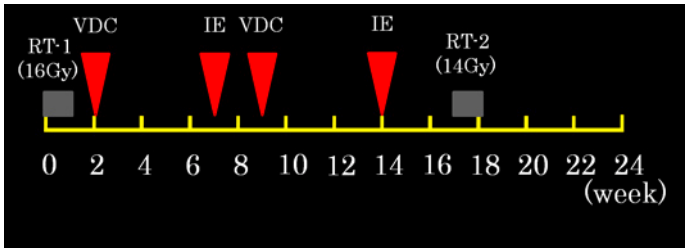

Fig. 4. Protocol of chemotherapy. RT-1 = Local radiation 16 Gy; RT-2 = radiation to brain and spinal cord 14 Gy; VDC = vincristine (1.5 mg/m^2) + doxorubicin (30 mg/m^2) + cyclophosphamide (1,200 mg/m^2); IE = ifosfamide (1.8 g/m^2) + etoposide (100 mg/m^2).

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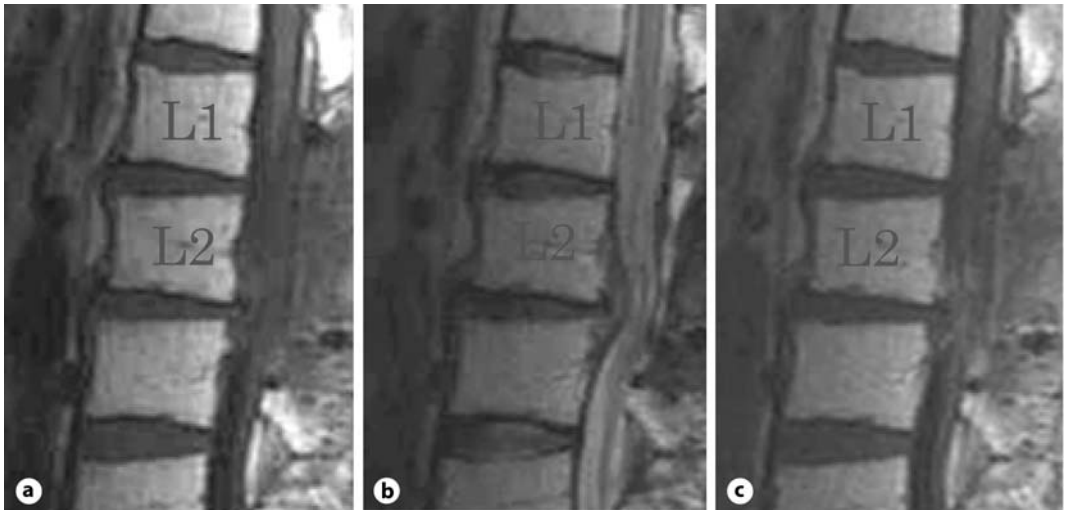

Fig. 5. MRI after chemotherapy and radiation. **a** T1-weighted image. **b** T2-weighted image. **c** T1-weighted image with gadolinium enhancement.

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