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Primary Intraspinal Primitive Neuroectodermal Tumor at Conus Medullaris

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A primary intraspinal primitive neuroectodermal tumor is very rare, with only 24 cases having been reported in the literature. In general this type of tumor is treated with surgery followed by radiotherapy and chemotherapy; however, the prognosis still remains poor. The case of a primary intraspinal primitive neuroectodermal tumor, at the conus medullaris in a 17 year old male patient is presented. He had sufferred from paraparesis, urinary difficulty and lower back pain of 1 month duration. A thoracolumbar MRI demonstrated a $2 \times 2 \times 8$ cm isointense intraspinal mass, on T1-weighted images, with strong contrast enhancement from the T11 to L2 level. There was no clinical or radiological evidence for the existence of an intracranial tumor. A histological examination revealed a small round cell tumor and immunohistochemical characteristics of PNET. The clinical, radiological and pathological features are discussed with a review of the literatures.

Key Words: Primitive neuroectodermal tumor, conus medullaris

INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are a group of malignant neoplasms that arise from pluripotent neural crest cells. PNETs are thought to arise from the neoplastic transformation of primitive neuroepithelial cells in subependymal zones.[1-3] These tumors are usually composed of undifferentiated, small, round, and hyperchromatic cells. In 1973, Hart and Earl proposed the term 'primitive neuroectodermal tumors' (PNETs).[2] In the central nervous system, these tumors most frequently arise in the cerebellum of children and are called medulloblastoma.[4,5] Compared with the high frequency of medulloblastoma in primary brain tumors, primary intraspinal PNETs are very rare. To date, there have only been 24 cases of primary intraspinal PNETs reported in the literature. A case of a primary intraspinal PNET at the conus medullaris is reported with a review of the literature.

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CASE REPORT

A 17-year-old male was admitted with a 1 month history of paraparesis, urinary difficulty, lower back pain. A neurological examination revealed a bilateral weakness of the lower extremities, with foot drop on both sides. Hyoesthesia and hypoalgesia were detected below the T11 level. Spinal magnetic resonance imaging (MRI) demonstrated a $2 \times 2 \times 8$ cm sized intradural, intramedullary lesion from the T11 lower vertebral body to the L2 lower vertebral body level. The T2 weighted magnetic resonance image showed an isosignal intramedullary mass, with a multifocal high signal intensity cyst like lesion (Fig. 1). On the T1 weighted magnetic resonance image, an isosignal intramedullary tumor, with strong enhancement, was demonstrated from the T11 to L2 level (Fig. 1). The radiological findings of the tumor were highly suggestive of a high grade malignancy such as an astrocytoma ependymoma. Total laminectomy at the L1, L2, L3 levels, and a subtotal laminectomy at the T12, and L4 levels were performed. After the dura was opened a grey-reddish hard consistency hyper-

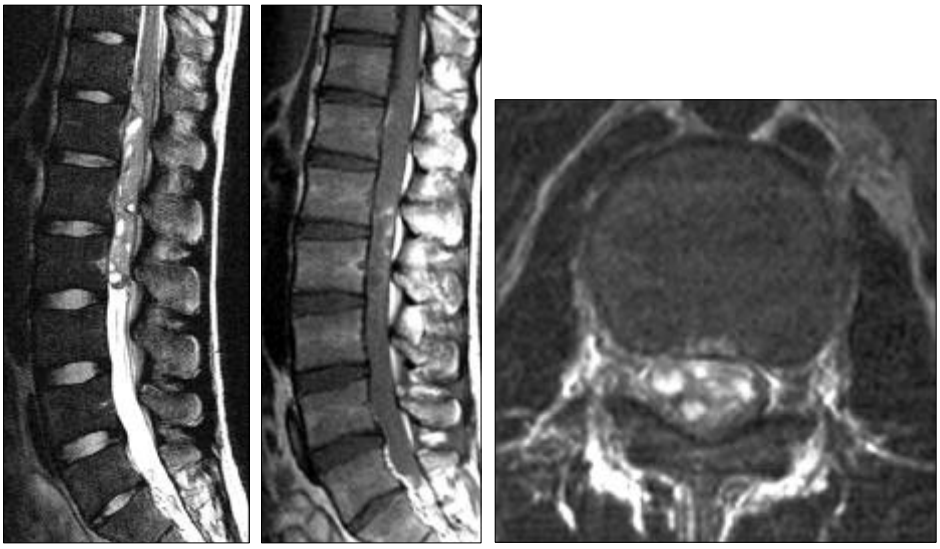

Fig. 1. T2 weighted magnetic resonance image demonstrated an isosignal intramedullary mass, with multifocal high signal intensity, cyst like lesion. On T1 weighted magnetic resonance image, an isosignal intramedullary tumor, with strong enhancement, was demonstrated from the T11 to L2 level.

vascular tumor mass, filling the intradural space was detected. The tumor was partly intramedullary and partly extramedullary, and the tumor margin was poorly demarcated. The arachnoid and pia mater around the mass were adherent to the spinal cord. A subtotal removal of the mass was performed. The histological examination revealed no definite Homer-Wright rosette, but undifferentiated small round cells with hyperchromatic nuclei were observed which showed positive immunoreactivity for MIC-2, neuron specific enolase (NSE) (Fig. 2). A brain MRI revealed no evidence of a tumor. Four weeks after the operation the patient received craniospinal irradiation with a total dose of 5040Gy.

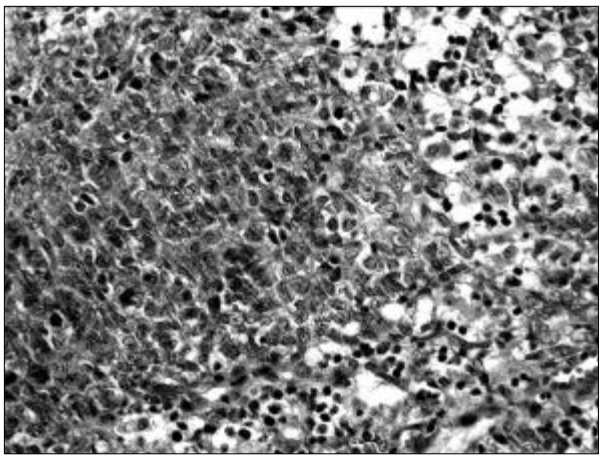

Fig. 2. Histopathology revealed a poorly differentiated small round cell tumor, with hyperchromatic nuclei observed. No definite Homer-Wright rosette was revealed. (H-E stain, × 400)

DISCUSSION

PNETs is the generic name used to describe a morphologically similar, undifferentiated or primitive small blue celled neoplasm showing the potential for multiple differentiations, irrespective of the site of origin. In 1973, Hart and Earl reported 23 cases of poorly differentiated central nervous system tumors in children, which were pathologically similar to a medulloblastoma. They defined that a primitive neuroectodermal tumor should contain more than 90% undifferentiated primitive cells. Since the initial definition by Hart and Earle the classification of this embryonal tumor has been controversial. In 1993, the World Health Organization Classification of brain tumors recommended to use PNET as the generic term for cerebellar medulloblastomas and other CNS tumors that are morphologically identical to medulloblastomas.[6]

A primary intraspinal PNET is extremely rare. Before the diagnosis of a primary spinal PNET can be confirmed, the more common 'drop' metastasis, of intracranial origin, must be excluded.[7,8] Our case was a true primary spinal PNET as there was no evidence of an intracranial tumor in the brain MRI. The neuroradiological features of PNETs have been best studied in cerebellar

medulloblastomas. In general, medulloblastomas tend to be iso-or hyperintense on CT, low signal on T1-weighted MRI and high signal on T2-weighted MRI, with varying amounts of tumor calcification, necrosis and surrounding edema.[9] There have only been a few reports of the neuro-radiological features of PNETs outside of the cerebellum. In our case, an isosignal intramedullary mass was observed on the T1-weighted magnetic resonance image, and a multifocal bright signal cyst like lesion from the T11 to L2 level, on T2-weighted magnetic resonance image. A gadollium enhanced T1-weighted magnetic resonance image demonstrated a strong enhancing mass, with an obliterated margin, from the T11 to L2 level. The major radiological differential diagnosis for intraspinal PNETs is ependymomas, which is the most common intramedullary tumors.[10] On MR imaging spinal ependymomas are isointense on T1-weighted images, with strong enhancement after contrast enhancement with Gadollium, which were the features observed in our case. Therefore the differentiation between the spinal ependymoma and an intraspinal PNET might be difficult.

Histologically, PNETs are undifferentiated small, round-celled tumors with hyperchromatic nuclei with neural differentiation features, which typically form Homer-Wright rosettes.[11,12] The amount and quality of rosette formation can vary substantially, and some tumors may only show abortive rosette formation. Strong immunoreactivities for MIC-2 and neuron specific enolase (NSE) are required in order to diagnose PNET.[13] In our case there was no definite Homer-Wright rosette but undifferentiated small round cells, with hyperchromatic nuclei were observed, with positive immunoreactivity for MIC-2, and neuron specific enolase (NSE). Histopathologically and immunopathologically, other small round cell tumors, lymphoma, small cell osteosarcoma and neuroblastoma were ruled out in our case.

These tumors tend to occur in young adults, with a male predominance (male:female-1.75:1) and average age of 29 years. Apart from our patient there were only 24 cases, with primary intraspinal PNET, reported in the literature. The levels of the involved spine were distributed as follows; lumbar 11cases (44%), thoracolumbar 6 (24%), thoracic 3 (12%), cervical 3 (12%), thoracic 3 (12%), lumbosacral 1 (4%), and sacral 1 (4%). The locations of the tumors were distributed as follows; cauda equina 8 cases(36%), intradural extramedullary 7 (31%), intramedullary 5 (22%), and extradural 2 (9%). The tumors seem to have a predilection for the cauda equina with 36% of the cases showing an origin from the cauda equina.[7,19] Tumor metastasis occurred in 11 cases (46%). The site of metastasis were distributed as follows; brain 2 cases (18%), leptomeninges 2 (18%), diffuse intraspinal 2 (18%), lung 2 (18%), bone, and lymph node 2 (18%), pleura 1 (9%). There were 6 cases (54%) and 5 cases (46%) cases of metastatsis that occurred within the central nervous system and distant metastasis, except in the central nervous system respectively.[14,15]

The symptoms and signs were back pain, radiating leg pain, lower extremity weakness, and urinary difficulty. In our case weakness in the legs, urinary difficulty, and lower back pain were the presenting symptoms.

The optimal treatment of a primary spinal PNET is unknown because of the rarity of the tumor. In the literature, almost all of the spinal PNET cases were treated with surgery and high dose radiotherapy of the tumor region, or the entire neuraxis, and sometimes with additional chemotherapy.[16] In our case, due to the diffuse tumor infiltration, fixation to spinal nerves and hypervascularity subtotal tumor resection were performed. Nearly all reported patients with primary intraspinal PNETs underwent radiation therapy as part of their primary treatment. However, the effect of radiation therapy on local control is unclear, as incidences are rare. With regard to the high propensity for intraspinal subarachnoidal spread in patients with primarily localized tumors, it would appear reasonable to indicate treatment of the whole neuroaxis. A dose of 5000 Gy has long been accepted as tolerable for the spinal cord.[17]

In the reported cases, summarized in Table 1, nine patients underwent chemotherapy as part of their initial therapy. Chemotherapy is now a standard therapeutic method in most protocols for children with infratentorial PNETs, either prior to, or following radiotherapy.[6] Chemotherapeutic regimens are the same as for infratentorial medul-

Table. 1. Summary of 25 Cases with Primary Intraspinal PNETs

No	age	sex	Level	location	Preop Sx, Sn	metastasis	Treatment	Survival (mo)	Reference
1	24	M	Lumbar	Cauda equina	NA	Lung	OP,RT	10	Smith et al.[5]
2	NA	NA	Cervical	Unknown	NA	None		<12?	Konsik et al.[14]
3	NA	NA	Cervical	Unknown	NA	None		<12?	Konsik et al.[14]
4	NA	NA	Thoraco-lumbar	Unknown	NA	Lung, Bone, Lymphnode		<12?	Konsik et al.[14]
5	24	M	Lumbar	Cauda equina		Leptomeningeal	OP,RT	18	Kepes et al.[12]
6	56	M	Lumbar	Cauda equina		None	OP,RT	Alive at 36	Kepes et al.[12]
7	39	M	Lumbar	Cauda equina		None	OP,RT	42	Kepes et al.[20]
8	26	M	Cervical	Intradural extramedullary	Dyspnea lethargy	Pleura, bone, lymph node	OP,RT	36	Sevick et al.[15]
9	26	F	Lumbosacral	Extradural	LBP urinary difficulty	None	OP, RT	Alive at 6	Liu et al.[18]
10	15	F	Thoraco-lumbar	Intramedullary Extramedullary	Paraparesis, Polyradiculitis	None	NA	18	Jaksche et al.[25]
11	26	M	Thoraco-lumbar	Cauda equina	Paraparesis Hydrocephalus	Brain	NA	36	Jaksche et al.[25]
12	7	M	Thoraco-lumbar	Intramedullary	Paraparesis Hydrocephalus, enuresis	None	Biopsy,CT,RT	20	Freyer et al.[5]
13	16	F	Lumbar	Intramedullary	LBP, spastic paraparesis	Brain	OP,CT,RT	29	Ogasawara et al.[1]
14	47	M	Lumbar	Cauda equina	LBP, LLP, urinary difficulty	None	Biopsy,CT,RT	16	McDermott et al.[11]
15	14	M	Lumbar	Cauda equina	LBP, LLP	None		Alive at 3	Hisaoka et al.[19]
16	14	F	Thoraco-lumbar	Intramedullary	Parapresis, LBP	None	OP	Alive at 15	Deme et al.[21]
17	23	F	Thoracic	Intradural extramedullary	LBP, bilateral foot weakness	None	OP,CT,RT	Alive at 12	Papadatos et al.[24]
18	32	M	Sacral	Intradural	RLP	Leptomeningeal	OP,RT,CT	29	Dorfmuller et al.[23]
19	17	M	Lumbar	Epidural	Paraparesis	None	OP,RT,CT	23	Dorfmuller et al.[23]
20	52	M	Lumbar	Cauda equine	Lt leg weakness, LBP	None	OP,RT	Alive at 12	Isotal et al.[22]
21	69	M	Thoracic	Intra-, extramedullary	Paraparesis, LLP	None	OP,RT	3	Christian et al.[7]
22	18	F	Lumbar	Intradural extramedullary	Paraparesis, LBP	None	OP,RT,CT	Alive at 25	Yavuz et al.[6]
23	49	F	Lumbar	Intradural extramedullary	LBP, RLP	Diffuse intraspinal	OP,RT,CT	23	Albrecht et al.[8]
24	29	F	Thoracic	Intramedullary	Rt leg weakness, paresthesia	Diffuse intraspinal	OP,RT,CT	17	Albrecht et al.[8]
25	17	M	Thoraco-lumbar	Intramedullary	Paraparesis, urinary difficulty	None	OP,RT	Alive at 4	Present case

NA, not available; Sx, symptom; Sn, sign; Op, operation; RT, radiotherapy; CT, chemotherapy; LBP, low back pain; RLP, right leg pain; LLP, left leg pain; Rt, right; Lt, left.

loblastomas. Multidrug chemotherapy was performed, such as vincristine, lomustine, cisplatin, and cyclophosphamide. The application of maintenance chemotherapy after radiotherapy seems to deliver better results. From the few patients with primary intraspinal PNETs described until now definite conclusions concerning chemotherapy cannot be drawn. Considering the poor prognosis, all efforts should be made to prevent local and distant tumor spread.[18,19]

Concerning the prognosis, of the 25 patients (including our patient) reported until now, 8 were reported to still be alive at the last follow up. However, the time of observation was often limited. The average survival time in the 17 patient listed in the Table 1 was 20 months, (ranging from 3- to 42 months). Despite multimodal treatment combining surgery, radiotherapy and chemotherapy, in most patients, the outcome was poor. The causes of death in these patients included metastatic disease, progressive spinal cord involvement and pneumonia.[20,21]

A primary intraspinal Primitive neuroectodermal tumor is rare and the prognosis is very poor. In our case, cyclic chemotherapy and a more prospective follow up time are needed, as the follow up period was short. An improvement in the treatment outcome may be achieved by intensification through multimodal treatment-surgery, radiotherapy, and chemotherapy.

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