Primary Spinal Primitive Neuroectodermal Tumor A Rare Case Report

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ABSTRACT
Primary spinal primitive neuroectodermal tumor (PSPNET) is an extremely rare lesion. As primitive neuroectodermal tumors, they are highly malignant with a poor prognosis. Very few cases of PSPNET have been reported in the English literature. Furthermore, histopathologic distinctions between central and peripheral primitive neuroectodermal tumors can be complex, but increasing awareness and the use of immunohistochemistry can aid in appropriate diagnosis and, hopefully, further improved management protocols. We report the clinical, radiological, pathological and management of 69 year female patient presenting with a PSPNET to our service, including a thorough review of literature.

Primitive neuroectodermal tumors (PNETs) are composed of small, round, blue-celled neoplasms with a poor prognosis and characteristic histological and molecular features. They are a group of highly malignant tumors of neuroectodermal origin that mainly exist in the central nervous system (CNS), chest wall, lower extremities, trunk, kidney, and orbit but rarely in the spine. Primary spinal primitive neuroectodermal tumors (PSPNET), is an extremely rare lesion, however, with the increasing awareness and use of immunohistochemistry, PSPNET is increasingly reported. Here, we present the clinical, radiological and pathological features of another rare case of a PSPNET in a 69 year old female patient, including her ongoing treatment options. We also perform a literature review of this rare entity.

CASE PRESENTATION
This is a 69 year old female patient with past medical history of lumbar radiculopathy and spondylolisthesis status post laminectomy, nerve root decompression, and posterior lumbar facet fusion at L4-5 and L5, S1 on the left. 14 months prior to presentation, she had improved initially, but approximately 6 months prior to this admission, patient had been managed by several other physicians due to lower back pain, lower extremity pain, left foot drop, urinary incontinence (for which an in-and-out foley catheter usage was ordered), and hemorrhagic cystitis. She was also practically bedridden four months before this last admission. This time, she presented with altered mental status, urinary and fecal incontinence, persistent lower back pain and bilateral lower extremity weakness. Important physical examination findings included confusion, decubitus sacral ulcers and decreased rectal sphincter tone. Power in proximal lower extremity group muscles was grade 4/5 bilaterally, 0/5 in distal left lower extremity, and 2-3/5 in distal right lower extremity. Figures 1 and 2 below illustrate the radiological findings.

The patient was prepared for surgery. Intraoperatively the first area that was approached was the mushroom formed by the tumor that had protruded through the lamina of S1 and S2. This was removed and sent to pathology. Decompressive laminectomies of L4, L5, S1 and S2 were performed. Additional pieces of the neoplasm were resected from the surrounding nerves. After the resection had been extended to the anterior part of the sacrum and having secured the hemostasis with difficulty, the dura was opened to visualize the nerve roots and the tumor itself to see the feasibility of resection. Upon opening the dura, it was noticed that there was no cerebrospinal fluid. The coalescence and the hemorrhagic arachnoiditis of the nerves were evident. There was thickening of the nerves in the middle of cauda equina and the nerves also were quite stuck together with inflammatory signs around the neoplasm. The surgeons felt it was impossible to separate the nerves. The choice was to do a duroplasty. Intraoperative diagnosis was that of an intradural spinal tumor with extradural extension. Histological findings are illustrated in fig. 3.

Hospital course was favorable and the patient was discharged for rehabilitation. Further management included radiotherapy and chemotherapy as per the multidisciplinary team involved in the case. Outpatient follow-up to 5 months after surgery was evaluated as stable. She however remained wheelchair bound due to lower extremity weakness.

Figure 1a. CT myelogram with sagittal and 1b. Coronal reconstructions, demonstrate an intraspinal soft tissue mass which extends from the lower lumbar spine (inferior L4 level) to the sacral and pre-sacral space through the left neural foramen, which appears enlarged.

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Figure 2 CT myelogram (axial) 2a. Normal appearance of the spinal canal, thecal sac and internal cauda equina. 2b, soft tissue mass producing complete obliteration of the spinal canal. 2c and 2d. Enlargement of the left S2 neural foramen and extension of the tumor to the presacral space.

Fig.3. a) Low power view of the tumor. Tumor cells show small nuclei with increase nuclear to cytoplasmic ratio. Some of the tumor cells show spindle nuclei. b) High power view of tumor to show mitotic figures and prominent nucleoli of some tumor cells. c) CD99 immunohistochemical stain shows a positive staining with membranous pattern

DISCUSSION
Stout first described PNETs in 1918, and these tumors were thought to arise directly from nerves. The pathologic and cytogenetic understanding of these tumors has significantly advanced. Hart and Earle in 1973 described PNETs as undifferentiated cerebral tumors. Reviewing this term, Rorke and Becker in 1983, defined PNETs as central nervous system tumors predominantly composed of primitive neuroepithelial cells. At the same time, they subclassified these tumors on the basis of their cellular differentiation. Following the WHO 2000 classification, PNETs have been considered embryonal tumors composed of undifferentiated neuroepithelial cells with a capacity of differentiation into different cell lines such as astrocytic, ependymal, melanotic and muscular. They have been considered to arise from a neoplastic transformation of primitive neuroepithelial cells, thereby making their presence possible in any part of the central nervous system. PNETs are relatively common, malignant CNS tumors in the pediatric age group that almost invariably arise intracranially. By the time they are discovered, they have often disseminated via subarachnoid spaces to involve other parts of the CNS, including the spinal cord. By contrast, the rare cases of PSPNET have been reported in a wide age group (3 months–69 years) with an adult predominance.

It must also be noted only 30 patients with the diagnosis of PSPNET have been reported in the literature reviewed. These include patients with peripheral PNET (pPNET); however, the histopathologic distinction between central and peripheral PNET has not commonly been made in these reported cases. pPNET is associated with a different spectrum of cytogenetic abnormalities (isochromosome 17q for example). pPNETs, on the other hand, are closely related to Ewing’s sarcoma (ES) and are part of the so-called Ewing’s family of tumors. Strong immunoreactivity for mi2 (CD99) and neuronal markers such as PGP 9.5, synaptophysin and neuron specific enolase strongly support the diagnosis of pPNET. This case was consistent with a pPNET.

The management of spinal cord PNET is a particularly challenging
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clinical issue. Complete excision is usually not possible, as the tumor infiltrates the spinal cord and/or nerve roots. This was evident in this case. In practice, it is also relevant to separate cPNET from pPNET regarding their differences in clinical evolution and medical treatment. Although both cPNET and pPNET are aggressive tumors, pPNET is known to metastasize and invade in tissues, while cPNET rarely metastasizes outside the CNS, but spreading along the CSF at diagnosis is present in 10–30% of cases. Survival rates for the ES/pPNET family to those for cPNET are quite similar (50–70% in localized disease) provided that treatment applied conforms with protocols based upon the results of successive multi-centre randomized clinical trials. In both cPNET and pPNET treatment management consists of a combination of local disease control by surgery, radiotherapy or a combination of both and multiagent chemotherapy based on the presence of high risk features in the patient. Crucial are the differences however in treatment protocol regarding the order of treatment sub-modalities and specific chemotherapeutic regimen and intensity. Furthermore, besides differences in radiation dose, in pPNET radiation therapy is used for local disease control only, as opposed to consistent entire neuraxis radiation in cPNET with predictable side effects regarding neurological development, which is particularly important in children. Spinal pPNETs have poor survival rates and there is no current consensus on the best treatment approach to these patients. Surgical tumor resection is the cornerstone of therapy. The role of adjuvant treatment modalities is not well defined, due the absence of prospective randomized trials for this extremely rare clinical entity.

CONCLUSION
It must be emphasized that most cases of PNET involving the spinal axis are secondary to subarachnoid seeding, which leads to leptomeningeal deposits (so-called drop metastasis from an intracranial primary tumor) along the nerve roots or pial surface of the spinal cord. A PSPNET, on the other hand, is a very rare lesion and thus reaching a final diagnosis entails excluding any other possible primary lesions in the rest of the body. In our case, imaging studies in the rest of the CNS failed to identify the presence of a primary lesion. Immunohistochemical staining is helpful in proper classification and to evaluate outcomes based on current treatment regimen.

REFERENCES

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