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Primary spinal primitive neuroectodermal tumor on MR imaging

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Abstract

Neoplasms in the region of filum terminale are not uncommon. Myxopapillary ependymoma is the commonest tumor at this location. The differentials reported for this entity are nerve sheath tumor, meningioma, paraganglioma, intradural metastases, lymphoma, other varieties of ependymoma, subependymoma, astrocytoma, ganglioglioma, hemangioblastoma, and primitive neuroectodermal tumor (PNET). PNET may very rarely present as an intradural thoracolumbar mass. We present pre- and post-therapy magnetic resonance imaging (MRI) features of a patient with proven primary spinal primitive neuroectodermal tumor (PSPNET) of peripheral subtype.

Key words: CD99; myxopapillary ependymoma; primary spinal primitive neuroectodermal tumor; primitive neuroectodermal tumor; spinal

Introduction

Primary spinal primitive neuroectodermal tumor (PSPNET) is diagnosed when one or more histopathologically proven primitive neuroectodermal tumor (PNET) lesions are present in the spinal axis, in the absence of a lesion in the brain, since most cases are secondary to subarachnoid seeding from primary cranial PNET. Therefore, concurrent brain imaging is a must (to rule out the possibility of metastasis from a primary PNET) before arriving at the diagnosis of PSPNET. Histopathological findings and immunohistochemical analysis of the spinal lesion are essential for confirmation of the diagnosis.[1-3]

PNET is used to describe cerebellar medulloblastoma and other neoplasms located at non-cerebellar sites in the central nervous system (CNS), sharing same histological features, including primary cerebral neuroblastoma, pineoblastoma,

ependymoblastoma, medulloepithelioma, and primary spinal PNET.[2,3]

Case Report

A 31-year-old female patient presented with a gradually progressive low backache and weakness of lower limbs for 4 weeks. Bowel and bladder functions were intact. There was no history of recent fever, cough, or vaccination. Focused neurological assessment revealed hyporeflexia with reduced muscle power and tone affecting bilateral lower limbs. Babinski sign was negative bilaterally. No focal tenderness was elicited in lumbar spinal vertebrae.

Magnetic resonance imaging (MRI) [Siemens, Magnetom Essenza, Erlangen, Germany] revealed an extramedullary intradural lesion in the region of filum terminale filling the lumbar spinal canal and replacing most of the normally visualized cerebrospinal fluid (CSF) signal intensity. The conus medullaris and cauda equina were not distinctly visualized possibly due to encasement. The lesion appeared sharply defined from the surrounding CSF and demonstrated an extensive longitudinal span (L2-L3 disc level to lower border of S1 vertebral body). The lesion appeared heterogeneously hyperintense on T2-weighted (T2W) fast spin echo (FSE) and short tau inversion recovery (STIR) images and isointense on T1-weighted (T1W) spin echo (SE) images (to normal lumbar spinal cord). No evidence of

intratumoral hemorrhage, syrinx formation, or calcification was noted [Figure 1A-C]. Few tiny, well-defined, randomly distributed foci were noted predominantly in the superior and inferior parts of the lesion which appeared isointense on T1W and hyperintense on T2W and STIR images (compared to rest of the lesion) indicating cystic changes [Figure 1A and C]. There was no spinal canal or neural foramina expansion, cortical bone erosion, or scalloping of the posterior margins of the vertebral bodies [Figure 1A-C].

On post-contrast T1 fat-saturated (FS) images, the entire lesion demonstrated significant contrast enhancement [Figure 2A and B]. There was no other enhancing focal soft tissue or bony lesion in the spinal axis [Figure 2C and D]. The lesion showed peripheral rim enhancement of previously noted cystic focus [Figure 2B]. On the basis of MRI imaging, a differential diagnosis of a typical filum terminale myxopapillary ependymoma (most likely) or nerve sheath tumor was suggested.

The patient underwent decompression laminectomy of lumbar vertebrae with gross excision of the lesion preserving the vital structures. Histopathological examination (HPE) using hematoxylin and eosin (H and E) stain (at original magnification, ×10 and original magnification, ×40) showed [Figure 3A and C] malignant round blue cells pointing to primitive neural ectodermal origin of the tumor. Immunohistochemical staining revealed diffuse positivity for vimentin [Figure 3D] which is a generalized soft tissue immunological marker found in a large variety of soft tissue tumors. The strong and diffuse immunoreactivity for CD99 [Figure 3B] confirmed the lesion as PNET of peripheral subtype.

Follow-up MRI imaging (8 months later) after initiation of chemotherapy showed an ill-defined lesion

appearing hyperintense on T2WI and hypointense on T1WI [Figure 4 A-C] with significant post-contrast enhancement at the site of primary lesion [Figures 4D and 5]. The perivertebral soft tissue in the lumbar region appeared edematous with absence of posterior segment of the lumbar vertebrae (postoperative) and previously visualized CSF signal intensity on the posterior aspect of the lesion [Figure 4 A-C]. Multiple small, well-defined, round-to-oval lesions were noted involving the intradural extramedullary space (suggested by absence of cord expansion and presence of focal expansion of the CSF signal referred to as CSF capping at the lesion-CSF interface on either side of the lesions) in the cervical [Figure 6A] and thoracic regions [Figure 6B, D and E] of the spinal canal. These lesions were hyperintense on T2WI and isointense on T1WI (to the spinal cord) and appeared to compress the cord at the thoracic level with resultant parenchymal cord signal intensity [Figure 6B]. On brain imaging, no focal lesion was noted on T2WI and T1WI. On post-contrast T1 FS images, all the lesions in the cervical and thoracic spinal canal showed intense homogenous enhancement [Figure 6C and f]. In view of primary pathological diagnosis of PNET, imaging findings indicated development of multiple intradural metastases in cervical and thoracic regions.

The second follow-up MRI study (12 months after the first scan) findings appeared similar to the previous scan with no significant interval changes at the site of primary lesion; however, the multiple intradural metastases in thoracic region appeared to progress with resultant marked compression of the cord at multiple levels [Figure 7 B-E]. This was in contrast to the metastatic lesion in the cervical region which appeared to regress (indistinct on plain images, but visualized on postcontrast images) [Figure 7 A and F]. Brain imaging revealed no focal enhancing lesion on postcontrast T1W FS images.

Figure 1 (A-C): MRI of lumbosacral spine - sagittal section STIR (A), T1 weighted image (B) and, T2 weighted (C) image (WI). 31 year-old female with PSPNET of filum terminale. Well defined lesion (thick white arrow) in the region of filum terminale in the spinal canal appearing hyperintense on T2-WI FSE and STIR images and isointense on T1-weighted SE images. No evident intratumoral hemorrhage, calcification [A, B, C] and few randomly distributed small cystic areas (thin white arrow in A and C).
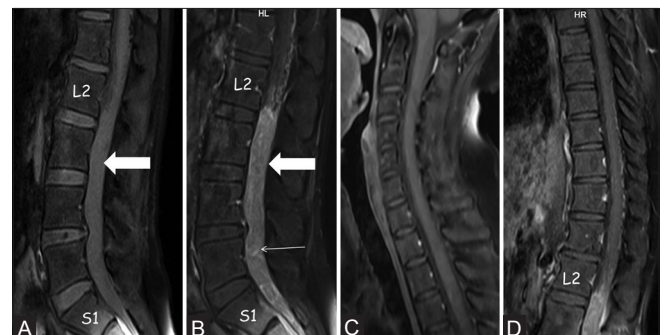

Figure 2 (A-D): Sagittal MRI of lumbosacral spine –pre contrast FS T1 (A), postcontrast FS T1 (B); postcontrast FS T1 cervical (C) and thoracolumbar region (D) images. 31 year-old female with PSPNET of filum terminale. The lesion demonstrates significant contrast enhancement (thick white arrow). No other focal enhancing lesion noted in the spinal axis. Peripheral rim enhancement of previously noted cystic focus in the lesion can be noted (thin white arrow in B), when compared to pre contrast T1 FS image (A)
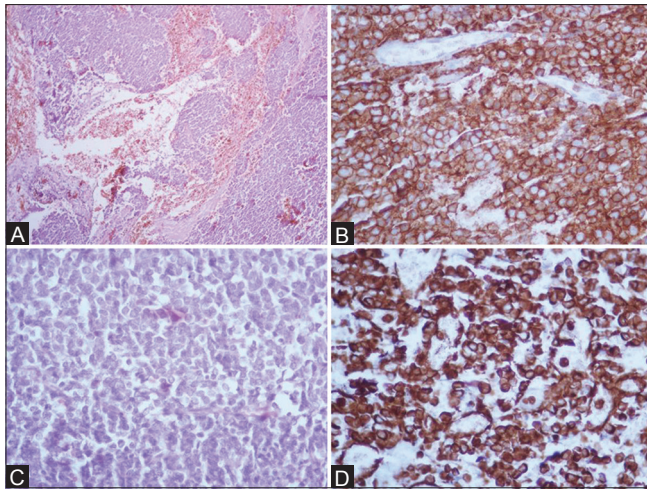
Figure 3 (A-D): Microscopic pathology (A and C) and Immunohistochemical staining (B and D). 31 year-old female with PSPNET of filum terminale. Histopathological examination using (H and E) stain (original magnification, ×10) and (original magnification, ×40) showed a sheet of uniform round cells suggesting a round cell tumor (A and C). Immunohistochemical staining revealed diffusely positive immunoreactivity for vimentin (D) and CD99 (B) markers
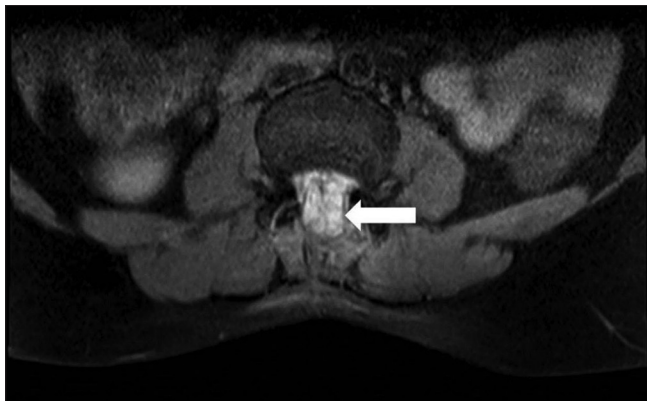

Figure 5: MRI of lumbosacral spine - Axial post contrast FS T1WI [post-operative status-8 months after first imaging]. 31 year-old female with PSPNET of filum terminale. Ill-defined intensely enhancing residual lesion noted at the site of primary lesion (thick white arrow)

On the most recent follow up visit, patient did not show significant clinical improvement.

Discussion

PSPNET is typically found in young adult males in the age group of 20-30 years. PSPNETs are aggressive lesions characterized by rapid growth, short duration of symptoms, inadequate or no response to chemoradiotherapy, and recurrence of the tumor in most patients. Presence of cranial symptoms in a known case of PSPNET indicates development of intracranial metastases.[4]

PNET histologically appears as predominantly undifferentiated small, blue, round cell tumor with hyperchromatic nuclei, scanty cytoplasm, and frequent
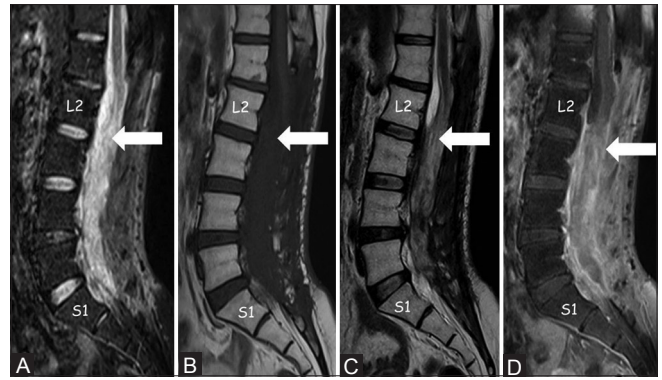

Figure 4 (A-D): MRI of lumbosacral spine - sagittal section STIR (A) T1 WI (B) T2 WI (C) and post contrast FS sagittal T1 WI (D) [post-operative status-8 months after first imaging]. 31-year-old female with PSPNET of filum terminale. Ill defined heterogenous lesion noted in lumbosacral spinal canal at the site of primary lesion [thick white arrow] (A, B, C). Postcontrast scan demonstrated significant enhancement of the spinal canal lesion (D) Perivertebral soft tissue in the lumbosacral region showed post operative changes

Figure 6 (A-F): MRI - sagittal T2 cervical (A) sagittal T2 thoracic (B) post contrast FS sagittal T1 thoracic (C) axial T2 (D and E) and post contrast FS sagittal T1 cervical (F) [post-operative status-8 months after first imaging]. 31-year-old female with PSPNET of filum terminale. Intensely enhancing multiple intradural metastases noted in the cervical (thick white arrow) and thoracic (thin white arrows) regions of the spinal canal compressing the cord at the thoracic level

mitotic figures. On immunohistochemistry, variable positivity may be noted depending on differentiation (neuronal, glial, or myogenic). The tumor usually presents with nonspecific symptoms like paraparesis, paresthesias, gait disturbance, and low back pain.[5,6]

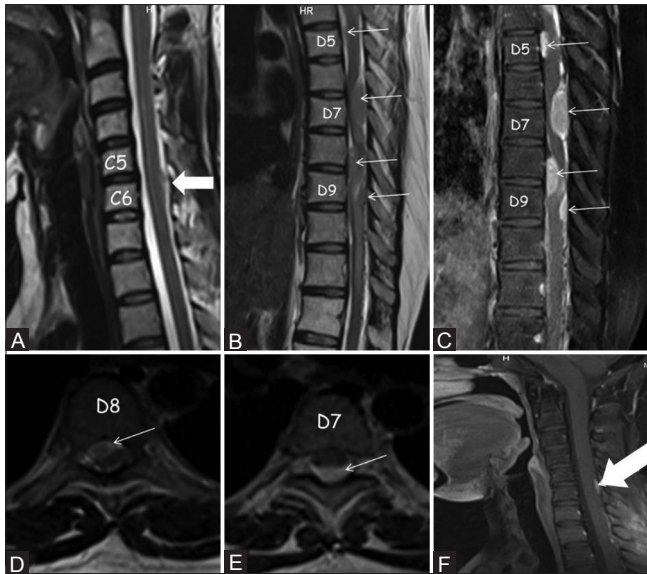PSPNET is a rare neoplasm with less than hundred confirmed cases in adults reported till date. The incidence

Figure 7 (A-F): Magnetic resonance imaging of cervico-thoracic spine - sagittal T2 cervical (A) sagittal T2 thoracic (B) post contrast FS sagittal T1 thoracic (C) axial T2 (D and E) and postcontrast FS sagittal T1 cervical (F) [Second follow up study-12 months after first imaging] 31 year-old female with PSPNET of filum terminale. Multiple intradural metastases in thoracic region (thin white arrow) appeared to progress (compared to Figure 6), in contrast to the regressing metastatic lesion in cervical region (thick white arrow)

in the pediatric age group appears to be even lower. PNETs are classified into central type (cPNET) and peripheral type (pPNET) based on their origin. cPNET frequently spreads via the CSF, but very rarely metastasizes outside CNS, and pPNET metastasizes to distant sites like bone, lung, lymph nodes, and liver. Immunohistochemistry can distinguish these subtypes and is recommended in all suspected cases. [7-9]

All PNETs are divided based on their embryological origin (not anatomical location) into those with CNS origin (cPNET) and those arising from outside the CNS (pPNET). This implies that lesions anatomically outside the CNS may be of CNS origin on immunohistochemical analysis and vice versa. Our case report is a demonstration of this principle since the lesion was intradural in location on imaging but was actually a peripheral subtype lesion.

Review of previous cases reported in literature suggests that PSPNET may arise from all levels of the spine and can be intramedullary, intradural-extramedullary (most common site being cauda equina), or extradural. Review of previous cases suggests intradural-extramedullary and intramedullary location to be almost equal in frequency.[10] The tumor is most frequently located at lower spinal levels, in lumbar and lumbosacral regions.[4,5,11]

MR imaging features of PSPNET are also usually nonspecific, with most of them being hyperintense on T2WI and iso- to-hypointense on T1WI, with heterogeneous

enhancement on postcontrast sequences. Intratumoral hemorrhage is highly uncommon. According to Duan *et al.*, although imaging findings are not specific, the diagnosis could be suggested when MR imaging depicts intradural, extramedullary, or extradural large, well-circumscribed mass which extends out from intervertebral foramen and invades paraspinal soft tissues or vertebral bones in a young patient.[12] However, their conclusion was based on a very small sample size. On positron emission tomography (PET) with 18F-fluoro-2-deoxy-glucose (FDG), it appears as a hypermetabolic focus. FDG/PET appears to be an effective imaging modality for the evaluation of suspected tumor recurrence.[11,13,14]

pPNET strongly expresses glycoprotein CD99, encoded by the microneme protein 2 (*MIC2*) gene and shows reciprocal translocation between chromosomes 11 and 22 showing the specific chimeric gene of *EWS–FLI1*. In contrast, all central PNETs are negative for *MIC2* and *EWS–FLI1*. This distinction is critical because of differences in specific chemotherapeutic regimen, radiation dose, and its extent.[15-17]

Myxopapillary ependymoma along with other less common ependymoma subtypes constitute 90% of primary tumors in the filum terminale region. The mean age at presentation is 28 years (average 15 years before intramedullary ependymomas). Myxopapillary ependymoma is histologically characterized by abundant fibrous connective tissue stroma showing mucinous degeneration. Cellular areas often display rosettes and pseudorosettes intermixed with papillary regions containing a vascular core.[18,19]

On imaging, myxopapillary ependymomas present as masses of the filum terminale, but may also incorporate the conus medullaris (in contrast to cervico-thoracic cord ependymomas which are intramedullary). These are slowly growing neoplasms that frequently become large (average tumor spans four vertebral levels). The MR imaging features are nonspecific with most being hyperintense on T2WI and hypo- to-isointense on T1WI (relative to the spinal cord). Hyperintense signal relative to the spinal cord on unenhanced T1WI may be due to proteinaceous mucoid matrix of myxopapillary ependymomas (distinguishing them from other ependymoma subtypes, which are always hypo- or isointense on T1WI). Lesions of mixed signal intensity are seen if intralesional cyst formation, tumor necrosis, or hemorrhage has occurred. Frequently, exophytic growth pattern may cause expansion of the spinal canal and neural foramina with scalloping of the posterior vertebral body margins and pedicles. Calcification is extremely unusual in spinal ependymoma (in contrast to ependymomas of the brain). Occasionally, myxopapillary ependymomas may show superficial siderosis caused by the deposition of hemosiderin on the cord surface due to repeated episodes of hemorrhage from the tumor, appearing as a rim of hypointensity on the surface of

the spinal cord, best seen on T2W gradient-echo MR images. Most ependymomas enhance intensely after administration of contrast material. Enhancement is usually homogeneous, but may be heterogeneous when hemorrhage or necrosis is present. Contrast-enhanced imaging is useful in differentiating the tumor from the spinal cord, defining intratumoral cysts, and identifying intradural metastases.[18-20]

The common differential reported for a myxopapillary ependymoma in the region of filum terminale includes intradural extramedullary neoplasms such as nerve sheath tumors (small lesions may be difficult to distinguish on imaging alone; large lesions show foraminal widening), meningiomas (uncommon site, uniformly isointense on T1WI and T2WI, no bone erosion), paraganglioma (well-encapsulated mass, isointense on T1WI and iso- to-hyperintense on T2WI, frequently heterogeneous signal intensity due to hemorrhagic areas, intense enhancement, serpentine enhancing structures adjacent to the mass in large lesions), intradural metastases, and lymphoma (uniform signal intensity and enhancement, nodularity of the nerve roots, aggressive bony lesions without bone remodeling). Other uncommon lesions include other ependymoma subtypes, subependymoma, astrocytoma, ganglioglioma, and hemangioblastoma. Rare conditions that may present as intradural thoracolumbar masses include primitive neuroectodermal tumor, lipoma, dermoid cyst, cholesteatoma, and neurenteric cyst.[18-20]

Conclusion

Primary spinal PNET is an extremely rare neoplasm. On imaging, it usually presents in the lumbosacral region as an aggressive lesion showing intralesional hemorrhage, spinal canal expansion, bone erosion, or scalloping of the vertebral body margins, however, absence of these features do not rule out the diagnosis. Also, PNET of spinal axis may demonstrate cystic changes on imaging mimicking commoner neoplasms at this location.

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