Primary intramedullary primitive neuroectodermal tumor of the cervical spinal cord

Case report

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Primary intramedullary primitive neuroectodermal tumors (PNETs) of the spinal cord are rare. Only six cases have previously been reported, all involving tumors in the thoracic or lumbar spine. The authors report the case of a 54-year-old woman who presented with quadriplegia and bladder and bowel dysfunction. The patient had suffered symptoms of neck pain for 1 month and left shoulder weakness for 10 days. Magnetic resonance imaging of the cervical spine revealed an intramedullary mass extending from C-2 to C-5 with an exophytic component in the adjacent left subarachnoid space. Multiple biopsy specimens were obtained, and a partial excision was performed. Histological examination revealed nodular growth and neuronal differentiation, with a striking resemblance to desmoplastic medulloblastoma. A positron emission tomography scan did not reveal uptake at any site. These findings confirmed the diagnosis of a primary intramedullary PNET. Postoperatively, the patient was given craniospinal radiotherapy with a radiation boost to the tumor bed.

KEY WORDS • intramedullary tumor • spinal cord neoplasm • primitive neuroectodermal tumor

PRIMITIVE neuroectodermal tumors of the CNS are malignant neoplasms with distinct histopathological and immunohistochemical characteristics. Typically, CNS PNETs occur in the brain and are seen primarily in pediatric patients, most often as infratentorial medulloblastomas, and less commonly as supratentorial PNETs. In contrast, PNETs of the spinal cord are rare and have been documented more frequently in adults than brain PNETs have been. To the best of our knowledge, only six cases of spinal cord intramedullary PNET have been reported in the literature to date and none of these involved a cervical tumor.1,4,6,10,14,16 We report a unique case of a primary intramedullary PNET of the cervical cord in an adult.

Case Report

History and Examination. This 54-year-old woman presented with quadriplegia, hypotonia in all limbs, and bladder and bowel dysfunction. She had a 1-month history of neck pain radiating to the left shoulder, which rapidly progressed to complete quadriplegia along with bladder and bowel dysfunction over a period of 10 days. Additionally, the patient was short of breath and was using her accessory muscles of respiration. She experienced sensation to the C-5 level.

Cervical MR imaging revealed an intramedullary mass that extended from the distal edge of C-2 to the distal edge of C-5. The cord was enlarged and an exophytic component of the mass extended left into the subarachnoid space. The tumor was iso- to hypointense on T1-weighted images and was heterogeneously hyperintense on T2-weighted images. The lesion enhanced on the administration of contrast agent (Fig. 1). The tumor did not seem to be separately demarcated, and no distinct planes were evident between the cord and the mass. Cord edema was visible on T2-weighted images on either side of the mass from the cervicothalamic level to the C-7 level. The images revealed no other cord lesion and no osseous or soft-tissue abnormality of the spine. Routine hematological investigations and a chest radiograph were nondiagnostic. A provisional diagnosis of astrocytoma/ependymoma was entertained and the patient was transferred to an operating room.

Procedure. With the patient in the seated position, a wide decompressive cervical laminectomy was performed.
from C-3 to C-5. The dura mater was opened in the midline. The cervical cord was found to be distinctly displaced to the right and posteriorly by a mass in the left anterior subarachnoid space. The arachnoid mater appeared normal and was opened. The cervical cord was observed to be enlarged from C-3 to C-5. A well-defined, yellowish, fleshy tumor was noted in the left anterior subarachnoid space. During the biopsy procedure, the tumor was found to be soft, easily suctioned, and moderately vascular. At C-3 and C-4 the left nerve roots were enmeshed in the mass. Because the left hemicord and nerve roots were infiltrated by the tumor, a partial excision was performed. Multiple biopsy specimens were obtained. After the excision, the spinal cord was lax and pulsating with a free egress of cerebrospinal fluid. A lax duraplasty was performed; the patient tolerated the surgery well.

Postoperative Course. Postoperatively, the patient’s limb strength improved to Grade 3 in her right limbs and left lower limb, and to Grade 2 in her left upper limb, according to the manual muscle test. Her breathing also improved, but her constipation and urinary retention persisted.

Pathological Examination. Histological examination of biopsy specimens revealed the tumor to be densely cellular, essentially consisting of small- to intermediate-sized cells with hyperchromatic, round-to-oval, mitotically active nuclei. The tumor cells were arranged in nodules of varying sizes with intervening sheets of cellular tumor tissue. The nodules had a relatively differentiated appearance; they were less cellular and had slightly larger, more uniform nuclei with relatively open chromatin, a more prominent fibrillary network with Homer–Wright rosettes,
and small neuropil islands. In contrast, the internodular tumor tissue was more densely cellular with overlapping, more hyperchromatic nuclei. This tissue contained less intercellular fibrillary matrix and fewer rosettes (Fig. 2A). A separate fragment containing many ganglion cells was also seen.

Immunohistochemical analysis showed the nodules to be rich in synaptophysin, particularly in the rosettes and neuropil islands, and poor in reticulin content. In contrast, the intermodal tumor tissue showed decreased synaptophysin and increased reticulin content (Fig. 2 B and C). The MIB-1 labeling index was more than 90% in hot spots of the intermodal tumor and between 10 and 20% within the nodules (Fig. 2D). Stains for thyroid transcription factor–1 and MIC2 were also negative. Additional immunostains for MYCC, MYCN, Trk-c, and β-catenin were negative (courtesy of Dr. Shirsat from the Advanced Centre for Treatment, Research, and Education in Cancer, Tata Memorial Centre, Navi Mumbai, India). The overall morphological characteristics and immunophenotype were those of a PNET with nodular growth and neuronal differentiation. The tumor had a striking resemblance to desmoplastic medulloblastoma.

Further Evaluation and Treatment. Because primary PNET of the spinal cord is a very rare disease and because of the patient’s age, after the histopathological diagnosis of spinal cord PNET was established, additional imaging studies were performed to rule out the possibility of the spinal cord lesion representing metastasis from a primary tumor elsewhere in the body or having itself metastasized. A whole-body FDG-PET–CT scan showed intensely increased uptake (standardized uptake value 9.7) in the spinal canal from C2–3 to C4–5. Corresponding plain CT images obtained using the same scanner showed an ill-defined residual soft-tissue mass in this region (Fig. 3). Postlaminectomy changes were also seen from C-3 to C-5. The remaining scans were otherwise unremarkable, ruling out any other focus of neoplastic disease. A brain MR image was also nondiagnostic (Fig. 4). The diagnosis of primary intramedullary PNET of the spinal cord was thus established.
The patient was given craniospinal radiotherapy with a radiation boost to the tumor bed. Since she received radiotherapy, the patient has remained neurologically stable with no further improvement. As we write this paper, adjuvant chemotherapy is being considered.

Discussion

Management of PNETs of the brain consists of surgical excision followed by craniospinal radiotherapy with a radiation boost to the primary tumor with or without chemotherapy. A PNET originating from the spinal cord, however, is a rare occurrence. We have been able to identify only 26 cases of intraspinal PNET in the literature.\(^{2,5,8,11–13,15,17,20–24}\) The tumors were classified as intramedullary, intradural–extramedullary, or epidural, with the majority arising from the cauda equina. Intradural–extramedullary and epidural PNETs can be considered peripheral tumors. Compared with brain PNETs, which occur primarily in pediatric patients, intraspinal PNETs tend to occur in an older age group. (The median age of patients in the reported cases is 28 years, and five of the patients were older than 45 years of age at diagnosis.)

Six cases of central primary PNET arising from the spinal cord have previously been reported. Four of these were exclusively intramedullary and two had an extramedullary component as well.\(^{1,4,10,14,16}\) In all six cases with intramedullary involvement, the tumors occurred in the thoracic or lumbar cord (Table 1). To the best of our knowledge, this present case represents the first well-documented cervical intramedullary PNET.

Central nervous system PNETs are believed to arise from malignant transformation of primitive neuroepithelial cells in subependymal zones.\(^{18}\) Subependymal zones of the spinal cord should also harbor these primitive cells, and why it is so rare for these cells to undergo malignant transformation is still an enigma.

Our patient was 54 years of age at diagnosis, and her case is only the second case of intramedullary PNET reported in the literature as having been diagnosed in a middle-aged or elderly patient. The patient described by Mawrin and colleagues\(^{14}\) was 69 years of age at diagnosis. The other reported cases of intramedullary PNETs involve children and young adults.

The imaging presentation of spinal cord PNET does not seem to be distinct from that of spinal cord astrocytoma or ependymoma, and the diagnosis is usually based on the histopathological findings. A diagnosis of spinal cord PNET should be established on histopathological exami-
Intramedullary PNET of the cervical spinal cord

TABLE 1
Six cases of primary intramedullary PNET

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Tumor Level</th>
<th>Tumor Location</th>
<th>Survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaksche, et al., 1988</td>
<td>1</td>
<td>15, F</td>
<td>thoracolumbar</td>
<td>intra- &amp; extramedullary</td>
<td>18</td>
</tr>
<tr>
<td>Freyer, et al., 1989</td>
<td>2</td>
<td>7, M</td>
<td>thoracolumbar</td>
<td>intramedullary</td>
<td>20</td>
</tr>
<tr>
<td>Ogasawara, et al., 1992</td>
<td>3</td>
<td>16, F</td>
<td>lumbar</td>
<td>intramedullary</td>
<td>29</td>
</tr>
<tr>
<td>Demel, et al., 1997</td>
<td>4</td>
<td>14, F</td>
<td>thoracolumbar</td>
<td>intramedullary</td>
<td>alive at 15</td>
</tr>
<tr>
<td>Mawrin, et al., 2002</td>
<td>5</td>
<td>69, M</td>
<td>thoracic</td>
<td>intra- &amp; extramedullary</td>
<td>3</td>
</tr>
<tr>
<td>Albrecht, et al., 2003</td>
<td>6</td>
<td>29, F</td>
<td>thoracic at 2 levels</td>
<td>intramedullary</td>
<td>17</td>
</tr>
</tbody>
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References
15. McDermott VG, el-Jabbour JN, Sellar RJ, Bell J: Primitive neu-

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