Giant cell ependymoma of the spinal cord

Case report and review of the literature

DAWY R. FOURNEY, M.D., F.R.C.S.(C), ABDOLREZA SIADATI, M.D., JANET M. BRUNER, M.D., ZIYA L. GOKASLAN, M.D., AND LAURENCE D. RHINES, M.D.

Division of Neurosurgery, Royal University Hospital, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland; and the Departments of Neurosurgery and Pathology (Neuropathology), The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Several rare histological variants of ependymoma have been described. The authors report on a patient in whom cervical spinal cord astrocytoma was originally diagnosed after evaluation of a limited biopsy specimen. More abundant tissue obtained during gross-total resection included areas of well-differentiated ependymoma. The histological features of the tumor were extremely unusual, with a major component of pleomorphic giant cells. Its histological, immunohistochemical, and electron microscopic features, however, were consistent with ependymoma. Only two cases of terminal filum and two of supratentorial giant cell variant of ependymoma have been reported. To the authors’ knowledge, this represents the first case of giant cell ependymoma of the spinal cord. The clinical significance is the potential for misdiagnosis with anaplastic (gemistocytic) astrocytoma, especially in cases in whom limited biopsy samples have been obtained.

KEY WORDS • giant cell ependymoma • intramedullary tumor • spinal cord

Ependymomas are slow-growing tumors of the cells that line the ventricular spaces of the central nervous system, including the central canal of the spinal cord. They are the most common neuroepithelial tumors of the spinal cord, accounting for 50 to 60% of spinal cord gliomas. In adults, ependymomas represent the most common intramedullary spinal tumors. Approximately two thirds of spinal cord ependymomas involve cervical levels.

Their morphological features and biological behavior may vary considerably. The World Health Organization classifies these tumors as ependymoma (with cellular, papillary, clear cell, and tanycytic variants), anaplastic and myxopapillary ependymoma, and subependymoma. In recent years, a rare variant composed mainly of pleomorphic giant cells has been reported, two cases involving the terminal filum, and two the cerebral hemispheres.

We report a case of this unusual histological type of ependymoma arising from the cervical spinal cord. To our knowledge, this represents the first report of a giant cell ependymoma arising from the spinal cord.

Case Report

History. This previously healthy 22-year-old man presented with a 2-year history of progressive bilateral upper-extremity weakness, predominantly on the left side, and clumsiness of gait. Magnetic resonance imaging revealed a large cervical spinal cord tumor. A multilevel laminectomy and biopsy procedure were performed at an outside institution. Complete closure of the dura mater was not possible because of expansive tumor; the postoperative course was complicated by cerebrospinal fluid leakage, wound dehiscence, and meningitis. The pathological diagnosis was reported as low-grade astrocytoma by two centers. Pathological examination of the small amount of tissue available showed anaplastic (gemistocytic) astrocytoma.

Presentation. Since undergoing biopsy four months earlier, the patient had reported progressive deterioration in ambulation and upper-limb strength.

Examination. The cervical wound was healed by secondary intention. Cranial nerve function was intact. Motor strength was reduced in both upper extremities (Grade 3–4/5), with particular weakness of the intrinsic muscles of the left hand. Deep tendon reflexes were reduced in the upper extremities; the lower extremities were hyperreflexic, with positive Babinski sign bilaterally and sustained clonus in the left ankle. Proprioception and light touch sensation were reduced in all four limbs. Gait was spastic, but the patient could walk unassisted.

A large multicystic and partially enhancing cervical
cord tumor, extending from the caudal medulla to C6–7, was demonstrated on MR imaging. A syringohydromyelic cavity was observed to extend from the lesion to T-3. Postoperative changes, including C1–7 laminectomies and a large posteriorly located pseudomeningocele, were also noted (Fig. 1).

**Operation.** The patient was positioned prone on bolsters with his head supported by three-pin fixation. After making a midline incision, a large pseudomeningocele cavity was observed. The occipital bone, the C1–7 lateral masses, and the T-1 posterior elements were identified. The tumor protruded through the dura in the midline in several areas. We extended the dural opening from C-1 to C-7, and careful microdissection allowed identification of the tumor and surrounding pia mater. The dura and the pial edges were retracted separately by using sutures.

A small biopsy sample of the tumor, obtained from the C-4 level, was interpreted as anaplastic astrocytoma, based on examination of the initial frozen sections. Using microsurgical techniques, however, a plane was eventually identified between the tumor and the spinal cord. The plane was more tenuously delimited in regions with postoperative scarring and cyst formation. A larger specimen was removed, sent for further frozen section analysis, and its histological profile was found to be more consistent with that of ependymoma. Encouraged by the possibility of a surgical cure, we continued to dissect along the somewhat challenging peritumoral plane and achieved a gross-total resection of the lesion (Fig. 2). Somatosensory evoked potential monitoring, performed throughout the procedure, did not demonstrate any change from that observed on preoperative studies.

A dural patch graft was required for watertight closure. The wound was closed in layers, mobilizing the paraspinal muscles to cover the midline defect. A lumbar drain was placed.

**Postoperative Course.** The patient was quadriplegic and required a tracheostomy and gastrostomy tube placement.
His inpatient course was complicated by cerebrospinal fluid leakage and meningitis. By 10 weeks postoperatively, he was ambulating with assistive devices but had little control of his left arm. At the time of manuscript preparation, 9 months postoperatively, he ambulated independently, his tracheostomy and gastrostomy wound had healed, and there was no radiographic evidence of tumor recurrence. He continues to improve with rehabilitation.

Pathological Examination. The surgical specimen consisted of a nodular mass of soft red-to-gray tissue fragments measuring up to 3 cm in greatest dimension. Frozen section analysis of the initial few small tissue fragments, stained with H & E, showed a moderately cellular glioma consisting of numerous gemistocytic cells, some with large, pleomorphic or multiple nuclei. No areas of pseudorosette formation were present. Frozen section analysis and subsequent examination of the more abundant material obtained from the gross-total resection, however, showed definite areas of well-differentiated ependymoma, with obvious perivascular pseudorosettes.

Fresh tissue was fixed in 4% glutaraldehyde for electron microscopic examination. The remainder of the specimens were fixed in 10% phosphate-buffered formalin and embedded in paraffin. Paraffin sections (6 μm) were stained with H & E.

Examination of the H & E–stained sections revealed a moderately cellular neoplasm populated by frequent pleomorphic giant cells with abundant eosinophilic cytoplasm (Fig. 3A). In some areas, the neoplastic cells were oriented around vascular lumina forming perivascular pseudorosettes (Fig. 3B). True ependymal rosettes were not identified using routine light microscopy. No areas of necrosis, excess mitotic activity, or other features of anaplasia (that is, high cellularity or microvascular proliferation) were identified. Several nodular areas of hyalinization were present within the tumor, suggesting a longstanding process.

Immunohistochemical staining for GFAP and the Ki-67 proliferation antigen (using monoclonal antibody MIB-1) were performed on 4-μm paraffin sections by using a standard avidin–biotin peroxidase complex. The primary antibodies were monoclonal (GFAP 1:150, NovoCastra [Newcastle upon Tyne, UK]; MIB-1 1:100, Dako Corp. [Carpinteria, CA]). Both staining procedures involved citrate buffer pretreatment for antigen retrieval. Diaminobenzidine was used as the chromogen. Appropriate positive and negative controls were included.

Immunohistochemical staining for GFAP was positive in the cytoplasm of all neoplastic cells (Fig. 3C). The MIB-1 antibody showed a low proliferation index, with less than 1% of the nuclei of the neoplastic cells staining positive.

Electron microscopic examination showed an epithelioid architecture with pleomorphic nuclei and abundant cytoplasmic intermediate filaments. Junctional complexes and multiple small lumina filled with slender microvilli were easily identified (Fig. 4). Occasional cilia were also present.

Discussion

Ependymomas are a histologically heterogeneous group of tumors. In addition to the well-recognized ependymoma subtypes (cellular, papillary, clear cell, and tanycytic), several exceptionally rare histopathological variants have been identified. These include ependymoma with extensive tumor cell vacuolation, ependymoma with lipomatous differentiation, signet ring (castration) cell ependymoma, and giant cell ependymoma (Table 1).

The microscopic, immunohistochemical, and ultrastructural features of the tumor in our case provide un-
equivocal evidence of ependymal origin, albeit with an unusual giant cell morphological profile. The light microscopic appearance, including the identification of perivascular pseudorosettes, is that of an ependymal neoplasm. The expression of GFAP in the tumor cells and the ultrastructural appearance of small lumina filled with microvilli in the presence of surrounding junctional complexes support a tumor of ependymal origin. Despite the pleomorphic nature of the giant cells, criteria for anaplastic (Grade III) ependymoma, as established by the World Health Organization, were not fulfilled. The tumor was only moderately cellular and had no significant mitotic activity or vascular endothelial proliferation.

This case is of clinical significance because it underscores the importance of obtaining a sufficient amount of tissue to establish an adequate pathological diagnosis, especially at the time of frozen section analysis when the decision to simply biopsy the tumor or attempt a complete resection is in question. Second, it shows how easily the giant cells of this rare ependymoma variant can be mistaken for gemistocytes (that is, anaplastic astrocytoma) in the absence of perivascular pseudorosette formation. The distinction obviously has clinical implications, because careful microdissection of ependymomas often distinguishes a cleavage plane that makes the tumor amenable to complete resection. The extent of tumor resection is the single-most important prognostic factor for disease-free survival in ependymomas.

The degree of pleomorphism of the neoplastic giant cells in the tumor we described suggests it might be anaplastic and have the potential for aggressive behavior. The presence of pleomorphic giant cells in other gliomas, however, such as subependymal giant cell astrocytoma or pleomorphic xanthoastrocytoma, is not linked to an adverse prognosis. Although the follow-up interval in the present case was short, no recurrence was reported in the two published cases of completely resected low-grade giant cell ependymomas of the terminal filum after 35 and 16 months, respectively. In the case of the anaplastic supratentorial lesion reported by Brown, et al., imaging studies revealed enhancement consistent with recurrence at the tumor resection site 8 months after gross-total resection and radiotherapy. The tumor in that report, however, in addition to having clear microscopic features of anaplasia, had an exceptionally high (50%) MIB-1 proliferation index. Thus, although the number of cases reported to date is limited, it appears that the presence of giant cells, in the absence of other features of anaplasia (high cellularity,
increased mitotic activity, or vascular endothelial proliferation), is without prognostic significance. The cellular pleomorphism of giant cell ependymoma has been attributed to degenerative changes. The areas of tumor hyalinization observed in our case tend to support this proposal. All giant cell ependymomas thus far described in the spinal cord or terminal filum have shown a well-differentiated histological appearance.

It is important to recognize the occurrence of this very rare (and sometimes difficult to diagnose) entity at the time of frozen section examination, in additional anatomical locations to those previously reported.

### References


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**TABLE 1**

Summary of cases of giant cell ependymoma reported in the literature

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs), Sex</th>
<th>Location of Lesion</th>
<th>Histopathology</th>
<th>Treatment</th>
<th>Outcome (mos postop)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zec, et al., 1996</td>
<td>14, M</td>
<td>terminal filum</td>
<td>low grade</td>
<td>gross-total resection</td>
<td>no recurrence (35)</td>
</tr>
<tr>
<td></td>
<td>14, M</td>
<td>terminal filum</td>
<td>low grade (myxo-papillary features)</td>
<td>gross-total resection</td>
<td>no recurrence (16)</td>
</tr>
<tr>
<td>Brown, et al., 1998</td>
<td>26, M</td>
<td>lt frontal &amp; corpus callosum, intraventricular extension</td>
<td>anaplastic</td>
<td>gross-total resection</td>
<td>probable recurrence (8)</td>
</tr>
<tr>
<td>Pimentel, et al., 2001</td>
<td>13, F</td>
<td>lt temporoparietal, extraventricular cervical spinal cord</td>
<td>anaplastic</td>
<td>gross-total resection, radiotherapy</td>
<td>no recurrence (24)</td>
</tr>
<tr>
<td>present case</td>
<td>23, M</td>
<td>cervical spinal cord</td>
<td>low grade</td>
<td>gross-total resection</td>
<td>no recurrence (9)</td>
</tr>
</tbody>
</table>

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