Central neurocytomas of the cervical spinal cord

Report of two cases

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Central neurocytoma is a neuronal neoplasm that occurs supratentorially in the lateral or third ventricles. The authors report the clinical, neuroradiological, and neuropathological features of two neurocytomas arising in the spinal cord of two men, aged 65 and 49 years. The patients presented with progressive neurological deficits referable to the cervical spinal cord. Magnetic resonance imaging revealed isodense intramedullary spinal cord tumors at the C3–4 level. Both tumors were initially misdiagnosed as gliomas. In Case 1 the correct diagnosis was made after electron microscopy revealed neuronal features. Immunostaining in Case 2 revealed that tumor cells were positive for synaptophysin and negative for glial fibrillary acidic protein, strongly indicating a neuronal tumor. It is suggested that this spinal cord neoplasm be included under the designation "central neurocytoma."

KEY WORDS • central neurocytoma • synaptophysin • spinal cord neoplasm • differential diagnosis

Central neurocytoma is a small cell neuronal tumor that occurs in the lateral or third ventricle. Neurocytoma generally presents in the second through seventh decade of life and follows a relatively benign clinical course, responding to resection with or without radiation therapy. Although neurocytomas were believed to be relatively rare, many cases have now been reported. Recent pathological studies have stressed the rather typical light microscopic features, the distinctly neuronal immunohistochemical profile, and the electron microscopic findings of neuronal differentiation. As a result, the possibility of central neurocytoma is now often raised in the differential diagnosis of an intraventricular tumor in an adult. To date, however, definite neurocytomas have not been documented below the tentorium. We report two cases of cervical spinal cord tumors that are pathologically identical to central neurocytoma on light microscopic, immunohistochemical, and ultrastructural examination.

Case Reports

Case 1

This 65-year-old man noted numbness and paresthesias in the left upper extremity. One year later he began experiencing paresthesias in the right hand, followed by the subacute onset of progressive left-hand weakness. A computerized tomography (CT) myelogram obtained elsewhere revealed an intrinsic spinal cord tumor at the C3–4 level.

Examination. The patient exhibited marked atrophy of the proximal left upper-extremity musculature and inability to abduct the left arm above the shoulder. He had greater strength distally with almost normal power in the intrinsic hand muscles, but decreased fine motor control and reduced ability to perform rapid alternating movements with the left hand. The left lower extremity showed minimal proximal weakness and there was mildly decreased proprioception of the left fingers and toes. Pinprick sensation was decreased in the left C-5 and C-6 dermatomes and slightly reduced in the right C-5 dermatome. Deep tendon reflexes were decreased only in the left biceps and triceps; plantar responses were equivocal. Magnetic resonance (MR) T<sub>1</sub>-weighted imaging revealed a homogeneously isodense tumor widening the cord from C-2 to C-6. There was no evidence of associated syrinx.

Operation. Laminectomy of C3–5 with midline dural opening were performed. A slight yellow discoloration was encountered on both sides of the midline at the superior margin of the visible spinal cord. A midline
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myelotomy was carried out and pathological tissue was identified approximately 4 mm beneath the dorsal surface of the cord. Biopsy led to a frozen-section diagnosis of glioma.

**Pathological Examination.** Light microscopy of the biopsy specimen revealed small, densely aggregated cells with round nuclei. There were several small Homer Wright rosettes scattered throughout the tumor, and several less well defined areas free of nuclei (Fig. 1). The background was finely fibrillar, appearing more similar to delicate neuropil than to the coarser glial fibrillary background of astrocytic and ependymal tumors. There were some areas with perinuclear halos that suggested a differential diagnosis of oligodendroglioma. There was no evidence of perivascular pseudorosettes, true rosettes, calcospherites, necrosis, or endothelial proliferation. The vasculature was delicate without complex branching. Rare, larger ganglion-like cells appeared cytologically normal; most likely these represented trapped spinal cord neurons since reactive astrocytes were noted in adjacent portions of the surrounding parenchyma.

Tissue was taken for ultrastructural analysis because of the small size of the biopsy and the equivocal diagnosis on frozen section. Electron microscopy revealed neuronal features: tumor nuclei were round to oval with smooth nuclear contours and the cytoplasm was drawn into long processes that formed the background neuropil of the tumor. These cell processes were filled with microtubules and many had scattered dense-core granules as well (Fig. 2). None of the processes had aggregates of intermediate filaments, lumen formation, or other ependymal features. Clusters of synaptic-type vesicles were not observed. The ultrastructural findings provided the diagnosis of central neurocytoma.

**Postoperative Course.** The patient was treated with 43.2 Gy of 10-MV irradiation, given in 24 fractions over a 34-day period. His neurological condition remained stable and he experienced a slight increase in left arm strength over the year following irradiation. At 71 years of age he experienced a gradual progressive dementia consistent with Alzheimer's disease. A ventricular shunt was placed at another institution and, despite adequate shunt function, his cognitive function continued to decline. A CT scan was normal except for cortical atrophy. His extremity strength and sensation were slightly improved from the pretreatment level and remained stable 10 years after presentation (9 years after irradiation). This case has been described briefly in a previous report.13

**Case 2**

This 49-year-old man with thalassemia minor noted paresthesias in his left hand for 6 months before presentation. Plain roentgenograms and an electromyelogram were normal. An MR image of the cervical spine, obtained at another institution, demonstrated an enhancing intramedullary spinal cord mass at the level of the C-4 vertebral body. The paresthesias progressed, subsequently involving the finger tips.

**Examination.** The initial neurological examination revealed bilateral weakness in the intrinsic muscles of the hand, with sensations of warmth in the radial aspect of the right foramen and of tingling in the tips of all fingers bilaterally. There was no corresponding deficit in temperature, light touch, or pinprick sensation. The deep tendon reflexes were at the upper limit of normal in the left biceps, triceps, and brachioradialis muscles;
the right-sided and lower-extremity reflexes were normal. There were no other long-tract or focal deficits.

On T₁-weighted MR imaging, an isodense lesion was seen in the midline centered at the C3–4 level. The tumor extended from the anterior to the posterior aspects of the cord in two lobules, divided by the median septum. The lesion was isointense on T₁-weighted imaging (first and second echo).

First Operation. Seven months after the onset of symptoms, laminectomies of C2–5 were performed. A tumor was visible as a bulge beneath the dura, which was opened in the midline. The cord was markedly widened at the C3–4 level, with increased surface vascularity due to abnormal vessels but no arterialized veins. A midline myelotomy was performed and deepened to 1 mm, at which point a highly vascular tumor was encountered with its superior margin appearing to infiltrate the spinal cord. The inferior portion of the tumor was resected. Hemostasis was achieved with bipolar electrocautery, and the dura was closed with a patch. The pathological diagnosis was probable ependymoma, although an astrocytoma could not be excluded. Hemosiderin and gliosis were noted. The diagnosis of neurocytoma was not entertained and therefore no special studies were pursued.

First Postoperative Course. The patient had no new neurological deficits postoperatively. He received 50.7 Gy of 10-mV irradiation (minimum tumor dose) in 27 fractions over a 37-day period. He remained stable for 2 years, then began to notice the onset of right arm weakness followed by slight left arm weakness and increased paresthesias in both upper extremities. An MR image revealed only slight enlargement of the residual tumor in comparison with the MR imaging appearance 6 months previously. Gadolinium diethylenetriamine penta-acetic acid enhancement was homogeneous and intense (Fig. 3). Six months later the patient developed lower-extremity weakness, most marked in the proximal right muscles. He had decreased sensation to pinprick, vibration, and proprioception on the left side below C-5 and in the right upper extremity. Left upper-extremity hyperreflexia was observed and his toe reflexes remained downgoing. His symptoms were not responsive to increasing doses of glucocorticoids.

Magnetic resonance imaging revealed an increase in the tumor size (Fig. 4). Angiography, performed because sagittal and axial MR images showed hypointense regions consistent with either flow-void areas or hemosiderin, showed faint tumor blush but no other abnormalities. The tumor was fed predominantly by the left vertebral artery via a descending left lateral spinal artery. A single small early-filling vein draining infracranially was identified posteriorly near the dura. This study supported the hypothesis of hemorrhage as the source of the MR imaging hypointense areas. No feeding vessels appropriate for endovascular embolization were identified.
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Second Operation. The dura was opened in the midline. Tumor was visible in the midline separating the posterior columns laterally. It was tethered by the posterior median septum but extruded on either side. A plane was developed between the tumor and spinal cord, although cord invasion by the tumor was somewhat more extensive rostrally and laterally to the left. A cyst containing yellow fluid was encountered rostrally, which aided in development of the ventral plane. The tumor was highly vascular with its arterial supply arising from the posterior spinal arteries, anterior spinal artery, and many arterial branches that projected directly through the lateral funiculus to the tumor, some from the lateral spinal arteries. The tumor extended ventrally and bilaterally around the median septum. There was an arterialized vein on the dorsal surface of the left tumor mass, which drained intracranially. A gross total resection was achieved. The excised tumor was light brown to dark red and friable.

Pathological Examination. The light microscopic appearance of both tumor specimens was similar to that in Case 1 (Fig. 5 left); however, a single mitotic figure and regions of hemosiderin deposition were also noted. Immunohistochemical examination revealed strong staining for synaptophysin and neuron-specific enolase. Synaptophysin staining showed a typical granular positivity of the delicate cell processes (Fig. 5 right), strongest in the center of the rosette-like structures. None of the entrapped neurons showed synaptophysin immunoreactivity. The cells were not positive on glial fibrillary acidic protein staining except for occasional trapped astrocytes at the periphery of the lesion.

Second Postoperative Course. The patient awoke from general anesthesia with a marked increase in weakness in the right upper and lower extremities, decreased sensation in the right upper extremity, and decreased joint position sense in the right lower extremity. Postoperatively, he has recovered some ability to move these limbs, but without gaining functionally significant strength. His left-sided strength has continued to improve in the 5 years that have elapsed since the onset of his initial symptoms.

Discussion

Classification

Central neurocytoma is a benign neuronal tumor that occurs in the supratentorial ventricular system. This tumor must be distinguished pathologically from histologically similar gliomas, such as oligodendroglioma and ependymoma, and from other central nervous system small cell neuronal tumors such as neuroblastoma. This latter distinction is usually straightforward because neuroblastomas appear histologically malignant, with anaplastic cells, mitoses, and necrosis. Yaşargil et al., however, described in adults two ventricular neurocytomas with mitotic figures, necrosis, and vascular proliferation. While such cases might represent transitional entities, clinical data have not been reported to confirm the histological impression of malignancy. In addition, we have previously documented two ventricular neurocytomas with necrosis that did not have a worse outcome. Thus, the significance of mitoses and necrosis in neurocytomas remains unclear. The tumors presented here had light microscopic features of neurocytoma and either immunohistochemical or ultrastructural proof of neuronal differentiation. Although the specimen from Case 2 exhibited a single mitotic figure, the tumors had no other anaplastic fea-
Differential cord histological ependymoma arising tomas periventricular ganglion cells, predominantly associated with dysplastic changes in the adjacent cortex, suggesting a hamartomatous lesion. Many of these patients were infants or children, with long-standing seizure disorders. These rather distinctive features are similar to those in lesions previously reported as dyssembryoplastic neuroepithelial tumors; because of the distinctive clinical, radiological, and pathological features, it seems prudent to separate dyssembryoplastic neuroepithelial tumors from typical ependymoma.

Ellison, et al. recently described a cerebellar tumor composed predominantly of cells immunochemically and histologically distinguishable from neurocytoma. An unusual feature of their tumor was that it contained small groups of lipocytes. Miller, et al. briefly mentioned three possible cases of spinal neurocytoma that occurred in infants or children. It is likely that these cases and ours represent examples of neurocytomas arising outside the supratentorial ventricular system. Since it has been proposed that supratentorial central neurocytomas arise from neuronal precursors in the periventricular germinal matrix, spinal neurocytomas may be derived from neuronal precursor cells that surround the central canal in fetal life.

Differential Diagnosis

The differential diagnosis of intramedullary spinal cord tumors primarily includes gliomas such as ependymoma, astrocytoma, oligodendroglioma, and mixed glioma, hemangioblastoma, and rarely metastasis. Central neurocytoma has clinical and pathological similarities to many of these tumor types and thus has probably been overlooked in the past. Gadolinium-enhanced axial MR images suggest a low-grade tumor arising near the central canal. The presence of two midline tumor lobules divided by the median septum may distinguish our Case 2 from the usual appearance of ependymoma or other spinal cord gliomas. It has been reported that hypointense areas in and around a tumor on T1- and T2-weighted MR images correlate with a histological diagnosis of ependymoma, but our Case 2 demonstrates that a diagnosis of neurocytoma must be considered in such cases. A range of intravenous contrast enhancement intensities from moderate to marked is observed among supratentorial neurocytomas, and might be expected among spinal neurocytomas. In our Case 2, the MR images enhanced densely and homogeneously before spontaneous hemorrhage occurred into the tumor.

When examined pathologically, the spinal cord neurocytomas were initially mistaken for mixed glioma in Case 1 and for ependymoma in Case 2. A number of histological features should alert the pathologist to the correct diagnosis. The tumors have a characteristic fine fibrillary background that more closely resembles neuronal neuropil than the gliad fibrillarity of astrocytomas or ependymomas. This fine fibrillarity is most clearly seen in the areas free of nuclei or in the center of Homer Wright rosettes. The nuclei are round, more like those of oligodendrogliomas than the angular nuclei of ependymomas. However, the chromatin pattern is more delicate than in either oligodendrogliomas or ependymomas. Perinuclear halos may be present and account for the sometimes striking similarity to oligodendroglioma. In the neurocytomas, delicate vasculature is not as branched as in classic oligodendrogliomas, and distinct perivascular pseudorosettes are not seen.

Natural History and Treatment

It is not possible to generalize from our two cases about the natural history of spinal neurocytoma. The tumors likely consist of relatively mature cells and, like their supratentorial counterparts, will follow a relatively benign course. It is of interest that the disease in Case 2 progressed more rapidly than in Case 1. This coincided with the presence of a single mitotic figure and hemosiderin deposition, features absent in Case 1. The rapid increase in size of the tumor in the second patient and the bilirubin-stained cyst cavity detected at his second operation are most consistent with hemorrhage into the tumor, causing enlargement and clinical deterioration. Only a single case of supratentorial neurocytoma has been reported in which hemorrhage was a prominent feature.

Like their supratentorial counterparts, both tumors reported here proved at surgery to be vascular; however, angiography did not reveal feeding vessels accessible for embolization. Furthermore, our experience with gross total resection proves that great care must be taken at surgery to avoid compromising vessels of passage feeding the remainder of the spinal cord.

Both of our patients were treated with radiation therapy. It is uncertain what effect, if any, this may have had on the natural history of these lesions. It has been recommended that radiation therapy be reserved for progressive, recurrent, or anaplastic variants in supratentorial neurocytoma. We advocate a similar approach in cases of spinal central neurocytoma until more data are available.

References

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