CENTRAL neurocytoma is a rare tumor of the central nervous system (CNS). It was first reported by Hassoun and colleagues,9 who examined an intraventricular neoplasm that, on light microscopy, shared features with an oligodendroglioma but on electron microscopy was found to be composed of neuronal elements. This neoplasm is most often encountered in a lateral ventricle, near the foramen of Monro, but it may also be found in the third ventricle,7 in extraventricular locations of the cerebrum,8,13 in the cerebellum,5 and in the spinal cord.4,12,13,20 It represents about 0.1 to 0.25% of all neural tumors. This neoplasm occurs most commonly in adults, aged 30 to 50 years, with no significant difference in incidence rates between men and women.2 The tumor contains cells with features of neuronal differentiation, as demonstrated by Hassoun, et al., who found neuritic processes of the tumor cells with occasional synaptic structures and neurosecretory granules.

Case Report

Presentation. This 46-year-old Caucasian woman presented with a 2-month history of progressive left lower-extremity weakness and pain and decreased ability to walk, as well as complaints of incomplete voiding. A magnetic resonance image revealed a 7-mm oval mass that was located intrathecally and extended from T-12 to L-1 and was adjacent to a nerve root. No lesions were identified at higher vertebral levels. The mass was excised. On histological examination it was found to have classical features of a neurocytoma. To the best of the authors’ knowledge, this is the first report of a neurocytoma occurring in that region. A detailed histological description of this case and review of the pertinent literature are provided.

Examination. A magnetic resonance (MR) image of the lumbar spine revealed a 7-mm intradural mass at the T12–L1 level, which was slightly hypodense relative to the adjacent nerve roots within the thecal sac; it measured approximately $2 \times 1.5 \times 0.4$ cm (Fig. 1). The differential diagnosis included schwannoma and neurofibroma. The possibility that the mass represented metastatic disease or seeding from another neoplasm higher in the CNS was considered unlikely because evaluation of the MR images obtained in higher regions of the spinal cord and in the brain itself showed normal findings with no additional masses identified.

Operation. The patient underwent laminectomy at the radiographically confirmed L1–2 level. After the ultrasonography provided confirmation of the abnormal tissue in the intradural compartment, a linear incision was made in the dura. An oval mass densely adherent to a single nerve root was identified and dissected free of the arachnoid and the nerve root. The tumor was well circumscribed and was composed of pink-white-gray tissue. A biopsy sample was obtained and submitted for frozen-section examination; the results were suggestive of a benign schwannoma. The residual tumor was dissected free without sacrificing the nerve root.

Pathological Examination. The tissue sample obtained
at surgery was fixed in 10% aqueous formaldehyde and embedded in paraffin for routine histopathological processing and immunohistochemical study. Histological sections of 10 μm in thickness were prepared and stained with hematoxylin and eosin and with Wilder’s reticulin stain. Immunohistochemical staining was performed by using primary antisera against synaptophysin (BioGenex, San Ramone, CA), chromogranin (Boehringer Mannheim, Indianapolis, IN), glial fibrillary acidic protein (GFAP), S-100 protein, epithelial membrane antigen, and neuron-specific enolase (gamma enolase) (Dako, Carpinteria, CA). For proliferative index analysis of tumor cell nuclei, sections were stained for MIB-1 antigen (Immunotech, Westbrook, ME).

Microscopic Findings. Examination of the surgical specimen showed no normal tissue; rather, only a moderately cellular neoplasm was revealed, its cells round to elongated against a finely fibrillar background. The tumor cells formed loosely packed clusters in some areas (Fig. 2 upper left) and parallel rows in others (Fig. 2 upper right), and in additional areas the cells surrounded thin-walled blood vessels with a fibrillary network seen between the tumor cells and the adventitia of the blood vessels. The latter arrangement was somewhat similar to that seen in ependymomas; however, as indicated by the results of special stains, this similarity was only superficial. The nuclei of many tumor cells had a finely stippled salt-and-pepper distribution of chromatin. (Fig. 2 center left). Occasional cells had large, irregular hyperchromatic nuclei. Mitotic figures were not conspicuous, and there were no areas of necrosis present. The tumor differed from the most common neoplasm that involves the spinal nerve roots, neurilemmomas (schwannomas), in two important aspects. First, schwannomas, as a rule, are very rich in reticulin fibers that represent the basal laminae of neoplastic Schwann cells. In our tumor, reticulin fibrils were entirely restricted to the walls of blood vessels. The tumor cells and their immediate surroundings showed no stainable reticulin whatsoever (Fig. 2 center right). Second, the tumor was entirely negative for S-100 protein, a substance richly present in normal Schwann cells as well as their neoplastic equivalents. As to other immunostains, GFAP was not expressed by any of the tumor cells, and the fibrillary areas between tumor cells and vessel walls were also free of GFAP (the latter areas usually contain GFAP in the perivascular tumor cell processes of ependymomas). On synaptophysin staining, granular cytoplasmic positivity could be observed next to cell nuclei in a number of tumor cells (Fig. 2 lower left). The cell outlines, including their cytoplasmic processes, were keenly brought into focus when performing neuron-specific enolase (gamma enolase) staining. This helped more by highlighting the axon-like long cytoplasmic processes that extended from one pole of tumor cells (Fig. 2 lower right) than by simply staining the cytoplasm of the cells, because gamma enolase does not possess high specificity. The immunostaining procedure for chromogranin was entirely negative in the tumor, which strongly indicated that the lesion was not a paraganglioma. In addition, the tumor formed no closely packed cell clusters (“Zellballen”) surrounded by reticulin fibers nor did it contain “sustentacular cells” of a paraganglioma, which are usually positive on S-100 immunostaining. The histological appearance of the tumor did not suggest a meningioma, and an epithelial membrane antigen immunostaining test was entirely negative throughout.

The morphology of the individual tumor cells and of their nuclei—their arrangement in clusters, single-cell rows, and perivascular pseudorosette-like formations; their negativity on reticulin, S-100, and GFAP stains; their focally positive cytoplasmic stain for synaptophysin; and their axonlike processes that were highlighted with neuron-specific enolase stain—were all consistent with the microscopic structure of a central neurocytoma. On MIB-1 staining (paraffin-section method for Ki-67 immunostain for proliferative-phase nuclei) only 1.2% of the nuclei were shown to stain positively, thus indicating a low rate of proliferative activity. As mentioned earlier, because MR images of the upper spinal cord and of the brain revealed no evidence of an intracranial or a higher vertebral level spinal tumor that could have spread to a lumbar nerve root through seeding via the cerebrospinal fluid, we were led to conclude that the tumor in this instance truly represented a central neurocytoma that developed as a primary neoplasm of a nerve root in the cauda equina.

Discussion
Our case is unusual in that it is, to the best of our knowledge, the first reported neurocytoma involving the cauda equina. On histological analysis the surgically removed mass was found to represent a moderately cellular neoplasm, the cells of which were of a neurocytic character embedded in a fibrillary background, a distinctive feature of neurocytoma. Louis, et al., and others have noted distinguishing characteristics of neurocytomas. The nuclei of tumor cells in such neoplasms are varied and euchromatic, and there is an extensive and delicate fibrillary background present, together with

FIG. 2. Photomicrographs of the tumor.  Upper Left: A portion of the tumor shows scattered small round cells with their cytoplasm blending into an eosinophilic fibrillary background and larger islands of the latter (right-hand lower corner) resembling neuropil. H & E, original magnification × 120.  Upper Right: In this area, the tumor cell nuclei form parallel rows, separated by a fibrillary background. H & E, original magnification × 130.  Center Left: In many tumor cell nuclei the chromatin substance is arranged in a speckled “salt-and-pepper” pattern. Hematoxylin with little eosin added, original magnification × 200.  Center Right: The tumor was free of reticulin fibrils; only the basement membranes of blood vessels (center of image) stained for reticulin. Wilder’s stain for reticulin, original magnification × 130.  Lower Left: The cytoplasm of some tumor cells stained positively for synaptophysin. Immunoperoxidase stain for synaptophysin, original magnification × 140.  Lower right: Long tapering cytoplasmic processes of some tumor cells resembled formation of dendrites and axons. Immunoperoxidase stain for gamma enolase (“neuron-specific enolase”), original magnification × 150.
anuclear zones, as were also found in our case. Ng and colleagues have noted the challenge in differentiating these tumors from CNS neoplasms such as oligodendrogliomas, noting that 54% of the latter may be synaptophysin positive. However, Pearl, et al., have stressed the importance of differentiating central neurocytomas from the more primitive and much more aggressive cerebral neuroblastosomas.

Intraventricular tumors derived from a neuronal lineage and presenting with the histological profile found in our case also appear to have a spectrum of differentiation. In some cases, a number of tumor cells may differentiate into gangliocytes whereas Yaşargil, et al., have observed in two of their eight cases of neurocytomas that the tumors became dedifferentiated and malignant.

Cerda-Nicolas, and colleagues have reported cytogenetic studies on neurocytoma tumor cells that indicated loss of chromosome 17. The tumor suppressor gene p53 is located on chromosome 17, which may possibly account for the unchecked tumor growth. It is possible that the actual number of central neurocytomas has been historically underreported, given the tendency for histological misdiagnosis; many of the tumors could have been termed either oligodendrogliomas or ependymomas of the foramen of Monro.

Our case is unusual in that it is the first reported neurocytoma to involve the cauda equina. Although the radiological, histological, and surgical findings of our patient’s tumor are consistent with those of a neurocytoma, the question remains as to the origin of such tumor (typically a neoplasm of the CNS) arising from the cauda equina, the nerve roots of which belong to the peripheral nervous system. One possibility is that the tumor may have developed from the central stump of a nerve root, which still represents central nervous tissue, or possibly from an ectopic island of central nervous tissue in a more peripheral segment of a nerve root. Indeed, cases of gliomas that arise within cranial nerves are on record, such as a glioma of the acoustic nerve and a glioblastoma of the oculomotor nerve. Furthermore, the cauda equina fibers are in close contact with the leptomeninges, and the latter on occasion may be the sites of primary extramedullary CNS tumors. Whereas most of such neoplasms were found to be gliomas, ectopic central nervous tissue could also harbor some residual progenitor cells of the neural series.

Treatment and Prognosis

Söylemezoglu, et al. in a review of 36 central neurocytomas in which they compared MIB-1 proliferative indices and the clinical behavior of their patients, found that tumors with a proliferative index above 2% were associated with much more aggressive behavior than those having less than 2% proliferative-phase nuclei (based on MIB-1 stain analysis). In general, the prognosis of patients who undergo resection of central neurocytomas is good; however, in some cases local recurrences after surgery have been reported. In addition, in some patients craniospinal dissemination of this tumor has also been observed. Surgical resection may be followed by radiation therapy, but long-term follow-up review of patients who did not undergo radiotherapy has also revealed no tumor recurrence.

One year post surgery our patient is doing well. Repeated MR imaging of the thoracolumbar spine has shown no evidence of tumor recurrence.

Conclusions

Our case is unusual in that it represents, to the best of our knowledge, the first report of a neurocytoma involving the cauda equina. The neuroimaging-documented absence of cerebral or spinal cord masses suggested that this tumor was a primary lesion in its location rather than a “drop metastasis.” This tumor was histologically benign and was completely excised. This allowed us to be optimistic regarding our patient’s complete recovery. We concluded that this neoplasm, which, as a rule, develops in central rather than peripheral nervous tissue, originated from the central stump of a cauda equina nerve root or possibly from an island of distally displaced central nervous tissue within the peripheral portion of the nerve root.

Acknowledgments

The authors wish to thank Ms. Julie Collins, H.T. for performing the immunohistological tests and Mrs. LaShon Forté for the careful typing of the manuscript.

References

Neurocytoma of the cauda equina


Manuscript received July 20, 1998. Accepted in final form December 4, 1998.
Address reprint requests to: Christina L. Stephan, Post-Sophomore Fellow, Department of Pathology and Laboratory Medicine, University of Kansas School of Medicine, 3901 Rainbow Boulevard, Kansas City, Kansas 66160-7410.