Gliofibroma

Case report

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The case history of an infant with a large gliofibroma is presented. Gliofibromas are rare mixed glial-mesenchymal tumors that have been poorly characterized. The computerized tomography appearance and a detailed light and electron microscopic description are presented, along with immunoperoxidase studies of this tumor. This case is compared with gliofibromas described elsewhere in the literature.

Key Words • gliofibroma • gliosarcoma • intraventricular tumor

Benign tumors with features of glial and mesenchymal differentiation are rarely found in the central nervous system, which may be related to the relatively small number of mesenchymal cells in the nervous system. Alternatively, these neoplasms may not be widely recognized as nosological entities because they are morphologically similar to the more common low-grade glial neoplasms and, therefore, are underreported. The benign glial-mesenchymal tumors that have been identified include gliofibromas, benign mixed glial-mesenchymal tumors, intracerebral fibromas, and sclerosing astrocytomas. In contrast, malignant tumors comprising glial and mesenchymal elements, such as gliosarcomas and sarcogliomas, are much more widely recognized and may provide a paradigm for understanding their more benign counterparts.

We have recently encountered a case with a striking radiographic presentation and the pathological findings of a benign glial-mesenchymal neoplasm which has many of the features of the previously described gliofibromas. In this report, we characterize this neoplasm by electron microscopy, immunoperoxidase studies, and histochemical findings, and compare its properties to those of other mixed glial/mesenchymal central nervous system neoplasms.

Case Report

This 2-month-old baby girl was brought for evaluation of a decreased level of consciousness, poor feeding, and frequent episodes of projectile vomiting. The child was previously healthy but was being followed for increased head circumference (39.3 cm at 20 days and 43 cm at 2 months). At 13 weeks of age, the patient's head circumference was 44.5 cm and the anterior and posterior fontanelles were tense.

Examination. A noncontrast-enhanced magnetic resonance (MR) image performed on the day of admission showed both a large intraventricular mass involving the right basal ganglia, thalamus, hypothalamus, and temporal lobe (Fig. 1A) and an infratentorial tumor beneath the fourth ventricle involving the cerebellar tonsils and possibly filling an enlarged cisterna magna (Fig. 1B). The supratentorial tumor did not appear to be contiguous with the infratentorial mass. Both lateral ventricles were enlarged; the left greater than the right. Neurological examination revealed intermittent lethargy without focal deficits.

Operations. A right parietal craniotomy was performed on the next day. At surgery a large gray-white intraventricular tumor with regions of soft, gelatinous as well as firm consistency was found arising from the right thalamus and extending anteriorly, posteriorly, and across the midline. The tumor was debulked. A ventricular catheter was left for external drainage of cerebrospinal fluid. Bilateral frontal ventriculoperitoneal shunts were placed 1 week later for persistent hydrocephalus.

A repeat MR image with gadolinium enhancement
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(Fig. 1C) performed 2 weeks after the right parietal craniotomy revealed significant growth of both supratentorial and infratentorial masses, which now involved the optic chiasm, hypothalamus, medial right temporal lobe, and inferior basal ganglia on the right, with the intraventricular component of the right lateral ventricle extending into the left side. There was no enhancement around the aqueduct and fourth ventricle. The infratentorial part of the tumor involved much of the cisterna magna and medial tonsils, and extended into the inferior vermis, appearing to compress the medulla forward.

Eighteen days after the first operation, a posterior fossa craniotomy with fourth ventricular tumor resection was performed. At surgery, a 30-cc multilobulated well-encapsulated mass arising from the floor of the fourth ventricle at the level of the lower pons and upper medulla was removed. The child did well after the second procedure. One month following the first operation, a right pterional craniotomy was performed for partial resection of a large firm white exophytic suprasellar and frontotemporal extensions of the right thalamic mass.

Postoperative Course. A follow-up MR image performed 4 months later showed no residual tumor in the posterior fossa, but the diencephalic and suprasellar tumor were unchanged in appearance from the previous postoperative MR image. The patient’s clinical status slowly deteriorated while the tumor continued to grow, as assessed by increasing head and fontanel size. She died at 1 1/2 years of age, and no autopsy was performed.

Pathological Examination. Grossly, the tumor fragments from all three resections were firm and white. Microscopically, the tumor was composed of two populations of spindle-shaped cells which could be distinguished by their staining characteristics. The first and most prevalent cell type was characterized by an eosinophilic cytoplasm with coarse processes and an extracellular matrix which stained green with Masson’s trichrome (Fig. 2A) and displayed abundant extracellular reticulin fibers which invested individual cells (Fig. 2B). These cells exhibited variable but significant positivity by immunoperoxidase staining for alpha-1-antitrypsin and muscle actin. The nuclei had a delicate chromatin pattern with indistinct nucleoli and were predominantly round or elliptical, although indented or irregular forms were occasionally present. These cells were sometimes arranged in a vague storiform pattern and were associated with rare myxoid areas. The second cell type formed dense cellular bands throughout the tumor and was characterized by a more eosinophilic fibrous cytoplasm which stained slate gray with Masson’s trichrome and expressed glial fibrillary acidic protein (GFAP) (Fig. 2C) and S-100 immunoreactivity. These cells were often perivascular. The nuclei of these cells were indistinguishable from those of the first type, but indented or irregular forms were more frequent, particularly in the tumor from the second and third resections. Mitoses numbering up to 5/10 high-power fields were readily identified throughout the tumor resected from the posterior fossa, but were scant in the tumor from both supratentorial resections. The tumor was negative for carcinoembryonic antigen and the histiocytic marker KP-1, and gave equivocal immunohistochemical staining for factor VIII and lysozyme. There were no areas of necrosis, hypertrophied endothelial cells, or inflammatory cell infiltrates.

Electron microscopic examination of the tissue obtained from the second supratentorial tumor debulking highlighted the dual glial and mesenchymal nature of...
the neoplasm (Fig. 2D). Groups of astrocytic cells with numerous processes rich in intracytoplasmic glial filaments were often observed to be invested by a basement membrane. Spindle cells with oval nuclei, peripherally placed heterochromatin, and prominent Golgi apparatus, but overall nondistinctive cytoplasmic features were present on the opposite side of the basement membrane, in a loose connective tissue matrix which included abundant collagen fibers. There was no evidence for myofibroblastic differentiation, phagocytic activity, interdigitating cellular processes, Weibel-Palade bodies, or long-spaced collagen.

Discussion

We have described a benign tumor composed of cells that exhibited both glial and mesenchymal differentiation. The glial differentiation was highlighted by positive immunoperoxidase staining with GFAP and S-100, while the mesenchymal differentiation was mainly characterized by the ultrastructural demonstration of basement membrane and collagen production, and non-descript cytoplasmic organelles. Thus, this tumor bore a striking resemblance to other collagen-forming nervous system tumors which are characterized by a proliferation and dense intermingling of neoplastic glial and mesenchymal spindle cells, such as the gliofibromas, and intracerebral fibroma, sclerosing astrocytomas, and mixed mesenchymal-glial tumors.

Comparisons between the present tumor and previous reports of benign glial-mesenchymal tumors deserve some discussion. This tumor clearly differed from intracerebral fibromas and desmoid tumors that show no evidence of glial differentiation. The present tumor resembled the “gliofibroma” occurring in the lower medulla of a 3-year-old girl reported by Friede, in that both tumors contained a well-differentiated astrocytic neoplasm with a dense intermingling of astroglial processes and collagen fibers with large zones of hyaline stroma. The present tumor is distinguished by its lack of a highly cellular second component exhibiting mitoses and necrosis, and by the clear anatomical demarcation, at the ultrastructural level, between the astroglial and connective tissue elements. By electron microscopy, Friede’s case lacked fibroblast-like cells, although basement membranes were occasionally observed between the astrocytic processes and the collagen fibers in the better differentiated areas. Despite irradiation and chemotherapy, his patient died 3 months after the original diagnosis with evidence of extra-axial seeding of the tumor.

Llena, et al., described a 19-year-old man with a cerebellar “fibroma” and reviewed additional cases of predominantly fibrous brain tumors which collectively showed the presence of a myxoid component, multinucleated neoplastic cells, abundant collagen production, chronic inflammatory cells, and a storiform pattern of spindle cells. They compared their cases with either nodular fasciitis or fibrous histiocytomas. Budka and Sunder-Plassmann described the light microscopic findings in a “glial-fibroma” of the cervical spinal cord from a 45-year-old woman; that tumor showed a sharp demarcation between the mixed hypocellular fibrous component and the more cellular glial component. Neither component displayed pleomorphism or mitotic activity. There was no clinical evidence of tumor progression in that patient 1 year after resection. Reinhardt and Nahser described a temporoparietal gliofibroma in a 16-year-old girl who had a 6-year history of seizures. The neoplasm contained anaplastic GFAP-containing cells admixed with strands of collagen with small zones of hyaline myxoid matrix and multinucleated cells. Mitotic figures were infrequent. By electron microscopy, “basement membranes between collagen and glial fibers could frequently not be identified.” The authors interpreted that gliofibroma as arising from neoplastic transformation of a pre-existing hamartoma-like lesion. Their patient had no clinical evidence of tumor 6 months following resection. Gass, et al., reported an intramedullary spinal cord “sclerosing astrocytoma” in a 46-year-old retired boxer, which consisted of a fibrous nodule surrounded by mildly pleomorphic astrocytes without significant mitotic activity intermixed with inflammatory cells. Their patient was asymptomatic 3 years after resection of the intramedullary lesion.

In contrast to these neoplasms, the present tumor lacks multinucleated cells, a significant inflammatory infiltrate, and a hyaline stroma; in addition, while myxoid areas are present, they are sparse. The tumor in our patient most resembles the gliofibroma described by Igsias, et al., which consisted of a congenital intramedullary tumor composed of intermingled benign astrocytes and fibroblasts without mitotic activity. By electron microscopy, a common basement membrane was observed investing both the astrocytes and fibroblasts. In contrast, in our case there were foci of high mitotic activity and the basement membrane clearly separated the glial from the mesenchymal component. In conclusion, although differences exist between the tumor presented here and previously described neoplasms in regard to histology or its interpretation, we have designated the present tumor as a gliofibroma.

As previously mentioned, a major class of mixed glial-mesenchymal tumors consists of gliosarcomas and sarcogliomas. The mesenchymal cell of origin in the gliosarcoma/sarcoglioma has variously been proposed to be endothelial, histiocytic, fibroblastic, and myofibroblastic. These same cells are candidates as the cell of origin of the gliofibroma. It is possible that the gliofibroma may represent a more benign form of the sarcomatous element more commonly observed in association with glioblastomas and sarcogliomas. The immunoperoxidase studies in our case, which demonstrated positive staining for muscle actin, and the failure of electron microscopic studies to provide evidence for specific myofibroblastic or histiocytic differentiation support the contention that gliofibromas arise from a multipotent glial/mesenchymal progenitor, as suggested.
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Fig. 2. A: Photomicrograph of the tumor demonstrating a dense admixture of darker-staining glial cells (arrow) in a loose connective tissue matrix. Masson's trichrome. × 80. B: Photomicrograph showing a rich network of reticulin-positive fibers. Reticulin, × 40. C: Immunoperoxidase glial fibrillary acidic protein (GFAP) staining highlights the glial islands and individual GFAP-positive cells in the connective tissue areas. × 80. D: Electron micrograph showing an island of glial cells and astrocytic processes (asterisk) invested by a basement membrane (small arrows) and surrounded by collagen and a fibroblast-like cell (large arrow). × 7050.

by Grant, et al., for the sarcomatous element of the gliosarcoma. It is also possible that the tumor comprises metaplastic glial cells which focally are producing extracellular matrix components as suggested by Kepes, et al., in the formation of cartilage in gliomas. Kepes, et al., also reviewed studies showing that astrocytes can be induced to secrete basement membrane components. Previous authors have also suggested that astrocytes can produce collagen. We cannot totally exclude the possibility that a gliosarcoma or sarcoglioma coexisted in our patient since an autopsy was not performed; however, this seems unlikely since three separate biop-
sies in this case have failed to identify such an aggressive neoplasm. Alternatively, the storiform pattern in this tumor raised the possibility that this was a primarily mesenchymal neoplasm, such as a rare intracranial malignant fibrous histiocytoma,\(^1\) invading the brain and trapping islands of reactive glial cells; however, this was considered less likely since the astrocytic cells had neoplastic features.

While all of the relatively benign neoplasms previously described share the feature of mixed glial and mesenchymal differentiation, they differed, however, in the degree to which the glial or mesenchymal characteristics are expressed. At the extremes of this continuum would lie the intracerebral fibroma and the low-grade astrocytoma. Thus, these intermediate tumors may represent either isolated unrelated neoplasms or a single neoplasm expressing a phenotypic continuum from predominantly mesenchymal to predominantly glial differentiation. Certain features do emerge from review of the literature. Collectively, these tumors may occur throughout the entire neuraxis and, as is apparent in this case, they may be massive. They appear to be more prevalent in young patients, but some do occur in adults. The prognosis seems related more to location rather than to any morphological feature of the tumor, although the degree of anaplasia (as in the original gliofibroma described by Friede\(^3\)) and the mitotic index (as in our case) may prove to be important. Additional cases are necessary to establish the validity of the assertion that the entities described and reviewed here represent related neoplasms.

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References


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