Primary angiosarcoma of the central nervous system

Study of eight cases and review of the literature

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Angiosarcoma arising in the central or peripheral nervous system has rarely been reported. Eight patients with primary angiosarcoma of the central nervous system are described here; these included five males and three females ranging in age from 2 weeks to 72 years (mean 38 years). Of the eight neoplasms, six were located in the cerebral hemispheres and one was in the meninges; the site was unknown in the other. All patients underwent surgical resection. Five of the eight patients died, four within 4 months after surgery and one after 30 months. Two of the remaining three patients were 17 and 27 years old at the time of diagnosis and were alive at follow-up review 39 and 102 months after surgery, respectively. One patient was lost to follow-up monitoring.

Microscopically, all eight tumors demonstrated a well-differentiated pattern with irregular vascular channels and intraluminal papillae; in addition, four showed poorly differentiated solid areas. Immunohistochemical staining of neoplastic cells to factor VIII-related antigen and Ulex europaeus agglutinin I was performed in five tumors and was focally positive in four. No correlation could be shown between the histological features and the growth and biological behavior of the tumors.

KEY WORDS • angiosarcoma • central nervous system • immunohistochemistry

ANGIOSARCOMA is a rare malignant neoplasm of the vascular endothelium that occurs chiefly in skin and soft tissue. Angiosarcoma arising in the central or peripheral nervous system has been reported only rarely. Within the central nervous system (CNS), it may present in several ways: 1) as a “pure” neoplasm with no other component; 2) mixed with glioblastoma multiforme (gliosarcoma); or 3) as a metastatic neoplasm. This report describes eight new cases of “pure” primary CNS angiosarcoma and reviews previously published cases.

Clinical Material and Methods

Patient Population

Among 184 primary brain sarcomas and 267 gliosarcomas recorded at the Armed Forces Institute of Pathology between 1970 and 1987, we found eight cases of primary angiosarcoma, one case of gliosarcoma with a complex mesenchymal component that included fibrosarcoma and angiosarcoma, and one case of primary angiosarcoma of the mediastinum metastatic to the brain. These cases of “pure” angiosarcoma constitute the basis of this report. Follow-up information regarding clinical course, vital status, incidence of recurrent or metastatic disease, treatment, length of survival, and cause of death was available for seven of the eight patients.

Tissue Preparation

Tissue sections from all cases were stained with hematoxylin and eosin, reticulin, and Masson’s trichrome techniques. For immunohistochemical study, the avidin-biotin complex (ABC) method was applied to deparaffinized sections from three cases, using antibodies to glial fibrillary acidic protein (GFAP), cytokeratin, S-100 protein, myoglobin, desmin, vimentin, fibronectin, homatropine methylbromide-45, leukocyte common antigen, factor VIII-related antigen, and Ulex europaeus agglutinin I (UEA-I). In another case, immunostaining was limited to GFAP, factor VIII-related antigen, and UEA-I antibodies. In still another case, sections were treated with factor VIII-related antigen and UEA-I only. The secondary antibody was either...
Fig. 1. Photomicrographs of a surgical specimen.  A: Area with a vascular pattern comprised of irregular anastomosing channels lined by flat-to-plump neoplastic endothelial cells. H & E, \times 113.  B: The vascular pattern is well delineated by a network of reticulin fibers. Reticulin stain, \times 180.  C: Area of solid pattern composed of closely packed polygonal cells with large and irregular hyperchromatic nuclei, homogeneous cytoplasm, and indistinct cellular borders. Mitoses are present (arrows). H & E, \times 180.  D: A large vascular space is partially filled with papillary structures which are lined by neoplastic endothelial cells. H & E, \times 75.  E: Poorly differentiated area with neoplastic endothelial cells showing cytoplasmic immunoreactivity to factor VIII-related antigen. ABC method, \times 235.  F: Vascular component with neoplastic endothelial cells displaying positive staining to Ulex europaeus agglutinin I. ABC method, \times 235.
Primary angiosarcoma of the central nervous system

biotinylated mouse or rabbit immunoglobulin G and detection was by an ABC kit.* Material for immunohistochemical study was not available in three cases.

Illustrative Case

This 61-year-old woman had a 4-week history of blurred vision and headaches when she developed loss of balance and left-sided weakness that progressed to an inability to walk. On physical examination, she was alert, cooperative, and oriented. There was left hemiparesis with hyperreflexia and impaired graphesthesia. A brain scan showed an area of increased uptake in the right parietal region. Right carotid angiography revealed slowing of the arterial circulation and early vein filling in the right posterior parietal region.

At surgery, a well-demarcated subcortical lesion was removed from the right parietal lobe. The excised mass measured 4 × 3 cm and was cystic and hemorrhagic. Histopathological examination of the specimen showed a tumor with a admixture of vascular and solid patterns; the microscopic features are demonstrated in Fig. 1. Postoperative radiographic studies showed extension of the lesion into the right frontal region. The patient died 6 weeks later of cerebral edema. No autopsy was performed.

Results

In our series of eight patients with primary CNS angiosarcoma, there were five males and three females, with age at diagnosis ranging from 2 weeks to 72 years (mean 38 years). The clinical course was characterized by a rapid onset of symptoms. All patients underwent total or partial surgical resection. Only one patient received additional treatment, consisting of 3000 rad of radiation therapy. The median survival time in the five patients known to have died was 8 months. Two patients who were 17 and 27 years old at the time of diagnosis were alive at 39 and 102 months, respectively, after surgery. A 56-year-old man was lost to follow-up review after surgery. Seven of the eight neoplasms were supratentorial in location; seven were parenchymal and one was meningeal. At surgery, the tumors appeared well circumscribed and hemorrhagic, and were considered by the neurosurgeons to have been resected with ease.

Microscopically, all eight tumors exhibited well-differentiated areas with ramifying vascular channels of different shape and caliber and intraluminal papillary structures lined by plump endothelial cells often with hyperchromatic nuclei. In addition, four of the eight cases showed clusters and solid sheaths of poorly differentiated cells exhibiting an epithelioid or spindle-cell configuration. In one of the latter cases, the tumor was composed almost exclusively of large polygonal epithelioid-like cells frequently marked by intracytoplasmic vacuoles. The number of mitotic figures varied considerably and ranged from 0 to 3/10 high-power fields. Necrosis and hemorrhage were striking features in most cases. Six of the eight tumors were poorly circumscribed and infiltrated adjacent brain parenchyma and/or meninges. Massive invasion of bone and soft tissue was noted in one case. Focal staining of the neoplastic cells for factor VIII-related agent and UEA-I was present in four cases, and in one case both markers were negative. Two neoplasms immunoreacted with vimentin and, in a third case, immunoreactivity to S-100 protein was present. All tumors tested were negative for GFAP, cytokeratin, myoglobin, desmin, fibronectin, and leukocyte common antigen. In three cases, paraffin sections were not available for immunohistochemical examination.

Discussion

Literature Review

Primary CNS angiosarcoma has seldom been reported in the literature. To our knowledge, only five well-documented cases have been described. Menas and Garcia† reported the light microscopy and ultrastructural features of a primary angiosarcoma in the left frontal lobe of a 15-year-old girl. Charman, et al.,4 described a 65-year-old man with primary angiosarcoma of the left parieto-occipital area that stained with factor VIII-related antigen, UEA-I, and alkaline phosphatase. Kristoferitsch and Jellinger10 studied a dural angiosarcoma of the thoracic spinal region in a 60-year-old man; the tumor had invaded the spinal cord parenchyma and had metastasized to the lumbar region. Two additional examples were reported briefly by Russell and Rubinstein.18 One of their tumors involved the dura of the anterior cranial fossa in a 1½-year-old child; the other involved the cervicomedullary region in a 6-year-old girl.

In the five previously published cases and our eight cases, no age predilection was found. Males (eight cases) were more frequently affected than females (five cases). The most frequent site of origin was the cerebral hemispheric parenchyma (eight cases), with the parietal lobe being the most common location (five cases). The only two spinal cord angiosarcomas reported arose in the dura.10,18

Clinical Course

The clinical course in our patients was characterized by the rapid onset of symptoms, usually appearing within 6 months prior to surgery. All patients underwent surgical resection of the tumor and only one received postoperative radiation therapy.

A primary CNS angiosarcoma has been described with the appearance on computerized tomography and magnetic resonance imaging of a well-demarcated lesion with hemorrhagic characteristics.4 In our cases, despite apparent good demarcation seen both by radiology and by visual inspection at the time of surgery, microscopically, the tumor was invasive with the po-

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* Vectastain Elite ABC kit manufactured by Vector Laboratories, Burlingame, California.
tential for a high rate of recurrence. As in previously reported cases of cutaneous and soft-tissue angiosarcoma,5,9 we were unable to demonstrate any correlation between histological features and biological behavior.

**Differential Diagnosis**

Poorly differentiated CNS angiosarcomas that have a solid pattern should be distinguished from other neoplasms, including anaplastic gliomas, metastatic carcinoma, amelanotic melanoma, hemangioblastoma, and various richly vascular sarcomas. The judicious application of immunohistochemical techniques to CNS neoplasms has become a useful diagnostic adjunct.1,17 Factor VIII-related antigen and UEA-I have gained acceptance in diagnostic pathology as useful markers for endothelial cells;11,13,16 however, as in some of our cases, these agents may not stain poorly differentiated neoplastic endothelial cells. In a recent immunohistochemical study of angiosarcoma, factor VIII-related antigen was found in 20 (74%) of 27 tumors, whereas UEA-I was detected in all 27 cases.10 In our series, four of five tumors stained with factor VIII-related antigen and UEA-I. Immunohistochemical results should be interpreted with caution, however, when only one of these markers is used in analyzing angiosarcoma, since some carcinomas stain with UEA-I11,16 and factor VIII-related antigen cannot be demonstrated in every angiosarcoma.1 Cytokeratin, S-100 protein, and homatropine methylnemethide-45 are useful markers in the differential diagnosis of angiosarcoma from metastatic carcinoma and malignant melanoma. Epithelial hemangioblastoma, like angiosarcoma, stains positive for factor VIII-related antigen but usually can be recognized by the arrangement of the tumor cells in distinct rows or cords, the presence of prominent interstitial hyaline fibrosis and intracellular vacuoles (incipient lumen formation), and the frequent association of the tumor cells with medium-sized vessels. Hemangioblastoma, a tumor characterized by its large, foamy, lipid-containing cells, stains negative for factor VIII-related antigen but positive for S-100 protein and GFAP.

Electron microscopic examination of both CNS angiosarcoma14 and extraneural angiosarcoma13 has confirmed their vascular endothelial origin. Non-neoplastic and neoplastic endothelial cells display similar ultrastructural features, including lumen formation and the presence of basal lamina, tight junctions, pinocytic vesicles, cytoplasmic filaments, and Weibel-Palade bodies.3 Well-differentiated angiosarcomas usually display several of these ultrastructural features.13,21 Even in less well-differentiated angiosarcomas, the combination of immunohistochemical studies and electron microscopy may permit an accurate diagnosis.

**References**


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