

BRIEF COMMUNICATIONS

Mixed Glioma and Rhabdomyosarcoma in Brain of a Wild Deer

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Tumors of the central nervous system occur in the horse, cow, pig, cat, dog, chicken and laboratory rats and mice, but there are few reports of these tumors in other mammals [2, 8, 9]. We found an unusual brain tumor in a wild deer and suggest a new concept for the pathogenesis of tumors that arise in the nervous system and contain muscle.

A young adult female white-tailed wild deer was found wandering in a wooded area of Tennessee. She was weak and dazed and died 24 hours later.

The deer was necropsied at the Tennessee Animal Disease Diagnostic Laboratory. Tissues were fixed in 10 percent buffered neutral formalin, embedded in paraffin, sectioned at 6 micrometers, and stained with hematoxylin and eosin (HE) and phosphotungstic acid-hematoxylin (PTAH). Formalin-fixed tissues were processed for electron microscopic study.

Lesions were confined to the central nervous system. The frontal lobes of the brain contained a gelatinous mass 3.8 centimeters at its greatest diameter. The tumor was in the midline in the region of the frontal lobes (fig. 1). The upper part of the mass was sharply demarcated, but the neoplasm infiltrated part of the brain below, leaving a rim of uninvolved brain inferiorly. The fixed brain weighed 170 grams and was otherwise normal.

The histologic pattern of the tumor correlated with the gross appearance. There were some zones of abrupt demarcation between neoplasm and affected brain, and other regions in which the tumor merged gradually with surrounding normal brain. Mild degenerative changes of neurons and a slight increase in astrocytes were noted in the adjacent compressed brain.

At the border of the tumor in the regions abruptly demarcated from normal brain or within 2 to 3 millimeters of normal brain in gradually merging zones, the tumor had a regular population of cells with a delicate neurofibrillary background and small, round nuclei with a stippled pattern of chromatin. In many foci near the borders, these small nuclei were perivascular (fig. 2) and were more densely packed than elsewhere. Proliferation of vascular endothelial cells and focal zones of necrosis occasionally were seen.

The more central parts of the tumor also contained small, undifferentiated cells

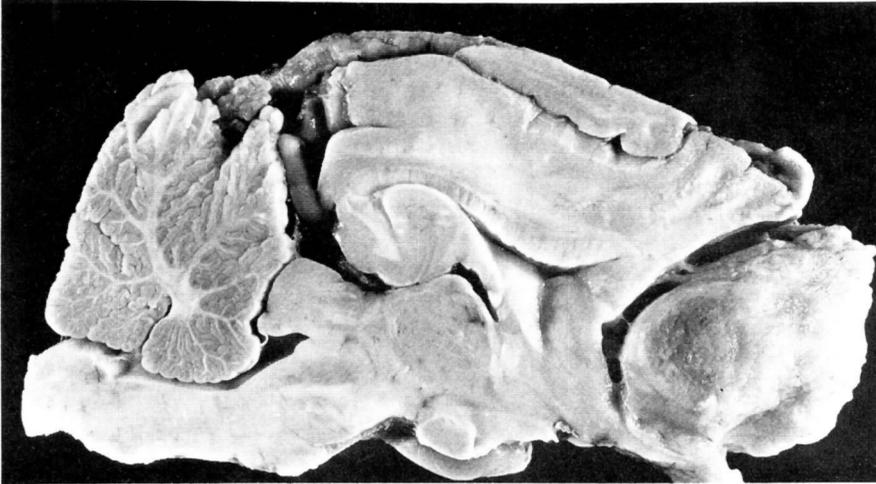


Fig. 1: Sagittal section of brain. Tumor, 2.8×3.0 cm, at far right.

with little cytoplasm. They were mixed with other cells with voluminous spindle-shaped cytoplasm (fig. 3a). Cross-striations of skeletal muscle frequently were seen in the elongated parts of cytoplasm (fig. 3b). The cells often were pleomorphic and bizarre. Ultrastructurally, the large cells containing circular eosinophilic cytoplasmic masses (fig. 3b) were formed by radially arranged fibers (fig. 4). The microscopic diagnosis was mixed glial and mesenchymal tumor (astrocytoma and rhabdomyosarcoma).

Although intracranial malignant neoplasms occur in animals, we have found only three cases in deer [5, 6]. Two of the tumors were classified as ependymomas and the third as an astrocytoma. The tumor we are reporting is unique in a nonhuman species. Intracranial tumors containing muscle have previously been found only in man. They have been designated by several names, such as medulloblastoma and gliomyosarcoma. A review of the literature found seven rhabdomyosarcomas that mingled with neural cells [12]. One report contains a description of a pure rhabdomyosarcoma and an analysis of eight others [11]. Most of these tumors in children are in the midline of the cerebellum, but in adults are in the cerebral hemisphere. In most instances the rhabdomyoblastic cells, when mixed, were associated with small, undifferentiated cells resembling those found in medulloblastoma. Skeletal muscle in the form of typical rhabdomyoblastic cells has been mixed with glial cells in both the cerebrum and the cerebellum. Rhabdomyoblastic differentiation is more often related to primitive tumors of neural origin. The term medulloblastoma was used as long ago as 1933 [10], but greater degrees of differentiation may be encountered than is indicated by the term medulloblastoma. The name gliomyosarcoma also has been suggested [3].

The site of the tumor in our case was unique, as it was in the midline between

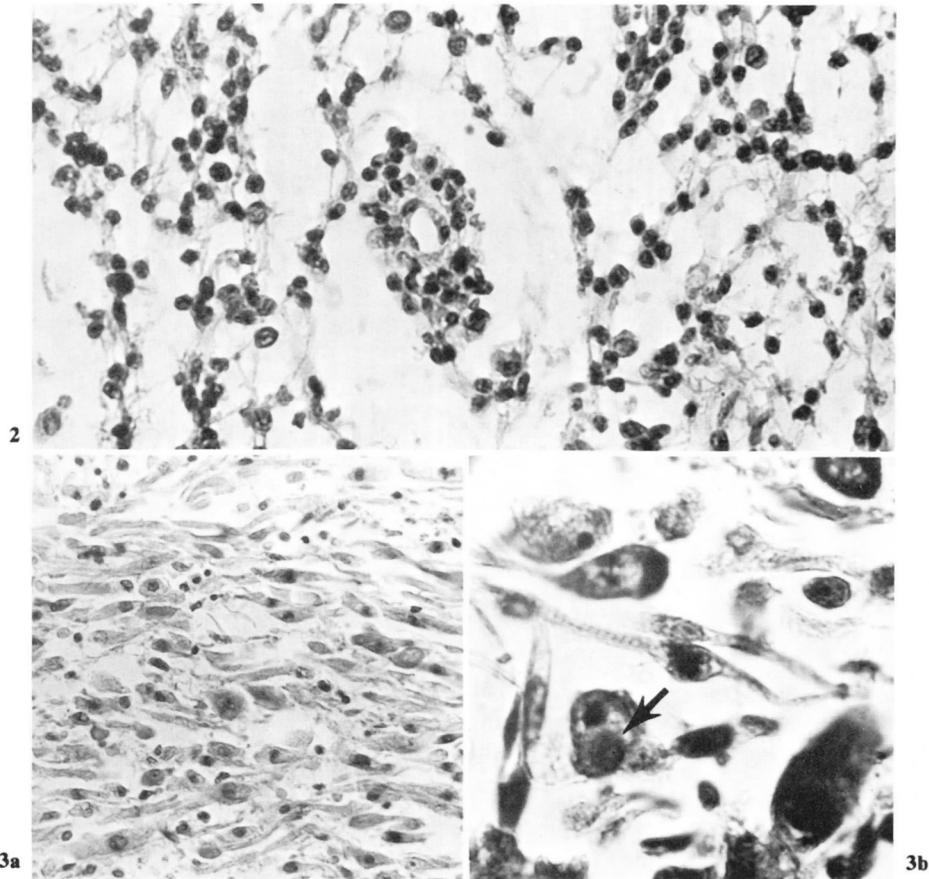


Fig. 2: Small, undifferentiated tumor cells with a fibrillary glial stroma, grouped around small vessels. HE.

Fig. 3: *a.* Rhabdomyoblastic focus. Cells with elongated cytoplasm. *b.* Regular cytoplasmic cross-striations (center of picture) and plump cells with dense round cytoplasmic region (arrow).

the frontal lobes. Origin from the olfactory nerve was unlikely because a complete shelf of normal brain was below the tumor. Around most of the border, the separation of tumor and brain was abrupt. We assumed that the small areas producing imperceptible merging of brain and tumor were astrocytic responses to the intracerebral tumor.

The intracytoplasmic inclusions were unusual. Similar aggregates attributed to myofibrillar clustering have been found by light and electron microscopy in the subsarcolemmal space of the gastrocnemius in a woman with an atypical myopathy [4]. Other disorders associated with these cytoplasmic bodies include polymyositis, progressive muscular dystrophy, myotonic dystrophy, denervation of muscle and periodic paralysis [4]. Disorganization and aggregation of myofibrillar filaments

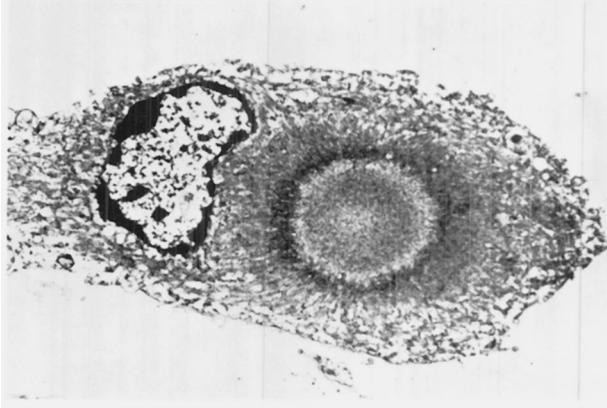


Fig. 4: Plump cell similar to that in figure 3b. Circular area of radial bundles of fibrils.

therefore have multiple causes, including neoplasms. Striated muscle has been found in the non-neoplastic cerebellum of the rat [13]; there were five reports of striated muscle in bovine pineals and one each in fish vagal ganglia and human laryngeal nerve.

Mixed tumors containing neuroepithelial and skeletal muscle cells usually have been considered to be of teratoid origin when they arise in the midline of the brain in infants and children [20]. The tumor in our deer was not a teratoma because the medulloblasts and astrocytes were indigenous to the brain. It has been thought that brain tumors containing striated muscle arise from multipotential mesenchymal tissue that differentiates into aberrant muscle cells [19].

Recent chemical, histochemical and x-ray diffraction data on the similarity of glial fibers and proteins of the myosin group [17] offer another insight into the possible origin of skeletal muscle in tumors of the central nervous system. A protein with characteristics similar to actomyosin has been isolated from whole brain of rat and cat [14]. The actin- and myosin-like components of this protein interacted with each other as well as with counterparts isolated from muscle [1, 15, 16]. Distinct differences, however, were detected in the actomyosins from striated muscle, smooth muscle of aorta and from brain [1]. A protein similar to skeletal muscle α -actinin has been isolated from embryonic chick brain [7].

A properly controlled phosphotungstic acid-hematoxylin stain gives chromatic distinction between collagenous (orange-red) and glial fibers (blue). Muscle fibers also stain blue. We suggest that actomyosin in brain and in muscle may account for the similar staining reaction.

A recent report of polarization microscopic studies with Levafix Red Violet E-2BL stain indicated similar staining properties in the polarization microscopy of glial fibers and smooth muscle. This is further evidence that glial fibers contain a myosin-like protein [18]. Morphological changes of the fibrillary glia caused by the neoplastic process may result in the rhabdomyoblastic appearance of some neural tumors.

References

- 1 BERL, S.; PUSZKIN, S.: Mg²⁺-Ca²⁺-activated adenosine triphosphatase system isolated from mammalian brain. *Biochemistry* **9**:2058, 1970
- 2 FANKHAUSER, R.; LUGINBÜHL, H.; McGRATH, J. T.: Tumors of the nervous system. *Bull WHO* **50**:53-69, 1974
- 3 GOLDMAN, R. L.: Gliomyosarcoma of the cerebrum-report of a unique case. *Am J Clin Pathol* **52**:741-744, 1969
- 4 KINOSHITA, M.; SATOYOSHI, E.; SUZUKI, Y.: Atypical myopathy with myofibrillar aggregates. *Arch Neurol* **32**:417-420, 1975
- 5 KRADEL, D.C.; DUNNE, H.W.: Diseases of the brain and spinal cord observed in Pennsylvania deer and other wildlife. *Proc Northeast Sec Wildlife Soc*, Hartford, Jan 1964
- 6 KRADEL, D.C.; DUNNE, H.W.: Brain tumors (ependymomas) in deer. *J Am Vet Med Assoc* **147**:1096-1098, 1965
- 7 LAZARIDES, E.; BURRIDGE, K.: α -Actinin: immunofluorescent localization of a muscle structural protein in nonmuscle cells. *Cell* **6**:289-298, 1975
- 8 LUGINBÜHL, H.: Comparative aspects of tumors of the nervous system. *Ann NY Acad Sci* **108**:702-721, 1963
- 9 LUGINBÜHL, H.; FANKHAUSER, R.; McGRATH, J.T.: Spontaneous neoplasms of the nervous system in animals. *Prog Neurol Surg* **2**:85-164, 1968
- 10 MARINESCO, G.; GOLDSTEIN, M.: Sur une forme anatomique, non encore décrite, de médulloblastome: médullor-myo-blastome. *Ann Anat Pathol (Paris)* **10**:513-525, 1933
- 11 MATSUKADO, Y.; YOKOTA, A.; MARUBAYASKI, T.: Rhabdomyosarcoma of the brain: case report. *J Neurosurg* **43**:215-221, 1975
- 12 MIN, K.W.; GYORKEY, F.; HALPERT, B.: Primary rhabdomyosarcoma of the cerebrum. *Cancer* **35**:1405-1411, 1975
- 13 OHANIAN, C.: The occurrence of striated muscle within the cerebellum of the albino rat. *Acta Anat* **71**:108-111, 1968
- 14 PUSZKIN, S.; BERL, S.; PUSZKIN, E.; CLARKE, D.D.: Actomyosin-like protein isolated from mammalian brain. *Science* **161**:170-171, 1968
- 15 PUSZKIN, S.; PUSZKIN, E.; CLARKE, D.D.; BERL, S.: The nature of the "contractile" protein isolated from brain. *Fed Proc* **28**:1733, 1969
- 16 PUSZKIN, S.; BERL, S.: Actin-like properties of colchicine binding protein isolated from brain. *Nature* **225**:558-559, 1970
- 17 WALDROP, F.S.; PUCHTLER, H.; VALENTINE, L.S.: Light microscopic demonstration of myoid fibres in the nervous system. *J Micr* **96**:45-56, 1972
- 18 WALDROP, F.S.; PUCHTLER, H.: Luxol fast blue MBSN-Levafix red violet E-2BL, a combined stain for myelin sheaths and glia fibers. *Arch Pathol* **99**:529-532, 1975
- 19 WILLIS, R.A.: *Pathology of Tumors*, pp. 757-771, 4th ed; Butterworth, London, 1967
- 20 WILLIS, R.A.: *Atlas of Tumor Pathology—Teratomas*. Sec 111, vol. 9, p. 11, Washington, AFIP, 1951

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