Malignant Intracranial Fibrous Histiocytomas. Histologic, Ultrastructural and Immunohistochemical Studies of Two Cases

A.A.F. Sima, R.T. Ross, G. Hoag, B. Rozdilsky and M. Diocee

ABSTRACT: Two cases of malignant intracranial fibrous histiocytoma are presented. In Case 1 the tumour arose from the meninges and showed a disseminated spread throughout the neuroaxis. In the second case the tumour appeared to arise from within the brain substance. In this case surgical intervention and radiotherapy appeared to have achieved a cure, since no residual tumour was found at autopsy.

The tumours were examined using ultrastructural and immunohistochemical techniques, which appeared advantageous in delineating this rare tumour from other intracranial neoplasms.

RÉSUMÉ: Histiocytomes fibreux malins intracrâniens. Des études histologiques, ultrastructurales, et immunohistochimiques dans deux cas Nous présentons deux cas de histiocytome fibreux malin intracrânien. Dans le premier cas, les méninges donnèront naissance au tumeur, qui répandit ensuite partout dans le nevraxe. Dans le second cas le tumeur apparut naître du parenchyme cérébral. Chez ce patient le traitement chirurgical et la radiothérapie semblent l'avoir gueré car on ne trouva pas de résidu du tumeur à l'autopsie. Les tumeurs one été explorés aux techniques ultrastructurales et immunohistochimiques, qui ont servi de distinguer ces tumeurs rares d'autres néoplasmes intracrâniens.

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Malignant intracranial fibrous histiocytoma (MFH) is rare. Only a few cases have been recorded, all arising from the meninges.[1-4] We report two patients with intracranial MFH, one arising from the meninges and one presumably from perivascular mesenchymal tissue within the brain substance. MFH is a pleomorphic sarcoma typically occurring in the deep, soft tissue of adults.[5-10] The studies by Kauffman and Stout,[11] and O'Brien and Stout[12] established the characterization of this tumour which is also known as malignant fibrous xanthoma, or fibroxanthosarcoma. The biphasic nature of MFH with evidence of both histiocytic and fibroblastic differentiations was emphasized by these authors. Recent studies however, have suggested a pluripotent tumour cell differentiation along various mesenchymal cell lines, arising from an undifferentiated mesenchymal stem cell.[6,10] The current findings of five distinct cell-types including an undifferentiated mesenchymal cell, support this notion. The present histological, ultrastructural, and immunohistochemical studies outline differential diagnostic criteria characterizing this unusual intracranial neoplasm.

Case 1

Clinical History

This 45 year old Caucasian male was admitted on February 9, 1984 because of a right hemiparesis and deteriorating vision. Since 1975 he had postural syncopal attacks followed by seizures and was treated with phenylhydantoin and phenobarbital. In 1979 a computerized tomogram (CT scan) of the head revealed a mass lesion on the left sphenoid ridge extending into the anterior fossa. Surgical exploration revealed a tumour attached to the olfactory tract on the left, and posteriorly to the dura of the floor of the middle fossa. The histologic diagnosis was meningioma. Postoperatively he was well except for complete anosmia.

In May of 1983 he complained of episodes of decreased hearing in the right ear, nausea, intense vomiting, and vertigo. Physical examination revealed deafness in the right ear and nystagmus on extreme lateral gaze to both sides. A repeat CT scan showed a small area of lucency in the left frontal lobe corresponding to the operative site. Examination in August 1983 showed multidirectional gaze nystagmus and substantially reduced hearing on the right of a sensory-neural type. Hearing on the left was normal. Vestibular testing showed poor pursuit tracking and caloric abnormalities of a central nature on the right.

He was readmitted on February 9, 1984. He had developed weakness of the right arm and leg and headaches in the left frontal area, an

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unsteady gait and blurred vision. He had no further seizures. There had been a gradual loss of memory for recent events since February 1983.

On examination he was apathetic, but in no acute distress. He had fine, fast, vertical downbeating nystagmus with the eyes in the primary position. It increased in amplitude on right or left lateral gaze. There was no light perception in the right eye and a complete nasal hemianopsia in the left eye. The pupils were equal. He had a right afferent pupillary abnormality with no direct response to light. Fundus examination revealed papilledema of 6 diopters with hemorrhages and cotton wool spots in the right retina. Early papilledema was seen in the left fundus. There were bilateral lateral rectus palsies. Complete anosmia was present. Cranial nerves III, IV and V were normal. There was upper motor neuron weakness of the lower portion of the right face and weakness and slight spasticity in the right upper and lower limbs. Coordination was normal, gait unsteady, and Romberg's test negative. Tendon reflexes in the right arm and leg were more active than on the left and the plantar responses were normal.

There was a large mass in the lower abdomen on the right. It was hard and fixed.

A ventricular drain was inserted on February 10, which revealed clear CSF under mildly increased pressure. A repeat CT scan revealed a left hemispheric mass. Bilateral carotid angiograms showed a normal right internal carotid. The left internal carotid was decreased in size and tapered in an irregular way to complete occlusion at the level of the anterior clinoid, suggestive of tumour encasement.

Exploration of the right iliac fossa tumour on February 22 revealed a mass infiltrating the underlying iliopsoas muscle. Due to massive bleeding, attempts to remove the tumour were abandoned. Biopsy material was not diagnostic.

On March 9, 1984 a repeat craniotomy was performed. A soft, hemorrhagic tumour was encountered under the left frontal lobe. There was tumour growth along the sphenoid ridge, which encased the carotid artery and the left optic nerve. The tumour extended into the overlying medial temporal area. Fragments of tumour were removed, but complete tumour removal was not possible. His postoperative course was characterized by frequent attacks of shortness of breath. Pulmonary emboli were confirmed on lung scan. He died on March 29, 1984 of a massive pulmonary embolus in spite of anticoagulant therapy.

Pathology

Methods

The biopsy material obtained at the craniotomy in March of 1984, consisted of small fragments of tissue aggregating 2x1x0.7 cm. Small cubes of tissue from 3 fragments were fixed in 2.5% cacodylate-buffered glutaraldehyde and processed for electronmicroscopy. The remainder was fixed in 10% neutral formalin and paraffin embedded. Paraffin sections were stained with hematoxylin-eosin (H-E), Masson's trichrome, oil red "o", Gordon-Sweet's reticulin stain, phosphotungstic acid-hematoxylin (PTAH), periodic acid-Schiff (PAS) with and without diastase treatment and with alcian blue at pH 2.5. For immunohistochemical examination sections were deparaffinized, rehydrated and the peroxidase anti-peroxidase (PAP) technique was employed for the following commercially available antisera; glial fibrillary acidic protein (GFAP), cytokeratin, vimentin, desmin, muramidase, alpha-1-antitrypsin and S-100 protein.

Ten ml of CSF obtained from the ventricular drain in March 1984 was centrifuged and the obtained pellet was fixed in 2.5% cacodylate buffered glutaraldehyde and processed for electronmicroscopy.

At the time of autopsy several tumour sites were sampled for electronmicroscopy. The brain, spinal cord and eyes were fixed in neutral 10% formalin for 15 days. Multiple samples from these tissues were processed for lightmicroscopy and immunohistochemistry as above.

Results

Case 1 Biopsy (March 9, 1984)

Lightmicroscopic Findings Several tumour fragments revealed a malignant pleomorphic tumour with small foci of necrosis and evidence of old hemorrhage. The tumour consisted of fibroblasts, histiocytic elements, xanthomatous cells and the occasional multinucleated giant cell of the Touton-type. Also small lymphocyte-like cells were seen scattered throughout the tumour. The proportions of these cell constituents varied. Some areas showed a predominant fibroblastic component with spindle-shaped nuclei of varying size with interspersed histiocytic elements. In these areas the tumour cells often formed whorls or a cartwheel or storiform pattern with a myxoid stroma that was weakly alcian blue positive (Figure 1). Other areas of the tumour were made up of mainly histiocytic elements. They varied in size and showed an abundant eosinophilic cytoplasm and pleomorphic nuclei. Multinucleated giant cells of Touton-type were present in variable numbers. Small undifferentiated cells with hyperchromatic nuclei were admixed with histiocytic cells in these areas (Figure 2). Foamy xanthomatous cells were also observed, which contained lipid. Mitoses were easily seen but varied in number from one area to the other. The distribution of collagen and reticulin fibers was irregular, being abundant in areas of fibroblast-like differentiation but scanty or absent in histiocytic foci. No glycogen or cross-striations were demonstrated in tumour cells. Areas of necrosis showed the presence of polymorphonuclear leucocytes and plasma cells. Review of the biopsy obtained in 1979 revealed a similar histologic picture.

Immunohistochemistry The histiocytic areas showed a moderate to strong positivity for vimentin (Figure 3), whereas in fibrocytic areas only the occasional cell showed weak positivity. Antibodies to other intermediate filaments were negative. Muramidase showed an irregular weak positivity in some tumour cells. No positivity was found with alpha-1-antitrypsin or S-100 protein.

Electronmicroscopy Five cell types could readily be identified; fibroblasts, histiocytes, xanthomatous cells, multinucleated giant cells and small undifferentiated cells. The fibroblasts displayed elongated irregular nuclei with conspicuous nucleoli. The cytoplasm showed numerous mitochondria, well developed Golgi-complexes and dilated cisternae of rough endoplasmic reticulum. They showed occasional lipid droplets and normally spaced collagen.

The histiocyte-like cells showed kidney shaped nuclei with one or two nucleoli. The cytoplasm showed a well developed Golgi-apparatus, free ribosomes and some rough endoplasmatic reticulum. The most conspicuous finding was the abundant presence of intermediate filaments often in a typical perinuclear location (Figure 4). The cytoplasm contained phagocytic vacuoles, multivesicular bodies, phagocytized myelin fragments and hemosiderin. The cell membrane was ruffled with abundant filopodia. No Langerhans granules were seen. Xanthomatous cells contained numerous lipid droplets, well developed cisternae of rough endoplasmic reticulum and plump cytoplasmic processes. They were sometimes found to produce mature collagen (Figure 5). The multinucleated giant cells showed a morphology similar to that of histiocytic elements and contained 4 to 6 nuclei. Small undifferentiated cells were also

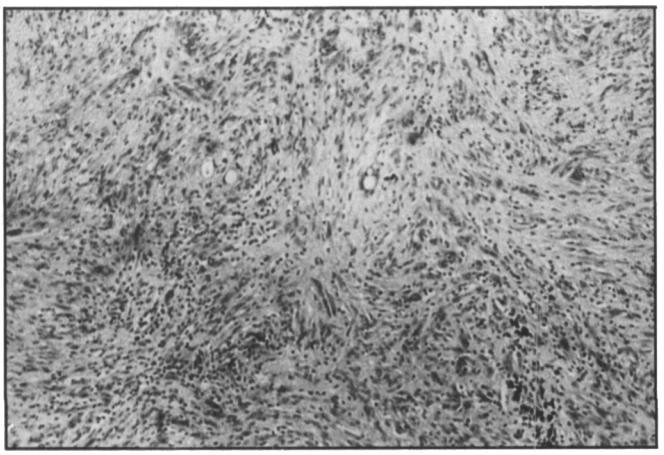

Figure 1 — Tumour obtained at second biopsy of Case 1 (March, 1984) exhibiting a predominant fibroblastic differentiation with spindle-shaped and pleomorphic nuclei. These areas showed the typical cartwheel or storiform pattern. Note scattered cells with small chromatin dense nuclei (mesemchymal stem cells) H-E Mag 108x.

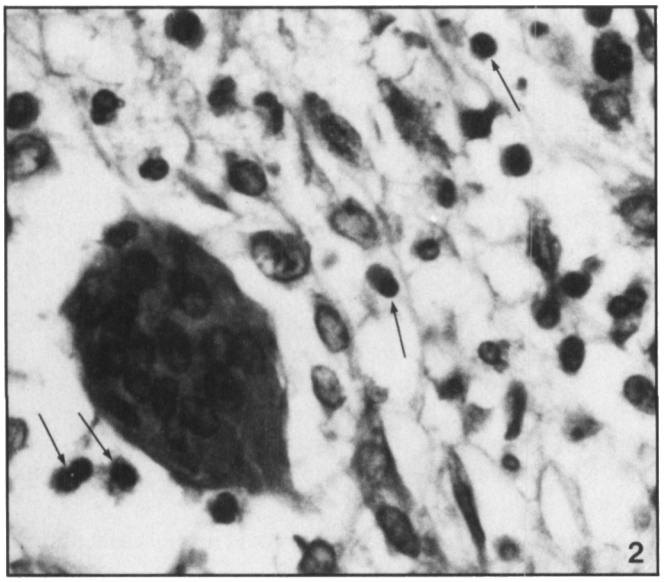

Figure 2 — Multinucleated giant cell with a bright eosinophilic cytoplasm in an area made up of mainly histiocytic elements. These areas also exhibited small undifferentiated cells with hyperchromatic nuclei (arrows). H-E Case 1, biopsy 1984, Mag 585x.

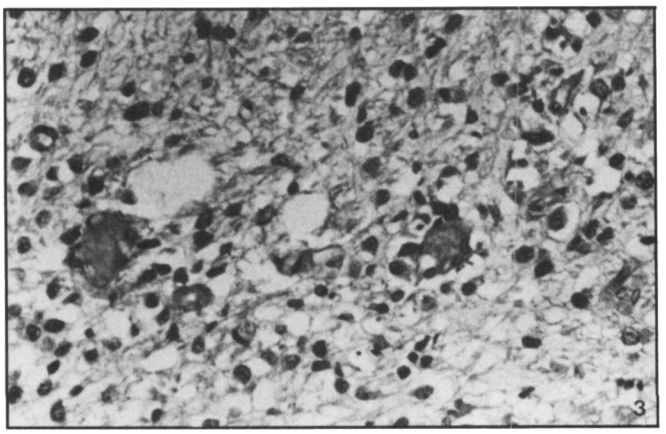

Figure 3 — Section stained with the PAP-technique for vimentin showing positivity in histiocytic elements. Case 1, biopsy 1984, Mag 410x.

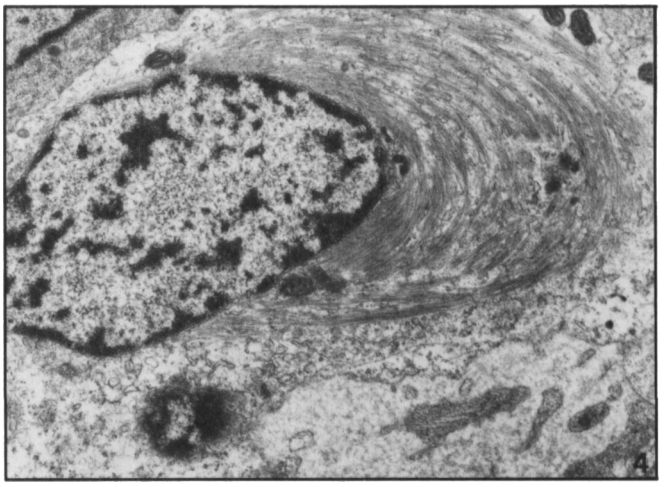

Figure 4 — Histiocytic tumour cell showing an abundance of intermediate filament in a typical perinuclear location. The cytoplasm shows rough endoplasmic reticulum and free ribosomes. Case 1, biopsy 1984, Mag 27,200x.

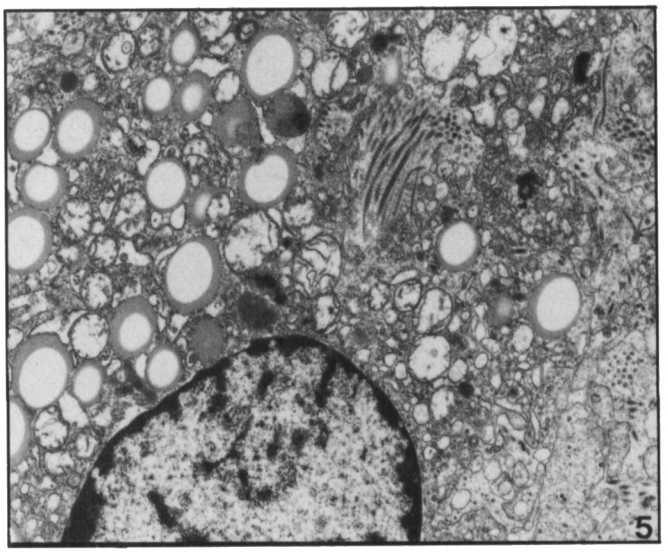

Figure 5 — Detail of xanthomatous cell containing numerous lipid droplets, dilated cisterne of rough endoplasmic reticulum, numerous mitochondria as well as mature collagen. Case 1, biopsy 1984, Mag 27,200x.

identified, which showed small chromatin dense nuclei surrounded by a thin rim of undifferentiated cytoplasm (Figure 6). Occasionally the presence of perinuclear filament could be demonstrated. The intercellular spaces showed the presence of collagen and particularly in histiocytic areas a finely granular extracellular matrix.

CSF The only tumour cells that could be identified in the CSF were undifferentiated cells and histiocyte-like elements. (Figure 7).

Autopsy Findings

General autopsy revealed massive bilateral pulmonary emboli as the cause of death. The right pelvic lesion was a 10 x 5 cm firm mass involving the right iliopsoas muscle. On lightmicroscopy this was a richly vascularized mass consisting of numerous capillary channels surrounded by spindle-shaped cells, consistent with a hemangiopericytoma. No metastases were found from this tumour.

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At autopsy the brain was noted to be adherent to tumour infiltrating the dura bilaterally in the middle fossae. The leptomeninges were thickened and opaque. The eyes were removed and were normal. The spinal cord and cauda equina were encased in a gray tumour mass occupying the subarachnoid and subdural spaces.

Coronal sections of the formalin fixed brain demonstrated generalized tumour involvement of the leptomeninges and subarachnoid space with multiple foci of tumour invasion into underlying brain tissue (Figure 8). There was direct spread of tumour into the inferomedial part of the left temporal lobe extending dorsally to involve the anterior caudate nucleus, and putamen, as well as the anterior limb of the internal capsule (Figure 8). A lesser area of invasion was found in the right inferior medial temporal lobe involving the amygdaloid nucleus and extending into the hypothalamic area. Sections of the brainstem revealed extensive tumour involvement of the floor of the fourth ventricle, with invasion into the pontine tegmentum, involving the 6th nuclei bilaterally, and the 7th on the right. The midbrain showed tumour involvement of the left inferior colliculus and the medial lemniscus of the left. Sections of the medulla revealed tumour invasion of the left lateral vestibular nucleus as well as involvement of the medial lemniscus in the lower medulla. Sections through the cerebellum revealed multiple small areas of tumour invasion from the subarachnoid space. At the base of the brain, the distal left internal carotid artery and optic nerve were encased in tumour and the optic chiasm revealed tumour growth of the right lateral aspect.

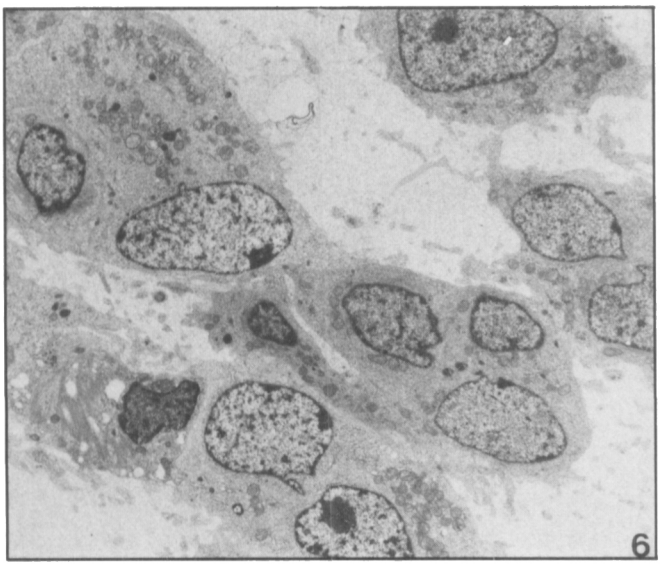

Figure 6 — Histiocytic tumour cells showing large vesiculated nuclei with prominant nucleoli. Note in the middle a small undifferentiated cell (mesenchymal stem cell) with a small chromatin dense nucleus. Case 1, biopsy 1984, Mag 8,100x.

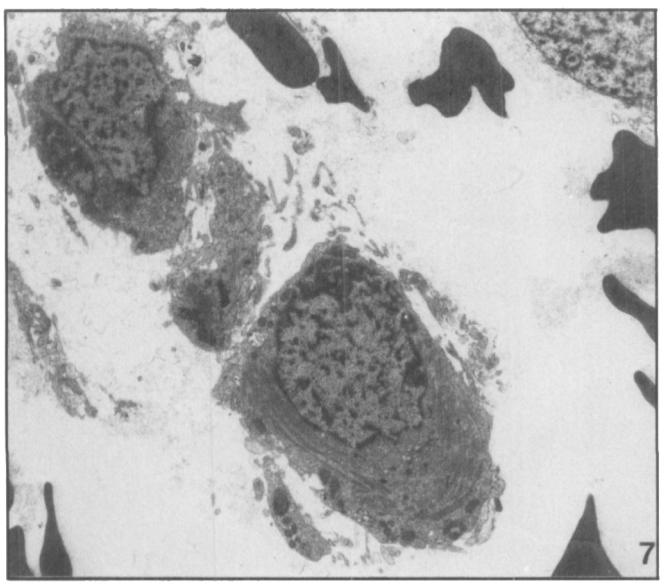

Figure 7 — Histiocytic tumour cells in centrifuged CSF-pellet. Note the similarity with Fig. 4. One cell shows dense bundles of intermediate filaments in the cytoplasm. The cell membranes are ruffled with multiple filopodia. Mag 14,700x.

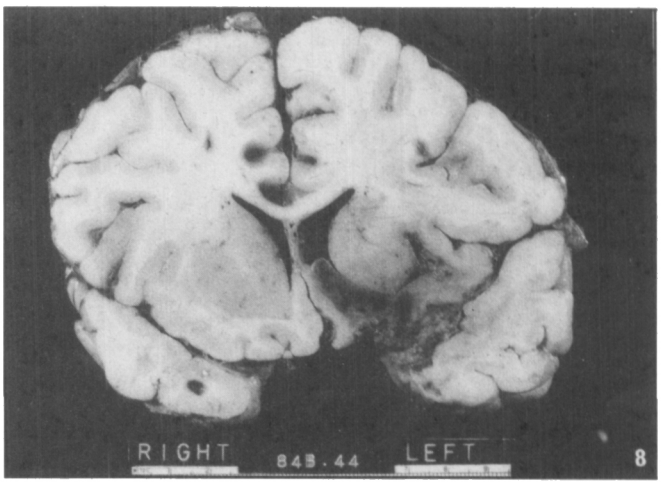

Figure 8 — Coronal section of the brain in Case 1. There is direct spread of tumour from the subarachnoid space into the inferomedial part of the left temporal lobe extending dorsally. Also note tumour involvement of the subarachnoid space over the left frontal lobe and Sylvian fissure.

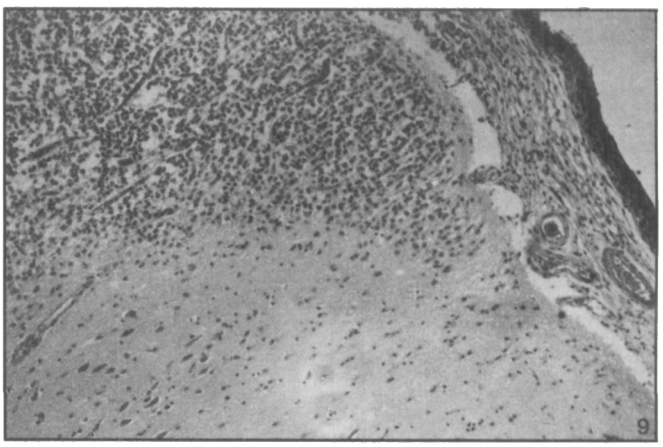

Figure 9 — Tumour invasion into the cerebral cortex. Note the predominant histiocytic differentiation of the tumour, which was characteristic of areas of brain parenchyma involvement. H-E Case 1, Mag 108x.

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Light Microscopy The tumour was histologically identical to tumour removed at the two previous craniotomies. The meninges were uniformly involved with spread in the subarachnoid space and with areas of tumour infiltration of underlying cortex. The tumour in the meninges and subarachnoid spaces displayed predominantly a fibroblastic differentiation with interspersed histiocytic elements and the typical storiform pattern. Tumour invading brain parenchyma showed a loose textured, more or less pure, histiocytic differentiation (Figure 9).

Immunohistochemistry and Electronmicroscopy Examination of several sections with the same immunohistochemical techniques employed on the second biopsy revealed positivity with vimentin and muramidase, whereas other immunostains were negative. Electronmicroscopic examination of multiple samples obtained at the time of autopsy showed well preserved morphology but did not add any further information.

CASE 2

Clinical History

A 65 year old Caucasian male was admitted to the University Hospital, Saskatoon, in January 1983. He was unable to give any history due to drowsiness. The family had noted personality changes, memory impairment, lack of spontaneous speech, and confusion for two months. Difficulty in walking, slowing of speech, weakness and lethargy then followed. He continued to deteriorate and one week prior to admission he ceased to speak spontaneously, replying to direct questions only and in vague terms. There were periodic tremors of the left arm, left sided focal seizures, and left facial droop.

On admission he was disoriented. He had a mild left facial weakness of the supranuclear type and no papilledema. There was weakness of all limbs, more on the left and more in the arm. Occasional intermittent tremors involving the left arm were present and the deep tendon reflexes were increased on the left side with equivocal plantar responses. The past history indicated that in August 1981 a wedge resection of his right lung was performed and an adenocarcinoma was confirmed. He had smoked greater than one package per day for the previous forty years.

Radiological examination of the skull was normal. A computerized tomogram (CT) scan of the head without contrast, revealed a large cystic lesion in the right frontal region extending to the midline and posteriorly. At the posterior and medial aspect of the lesion there was a triangular shaped, high density area, and in the most inferior and anterior aspect of the lesion, there was a second, slightly dense nodule. The left lateral ventricle was compressed and displaced (Figure 10a). Following contrast, the nodule in the inferior and most anterior aspect of the lesion was markedly enhanced, while the second dense lesion did not enhance (Figure 10b).

The patient was given dexamethasone sodiumphosphate 4 mg every six hours, and his mental status markedly improved. Speech became spontaneous and more coherent. Two days after admission, a right frontal craniotomy and removal of a tumour was performed. Intraoperatively, a cyst measuring 10 cm in diameter was found in the right frontal lobe. It contained at least 20 ml of thick, yellow fluid. The anterior floor of the cyst had a solid tumour nodule measuring 2.0 cm in its greatest dimension. The overlying cortex showed no tumour involvement.

Postoperatively, the patient's recovery was uncomplicated. He became oriented to time, place, and person. His speech and gait improved. Medications at this time included dexamethasone sodiumphosphate 4 mg four times per day, and phenylhydantoin 100 mg three times per day. The patient was discharged three weeks postoperatively on dexamethasone sodiumphosphate 1 mg three times per day.

Radiotherapy was started consisting of 2400 centigrays to the whole brain in ten equally divided fractions. The second phase consisted of a further 2400 centigrays to the anterior half of the brain. On review five months postoperatively, his neurological status was satisfactory.

He returned in August 1983, following a routine chest x-ray which revealed lung opacities. A right pneumonectomy was performed. Frozen section showed adenocarcinoma. Postoperatively he did well initially, however, he developed a bronchopleural fistula. On October 14, a pleurostomy was performed under local anesthesia. He developed episodes of chest pain, continued to deteriorate, and on October 24, 1983 had a respiratory-cardiac arrest. Resuscitation attempts were unsuccessful.

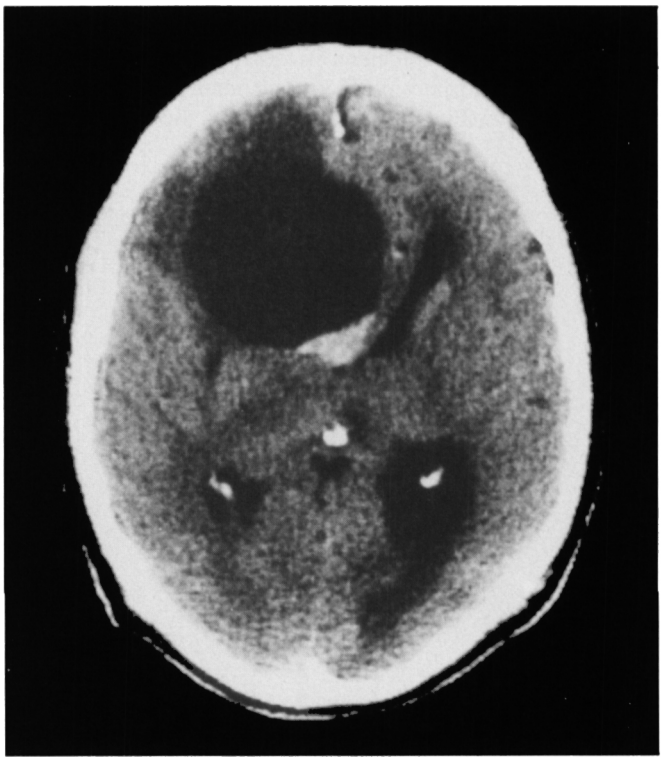

Figure 10a — Computerized tomograph (CT) scan of Case 2 showing a large cystic lesion in the right frontal area extending posteriorly with a high density area.

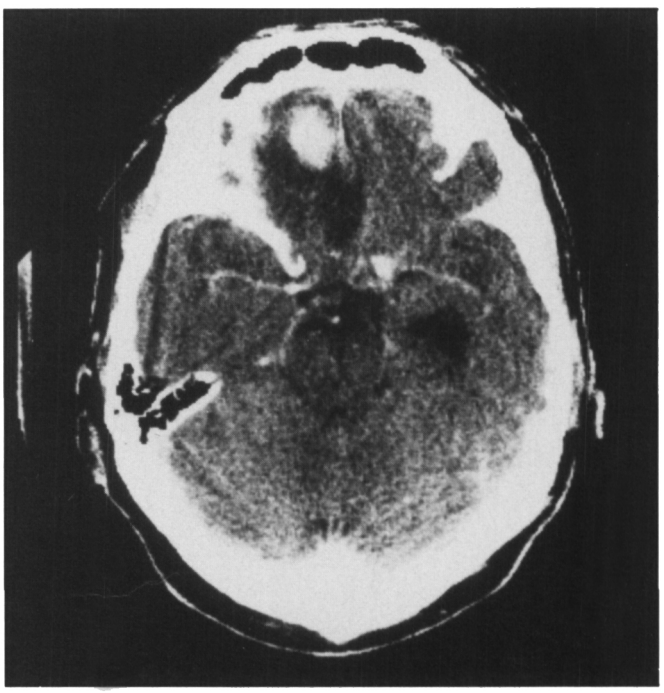

Figure 10b — Deeper cut following contrast injection displaying an anteroinferior enhancing nodule.

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Pathology

Methods

The same histotechnological techniques were used as in Case 1.

Results

Autopsy Findings

The autopsy demonstrated a coronary thrombosis of the left circumflex artery with evidence of previous myocardial infarction. There was secondary adenocarcinoma of the left lung and liver.

Removal of the skull was difficult as the dura mater in the right fronto-temporal region was tightly adherent at the site of the previous craniotomy. The brain weighed 1,560 g and a portion of the right frontal lobe was loosely adherent to the overlying dura mater. There was a brownish softened tissue defect. Sectioning revealed an underlying pinkish-brown hematoma measuring 3.5 cm in its greatest dimension. There were no abnormalities of the brainstem or upper spinal cord region.

Biopsy Findings

Histologically, the brain biopsy specimen showed a highly cellular tumour with numerous dilated vascular channels. There were focal areas of necrosis and hemorrhage. The cells were arranged in a storiform pattern with interlacing bundles of predominantly spindle shaped cells (Figure 11). The nuclei were spindle shaped and pleomorphic with both pointed and blunted ends. Occasional mitotic figures were seen. Reticulin stains demonstrated reticulin fibers surrounding the tumour cells (Figure 12). Focally there was abundant production of ground substance as demonstrated by the alcian blue stain. Intermixed with the spindle shaped cells were small cells with indistinct cytoplasmic borders and dense nuclei. In some areas of the tumour there were large and bizarre cells with large, irregular, convoluted nuclei and foamy eosinophilic cytoplasm. No cross striation was demonstrated in these cells. Some of them had the appearance of multinucleated cells. Prominent nucleoli were frequently seen, whereas mitotic figures were rarely seen in these histiocytic elements. Ultrastructurally, fibroblastic cells predominated (Figure 13). Histiocytic cells showed ultrastructural features similar to those in Case 1 with conspicuous bundles of intracytoplasmic filaments.

Immunocytochemical staining for S-100 protein, glial fibrillary acidic protein (GAFP), cytokeratin, desmin, and alpha-1-antitrypsin were negative. Staining for vimentin was moderately positive. Scattered cells showed positivity with muramidase.

Sections from the entire margin of the operative defect in the frontal lobe showed only reactive changes. There were numerous macrophages, large reactive astrocytes in the neuropil, and marked gliosis in the region corresponding to the surgical biopsy site. There was no evidence of tumour in any of the sections.

Discussion

Malignant fibrous histiocytoma (MFH) or fibroxanthosarcoma is a rare tumour of the CNS and its coverings. All of the previous seven cases reported in the literature [1-4,13] have arisen from the dura or the meninges, which was also the case in our Case 1 (Table 1). This neoplasm shares histological features with other CNS tumours. Spindle cells are seen in meningiomas and fibrosarcomas, and xanthomatous change is commonly

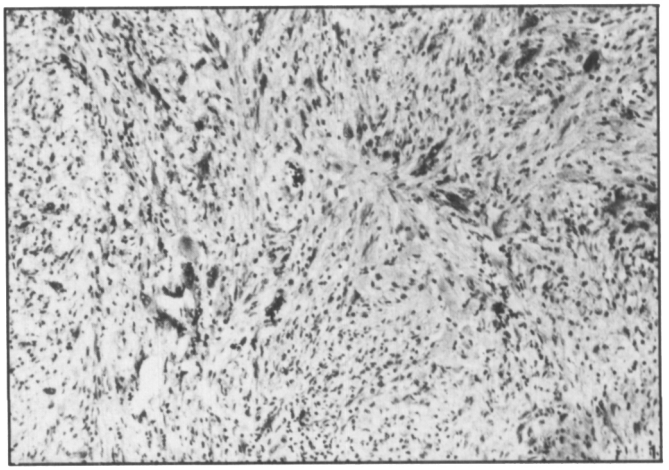

Figure 11 — Typical appearance of the biopsied tumour in Case 2 showing a storiform pattern with interlacing bundles of spindle shaped cells. H-E Mag 95x.

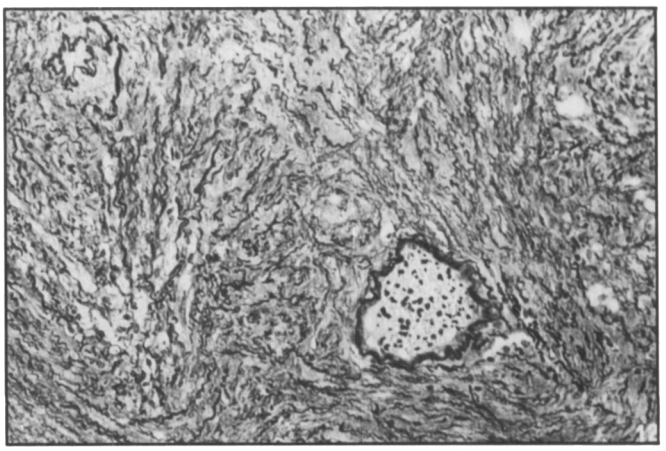

Figure 12 — Characteristic reticulin appearance of the biopsied tumour in Case 2, showing reticulin fibers surrounding single groups of tumour cells. Gordon-Sweet reticulin stain. Mag 540x.

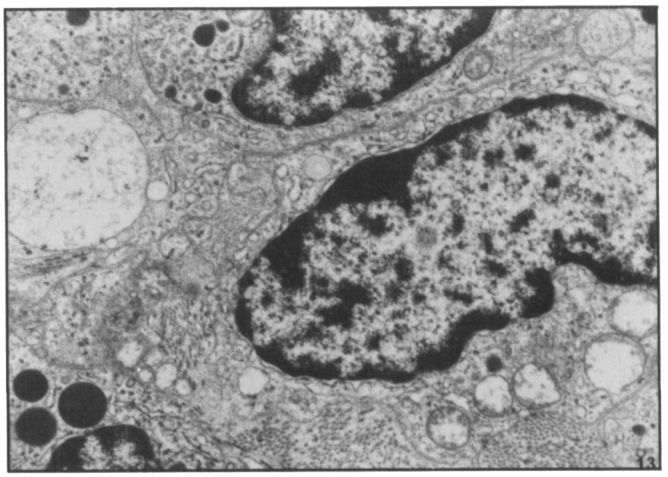

Figure 13 — Fibrocytic cells in Case 2 showing elongated nuclei, mildly dilated rough endoplasmic reticulum in the cytoplasm, and the production of mature collagen. Mag 28,500x.

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seen in meningiomas, neurolemmomas and lipidized astrocytomas. The resemblance to meningioma and the fact that MFH most commonly arises in the meninges led Kepes to suggest that they may be considered as a form of fibroblastic meningioma with histiocytic-xanthomatous differentiation.[3] This close resemblance between meningioma and MFH is also exemplified by the diagnosis of the first biopsy in Case 1. Hence the diagnosis of MFH may be difficult, not only when it occurs in soft tissue[14], but also when it presents as an intracranial neoplasm.

Although MFH is an uncommon tumour encountered in neuropathologic practice, it appears important to establish criteria for its correct diagnosis. By resorting to both ultrastructural and immunohistochemical techniques, as in the present two cases, it is possible to delineate MFH from other intracranial neoplasms.

The usefulness of applying immunohistochemical stainings has been pointed out by several authors.[2-4,13] In six previous cases staining for glial fibrillary acidic protein (GFAP) has been negative (Table 1), excluding the possibility of an astroglial tumour. On the other hand a previous report on three fibrous xanthomas of the meninges and the brain,[15] proved on subsequent immunohistochemical examination to be GFAP positive and were reclassified as pleomorphic xanthoastrocytomas.[3] The present tumours were negative for GFAP. The differential diagnosis between MFH and neurolemmoma may be more difficult. The latter, however, shows positivity for S-100 protein, which was not the case in the current MFH's. Instead, our cases showed positivity for the intermediate filament vimentin (Table 1), a finding which has not previously been reported. It may therefore be difficult to distinguish MFH from meningioma based on immunohistochemical criteria, since this latter tumour exhibits positivity for this intermediate filament.[16-18] In the present cases the differential diagnosis between MFH and meningioma was based on ultrastructural findings. The ultrastructural features of the two present cases were in agreement with previous ultrastructural reports on MFH.[6-10,14] They demonstrated five distinguishable cell types, none of which showed the typical features of meningioma, such as interdigitating processes, desmosomal complexes or basement membranes.

The histogenesis of MFH has been controversial. Earlier studies suggested a histiocytic derivation[11,19-22] but more recently, its origin from an undifferentiated multipotent mesenchymal cell has been proposed.[6,8,9,14] The present light- and electron-microscopic findings demonstrating fibroblasts, histiocytes, xanthomatous cells, multinucleated cells of the Touton type, as well as small undifferentiated cells, qualifying as stem forms as described by Fu et al,[6] give further support to the contention that this lesion arises from a primitive mesenchymal cell.

As in previous cases describing intracranial MFH, the tumour in our Case 1 appeared to arise from the meninges, whereas, in Case 2, there was no evidence to suggest a meningeal origin. Instead, it is plausible that this tumour arose from perivascular mesenchymal tissue within the brain substance, a situation which has not previously been reported.

A feature of intracranial MFH's not previously described was the dissemination of tumour in the subarachnoid space throughout the neuroaxis in our Case 1. Spontaneous hemorrhage into MFH is not unusual,[7,10] and was described in the intracranial case reported by Kalyanaraman et al.[4] A previous hemorrhage in the tumour of Case 2 most likely accounted for the cystic appearance. This is further supported by the intraoperative findings and the abundant presence of hemosiderin in both the biopsy and autopsy material.

Based on the present and previously described cases of intracranial MFH's, no correlation could be established between the histologic pattern and the clinical behaviour of these tumours. Even in much larger materials of extracranial MFH's no good prognostic histopathologic criteria have so far been identified.[7] Nevertheless intracranial MFH must be regarded as a potentially very aggressive neoplasm as examplified by our Case 1.

Both of these patients presented a second neoplasm, in Case 1 a hemangiopericytoma, and in Case 2 an adenocarcinoma of the lung. This has been reported as a common feature in patients with MFH arising at other locations. Weiss and Enzinger[7] found in material from 200 patients with MFH, a second neoplasm in 13% of the cases. The same authors[7] also pointed out

Table 1: Summary of reported intracranial MFH's depicting age, sex, location, origin and immunohistochemical features

	Age and Sex	Location	Origin	Immunohistochemical Features
Gonzalez-Vitale et al, 1976[1]	37, M	paracellar	meninges	not done
Kepes, 1979[3]	54, F	right parietal	dura	GFAP —
	16, F	right parietal	meninges	GFAP —
	17, F	spinal L2-3	meninges	GFAP —
Lam and Colah, 1979[2]	24, M	left frontal	dura	GFAP —
Kalyanaraman et al, 1981[4]	12, M	left frontal	meninges	GFAP —
Hille et al, 1983[13]	42, M	spinal, T10-S1	meninges	GFAP —
Present Case 1	45, M	left temporal	meninges	GFAP — vimentin + muramidase + alpha-1-antitrypsin − desmin − cytokeratin − S-100 protein −
Present Case 2	65, M	right frontal	perivascular tissue	GFAP — vimentin + muramidase + alpha-1-antitrypsin − desmin − cytokeratin − S-100 protein −

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that MFH is primarily a tumour of middle and late adult life. Intracranial MFH appears, however, to occur in a younger age group. The mean age in the total of 9 reported cases was 34 years (Table 1).

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REFERENCES

1. Gonzalez-Vitale JC, Slavin RE, McQueen DJ. Radiation-induced intracranial malignant fibrous histiocytoma. Cancer 1976; 37: 2960-2983.
2. Lam RMY, Colah SA. Atypical fibrous histiocytoma with myxoid stroma. A rare lesion arising from dura matter of the brain. Cancer 1979; 43: 237-245.
3. Kepes JJ. "Xanthomatous" lesions of the central nervous system; definition, classification and some recent observations. *In*: Zimmerman HM, ed. Progress in Neuropathology. New York, Raven Press 1979; 4: 179-213.
4. Kalyanaraman VP, Taraska JJ, Fierer JA, Elwood PW. Malignant fibrous histiocytoma of the meninges. Histologic, ultrastructural and immunohistochemical studies. J Neurosurg 1981; 55: 957-962.
5. Feldman F, Norman D. Intra- and extraosseous malignant histiocytoma (malignant fibrous xanthoma). Radiology 1972; 104: 497-508.
6. Fu YS, Gabbiani G, Kaye GI, Lattes R. Malignant soft tissue tumours of probable histiocytic origin (malignant fibrous histiocytomas): general considerations and electronmicroscopic and tissue culture studies. Cancer 1975; 35: 176-198.
7. Weiss SW, Enzinger FM. Malignant fibrous histiocytoma. An analysis of 200 cases. Cancer 1978; 41: 2250-2266.
8. Lagacé R, Delage C. Siemayer TA. Myxoid variant of malignant fibrous histiocytoma. Ultrastructural observations. Cancer 1979; 43: 526-534.
9. Merkow LP, Frich JC, Slifkin M, Kyreages GG, Pardo M. Ultrastructure of a fibroxanthosarcoma (malignant fibroxanthoma). Cancer 1979: 28: 372-383.
10. Limacher J, Delage C, Lagacé R. Malignant fibrous histiocytoma. Clinicopathologic and ultrastructural study of 12 cases. Am J Surg Path 1978; 2: 265-274.
11. Kauffman SL, Stout AP. Histiocytic tumours (fibrous xanthoma and histiocytoma) in children. Cancer 1961: 14: 469-482.
12. O'Brien JE, Stout AP. Malignant fibrous xanthomas. Cancer 1964; 17: 1445-1455.
13. Hille TL, Hanbery JW, Becker DH. Meningeal malignant fibrous histiocytoma arising from a thoracolumbar myelomeningocele. J Neurosurg 1983; 58: 593-597.
14. Taxy JB, Battifora H. Malignant fibrous histiocytoma. An electronmicroscopic study. Cancer 1977; 40: 254-267.
15. Kepes JJ, Kepes M, Slowik F. Fibrous xanthomas and xanthosarcomas of the meninges and the brain. Acta Neuropath (Berl) 1973; 23: 187-199.
16. Alguacil-Garcia A, Pettigrew NM, Sima AAF. Secretory meningioma. A distinct subtype of meningioma. Am J Surg Path 1986; 10: 102-111.
17. Lolait SJ, Underwood JR, Mu F-T, Alderuccio F, Dow CA, Pedersen JS, Chalmers PJ, Toh BH. Vimentin intermediate filaments in cultures of human meningiomas. Neuropath Appl Neurobiol 1984; 10: 321-331.
18. Schwechheuner K, Kartenbeck J, Moll R, Franke WW. Vimentin filament-desmosome cytoskeleton of diverse types of human meningiomas. A distinctive diagnostic feature. Lab Invest 1984; 51: 589-591.
19. Kempson RL, Kyriakos M. Fibroxanthosarcoma of the soft tissues. A type of malignant fibros histiocytoma. Cancer 1972; 29: 961-976.
20. Kobak MW, Perlow S. Xanthomatous giant cell tumours arising in soft tissue. Report on an instance of malignant growth. Arch Surg 1949; 59: 909-916.
21. Ozzello L, Stout AP, Murray MR. Cultural characteristics of malignant histiocytomas and fibrous xanthomas. Cancer 1963; 16: 331-334.
22. Alguacil-Garcia A, Unni KK, Goellner JR. Malignant fibrous histiocytoma. An ultrastructural study of six cases. Am J Clin Path 1978; 69: 121-129.