Multifocal Primary Intracerebral Malignant Fibrous Histiocytoma

—Case Report—

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Abstract

A 58-year-old female presented with a unique case of multifocal primary intracerebral malignant fibrous histiocytoma (MFH) manifesting as partial seizure. Neuroimaging showed a mass lesion in the right frontal lobe, which was totally removed. The histological diagnosis was MFH. Follow-up neuroimaging one month after surgery showed another lesion rapidly growing in the left frontal lobe. This lesion was totally removed, and identified as MFH. Her condition gradually worsened. Neuroimaging performed 3 months after first operation revealed bilateral recurrence. She died of respiratory failure 7 months after the initial diagnosis of MFH. Primary intracranial MFH is an extremely rare entity with only 31 cases of solitary tumor previously reported.

Key words: brain, malignant fibrous histiocytoma, multifocal primary tumor

Introduction

Malignant fibrous histiocytoma (MFH) is a common soft tissue sarcoma arising from the extremities and retroperitoneum in older adults.^{7,8,32)} However, primary intracranial MFH is rare. The clinical findings of primary intracranial MFH are similar to other brain tumors, manifesting as a space-occupying lesion. The diagnosis of MFH is based on positive immunostaining for monocytes/macrophage markers in the tumor cells and identification of two cell types by electron microscopy. All previous cases have involved a single lesion. Here we describe a case of multifocal primary intracerebral MFH.

Case Report

A 58-year-old female was admitted to our institute complaining of left hemibody partial seizure. The patient sustained moderate left hemiparesis due to Todd's palsy. Chest radiography showed no abnormalities, and laboratory data including blood cell count and blood chemistry, and some tumor markers were within the normal ranges. Computed

tomography (CT) showed a slightly homogeneous high density mass in the right frontal lobe with homogeneous enhancement by contrast medium, and peritumoral edema. Magnetic resonance (MR) imaging showed the corresponding tumor as homogeneously isointense on the T₁-weighted image and homogeneously isointense on the T₂-weighted image, with homogeneous enhancement after intravenous administration of gadolinium-diethylenetriaminepenta-acetic acid. There was associated surrounding peritumoral edema appearing as hyperintensity on the T₂-weighted image (Fig. 1). Cerebral angiography demonstrated a right frontal tumor stain. Gallium-67 whole body scintigraphy detected no extracranial abnormal high uptake.

Tumor resection was performed via right frontal craniotomy. Part of tumor was exposed from the cortical surface. The tumor had no adhesion with the dura mater, and the cleavage from the normal brain tissue was clear. The tumor was totally removed. Postoperatively, the patient sustained mild left hemiparesis which improved with steroid administration.

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Fig. 1 Magnetic resonance images showing a mass in the right frontal lobe as homogeneously isointense on the T₁-weighted image (upper left), and homogeneously isointense on the T₂-weighted image (upper right), with homogeneous enhancement after intravenous injection of gadolinium-diethylenetriaminepenta-acetic acid (lower row).

Histological examination showed highly cellular and predominant fibroblastic differentiation with spindle-shaped cells. Mono- or multinucleated tumor cells were randomly interspersed in a typical storiform arrangement. Some tumor cells infiltrated into the adjacent normal brain parenchyma, which contained reactive astrocytes (Fig. 2). Reticulin fibers surrounded each tumor cell, and collagen fibers accumulated within the intercellular space in some areas. Immunohistochemical staining revealed positive reaction for α -1-antichymotrypsin and CD68 in the tumor cells (Fig. 3), but negative for glial fibrillary acidic protein and S-100 protein. MIB-1 index was remarkably increased to 37.1%. Electron microscopy revealed that the tumor consisted of two distinctive cell types (Fig. 4). The tumor cells contained many lysosomes and phagosomes. The more scattered spindle-shaped cells had features of fibroblastic differentiation. The histological diagnosis was MFH.

One month later, she developed dysarthria and

Fig. 2 Photomicrograph of the tumor showing fibroblastic differentiation with spindle-shaped cells in a storiform pattern. HE stain, $\times 400$.

Fig. 3 Photomicrographs of immunohistological staining for α -1-antichymotrypsin (A) and for CD68 (B) demonstrating positive reaction in the tumor cells. $\times 200$.

Fig. 4 Electron micrograph showing a spindle-shaped cell including deposition of glycogen granules around the invaginated nucleus, and the cytoplasm filled with copious tonofilaments and many lysosomes. Bar = 1 μ m.

Fig. 5 Magnetic resonance images, just before the first operation demonstrating a small mass lesion in the left frontal lobe (left, arrowhead), and after one month showing rapid increase in size and some postoperative change in the right frontal tumor bed (right).

right hemiparesis. MR imaging revealed a left frontal tumor with peritumoral edema and local recurrence of the right frontal tumor. The former had the same characteristics as the previously resected ipsilateral lesion on neuroimaging. Retrospective examination of the MR images taken one month before the first operation identified a left frontal lesion about 5 mm in diameter. The left frontal tumor had grown rapidly over one month (Fig. 5). A left frontal craniotomy was performed. The tumor was totally removed. The histological

diagnosis was MFH. The MIB-1 index was 27.4%.

During the second postoperative course, she developed status epilepticus, which gradually worsened her general condition. Three months after the first operation, MR imaging revealed bilateral local recurrence of tumors with peritumoral edema. Her respiratory condition gradually worsened. Chest radiography and chest CT showed multiple nodules of the pleura and massive effusion. She died of respiratory failure 7 months after the initial diagnosis of MFH. Autopsy was not permitted.

Discussion

The histological diagnosis of MFH is not easily made based on only light microscopy with hematoxylin and eosin staining, which demonstrates a storiform architectural arrangement with fibroblast-like spindle cells. Therefore, MFH is difficult to distinguish from pleomorphic xanthoastrocytoma, meningioma, schwannoma, gliosarcoma, and malignant gliomas with heavily lipidized tumor cells.^{11,17,20,24,27,29} Electron microscopic examination combined with immunohistochemical study is required to differentiate MFH from other tumors. In our case, the histological studies indicated the presence of pleomorphic spindle cells in a storiform pattern and positive reaction in the tumor cells for the monocytes/macrophage markers, α -1-antitrypsin and CD68. These findings are highly suggestive of the histiocytic origin of the tumor cells. Electron microscopy revealed the characteristic two cell types, which was valuable for the diagnosis of MFH. Immunohistochemistry and electron microscopy are essential for identifying this rare tumor.

Primary intracranial MFH is extremely rare with only 32 cases reported since 1976 (Table 1).^{1-6,9-11,13-26,28-32} The 21 male and 11 female patients were aged from 0 to 81 years (mean 38.7 years). We classified these cases of intracranial MFH into three types: Meningeal MFH arising from histiocytes or undifferentiated multipotential cells found in the meninges (18 cases)^{17,27}; parenchymal MFH originating from perivascular mesenchymal cells or the pial sheath surrounding the Virchow-Robin space (11 cases)^{27,29}; and ventricular MFH arising from mesenchymal precursor cells of the tela choroidea (1 case).²⁶ The present case corresponds to parenchymal MFH. Table 1 summarizes the previous 31 cases of intracranial MFH described in detail. The present case is the only example of multifocal parenchymal MFH.

Six cases of parenchymal MFH originated in the frontal lobe and three cases in the temporal lobe. Four cases were recurrence, and usually resulted in

Table 1 Primary intracranial malignant fibrous histiocytoma

Case No.	Author (Year)	Age	Sex	Origin	Treatment	Recurrence over 3 mos	Metastasis	Outcome
1	Gonzalez-Vitale et al. (1976) ¹⁰⁾	37	M	parenchyma	VP shunt + I			died at 3 days of pneumonia
2	Kepes (1979) ¹⁸⁾	54	F	meninges	S	yes		died at 11 mos
3		16	F	meninges	S	no		alive at 24 mos
4	Lam and Colah (1979) ¹⁹⁾	24	M	meninges	S	no		alive at 8 mos
5	Kalyanaraman et al. (1981) ¹⁷⁾	12	M	meninges	S + I	no		alive at 18 mos
6	Nakamura and Becker (1985) ²²⁾	10	M	meninges	S	no		alive at 3 yrs
7		12	F	meninges	S	no		alive at 5 yrs
8	Grant and Gallagher (1986) ¹¹⁾	22	F	meninges	S	unknown		died at 11 mos
9	Swamy et al. (1986) ³²⁾	22	M	meninges	S			died at 10 days of meningitis
10	Sima et al. (1986) ²⁹⁾	65	M	parenchyma	S + I	unknown		died at 9 mos of lung cancer
11		45	M	meninges	S		CSF dissemination	died at 20 days of pulmonary embolus
12	Simpson et al. (1986) ³⁰⁾	65	M	parenchyma	S + I + C	no		alive at 5 mos
13	Berry et al. (1988) ⁴⁾	75	M	parenchyma	S + I	yes		alive at 6 mos
14	Paulus et al. (1989) ²⁴⁾	40	M	parenchyma	S	unknown		died at 8 mos
15	Roosen et al. (1989) ²⁶⁾	45	M	parenchyma	S	yes		died at 8 mos
16	Schrader et al. (1989) ²⁸⁾	45	M	meninges	S + I	yes		alive at 6 mos
17	Sugita et al. (1990) ³¹⁾	73	M	meninges	unknown	unknown		unknown
18	Castillo et al. (1990) ⁶⁾	4 mos	F	meninges	S + I	no		alive at 4 yrs
19	Pople and Harding (1991) ²⁵⁾	5	M	unknown	S + I + C	yes		alive at 20 mos
20	Hughes et al. (1991) ¹⁶⁾	6	M	meninges	S + I	no		alive at 6 mos
21	Biegel et al. (1992) ⁵⁾	6	F	unknown	S + I + C	yes		died at 3 mos
22	Ho et al. (1992) ¹⁵⁾	45	F	parenchyma	S + I	no	lung and T-5 drop metastasis	alive at 3.5 mos
23	Hirato et al. (1994) ¹⁴⁾	57	F	meninges	S			died of post-surgical bleeding
24	Matsuzaki et al. (1996) ²¹⁾	81	F	meninges	S	no		alive at 5 mos
25	Ogino et al. (1996) ²³⁾	70	M	meninges	S	unknown		unknown
26	Berchtenbreiter et al. (1996) ³⁾	41	M	meninges	S + I	unknown		unknown
27	Martinez-Salazar et al. (1997) ²⁰⁾	14	F	parenchyma	S	no		alive at 9 mos
28	Akimoto et al. (1998) ¹⁾	61	M	meninges	S + I + C	yes	lung and CSF dissemination	died at 1 yr
29	Baehring et al. (2001) ²⁾	57	M	ventricle	S + I	unknown		unknown
30	Higashiyama et al. (2002) ¹³⁾	73	M	parenchyma	S + I	yes		died at 15 mos
31	Fujimura et al. (2002) ⁹⁾	2	M	parenchyma	S	no		alive at 3 yrs
32	Present case	58	F	parenchyma	S	yes	lung	died at 7 mos

C: chemotherapy, CSF: cerebrospinal fluid, I: irradiation, S: surgery, VP: ventriculoperitoneal.

death. Overall six patients died and the mean survival period was 9.4 months. Eight cases of meningeal MFH occurred in the frontal lobe, four cases in the temporal lobe, and two cases in the parietal lobe. Three cases were recurrence. Seven patients survived and the mean survival period was 25.63 months. Metastatic parenchymal MFH and menin-

geal MFH accounted for only two cases. Six patients with parenchymal MFH and meningeal MFH died within one year. One patient with no recurrence had meningeal MFH rather than parenchymal MFH. Long-term survival is conspicuous among cases of meningeal MFH. One patient with meningeal MFH survived for more than 5 years. MFH frequently

recurs locally,³³⁾ so adequate surgical excision is the significant point for survival. In our case, histological examination showed infiltration of the tumor cells into adjacent brain parenchyma. MFH tends to permeate like an invasive tumor. Meningeal MFH may have a better prognosis than parenchymal MFH because of the potential for radical surgery. Only one case of ventricular MFH was reported, so the tendency for the prognosis was not clear. Although we only have one case of multifocal MFH, the prognosis is probably improved by radical removal.

The prognosis for patients with primary intracranial MFH is poor, with most deaths occurring within 12 months.⁶⁾ Simultaneous radiotherapy has been performed as an adjunctive method in some cases.^{10,14,21,27)} However, therapeutic efficacy is difficult to evaluate for the variable irradiation methods and doses used. Presumably radical removal followed by some adjuvant therapy is required. Chemotherapy may be effective for extracranial soft tissue MFH,¹²⁾ but the effectiveness for intracranial MFH is undetermined.

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