



Intracranial Malignant Fibrous Histiocytoma; a Tumor with Pathologic Challenge and Poor Prognosis

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Abstract

Primary intracranial Malignant Fibrous Histiocytoma (MFH) is an extremely rare entity, with only 39 cases reported in the literature. Herein, we present a case of intracerebral MFH in a 57 year-old man presented with decreased level of consciousness, nausea, and headache who underwent tumor resection and adjuvant Radiation and he was alive up to 6 months after completion of treatment. We also present a literature review including 39 cases of Intracranial MFH reported previously.

Keywords: Primary intracranial; Malignant Fibrous Histiocytoma; Clinical and pathologic characteristic

Introduction

Primary intracranial sarcomas are rare tumors. Intracranial Malignant Fibrous Histiocytoma (MFH), pleomorphic xanthoastrocytoma, meningioma, schwannoma, and gliosarcoma are the histologic types difficult to diagnose and may be confused. Differentiating these tumors based on light microscopic study alone may be difficult and cause diagnostic error.

MFH is a neoplasm composed of proliferating histiocytes and is characterized by a rapid and fatal course [1]. MFH is considered a rare tumor which comprises no more than 5% of all soft tissue sarcomas diagnosed in adults [2]. MFH affects the lower extremities, the upper extremities, and the retroperitoneum in order of decreasing incidence [3]. Primary intracranial MFH is an extremely rare entity, with only 39 cases reported in the literature to date (Table 1). Some of the reported Intracranial MFHs have a history of radiation therapy or surgical trauma [4,5].

Herein, we present a case of Primary intracranial MFH in a 57 year-old man without previous history of radiation therapy or craniotomy who underwent Tumor resection plus adjuvant local brain Radiation. We will review previously reported Primary intracranial MFHs in literature as well.

Case Presentation

A previously healthy 57-year-old man presented with a 20- day history of decreased level of consciousness. He also reported a subjective impression of headache and nausea. Magnetic Resonance Imaging (MRI) revealed a cortical based mass measuring 3.5 cm × 3.5 cm in left temporal lobe. T1-Weighted Images (T1WIs) obtained after administration of gadoterate meglumine showed a ring enhancement of the Peripheral portion of the mass. T2 Weighted Images (T2WIs) showed a sever surrounding edema and mass effect on brain parenchyma causing midline shift. In order to rule out the extracranial origin of brain mass, whole body Fluorodeoxyglucose (FDG) Fusion Positron Emission Tomography (PET) – CT was done and it revealed increased FDG uptake only at the brain mass and adjacent petrosal bone with Standardized Uptake Value (SUV) of approximately 4.0 without any extracranial lesion (Figure 1). Tumor resection was performed *via* left parieto-temporal craniotomy followed by 60 Gy adjuvant local radiation to tumor bed. Surgical findings revealed that the mass was located in the brain parenchyma of the left temporal lobe, with no adhesion to the dura matter.

Microscopically, the tumor consisted of multiple large pleomorphic cells and giant cells with storiform pattern (Figure 2). Immunohistological (IHC) staining was positive for alpha-1 anti trypsin (A1AT), Glial Fibrillary Acidic Protein (GFAP), vimentin, and CD68 and negative for SMA, S 100, Desmin, and CD30 (Figure 3). Our patient had fluctuating level of consciousness and slurred speech after surgery and radiotherapy. At the time of writing this paper (6 months after treatment), the patient's neurological status is stable and there is no evidence of recurrence or deterioration of neurological symptoms.

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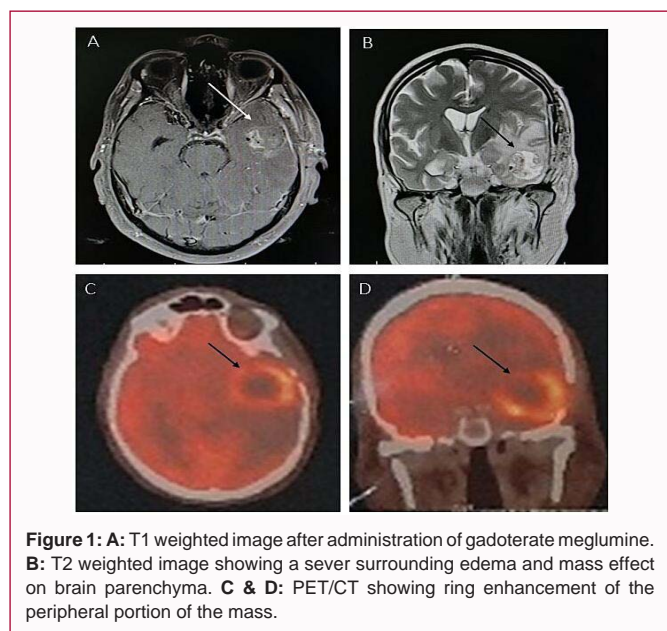
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Table 1: Primary Intracranial MFHs reported in literature since 1976.

No	Reference	Age/Sex	Location/Origin	Treatment	Follow up
1	[19]	12/M	Frontal/Menenge	Complete Resection	---
2	[20]	58/Fe tumor	Multifocal/Parenchyma	Resection (2 times craniotomy)	Recurrence/Died 7 months after initial diagnosis
3	[17]	45/M	Olfactory tract/Parenchyma	Resection (2 times craniotomy)	Recurrence/Died 2 month later due to PTE after second surgery
4	[17]	65/M	Frontal/Parenchyma	Resection Radiation (24 Gy to the whole brain then further 24 Gy to the anterior half of the brain)	No recurrence/died 5 months later due to lung adenocarcinoma
5	[13]	2.5/M	Clivus/Unknown	Resection (2 times craniotomy) Radiation Chemotherapy (after second craniotomy)	Recurrence/died 41 month after initial diagnosis
6	[14]	9/F	Temporoparietal/ Menenge	Subtotal Resection (2 times craniotomy) Chemotherapy (after first craniotomy) Radiation (59.4 Gy after second craniotomy)	Recurrence/alive at 15 th month
7	[15]	62/F	Frontotemporal/Menenge	Resection Radiation (60 Gy)	No recurrence/died 13 month later due to ovarian adenocarcinoma
8	[20]	50/F	Unknown/ Parenchyma	Resection	----
9	[18]	65/M	Unknown/Parenchyma	Complete resection Chemotherapy Radiation	No recurrence/alive at 5 th month
10	[21]	32/F	----	Resection	Died 4 days after surgery
11	[22]	47/M	Frontal/ Menenge	Resection	----
12	[16]	42/M	Frontoparietal/Menenge	Complete resection (2 times craniotomy) Radiation (60 Gy) Chemotherapy	Recurrence/died 1 year after initial diagnosis
13	[23]	61/M	Temporal/ Menenge	Resection (2 times craniotomy) Radiation(32 Gy whole brain then 40 Gy boost to the tumour bed) Chemotherapy	Recurrence/died 1 year after initial diagnosis
14	[6]	57/M	ventricle	Resection Radiation (refused to continue after 20 Gy)	----
15	[24]	41/M	Temporoparietal/ Menenge	surgery of unknown causes----	----
16	[25]	75/M	Temporal/Parenchyma	Resection Radiation (45 Gy whole brain then 14 Gy boost to the tumor bed)	Died 6 months after surgery of unknown causes
17	[26]	6/F	Hypothalamus/Parenchyma	Resection Radiation (craniospinal) Chemotherapy	Recurrence/died 3 months after initial diagnosis
18	[27]	44 month/F	Frontoparietal/ Menenge	Complete Resection Radiation (Whole Brain)	No recurrence/alive at 4 th year
19	[28]	2/M	Sylvian fissure/Parenchymal	Subtotal Resection	No recurrence/alive at 3 rd year
20	[29]	37/M	Pituitary Fossa/Parenchyma	Resection Radiation (14 Gy because he was thought to have a recurrence of the pituitary Adenoma)	Died 3 days after surgery due to septic shock
21	[30]	73/M	Parietal/Parenchyma	Resection (2 times craniotomy)	Recurrence/died 1 year after initial diagnosis
22	[9]	57/F	---	---	---
23	[31]	9/M	Unknown/ Menenge	----	---
24	[19]	12/M	Frontoparietal/ Menenge	Complete Resection	---
25	[32]	24/M	Frontal/ Menenge	Complete Resection	---

26	[33]	70/M	Frontoparietal/ Menenge	----	---
27	[5]	40/F	Frontal/Parenchyma	Resection	---
28	[34]	5/M	Frontal/ Menenge	Resection	Recurrence/alive at 20 th month
29	[35]	22/M	Unknown/ Menenge	Resection	Died 10 days after surgery
30	[36]	13/F	Frontal/Parenchyma	Resection	---
31	[37]	81/F	Frontal/Menenge	Resection	----
32	[20,38]	54/F	---	Resection	Recurrence/died 11 months after initial diagnosis
33	[20,38]	16/F	---	Resection	No recurrence/alive at 24 th month
34	[39]	12/M	Frontal/Menenge	Resection	No recurrence/alive at 3 rd year
35	[39]	13/F	Frontal/Menenge	Resection	No recurrence/alive at 5 th year
36	[40]	22/F	---	Resection	Died 11 months after initial diagnosis
37	[41]	45/M	Thalamus/Parenchyma	Resection	Died 8 months after initial diagnosis
38	[42]	45/M	Parietal/Menenge	Resection Radiation (60 Gy)	Recurrence/alive at 6 th month
39	[20]	73/M	---	---	---
40	Our Patient	57/ M	Temporal/Parenchymal	Resection Radiation (60 Gy)	No recurrence/alive at 6 th month

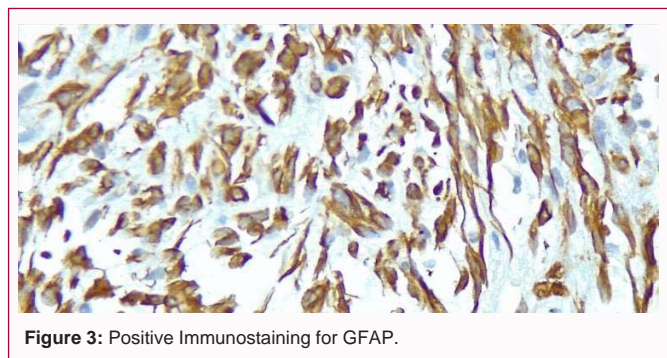
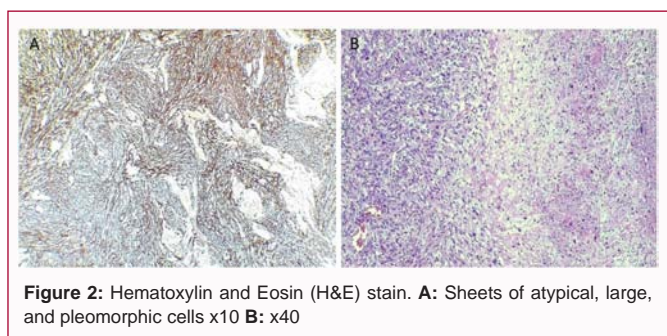
F: Female; M: Male



Discussion

Intracerebral MFH is an extremely rare disorder. To best of our knowledge only 39 cases have been reported since 1976 and current case is the 40th being reported.

We found 39 cases of Intracranial MFH (15 Females and 24 Males) reported in literature (Table 1). Mean age at diagnosis is 37.7 ± 24.6 by a range of 4 month to 81 year old. The most common site of intracranial MFH is frontal or frontal by another adjacent site e.g. Frontotemporal or Frontoparietal (50 % of reported cases). 55.9% of reported Intracranial MFHs arise from meningeal origin (18 patients) and 14 patients have parenchymal origin and one case has a Ventricular origin [6] and origins of 7 cases are undetermined in literature. Only 25 patients were followed up over the months after treatment, 12 patients received post operation radiotherapy, and 13



patients underwent surgery alone with 5-month Survival of 38% and 41% respectively.

Primary MFH of the CNS generally originates from the meninges and is revealed as an extra-axial mass lesion. The present case which originates from the parenchyma, suggests that parenchymal MFH without predisposing factors can mimic a high-grade glioma or gliosarcoma. Gliosarcoma is a rare (1% to 8% of all malignant gliomas) malignancy that presents very similarly to Glioblastoma Multiform (GBM) containing both glial and mesenchymal elements [7,8].

The histologic diagnosis of MFH is not easily based on only light microscopy with hematoxylin and eosin staining because it may be mistaken with pleomorphic xanthoastrocytoma, meningioma,

schwannoma, gliosarcoma and malignant gliosarcoma; so IHC study and electron microscopic examination is helpful to differentiate MFH from other tumors in addition to light microscopy study which demonstrates a storiform architectural arrangement with fibroblast like spindle cells.

In our case the light microscopic study revealed atypical proliferation of the spindle cells including marked pleomorphism and storiform pattern. IHC was positive for A1AT, CD 68, and GFAP and negative for SMA, S100, Desmin, and CD30.

Although traditionally presence of GFAP distinguishes gliosarcomas and pleomorphic xanthoastrocytomas, tumors of glial origin, from MFH, which is basically of mesenchymal origin but there have been reports of early intracranial MFHs or metastatic MFHs to the brain that are GFAP positive, possibly due to the presence of non-neoplastic glial cells within the mass [9-11].

In our patient, despite the microscopic appearance and cellular markers such as A1AT, Vimentin, and CD68 that are in favor of MFH, GFAP is also positive, which led to disagreement among pathologists between the diagnosis of gliosarcoma and MFH. This suggests that GFAP has limitations as a specific diagnostic marker for glial tumors and electron microscopic examination can be helpful in such situations.

Intracranial MFHs mostly recur locally so maximal and adequate resection is determining factor in survival [12]. Adjuvant radiotherapy or chemotherapy has been administered in some cases [13-18] but efficacy of adjuvant treatments is unknown.

Literature review revealed that only 25 patients of 39 were followed up over the months after treatment, 12 patients received post operation radiotherapy, and 13 patients underwent surgery alone with 5-month Survival of 38% and 41% respectively. Although 5 month survival rate was not significant in patients who received post operative radiation in comparison to surgery alone but this should be interpreted cautiously because the follow-up after treatment of some patients is very short and the information of others is incomplete in the literature and some have not been followed at all; our information about surgery (complete or Subtotal Resection) is not complete as well.

Eventually, after maximal tumor resection and despite disagreements about the pathological features of the tumor as a Primary intracranial MFH, the patient underwent adjuvant radiotherapy and his neurological symptoms were stable after treatment; although due to the rarity of intracranial MFH and limited studies, there is still no consensus on diagnosis and treatment of Primary Intracranial MFH.

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