

Case Report

Intracranial benign fibrous histiocytoma mimicking parasagittal meningioma: report of two cases and review of literature

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Abstract: Primary benign fibrous histiocytoma involving the central nervous system is an exceedingly rare tumor with most cases originating from the dura or parenchymal tissue. Diagnosis of primary benign fibrous histiocytoma is difficult due to its confusing histopathological characteristics. Two cases of primary intracranial benign fibrous histiocytoma mimicking parasagittal meningioma are presented in this report. Both tumors were gross totally resected and the patients showed no evidence of recurrence at follow-up of 12 months. The clinical features and prognosis of this rare tumor that were reported previously in the literature were also reviewed. Histopathological examination coupled with immunohistochemical staining is proved to be the convincing diagnostic method for the primary benign fibrous histiocytoma. Surgical resection is the recommendation for the therapy of the tumor.

Keywords: Fibrous histiocytoma, meningioma, intracranial tumors

Introduction

Primary benign fibrous histiocytomas occur most frequently in the skin of head and neck region of the elderly. However, there are few reports about the research on the intracranial benign fibrous histiocytoma [1-3]. The information about intracranial benign fibrous histiocytoma is so limited that it is often misclassified as other types of brain tumor. It's difficult to precisely distinguish this disease from other brain space-occupying lesion, like meningioma, lymphoma and gliosarcoma, using conventional neuroimaging and pathological hematoxylin-eosin staining [4, 5]. Immunohistochemistry (IHC) staining aiming at multiple molecular markers gives much information for the diagnosis of this intractable neoplasia. IHC would be a great help not only to identify the tumor initiating cells, but also to estimate the malignancy degree of tumor. With the development of the IHC and EMS (electron microscope) techniques, the etiology of benign fibrous histiocytoma becomes clearer and many uncertain tumors

are unveiled gradually [6]. Two cases of primary intracranial benign fibrous histiocytoma mimicking parasagittal meningioma are presented in this report. Both tumors were gross totally resected and the patients showed no evidence of recurrence at follow-up of 12 months. IHC was reconfirmed to be the most valuable diagnostic technique for primary benign fibrous histiocytoma.

Clinical report

Case 1

A 25-year-old female was admitted to this hospital because of sudden loss of consciousness three weeks ago: The patient had been doing well until 3 weeks before admission, when she suddenly lost her consciousness and fell down from the bicycle. She recovered consciousness spontaneously about half an hour later and then found the fracture of her left ankle. Then she was sent to the nearest hospital. There was no recent fever or chills, nausea, vomiting,

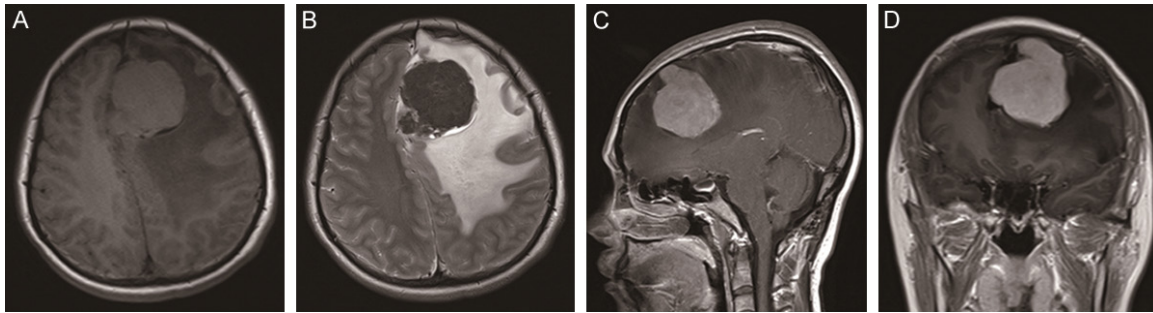


Figure 1. Imaging studies obtained at initial presentation of the first patient. A, B. Axial unenhanced MRI scan showing a large round lesion in the left frontal lobe with sharp borders and marked edema around. C, D. Sagittal and coronal contrast-enhanced T1-weighted MR image demonstrating obvious enhancement.

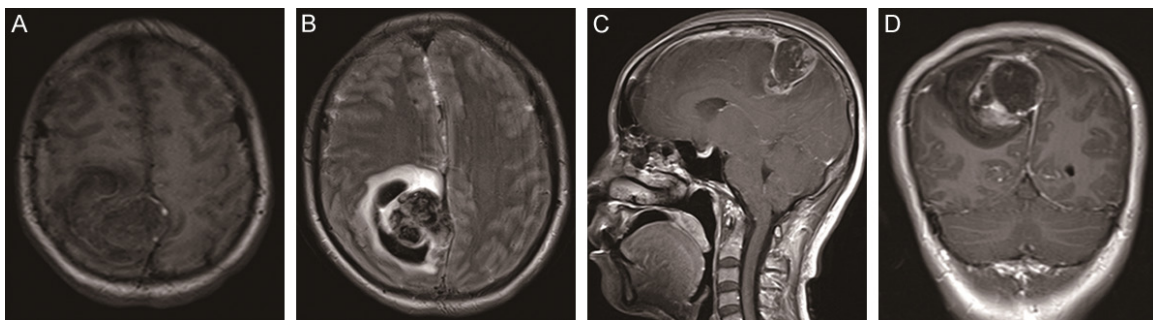


Figure 2. Imaging studies obtained at initial presentation of the second patient. A, B. Axial unenhanced MRI scan showing a large cystic lesion in the right occipital lobe. C, D. Sagittal and coronal contrast-enhanced T1-weighted MR image showing obvious enhancement. Axial T2-weighted MR image showing annular enhancement likely delineating the capsule of the tumor.

headache, weakness or history of seizures. On examination, except for symptom of the fracture in the left ankle, there were no abnormal signs or symptoms. A cranial computed tomographic (CT) scan was obtained immediately and an intracranial mass was found in the left frontal lobe adjacent to the cerebral falx. The fracture external fixation was performed before she was transferred to this hospital.

Case 2

A 34-year-old female was admitted to this hospital because of severe headache and subsequent sudden loss of consciousness combined with generalized seizure three days ago: The patient had been suffering from a mild irregular headache for one year, but she never went to see her doctor. Three days ago, the patient complaint that the headache got much worse and never relieved. Besides, her left extremities were some sort out of control. Then the patient was sent to the nearest hospital. An emergency CT scan was immediately per-

formed which showed an intracranial mass in the right occipital lobe. Mannitol was admitted for dehydration to decrease the intracranial pressure but the patient got no symptomatic relief. Even worse, she started to vomit. After a generalized seizure, her left extremities lost strength totally. Then the patient was transferred to this hospital to get further treatment.

Both patients were well-developed and functioning well before. Laboratory values, including a complete blood count, blood levels of electrolytes, calcium and glucose; and tests of coagulation, renal and hepatic function, were unremarkable. Ultrasonic test of uterus and both breasts revealed no obvious abnormalities.

Neuroradiological features

For case 1, magnetic resonance imaging (MRI) of the brain showed an oval mass in the left frontal lobe. The lesion showed homogeneously isointensity on the T1-weighted image and slightly short T2-weighted signal with clear bor-

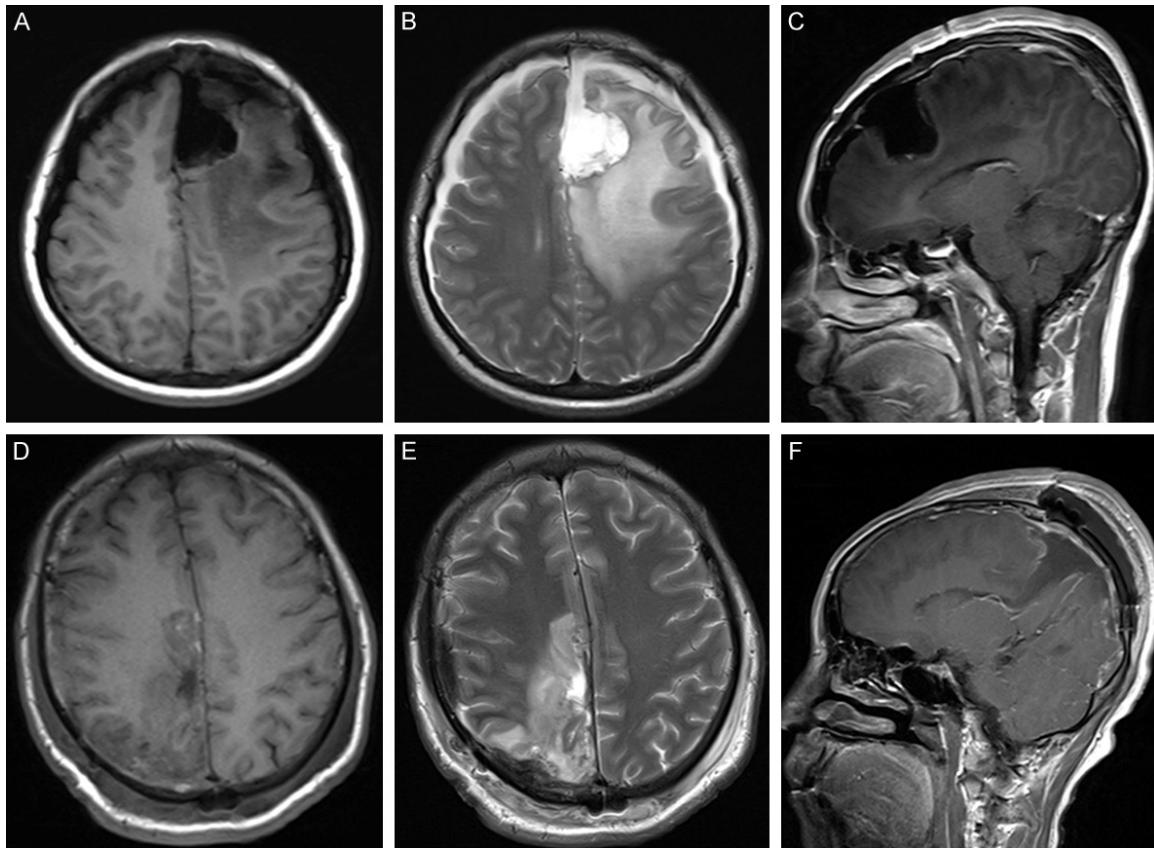


Figure 3. Postoperative MR images were acquired 72 hours after surgery, demonstrating that both tumors were totally removed. A-C. Axial T1-weighted image, axial T2-weighted image and sagittal T1-weighted image of the first patient, respectively. D-F. Axial T1-weighted image, axial T2-weighted image and sagittal T1-weighted image of the second patient.

ders (**Figure 1A, 1B**). T1-weighted image obtained after the administration of gadolinium showed relative well-distributed enhancement of the lesion. An axial T1-weighted image showed significant mass effect, midline shift, and compression to the cerebral falx and the lateral ventricle (**Figure 1C, 1D**). But dural tail sign was not observed. An axial T2-weighted showed marked edema surrounding the mass, especially in the back.

For case 2, MRI of the brain revealed a mass with relatively well-defined margins in the right occipital lobe. The lesion showed mixed low-isointensity on the T1-weighted image and iso-highintensity on the T2-weighted image (**Figure 2A, 2B**). The lesion was polycystic and protruded to the left side across the cerebral falx. T1-weighted image with contrast enhancement showed heterogeneous enhancement of the lesion (**Figure 2C, 2D**). Dural tail sign was not observed, neither. Edema around the lesion was remarkable.

Differential diagnosis

Both two young women have neither fever nor abnormal blood count recently that could exclude the possibility of infectious diseases. The chest X-ray and ultrasonic testing of uterus and bilateral breasts showed no evidence of lesions outside the brain, and then the metastatic tumor was excluded. The leading diagnosis of a primary intracranial tumor is the most probable choice. Human gliomas with a characteristic of infiltrating growth have no obvious boundary which was also excluded. All the proofs of contrast enhancement, clear boundary and peritumoral edema supported the diagnosis of meningioma except for negative dural tail sign. Previously, it was reported that no dural tail sign was present in 35-80% of patients with meningioma [7]. In addition, the appearance on imaging also makes CNS lymphoma and melanoma the possible diagnosis. The final diagnosis should be based on the pathological examination.

Primary intracranial benign fibrous histiocytoma

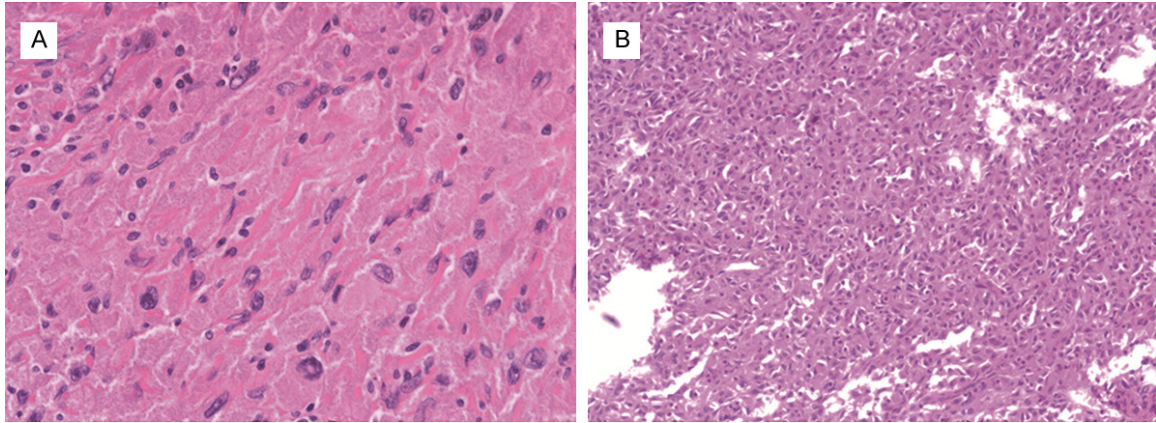


Figure 4. H&E-stained section showing pleomorphic histiocytoid neoplastic cells with spindly nuclei, arranged in streams or in a cartwheel fashion. A. H&E-staining $\times 400$. B. H&E staining $\times 40$.

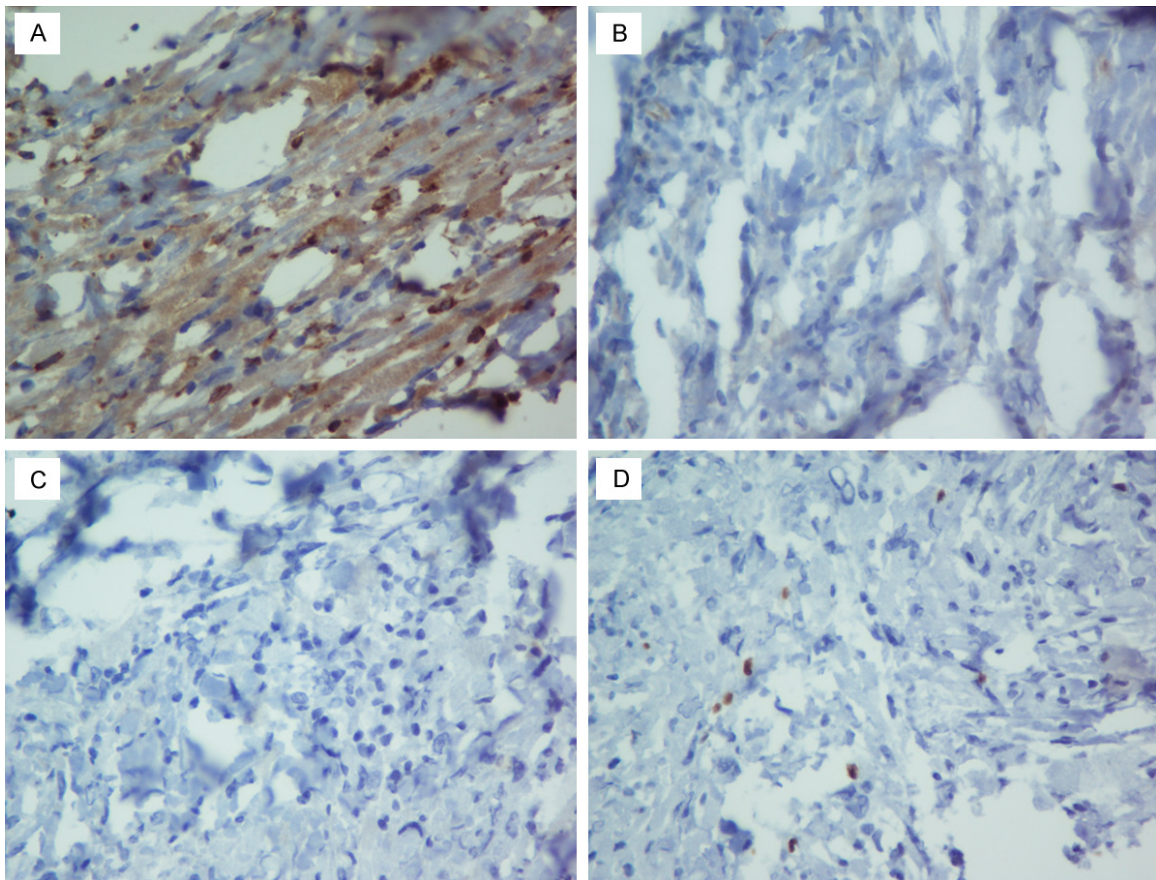


Figure 5. Immunohistochemical examination. A. Specimen strongly positive for CD68. B. Specimen positive for Nestin. C. Specimen weak positive for Ki-67. D. Specimen negative for EMA.

Neurosurgical intervention

Tumor resection was approached through left frontal and right occipital craniotomy for case 1 and 2, respectively. Up opening, grey and red,

solid tumors emerged partly under pressure. Both of the tumors were hard and tough in quality. Boundary between the tumor and the normal brain tissue was not very clear. Both tumors were quite vascularized with rich blood supply

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Table 1. Immunohistochemical results of case 1

Antigen	Intensity	Antigen	Intensity
GFAP	-	HMB-45	-
Vimentin	+/-	EMA	-
S-100	+/-	SOX-10	-
Nestin	+	CD163	+/-
CD68	+	Ki-67	<5%
PR	-	CK	-

“+” refers to positive reaction; “+/-”, weak positive; “-”, negative.

Table 2. Immunohistochemical results of case 2

Antigen	Intensity	Antigen	Intensity
GFAP	-	CD56	+/-
Vimentin	+	EMA	+/-
S-100	+/-	SOX-10	-
Nestin	+	CD34	+
CD68	+	Ki-67	<5%
CD31	+	CD1a	-

“+” refers to positive reaction; “+/-”, weak positive; “-”, negative.

from surrounding tissue but without obvious adhesion to the dura mater or cerebral falx. A distinct plane between the lesion and the brain was easily identified by color and texture, resulting in a gross total resection. Postoperative MRI demonstrated that two tumors were completely removed (**Figure 3A-C** for case 1; **Figure 3D-F** for case 2). Both patients had a good recovery after the surgical resection without neurological deficit.

Pathology

Hematoxylin-eosin staining for these two tumors was showed in **Figure 4**. Unfortunately, histopathological diagnosis of the tumor was still not very clear at the first time. Therefore, IHC staining corresponding to a serial of molecular markers were employed to further explore the nature of the tumors.

Further investigations showed that majority of tumor cells were randomly interspersed in collagenous fiber tissue (**Figure 5A**). The nucleus of these tumor cells was extremely irregular and atypical and many granular materials were scattered intracellularly. IHC staining revealed

the positive reaction for CD68 and Nestin (**Figure 5A, 5B**), weak positive for Vimentin, S-100 and Ki-67 (**Figure 5C**), negative for GFAP, PR, EMA (**Figure 5D**) and CK. Given the evidence of these molecular markers, the features were compatible with mesenchymal tumors, especially with tumors derived from fibrocytes. To eliminate the possibility of intracranial melanoma, SOX-10 and HMB-45 were stained and both were negative reaction in tumor specimens. The highest density of Ki-67 immunopositive nucleus was estimated to be <5%. The finally pathological diagnosis was intracranial benign fibrous histiocytoma which was confirmed by more than two independent neuropathologists.

Post-operative follow-up

The patients did not receive any adjuvant therapy and returned back to work consequentially. Both of these two patients were doing well without evidence of recurrence at follow-up of 24 months.

Discussion

Benign fibrous histiocytoma (BFH) was described as solitary tumor in dermis, soft tissue and bone. It occurs exceedingly rarely even in the skin. The prevalence of intracranial benign fibrous histiocytoma hasn't been reported up to date due to paucity of cases. BFH is mainly composed of two cell types, atypical fibroblasts and histocytes [8]. Histologically, benign or malignant fibrous histiocytomas (MFH) appear to be alike, belonging to “So-Called Fibrohistiocytic Tumors” according to World Health Organization (WHO) category.

The main tumor cells of intracranial BFH can also be seen in other tumors, such as pleomorphic xanthoastrocytoma and xanthomatous meningioma. Due to limited technical level of microscope and immunostaining in the past, BFH was commonly misclassified into other tumor types in the nervous system. Thus it is quite possible that there should be more cases of BFH, just concealed under a different diagnosis mistakenly.

These patients with intracranial FBH usually come to the doctor with the complaint of headache, seizure, vomiting, neurologic impairment or some other symptoms caused by intracranial

occupying effect and brain damage [2, 3, 8, 9]. Presentation of these symptoms is nonspecific and usually further verified by subsequent CT and MRI scan. In our present cases, MRI scan revealed a well-defined solid mass in one patient while a relatively fussy polycystic tumor in the other. In addition, after administration of gadolinium, the two tumors showed pretty different contrast-enhanced features. Therefore, the clinical manifestation of BFH varies greatly and the neuroradiological findings are always nonspecific, providing limited evidence to confirm the final diagnosis.

Conventional histopathological examination usually identified elongated neoplastic cells with spindly nuclei, arranged in a storiform pattern or in a cartwheel fashion (**Figure 4**). However, based on these histological features, we couldn't confirm the final diagnosis, failing to reach a final verdict between meningioma and fibrous histiocytoma. At present, the most practical method for distinguishing these similar tumors is immunohistochemistry (IHC). So the tumor specimens were detected by the immunostaining of several markers (**Tables 1 and 2**). Both histological specimens were evaluated by more than two independent pathologists.

Staining negative for GFAP excluded the possibility of tumors originated from glia such as pleomorphic xanthoastrocytoma [10]. For the xanthomatous meningioma, all tumor cells expressed Vimentin in their cytoplasm but in most fibrous histiocytoma, positive staining for EMA would be prevalent [11]. However, these tumors, including BFH, exhibit a very heterogeneous immunophenotype. Therefore, it is far from enough to distinguish these tumors from each other only depending on the markers of GFAP and EMA. Moreover, BFH is usually positive for CD68 which indicates a mesenchymal origin [12] and negative for S-100 and HMB-45. Although some of these tumor cells from the present cases were immunopositive for S-100, the majority of these cells showed no S-100 expression. In addition, the negative reaction of SOX-10 [13] helped to exclude the possibility of melanoma. Furthermore, considering the Ki-67 immunostaining with the highest density of less than 5%, the finally diagnosis of these two cases was intracranial benign fibrous histiocytoma.

Surgical resection is recommended for the treatment of these patients with intracranial benign fibrous histiocytoma, because removal of the lesion could reduce mass effect and intracranial pressure, leading to the clinical improvement. Furthermore, tumor specimen obtained by resection also provides materials for pathological detection, which will contribute to identifying the histopathological nature of these tumors.

Conclusions

In summary, intracranial BFH is extremely rare, especially in youths. Various imageological techniques including CT, MRI and even PET-CT, were utilized to identify the nature of this tumor. But the results were not very ideal. For final diagnosis, the histopathological examination coupled with immunohistochemical staining has proved to be a more straight-forward method. Surgical resection is the recommendation for the therapy of the tumor, and because of the benign biological behaviors, most patients would live a long survival postoperatively.

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Disclosure of conflict of interest

None.

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