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Cerebral Tufted Angioma with Gradually Developing Peritumoral Edema: A Case Report

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Abstract

Tufted angioma is a benign vascular tumor in which immature endothelial and pericyte cells and lymphatic vascular endothelium grow. It manifests as a flat, painful erythema that gradually expands mainly on the trunk and extremities. Although tufted angiomas can also occur in other areas of the body and may be more locally invasive, they rarely occur intracranially. A 63-year-old man underwent magnetic resonance imaging (MRI) for a brain check-up 8 years before his visit to our institute, which detected a mass lesion with surrounding cerebral edema in the left frontal lobe. The patient was followed up with annual MRI analysis, which indicated slow tumor growth and gradual development of peritumoral edema. The tumor was treated by gross-total resection. Histological analysis showed a slightly dilated microvascular core surrounded by many capillary aggregates in the brain parenchyma. Immunohistochemical findings indicated that the vascular endothelial cells were positive for CD34 and Brahma-related gene-1 and were surrounded by smooth muscle actin-positive pericytes. These findings were consistent with tufted angioma. Intracranial tufted angioma is uncommon, but it should be considered in the differential diagnosis for intracranial tumorous lesions. Long-term follow-up is necessary to unravel the natural history of the disease.

Keywords: tufted angioma, peritumoral edema, vascular tumor, Kasabach-Merritt phenomenon

Introduction

Tufted angioma consists of immature endothelial and pericyte cells and lymphatic vascular endothelium grow,[1,2] which is classified as a benign vascular tumor by the International Society for the Study of Vascular Anomalies classification.[3] This type of tumor is usually more prone to occur in infants than in adults, and is a flat, painful erythema that gradually expands and is located mainly on the trunk and extremities. Tufted angioma in infants can be classified into the following three types: uncomplicated, prolonged coagulopathy without thrombocytopenia, and complicated by Kasabach-Merritt phenomenon (KMP).[3-5] The cause of tufted angioma is unknown and it is not considered hereditary, although a familial variant has been reported.[6] About 10% of tufted angiomas resolve spontaneously; however, in most cases, they do not change or grow slowly.[7] In addition to the skin, the tumor can occur throughout the body, but it rarely occurs intracranially. To the best of our knowledge, there has been only one case report of intracranial tufted angioma.[8] Here, we describe another case of intracranial tufted angioma in the left frontal lobe without KMP complication, in which peritumoral edema gradually worsened concurrently with slow growth of the tumor.

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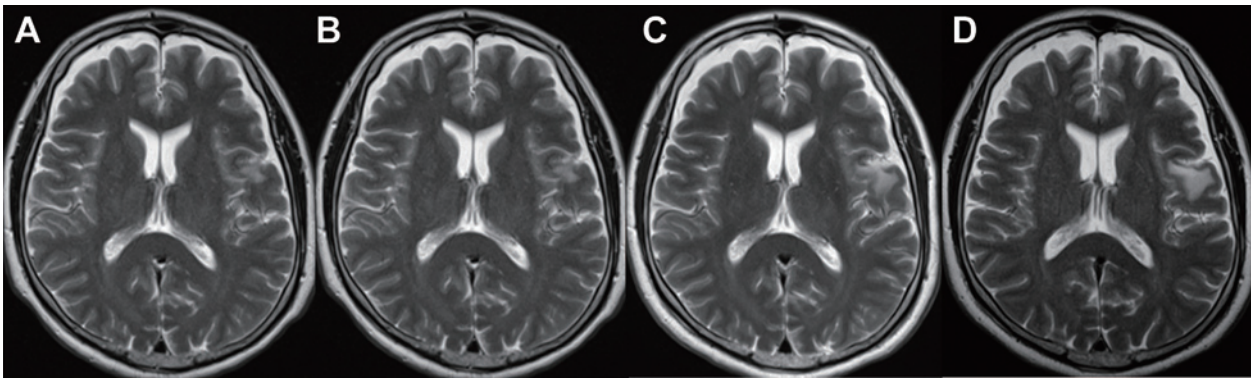

Fig. 1 Sequential magnetic resonance imaging (MRI) at initial diagnosis and before tumor resection.
T2-weighted MRI images: 8 years before (A), 6 years before (B), 2 years before (C), and immediately before surgery (D). The peritumoral edema showed gradual development concurrent with the slow growth of the tumor.

Case Report

A 63-year-old man, who had received medication for hypertension, underwent magnetic resonance imaging (MRI) for a brain check-up 8 years before his visit to our institute. The patient was found incidentally to have a mass lesion with surrounding cerebral edema in the left frontal lobe. The patient was followed up with annual MRI analyses, and the peritumoral edema showed gradual developing concurrently with slow growth of the tumor (Fig. 1). The patient had no family history of hereditary diseases or malignancies and no skin lesion. Blood analysis was normal, including normal platelet function.

Plain computed tomography (CT) of the head showed a low-density lesion in the cortical and subcortical areas of the left frontal lobe without bleeding or calcification (Fig. 2A). Post-contrast CT showed peripheral enhancement of the lesion (Fig. 2B). ^{18}F-fluorodeoxyglucose positron emission tomography showed no apparent accumulation in the lesion (Fig. 2C). T1-weighted images showed a hypointense tumor of 15 mm in diameter in the cortex of the left frontal lobe (Fig. 2D). Post-contrast T1-weighted images showed ring enhancement of the tumor (Fig. 2E). Fluid-attenuated inversion recovery images showed a hyperintense tumor with surrounding cerebral edema (Fig. 2F). Sagittal and coronal views of post-contrast T1-weighted images indicated that the tumor faced toward the sylvian fissure (Fig. 2G and H). There was no hyperintensity on diffusion-weighted images nor hypointensity on susceptibility-weighted images of the tumor. The initial differential diagnosis included lymphoma, brain metastasis, encephalitis, pilocytic astrocytoma, and high-grade glioma.

The patient underwent surgical resection of the tumor by awake craniotomy.[9] The tumor showed high neovascularization by draining of the red vein, which was hemorrhagic, elastic, and hard (Fig. 3). The brain parenchyma with edematous changes around the tumor was normal. The patient was discharged from the hospital on the 15th day after the surgery without any complications. No residual tumor was found in the postoperative MRI. No tumor recurrence has been identified 20 months after surgery.

Histological findings indicated that, in the parenchyma of the brain, a slightly dilated microvascular core was surrounded by many capillary aggregates. The vascular network was micronodular and had a glomerular-like structure. There were no atypical vascular endothelial cells, and no mitosis was observed. Immunohistochemical analysis showed that the vascular endothelial cells were positive for CD34 and were surrounded by smooth muscle actin-positive pericytes (Fig. 4). The Ki-67 labeling index was 5.8%. The histopathological features and immunohistochemical findings were compatible with tufted angioma.

Discussion

Although tufted angiomas can occur in any part of the body, they mainly affect soft tissues, such as the skin, and intracranial involvement is uncommon. Most cases (60%-70%) of tufted angioma develop before the age of 5 years, and fewer than 10% of cases with tufted angioma occur after the age of 50 years.[1,2] Therefore, our case is unusual because the tumor occurred intracranially and the patient was over the age of 50 years. To our knowledge, D'Amico et al. reported the first case of intracranial tufted angioma,[8] and interestingly, both the clinical and imaging features of this case were similar to our case. For instance, both the patients were in their 60s and both had MRI scans showing a contrast-enhancing small lesion within the gray matter of the frontal cortex that was associated with peritumoral edema of white matter.[8]

Histologically, tufted angiomas present as characteristic dense clumps and lobules of endothelial cells, and capillaries can be observed in capillary hemangiomas and crystalline lamellae.[10] Previously, tufted angioma was known as "angioblastoma of Nakagawa".[3,5] This tumor is not cancerous, but it can be locally aggressive. To our knowledge,

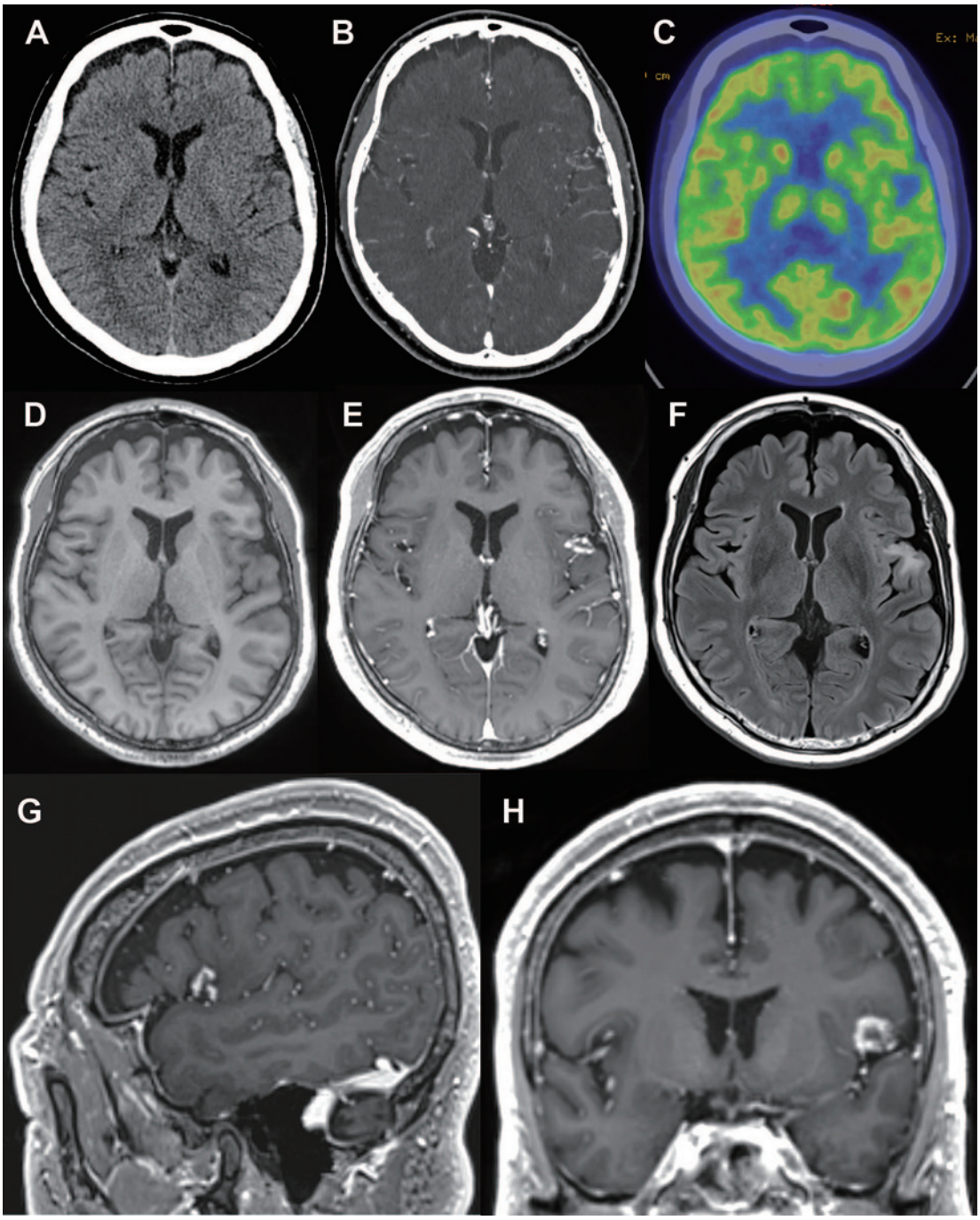

Fig. 2 Diagnostic image examinations before tumor resection.
A: Plain computed tomography (CT) showed a low-density lesion in the cortical and subcortical areas of the left frontal lobe without bleeding or calcification. B: Post-contrast CT showed peripheral enhancement of the lesion. C: ^{18}F-fluorodeoxyglucose positron emission tomography showed no apparent accumulation in the lesion. D: T1-weighted images showed a hypointense tumor (15 mm in diameter) in the cortex of the left frontal lobe. E: Post-contrast T1-weighted images showed ring enhancement of the tumor. F: Fluid-attenuated inversion recover images showed a hyperintense tumor with surrounding cerebral edema. G, H: Sagittal and coronal views of post-contrast T1-weighted images showed the tumor facing toward the sylvian fissure.

there have been only two cases of intracranial tufted angioma, including our case; however, both showed a high Ki-67-labeling index, although elevated proliferative indices are not uncommon in tufted angioma. The case reported by D'Amico et al. had a Ki-67 index that ranged from 9.5% to 25.6%, whereas our case had an index of 5.8%. The for-

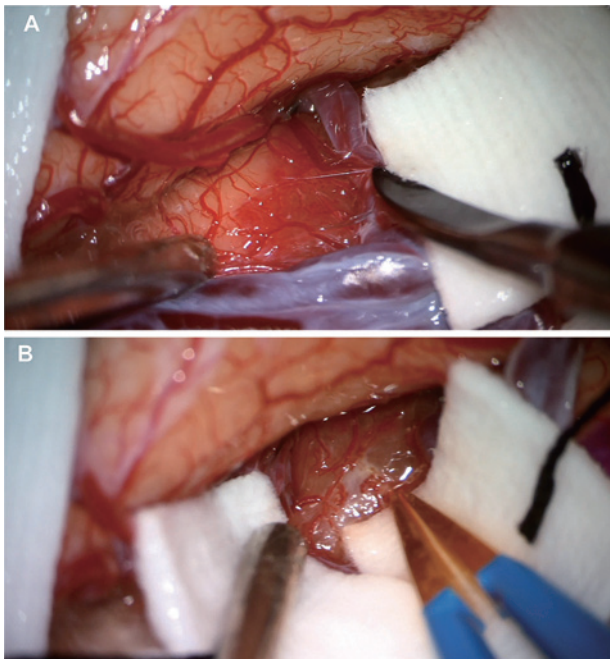

Fig. 3 Macroscopic images of the tumor.
A: A view of the tumor boundary showed that it occurred in the cortex. B: A view of the tumor showed that it had a brown jelly-like consistency with vascular formations.

mer case showed tumor recurrence, which was treated with Gamma Knife surgery. Although our patient had no tumor recurrence, tumor growth was observed prior to surgery. Because the natural history of the tumor remains unknown, follow-up examination is necessary to determine tumor recurrence.[8)]

Tufted angioma is considered to be closely related to kaposiform hemangioendothelioma. These conditions have been reported to have similar gene methylation profilings, pathological processes,[11)] and expression of *Prospero Homeobox 1*.[12)] A familial occurrence of tufted angioma has also been reported that suggested the involvement of the *kinase insert domain receptor*, *endoglin*, and *fms-like tyrosine kinase 4* genes.[6,13)] A somatic mutation in *G Protein Subunit Alpha 14* was reported in a case of tufted angioma with KMP.[14)] Genetic mutations were not examined in our case; however, genetic analysis could help understand the pathophysiology of tufted angioma in the brain.

Tufted angioma is a benign lesion that usually progresses slowly over a period of months to years. Most cases are asymptomatic, but a serious complication called KMP develops in about 10% of infant cases.[4,15)] The pathogenesis of KMP is that the local consumption of platelets and clotting factors in the lesions of kaposiform hemangioma and tufted angioma causes a tendency for systemic

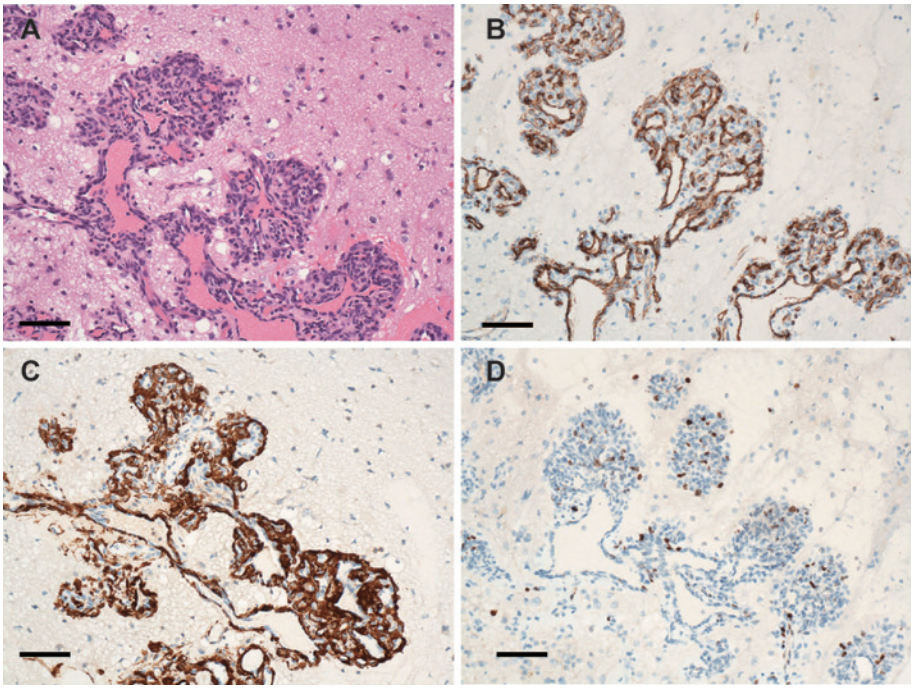

Fig. 4 Histopathological examination of the resected tumor.
A: The tumor showed a slightly dilated microvascular core surrounded by many capillary aggregates in the parenchyma of the brain (hematoxylin and eosin staining, original magnification ×20). The vascular network was micronodular and had a glomerular-like structure. We found no atypical vascular endothelial cells and no mitosis was observed. B–D: Immunohistochemical analysis showed that the vascular endothelial cells were positive for CD34 (B, CD34 staining, original magnification ×20) and were surrounded by smooth muscle actin-positive pericytes (C, smooth muscle actin staining, original magnification ×20). D: Ki-67 labeling index showed a cell proliferative potential of 5.8% (Ki-67 staining, original magnification ×20).

bleeding and coagulation disorders.[15,16] If KMP develops, the tumor grows rapidly, becomes painful, and the appearance changes to purple or brownish-red and spotty, caused by subcutaneous bleeding.[4] Neither our case nor the previous intracranial case reported by D'Amico et al. was complicated by laboratory abnormalities, such as thrombocytopenia or coagulation abnormalities.[8]

The initial treatment for intracranial tufted angioma is surgical resection. However, the appropriate treatment for recurrent tumors has not been determined. D'Amico et al. used Gamma Knife radiosurgery for treatment of a recurrent tumor, which was successful.[8] Other options include vincristine,[17,18] immunosuppressive agents,[19] or re-operation, all of which can be applied for tufted angioma in soft tissue. If the tufted angioma is complicated by KMP and the clotting problem is severe, intravenous transfusion of clotting factors may be performed to improve blood clotting and to add to drug therapy.[20]

Conclusions

The intracranial occurrence of tufted angioma is uncommon, and its natural history is unknown. Therefore, tumor recurrence and KMP complication in patients with tufted angioma should be carefully monitored.

Acknowledgments

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List of Abbreviations

CT: computed tomography, KMP: Kasabach-Merritt phenomenon, MRI: magnetic resonance imaging

Ethics Approval and Consent to Participate

This report was carried out in accordance with the principles of the Declaration of Helsinki and its later amendments. This study was approved by the institutional review board of the Kyoto University Hospital (approval number: R2088-3).

Conflicts of Interest Disclosure

All authors have no conflict of interest to declare.

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