Glioblastoma Multiforme Associated with Arteriovenous Malformation: A Case Report and Literature Review

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Abstract

Although microvascular proliferation can be observed in glioblastoma, obvious vascularity coupled with coexisting cerebral arteriovenous malformation (AVM) is extremely rare. This report is of a rare case of glioblastoma, coexisting with a cerebral AVM. A 20-year-old male presented with progressive right hemiparesis within 1 month. Cranial magnetic resonance imaging revealed a large bleeding tumor with surrounding dilated vessels. Cerebral angiography demonstrated a left frontal AVM with a 1.2 cm nidus. The patient underwent preoperative embolization and radical resection. The coincidence of glioma and AVM was a rare association. However, the concept of hypervascular glioblastoma has been used in different states from different literature reviews; therefore, the role of proangiogenic factors should be addressed.

Keywords: Angioglioma, arteriovenous malformation, glioblastoma, hypervascular glioblastoma

Introduction

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumors in adults. Although microvascular endothelial proliferation is one of the criteria for a histological diagnosis, grossly hypervascular glioblastoma is an unusual manifestation. The authors described a patient, who suffered from a combination between glioblastoma and cerebral arteriovenous malformation (AVM). This case also highlights the rare angiomatous manifestation of glioblastoma.

Case Report

A 20-year-old male developed progressive right hemiparesis on the right side within 1 month. Cranial magnetic resonance imaging (MRI) scans demonstrated a heterogeneously enhancing mass, 5.5 cm × 8 cm in size, with internal hemorrhage at the left frontal lobe. In addition, surrounding dilated arteries and veins at the adjacent cortex were noted on T1-weighted with gadolinium. On cranial computed tomography, the dense calcification located an inferior portion of the mass. Cranial magnetic resonance angiography revealed dilated peripheral branches of the anterior cerebral artery and middle cerebral artery (MCA) with dilated cortical veins [Figure 1a-d].

Moreover, a cerebral angiographic study revealed a nidus, approximately 1.2 cm wide in the subcortical region of the left precentral sulcus. This was fed from the distal branches of the left precentral artery and anterior parietal artery of the left MCA. The flow drained into a single cortical vein to the superior sagittal sinus [Figure 2a and b].

A preoperative embolization was performed for reducing blood loss during surgery before a craniotomy. Intraoperative findings revealed a well-defined, reddish tumor with obvious abnormal vessels occupying both superficial and deep portions of the tumor. Interestingly, the hypervascular tumor was toughly attached with dura. The tumor was completely removed.

Pathologic examination

Gross characteristics of the tumor were extra-axial mass, reddish-gray color, dural attachment, firm-solid consistency, and fed from multiple dilated arteries. In addition, calcification was observed at the inferior portion of the tumor. Therefore, the gross features mimic meningioma [Figure 3a-c].

A histopathological examination demonstrated nuclear polymorphism astrocytes and necrosis without sarcomatous spindle morphology. Therefore, gliosarcoma was excluded. The tumor was composed of numerous enlarged blood vessels of varying sizes, and dural morphology was normal. Finally, the diagnosis was glioblastoma associated with AVM [Figure 4a-d].

After tumor resection, the patient received postoperative adjuvant radiation. Six months after the first operation, the patient presented with alteration of consciousness and tumor recurrence was observed by neuroimaging. Due to these factors, he then underwent the second operation. Postoperatively, his consciousness improved, but tumor regrowth occurred, again, 1 year later, after the second

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operation. His family refused the third operation, and subsequently, he died in 2 years after the first operation.

Discussion

Glioblastoma is an aggressive primary brain tumor that has composites of necrosis and microscopic endothelial proliferation.[1] The term "angioglioma" had been used in glioma associated with various vascular abnormalities; however, this term was primarily defined by Russell and Rubinstein, who described angioglioma from patients with the cystic cerebellar tumors with coexisting glioma and hemangioblastoma.[2] Hence, the authors reviewed literature using the keywords such as "angioglioma," "glioblastoma AND arteriovenous malformation," "hypervascular glioma," "glioma AND arteriovenous malformation," and "vascular malformation AND glioma." We excluded "angiocentric glioma," because this entity is a distinct group of epileptogenic tumors, according to the 2016 WHO classification of tumors of the central nervous system. As a result, the cases are summarized in Supplementary Table 1. Histopathology of angiocentric glioma demonstrated spindled cells forming occasionally perivascular pseudorosettes.[3]

Form the literature review, the coexistence of glioma and vascular malformation is a rare entity. To the best of the authors' knowledge, at least 67 cases have been described before this present case. From Table 1, hypervascular gliomas are common in males (55.9%) and the distribution of age is between 2 and 72 years (mean age was 35 years).[2,4-31] In vascular malformation, AVM is the common coexisting vascular malformation. Using cerebral angiography, high blood flow passes through the arteriovenous shunt.[4,5,9,10,11,16-19,21-27,30] In addition, various tumors have been reported as having the coexistence of glial

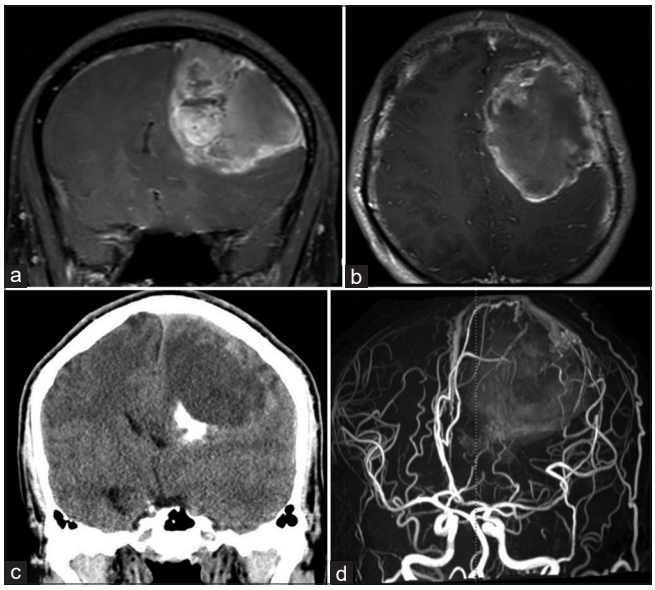

Figure 1: Preoperative neuroimaging. (a) T1-weighted coronal (b) and T1-weighted axial images with gadolinium administration demonstrated a large left frontal mass with flow void signs. (c) Cranial computed tomography revealed calcification at the inferior portion of the mass. (d) Cranial magnetic resonance angiography revealed multiple dilated vessels surrounding the tumor

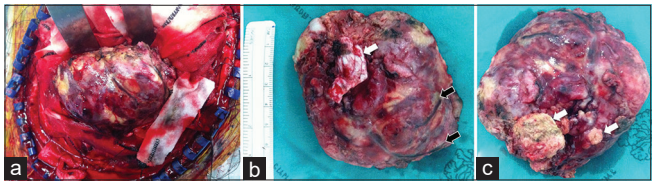

Figure 3: Gross appearance of the tumor. (a) Extra-axial mass was observed in the operative field. (b) The superior aspect of the tumor could be observed, the tumor attached dura matter (white arrow), and multiple feeding arteries (black arrow) were around the tumor. (c) The inferior aspect of the tumor could be observed, dense calcification (white arrow)

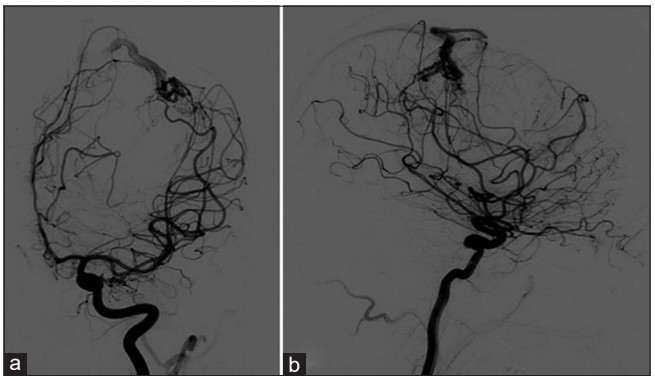

Figure 2: Preoperative cerebral angiography. (a) Anterior-posterior view and (b) lateral view showed a nidus in the subcortical region of the left frontal lobe. It was supplied by distal branches of the left precentral artery and anterior parietal artery of the left middle cerebral artery. The venous drainage was to the cortical vein to the superior sagittal sinus

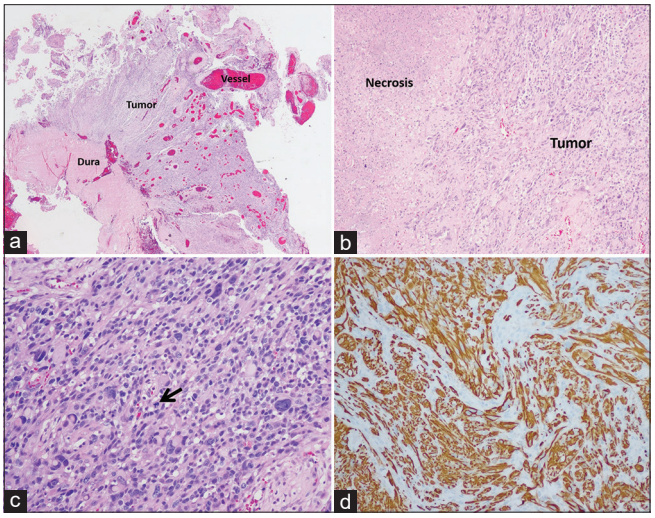

Figure 4: Histological examination of the tumor. (a) Tumor attached normal dura matter and numerous blood vessels in varying sizes were within the tumor. (b) The necrotic area was observed. (c) The neoplastic glial cells had nuclear enlargement with hyperchromatic nuclei, and irregular nuclear membrane and mitotic activity could be observed (black arrow). (d) Immunoreactivity of the tumor was positive for GFAP

cell tumors as well as other various tumors, either vascular tumor (cavernous, capillary hemangioma)[6,8,12,14,15,20] or other hypervascular tumors (hemangioblastoma).[2,7,32]

These coexistences have been found in both low-grade and high-grade gliomas. The common glial cell tumors are GBM, pilocytic astrocytoma, and oligodendroglioma. In histological features, GBMs usually found endothelial cell proliferation and glomeruloid appearance while pilocytic astrocytoma and oligodendroglioma found other characteristics of abnormal vessel pattern. Hyalinized and glomeruloid vessels could be prominent features in pilocytic astrocytoma whereas oligodendroglioma typically shows a dense network of branching capillaries resembling the pattern of chicken wire.[1] However, the overexpression of proteins of tumor angiogenesis pathway is proposed in the hypothesis of the pathophysiology of this coexistence.

Upregulation of angiogenetic-driven events has been hypothesized that induced abnormal vasculatures in hypervascular glioma.[33] C-X-C chemokine receptor type 4 (CXCR4) is a chemokine receptor for C-X-C motif chemokine ligand 12 (CXCL12) that is associated with angiogenesis and tumor progression. The receptors are upregulated by hypoxia-inducible factor-1 (HIF-1) and vascular endothelial growth factors (VEGFs). Reactivity of the HIF-1α subunit and VEGF was highly expressed in pseudopalisading tumor cells adjacent to necrosis. However, a high VEGF expression and overexpression of CXCL12-CXCR4 axis were observed in angiogenic vessels.[23,34]

In vascular malformation, it has been shown that VEGF expression is a fundamental part of intracerebral AVM pathogenesis. VEGF levels are increased in intracerebral AVM.[35] Upcoming molecular research should be studied to demonstrate the common angiogenetic-driven mechanisms between coexisting lesions. As the results, hypervascular glioma is the presence of dark vessel-like signals (flow void signs) on T2-weighted imaging located within the tumor. These represented the prominent serpiginous vessels.[21] Moreover, the histopathologic characteristics reveal clusters of numerous blood vessels of various size.[14]

As for the treatment strategy, radical resection is the treatment of choice in hypervascular glioma, but these tumors are challenging for total tumor resection. Unfortunately, significant intratumoral hemorrhage frequently occurs in this tumor. Emergency decompressive craniectomy with/without lesionectomy should be performed for saving of life. However, the risk of enormous bleeding during surgery has to be considered. Hence, in elective conditions, preoperative endovascular embolization is an alternative method for reducing blood loss, when the tumor is resected. Imai *et al*. proposed preoperative embolization as a strategy that tumors which located in eloquent areas need provocation testing beforehand. Presurgical embolization for tumor feeder vessels is recommended in negative provocation testing.[27]

Conclusions

We described a rare manifestation of GBM. Proangiogenic factors are most likely involved in the existence of both entities at the same location. Future molecular studies may reveal a common genetic pathway to explain this association. Surgical treatment is challenging due to the risk of massive intraoperative bleeding. Preoperative endovascular embolizations are alternative methods for controlling intraoperative blood loss.

What is already known on this topic?

GBM is the most common primary malignancy of the brain in adults. One of the histological characteristics involves microvascular proliferation such as endothelial proliferation and glomeruloid appearance.

What does this study add?

This case report demonstrated the rare coexistence between GBM and cerebral AVM. The hypothesis of pathophysiology is overexpression of proteins of tumor angiogenesis pathway.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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