

Glioma coexisting with angiographically occult cerebrovascular malformation: A case report

JUNHUI CHEN, LEI CHEN, CHUNLEI ZHANG, JIANQING HE, PEIPEI LI,
JINGXU ZHOU, JUN ZHU and YUHAI WANG

Department of Neurosurgery, 101st Hospital of People's Liberation Army, Wuxi, Jiangsu 214044, P.R. China

Received March 15, 2015; Accepted May 17, 2016

DOI: 10.3892/ol.2016.4916

Abstract. Angiographically occult cerebrovascular malformation (AOVM) is a type of complex cerebrovascular malformation that is not visible on digital subtraction angiography (DSA). Vascular malformation coexisting with glioma is clinically rare, and glioma coexisting with AOVM is even more rare. To the best of our knowledge, the present study is the first to report glioma coexisting with AOVM in the literature. The present study reports a rare case of glioma coexisting with AOVM in a 30-year-old male patient. Computed tomography (CT) scan revealed calcification, hemorrhage and edema in the right frontal lobe. CT angiography revealed a vascular malformation in the right frontal lobe, which was not observed on DSA. Finally, glioma coexisting with AOVM was confirmed by 2.0T magnetic resonance imaging and postoperative pathological examination. The present patient had a positive outcome and no neurological dysfunctions during the 6-month follow-up subsequent to surgery.

Introduction

Gliomas, as brain intrinsic neoplasms, are the most common primary brain tumors in adults, and are classified by the World Health Organization into four malignancy grades (I-IV) (1,2). When visualized using computed tomography (CT) or magnetic resonance image (MRI), glioma may appear as a solid or cystic lesion with an unclear boundary. The lesions are clearly enhanced on contrast enhanced CT or MRI scans (3). Glioma coexisting with cerebrovascular malformation in the brain is rare, with only a few cases reported in the literature at present (4-7). Angiographically occult cerebrovascular malfor-

mation (AOVM) is a small vascular malformation that is not visible on digital subtraction angiography (DSA). It comprises cavernous hemangioma, arteriovenous malformation (AVM), intravenous vascular malformation and capillary expansion. There may be no obvious symptoms of AOVM until hemorrhage occurs. Diagnosis of AOVM is difficult, but MRI may be considered as the first choice of diagnostic method, as it is superior to CT or DSA (8-11). This superiority is due to a number of reasons: MRI is able to show lesions more clearly compared with CT or DSA; MRI is able to more specifically identify AOVM compared with CT and DSA; MRI results may allow collection of data that can contribute to the surgical strategy; MRI allows visualization of the association between the AOVM and adjacent brain tissues; MRI allows clearer visualization of the feeding and draining arteries, compared with CT and DSA; and MRI is able to identify smaller AOVMs more easily than CT and DSA.

As its incidence is low and diagnosis is challenging, the diagnosis of glioma coexisting with AOVM is rare and has been reported in extremely few cases in the literature (4,5,12-14). Cemil *et al* (4) reported the case of a 58-year-old man presenting with sudden development of severe headache and vomiting, who was subsequently diagnosed with glioblastoma multiforme combined with arteriovenous malformation following MRI examination. Misdiagnosis and missed diagnosis are common in cases of glioma coexisting with AOVM, which can sometimes lead to unfavorable surgical outcomes. The present study reports a rare case of glioma coexisting with AOVM, in order to improve the understanding of this disease and prevent missed diagnosis and misdiagnosis.

Case report

A 30-year-old man presented in November 2014 as Huishan People's Hospital (Wuxi, China), with a sudden syncope and aphasia, with the symptoms gradually deteriorating over a 3-h period. The patient had no medical history of trauma, hypertension or any other condition. CT scans performed at the local community hospital (Huishan People's Hospital, Wuxi, China) revealed a calcified, edematous, minimal subarachnoid hemorrhage in the right frontal lobe. The patient was then referred to the 101st Hospital of People's Liberation Army (Wuxi, China) within 3 h of the original presentation, where physical examination and routine blood tests were performed, with normal

Correspondence to: Dr Yuhai Wang, Department of Neurosurgery, 101st Hospital of People's Liberation Army, 101 North Xingyuan Road, Wuxi, Jiangsu 214044, P.R. China
E-mail: wangyuhai67@126.com

Key words: angiographically occult cerebrovascular malformation, glioma, digital subtraction angiography, magnetic resonance imaging

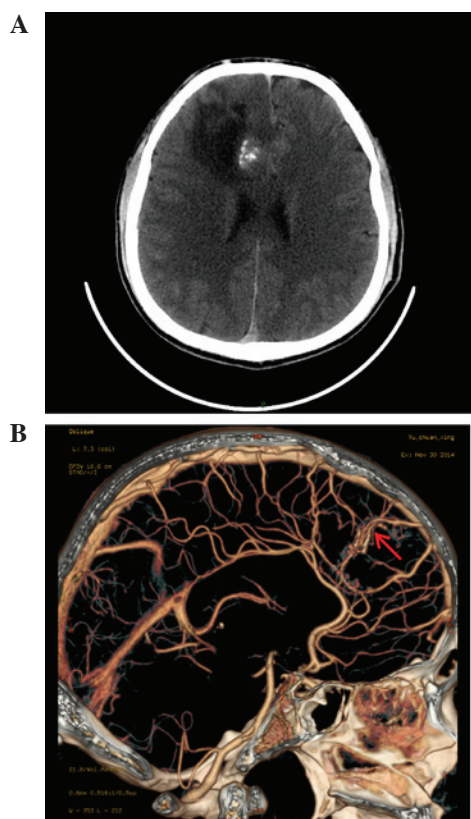


Figure 1. Preoperative imaging examinations. (A) CT scan revealed a right temporal lesion with a calcified shadow and edema. (B) CT angiography indicated arteriovenous malformation (arrows) on the pericallosal anterior cerebral artery. CT, computed tomography.

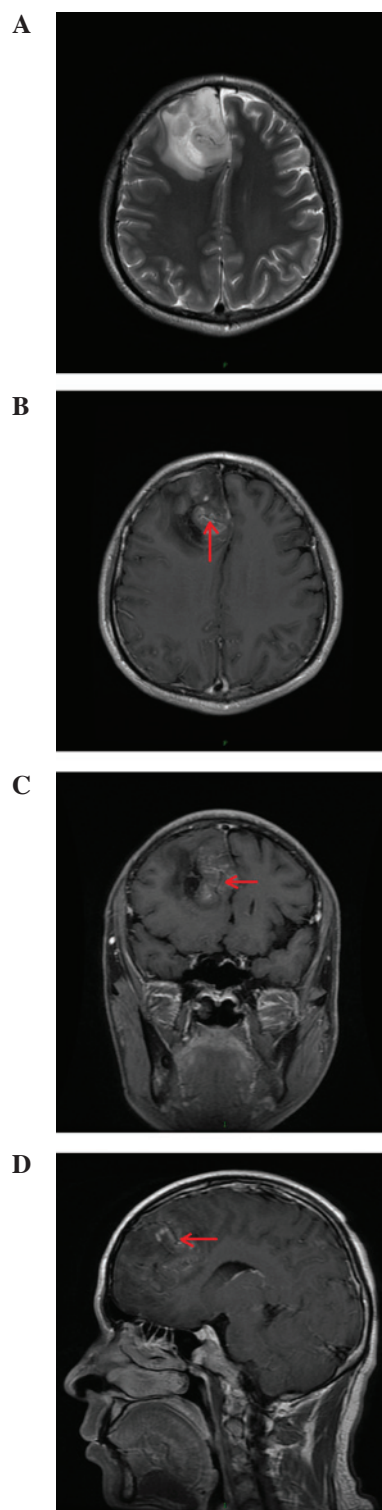


Figure 3. Preoperative magnetic resonance imaging scan demonstrating (A) a right temporal lesion with edema and distinct vessels centrally in axial T2-weighted imaging and (B-D) a 5.8x5.2x6.0 cm mixed density lesion and signal void with caput medusae-like vessels in the tumor in (B) axial, (C) coronal and (D) sagittal T1-weighted imaging.

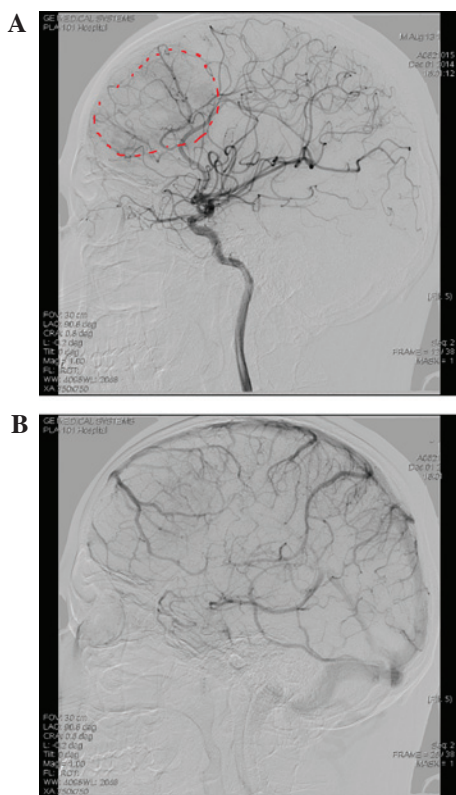


Figure 2. (A and B) Preoperative digital subtraction angiography demonstrated no arteriovenous malformation, but (A) revealed an area of abnormal staining (dotted circle). (B) This abnormal staining also can be observed in venous phase.

results. CT scans revealed a large area of edema and calcification in the right frontal lobe; however, no subarachnoid hemorrhage was observed in that area (Fig. 1A). Due to the similar radiologic characteristics on CT angiography (CTA) to cerebrovascular malformation, a cerebrovascular malformation in the right frontal lobe was suspected (Fig. 1B). However,

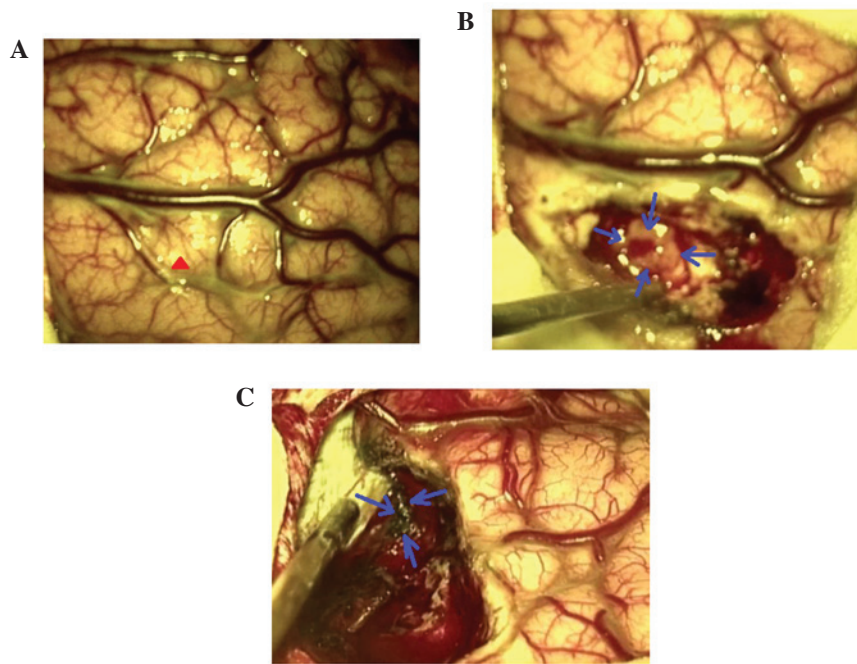


Figure 4. Intraoperative images. (A) The red triangle indicates the incision location in the cortex. The blue arrows indicate (B) the tumor, which has a rich blood supply, and (C) the angiographically occult cerebrovascular malformation.

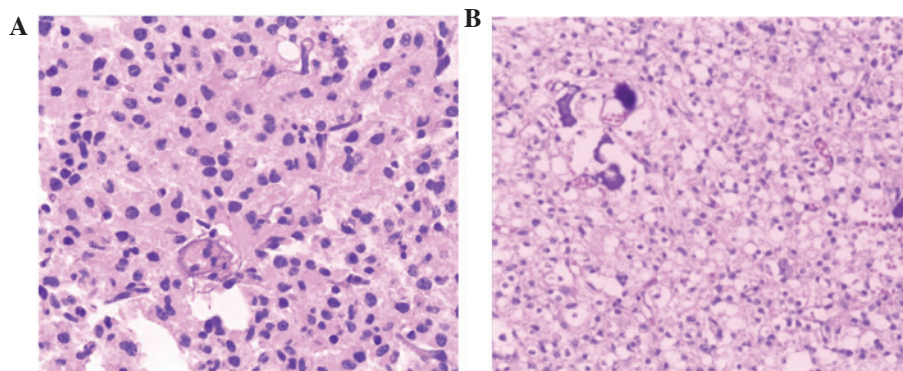


Figure 5. Histopathological examination showing (A) glioma (WHO TNM classification II; magnification, x1000), and (B) abnormal, tortuously distributed vessels, a feature of angiographically occult cerebrovascular malformation (magnification, x50).

abnormal cerebrovascular malformation was not observed at the arterial and venous phases during DSA, but an abnormally stained area was revealed following injection of contrast medium (Fig. 2A and B), which indicated the presence of abnormal tissue. MRI examination assessment by T1-weight (T1W), gradient-echo T2 (T2) and dynamic contrast-enhanced MRI revealed mixed signals with long T1 and long T2 signals, and a 5.8x5.2x6.0-cm cystic and necrotic lesion with no clear margin in the right frontal lobe. The lesion also exhibited dark signals similar to caput medusae on T2W images. In addition, an edema belt (Fig. 3A-D) around the lesion was observed. Thus, MRI confirmed the prediction that the lesion was a glioma with coexistence of a cerebrovascular malformation.

The negative DSA result led to an initial misdiagnosis and missed diagnosis. The bleeding, calcification and brain edema found on CT examination had indicated that an AVM was most likely, and the CTA appeared to confirm this. However, the gold-standard DSA examination did not confirm the diagnosis

of an AVM. In order to help explain this inconsistency, MRI was performed which found an AVM and a brain tumor; this explained the calcification and brain edema identified by the CT scans. It also explained the sole finding of an AVM by CTA and the abnormal staining on the DSA. In combination, these examinations provided the best interpretation of the results.

Following adequate imaging examination, as detailed above, physician-patient communication and academic discussion, surgery was performed. Following the administration of tracheal intubation and general anesthesia, the patient underwent right frontotemporal craniotomy (longitudinal fissure + pterion). The cerebral cortex was incised between the frontotemporal and middle frontal veins (Fig. 4A). A diseased tissue and abnormal honeycomb mass, 5x3x4-cm in size, was removed piece by piece (Fig. 4B). Frontotemporal craniotomy was closed after achieving a good haemostasis. A postoperative CT scan revealed no hemorrhagic complications and the patient was sent to the neurosurgery intensive-care unit.

Following removal of the lesion from the patient, the tumor was immediately fixed in neutral formalin liquid, followed by embedding in paraffin 24 h later. The tissue was sliced into 2 mm specimens and stained with hematoxylin and eosin. Stained tumor samples were observed under a light microscope (Olympus Corporation, Tokyo, Japan).

The patient received general treatment (0.4 g/day aminomethylbenzoic acid injection; 60 mg/day lansoprazole injection; 30 mg/day nimodipine injection; 1200 mg/day sodium valproate injection; 6 g/day piperacillin-sulbactam; 500 ml/day glucose injection) for 10 days, and was subsequently discharged 10 days after surgery without complications. MRI scan performed at the 6-month follow-up showed that the diseased lesion had been completely removed.

Postoperative histopathological examination revealed that glioma cells and Nidus confirmed an AOVN coexisting with glioma (Fig. 5).

Discussion

Glioma coexisting with AVM are rare, and as AOVN has a high rate of missed diagnosis and misdiagnosis, glioma coexisting with AOVN simultaneously in the same location are extremely rare in the clinic. Certain studies have suggested that the occurrence of two lesions within the same tissue may be coincidental (12,13,15). Other studies have reported that two lesions may be preoperatively diagnosed as one (4,14). This was the case in the present study, where the patient was initially diagnosed with AVM by CT and CTA. Intraoperative and histopathological examination finally confirmed the additional presence of the glioma, co-occurring with AOVN.

Other studies did not regard the coexistence of the two lesions as fortuitous, and it was suggested that the lesions had an effect on one another (4,5,16). Harris *et al* (16) reported that glioblastoma multiforme can improve the overexpression of vascular endothelial growth factor (VEGF); however, the expression of VEGF was high in the endothelial layer and media of AVM vessels (17). VEGF can promote growth of endothelial cells of blood vessels and the glioma cells can promote growth, migration and tubular formation of endothelial cells. VEGF plasma concentrations were significantly higher in patients with cerebral AVMs compared to a healthy control group (18). Zuccarello *et al* (19) observed notable glial cell proliferation around the AVM and large glial cells gathered among abnormal blood vessels.

The wide clinical use of CT, MRI and DSA may markedly improve the accuracy in the diagnosis of intracranial tumors and cerebrovascular disease. However, the incidence of missed diagnosis and misdiagnosis in the two diseases coexisting in the same lesion remains high, particularly in combination with AOVN. Despite DSA being considered the gold standard for the diagnosis of AVM, certain AOVNs cannot be found, which may lead to frequent misdiagnosis. Possible reasons for misdiagnosis include: i) Compression and destruction of blood vessels by tumor tissue, hematoma and edema, resulting in a lack of blood flow and vascular occlusion occurs at early time; ii) cerebral vasospasm or thrombus after bleeding caused by blood vessels in AVM; and iii) failure of DSA to detect the afferent arteries of AVM, due to their very fine nature; iv) small size meaning that the AVM is not identified by CT or DSA (20,21).

In the present case, CTA revealed a suspicious cerebrovascular malformation, but DSA examination was negative, which resulted in preoperative diagnosis being challenging. MRI confirmed AVM coexisting with GBM preoperatively, which was also confirmed by postoperative histopathological examination. MRI plays an important role in the diagnosis of intracranial tumors coexisting with AOVN, as it not only shows the size, boundary and blood supply of the tumor clearly, but may also provide an important diagnostic basis, as its special 'flow-empty actions'; as the blood flows very fast, this leads to the MR signal being produced a distance away from the reception range, meaning that no MR signal is produced (22). In addition, it is important that MR angiography (MRA) and MR venography (MRV) may clearly reveal the feeding arteries and drainage venous of AVM, which is valuable for surgery. Therefore, MRI, MRA and MRV should be performed in case of doubt or inconsistencies in CTA or DSA preoperative results.

Microsurgical treatment is considered the best treatment for glioma coexisting with AOVN (12,13). Both lesions should be removed through the same incision, unless they are in different sites. The more dangerous lesion of the two should be removed first to avoid intraoperative bleeding. In the present case, the glioma was concluded to be more dangerous than the AOVN, and thus was removed first. A definite preoperative diagnosis is key to the success of the surgery.

In conclusion, the present study reported an extremely rare case of glioma coexisting with AOVN. The imaging features of the disease, as detected by CT, CTA, DSA and MRI, that aided with the challenging diagnosis were described. Based on the findings of the present study, if CTA suggests cerebrovascular malformation AOVN should be considered, even if the DSA examination result is negative. MRI plays an important role in the diagnosis of combined lesions. When possible, complete microsurgical resection of those lesions is the best choice. Adequate preoperative imaging evaluation is key to the success of the surgery.

Acknowledgements

The authors would like to thank Yuan Gao (College of Life Science, University of Science and Technology of China, Hefei, China) for technical and language assistance.

References

- DeAngelis LM: Brain tumors. *N Engl J Med* 344: 114-123, 2001.
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW and Kleihues P: The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 114: 97-109, 2007.
- Ricard D, Idhah A, Ducray F, Lahutte M, Hoang-Xuan K and Delattre JY: Primary brain tumours in adults. *Lancet* 379: 1984-96, 2012.
- Cemil B, Tun K, Polat O, Ozen O and Kaptanoglu E: Glioblastoma multiforme mimicking arteriovenous malformation. *Turk Neurosurg* 19: 433-436, 2009.
- Aucourt J, Jissendi P, Kerdraon O and Baroncini M: Neuroimaging features and pathology of mixed glioblastoma-AVM complex: A case report. *J Neuroradiol* 39: 258-262, 2012.
- McKinney JS, Steineke T, Nochlin D and Brisman JL: De novo formation of large arteriovenous shunting and a vascular nidus mimicking an arteriovenous malformation within an anaplastic oligodendroglioma: Treatment with embolization and resection. *J Neurosurg* 109: 1098-1102, 2008.

7. Foy PM, Lozada L and Shaw MD: Vascular malformation simulating a glioma on computerized tomography: Case report. *J Neurosurg* 54: 125-127, 1981.
8. Lee BC, Vo KD, Kido DK, Mukherjee P, Reichenbach J, Lin W, Yoon MS and Haacke M: MR high-resolution blood oxygenation level-dependent venography of occult (low-flow) vascular lesions. *AJNR Am J Neuroradiol* 20: 1239-1242, 1999.
9. Russell DS and Rubinstein LJ (eds). *Pathology of tumors of the nervous system*. 3rd edition. William & Wilkins, Baltimore, pp93, 1971.
10. Ogilvy CS, Heros RC, Ojemann RG and New PF: Angiographically occult arteriovenous malformations. *J Neurosurg* 69: 350-355, 1988.
11. Lobato RD, Perez C, Rivas JJ and Cordobes F: Clinical, radiological, and pathological spectrum of angiographically occult intracranial vascular malformations. Analysis of 21 cases and review of the literature. *J Neurosurg* 68: 518-531, 1988.
12. Lombardi D, Scheithauer BW, Piepgras D, Meyer FB and Forbes GS: Angioglioma and the arteriovenous malformation-glioma association. *J Neurosurg* 75: 589-596, 1991.
13. Pallud J, Belaid H, Guillemin R, Vallee JN and Capelle L: Management of associated glioma and arteriovenous malformation-the priority is the glioma. *Br J Neurosurg* 23: 197-198, 2009.
14. Ziyal IM, Ece K, Bilginer B, Tezel GG and Ozcan OE: A glioma with an arteriovenous malformation: An association or a different entity? *Acta Neurochir (Wien)* 146: 83-86; discussion 86, 2004.
15. Goodkin R, Zaias B and Michelsen WJ: Arteriovenous malformation and glioma: Coexistent or sequential? Case report. *Neurosurg* 72: 798-805, 1990.
16. Harris OA, Chang SD, Harris BT and Adler JR: Acquired cerebral arteriovenous malformation induced by an anaplastic astrocytoma: An interesting case. *Neurol Res* 22: 473-477, 2000.
17. Moftakhar P, Hauptman JS, Malkasian D and Martin NA: Cerebral arteriovenous malformations. Part 1: Cellular and molecular biology. *Neurosurg Focus* 26: E10, 2009.
18. Scandalcioglu IE, Wende D, Eggert A, Müller D, Roggenbuck U, Gasser T, Wiedemayer H and Stolke D: Vascular endothelial growth factor plasma levels are significantly elevated in patients with cerebral arteriovenous malformations. *Cerebrovasc Dis* 21: 154-158, 2006.
19. Zuccarello M, Giordano R, Scanarini M and Mingrino S: Malignant astrocytoma associated with arteriovenous malformation. Case report. *Acta Neurochir (Wien)* 50: 305-309, 1979.
20. Wada M, Takahashi H, Matsubara S and Hirai S: Occult vascular malformations of the spinal cord: Report of four cases not detected by angiography. *Acta Neurol Scand* 101: 140-143, 2000.
21. Kim JH, Lee SH, Kim ES and Eoh W: Angiographically occult vascular malformation of the cauda equina presenting massive spinal subdural and subarachnoid hematoma. *J Korean Neurosurg Soc* 49: 373-376, 2011.
22. Osborn AG (ed): *Intracranial vascular malformation*. In: *Diagnostic Neuroradiology*. 1st edition. Mosby, St. Louis, MO, pp284-301, 1994.