CASE REPORT

Glioblastoma multiforme presenting with ischemic stroke: Case report and review of the literature


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Summary
A 58-year-old woman presented with acute onset of global aphasia. Imaging studies revealed a left frontotemporal enhancing tumor and ischemic stroke in the territory of the middle cerebral artery. The patient was operated on, and the diagnosis of glioblastoma multiforme was confirmed. At the time of surgery, several branches of the left middle cerebral artery were found embedded in the tumor. One branch, which was infiltrated by tumor and completely occluded, was resected to achieve complete resection. Postoperatively, the stroke area within the middle cerebral artery territory increased, together with worsening of the patient’s clinical status, thus requiring urgent decompressive craniectomy. Thereafter, the patient gradually improved, and received radiation therapy and chemotherapy with no recurrence after 24 months of follow-up. To our knowledge, glioblastomas presenting with ischemic stroke are rare, and such patients should be considered to be at high surgical risk.

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Introduction
Glioblastoma multiforme is the most frequent and most aggressive primary brain tumor. Common presenting symptoms include seizures and focal neurological deficits due to direct brain infiltration and/or mass effects, together with surrounding edema. Glioblastomas occasionally present with intracranial hemorrhage, but are rarely associated with cerebral infarction. This is a report of a patient who presented with acute onset of aphasia secondary to ischemic stroke as the initial manifestation of a glioblastoma.

Case report
A 58-year-old woman was admitted to the emergency room with acute onset of global aphasia. Magnetic resonance imaging (MRI) revealed a large cystic lesion, with a characteristic ring-like enhancement, in the left frontotemporal region associated with surrounding edema and a slight
Glioblastoma multiforme, stroke

Figure 1  MRI [T1-weighted, post-gadolinium (A) and T2-weighted (B)] demonstrates a large cystic lesion in the left frontotemporal region, with typical ring-like enhancement suggestive of malignant brain tumor.

Figure 2  Preoperative three-dimensional time of flight (TOF) MR angiography reveals the involvement of several branches of the left middle cerebral artery (MCA). Note the irregularity of those arteries (white arrow).

midline shift (Fig. 1A and B). This was highly suggestive of a high-grade tumor, and also showed tumor encasement of several branches of the left middle cerebral artery (Fig. 2). Diffusion-weighted MRI identified an ischemic stroke in the frontal part of the middle cerebral artery territory (Fig. 3A and B). The patient had no cerebrovascular risk factors, and the results of the laboratory and cardiovascular workups were normal.

The patient underwent tumor resection. At the time of surgery, several M3 branches of the left middle cerebral artery were found embedded within the tumor. One branch, which could not be separated from the tumor and was completely occluded, was resected to achieve complete resection. Postoperatively, the patient awoke with a worsened neurological status. Her global aphasia was complete, and she presented with severe right hemiparesis. Over the next few hours, her level of consciousness gradually decreased. The computed tomography (CT) scan demonstrated no hemorrhage, but there was a large region of hypodensity posterior to the resection cavity and a significant midline shift. Diffusion-weighted MRI confirmed enlargement of the stroke area within the middle cerebral artery territory (Fig. 4), prompting urgent left decompressive craniotomy. The patient progressively recovered and was sent to a rehabilitation center. At 3 months postoperatively, she was still complaining of weakness in her right arm, but she was able to walk. The aphasia had improved significantly. Pathological examination confirmed the diagnosis of glioblastoma. The patient was treated according to the Stupp protocol [1] as follows: temozolomide with concomitant radiotherapy, followed by 6-monthly temozolomide. There was no recurrence at follow-up 24 months later.

Discussion

In the present case, the hypothesis of glioblastoma causing ischemic stroke was supported by the sudden onset of clinical symptoms together with the typical features of stroke on diffusion-weighted MRI, and the surgically confirmed infiltration and occlusion of branches of the left middle cerebral artery. Occasionally, malignant brain tumors present with intracranial hemorrhage, and result in the acute onset of neurological symptoms mimicking hemorrhagic stroke [2]. On the other hand, ischemic strokes attributable to brain tumors are rare, and are more often related to benign tumors, such as meningiomas, that cause progressive vascular encasement and compression of intracranial vessels. To our knowledge, there are only a few reports of glioblastoma presenting with stroke [3].

Given the underlying mechanisms of tumor-related cerebral infarction, most of the available articles in the literature have attributed this to direct infiltration or dissection of the major cerebral arteries [3,4]. Indeed, several reports have shown that glioma cells are able to invade...
and weaken vascular walls, leading to arterial stenosis or rupture [5,6]. Other hypotheses, including vasospasm and a hypercoagulable state, which is commonly associated with malignancy, have also been suggested [3].

In our present case, the diagnosis of brain tumor causing stroke was obvious on both CT and MRI scans because of the clear cystic mass with ring-like enhancement, associated with surrounding edema and mass effect. However, misdiagnosis of brain tumor causing ischemic stroke could lead to the use of recombinant human tissue-type plasminogen activator (rt-PA), which has to be administered within 3 hours of the onset of symptoms [7], and may promote intratumor hemorrhage. Furthermore, it has been suggested that such rt-PA treatment of a malignant brain-tumor patient can promote tumor spread by degrading the extracellular matrix [8].

The differential diagnosis between ischemic stroke caused by atherosclerotic disease, non-atherosclerotic vasculopathy or cerebral embolism, and stroke secondary to brain tumor is difficult to make on clinical grounds. On rare occasions, radiological imaging can also lead to misdiagnosis. At present, many stroke centers follow a diagnostic protocol to investigate suspected stroke that includes CT and MRI without the use of contrast media. Furthermore, although MRI is the examination of choice, it is not always available. As described by Steinhoff et al. [9], 12 out of 295 glioblastoma patients had a completely normal non-contrast CT assessment.

With the use of MRI, the diagnosis of brain tumor associated with stroke is obvious in most cases. Gadolinium-enhanced MRI can usually identify brain tumor, while diffusion imaging has been shown to be highly accurate in detecting early stroke. Rarely, however, the non-necrotic part of a highly cellular solid brain tumor may show a decrease in the apparent diffusion coefficient (ADC) and hyperintensity on diffusion-weighted imaging (DWI), thus suggesting stroke. Nevertheless, the morphology and topography of the signal abnormalities usually argue against a diagnosis of stroke. When infiltrative brain tumor causes stroke, perfusion imaging with mapping of the cerebral blood volume (CBV) and the mean transit time (MTT) can indicate angiogenesis by revealing an increased CBV and decreased MTT within the lesion, and the opposite features in the ischemic territory [10]. On rare occasions, using MRI with contrast, non-necrotic infiltrative brain tumor may not be easily distinguishable from subacute ischemic stroke, especially if located in a vascular territory. In such cases, MRI spectroscopy may be helpful by demonstrating increased choline/creatine levels.

The early postoperative course of our present patient was marked by significant worsening of her neurological deficit, and enlargement of the stroke area within the middle cerebral artery territory on the postoperative MRI scan. During surgery, several left middle cerebral artery branches were
dissected from the tumor and no major permeable vessels were sacrificed. In our opinion, the unstable regional hemodynamics induced by the narrowing and occlusion of some of the middle cerebral artery branches might explain our patient’s complicated postoperative course and enlargement of the stroke area within the middle cerebral artery territory. Thus, patients with high-grade tumors and vascular encasement should be considered at high risk of postoperative complications, especially if they also present with stroke.

Conclusion

Infiltration or occlusion of the major cerebral arteries by glioblastoma can lead to ischemic stroke. The differential diagnosis between tumor-related and cerebrovascular brain infarction is not always obvious, but is nonetheless mandatory. MRI, including diffusion and perfusion imaging with gadolinium injection, are the examinations of choice when facing such a differential diagnosis, and should be included in the diagnostic protocol of stroke with the slightest signs of brain tumor. Patients presenting with glioblastoma causing ischemic stroke are at greater risk of complications associated with tumor resection.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References