

Glioblastoma Presenting Only as Cortical "Ribbon Sign" in the Early Stage: A Case Report and Literature Review

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Abstract

Background: Glioblastoma (GB) is the most common primary malignant brain tumor and occurs predominantly in the white matter of the brain. MRI often shows an irregular mass with uneven internal signals, necrosis, surrounding edema and a space-occupying effect. The malignant degree of GB is high, and it often relapses after surgery.

Case presentation: A 66-year-old male patient was admitted to our hospital due to sudden left superior strabismus and convulsions. During the patient's first hospitalization, MRI showed only an abnormal cortical signal, and the diagnosis was viral encephalitis. After the treatment of antiepileptic, antiviral and relieving brain edema, the patient was discharged. Seven months later, he was admitted to the hospital again because of memory impairment and slow reaction speed. MRI showed that there was an obvious mass in the original lesion area, and this was diagnosed as glioblastoma. Postoperative pathology confirmed glioblastoma (WHO) grade IV.

Conclusions: The clinical diagnosis, treatment and imaging manifestations of this case of GB are reported as follows to improve understanding of this type of GB, which only has cortical abnormal signals in the early stage, to reduce misdiagnosis.

Background

Glioblastoma (GB) is the most common primary malignant brain neoplasm[1] and mainly occurs in the white matter of the frontal lobe, temporal lobe and deep brain. The growth pattern of GB is invasive or central expansive growth along white matter fibers and meninges. Some glioblastomas may involve the cerebral cortex. However, GB with a main body located in the cortex is relatively rare, few imaging studies are related to it; GB with only cortical lesions is even rarer. It has been reported in the literature [2] that the survival time of patients with GB located in the cerebral cortex and subcortex is longer than in those with GB in other regions. Therefore, cerebral cortical and subcortical GB may indicate a better prognosis.

Case Presentation

History: A 66-year-old male patient was admitted to the hospital on June 12, 2017 due to sudden strabismus and convulsions for 2 days. The symptoms gradually aggravated to twitching three times in 24 hours, and he was confused. In the past 11 years, diabetes mellitus had been well-controlled by drugs. **Physical examination:** blurred consciousness, a poor mental state, and unclear speech. His left upper limb muscle strength was grade 4, left lower limb muscle strength was grade 4, right upper limb muscle strength was grade 5, right lower limb muscle strength was grade 5, and muscle tension was high. **Pathological reflex:** Babinski sign: left (+), right (+), Chaddock sign: left (+), right (+).

Imaging examination: A head MRI (Fig. 1–4) showed swelling of the right parietal temporal gyrus, thickening of the cerebral cortex, low signal intensity on T1WI, high signal intensity on T2WI, iso-signal on a FLAIR sequence, high signal intensity on a DWI sequence, and a ribbon-shaped lesion with a clear

boundary. There was no obvious involvement of the subcortical white matter, and the adjacent sulcus had become shallow. He was diagnosed with viral encephalitis.

Laboratory examination: cerebrospinal fluid glucose was normal; protein levels had increased to 1083.00 mg/L; cerebrospinal fluid immunoglobulin levels were high: albumin was 598.00 mg/L, IgA was 15.80 mg/L, IgG was 72.20 mg/L, and IgM was normal; no malignant tumor cells were found in cerebrospinal fluid smears; and cerebrospinal fluid bacterial smears showed no obvious abnormalities.

Treatment process: according to the patient's symptoms, signs and auxiliary examination, viral encephalitis with epilepsy was considered. After the treatment of antiepileptic, antiviral and relieving brain edema, the patient was discharged on June 20, 2017 after improvement. At the time of discharge, the patient did not complain of obvious discomfort. Physical examination: clear mind, fluent speech, both eyes can move in each direction, bilateral pupil and other large equal circle, bilateral nasolabial sulcus symmetrical, tongue extension in the middle; his left upper limb muscle strength was grade 4, left lower limb muscle strength was grade 4, right upper limb muscle strength was grade 5, right lower limb muscle strength was grade 5 left Babinski sign (-), right Babinski sign (-), Kernig sign (-).

On January 24, 2018, the patient was readmitted because of "memory loss with slow responses for 20 days". He showed lethargy, decreased calculating ability, and unstable walking. Physical examination: conscious state, good mental state, aphasia, short-term memory loss, normal long-term memory, normal instantaneous memory, decreased calculation ability. His character orientation was normal, his place orientation was decreased, his time orientation was decreased, and his judgment was normal.

Imaging examination: a head MRI scan (Fig. 5–8) showed abnormal signals caused by irregular masses in the right parietal occipital and temporal lobe, T1WI showed low signal intensity, T2WI showed isointense signals, and FLAIR and DWI sequences showed high and low mixed signals. The boundary was unclear, and a large area of necrosis could be seen in the center of the lesion. Edema signal could be seen around it. The trigone, inferior horn and posterior horn of the right ventricle were involved and deformed. MR Enhancement (Fig. 9): The lesion showed inhomogeneous circular enhancement and a central necrotic area without enhancement and was considered a malignant tumor, with GB likely. Magnetic resonance spectroscopy analysis (Fig. 10) showed that NAA was significantly lower in the lesion area than in the contralateral white matter, while Cho was significantly higher and Lac-Lip was significantly higher in the former than in the latter, suggesting that it was a malignant tumor with necrosis. ASL (Fig. 11) showed that the cerebral blood flow (CBF) of the solid components of the lesions had significantly increased, suggesting that the lesion was a malignant tumor.

Laboratory examination: cerebrospinal fluid glucose was high, at 6.40 mmol/L, and protein had significantly increased to more than 3000.00 mg/L. Immunoglobulin in the cerebrospinal fluid had increased: albumin > 1630.00 mg, IgA > 43.10 mg/L, IgG > 109.00 mg/L, and IgM > 4.95 mg/L. No malignant tumor cells were found in cerebrospinal fluid smears. There was no obvious abnormality in the cerebrospinal fluid bacterial smear.

Treatment process:the patient was diagnosed as intracranial malignant tumor. Craniotomy was performed under general anesthesia on February 3, 2018 after admission.The tumor was located in the right temporal and occipital lobes, and part of the tumor was protruding to the surface of the brain. The tumor was gray-red, soft, and rich in blood supply and had no capsule. The boundary between the tumor and the brain tissue was not clear. Under a microscope, the adhesion between the tumor and the brain tissue was separated along the edge of the tumor and reached the midline, down to the tentorium of the cerebellum and deep to the occipital horn of the lateral ventricle.The patient was discharged on February 11, 2018 with stable vital signs and clear mind. There was no obvious abnormality in cardiopulmonary and abdominal examination. The incision healed well and the stitches were removed.Both eyes can move in each direction, bilateral pupil and other large equal circle, bilateral nasolabial sulcus symmetrical.His left upper limb muscle strength was grade 5, left lower limb muscle strength was grade 5, right upper limb muscle strength was grade 5, right lower limb muscle strength was grade 5 left ;Babinski sign (-), right Babinski sign (-), Kernig sign (-). Eventually, he died in August 2018.

Pathological diagnosis: the part of the lesion in the brain tissue was 8 × 4.5 × 3 cm, the section was grayish white, its texture was soft, some areas were grayish brown, and the range was 6 × 5 × 5 cm (Fig. 12–13). Consideration was given to (right temporal occipital) glioblastoma (WHO grade IV, size 6 × 5 × 5 cm). Immunohistochemistry showed: GFAP (+), IDH1 (-), Vimentin (+), Olig-2 (+), S100 (+), NeuN (-), Syn (-), p53 (+), ATRX (-), CD34 (-), BRAFV600E (-), and a Ki-67 positive rate of approximately 60%.

Discussion And Conclusion

This report describes one case of glioblastoma with typical clinical and radiographic manifestations of viral encephalitis in the early stage of lesions. These findings are consistent with nine other English language reports describing patients with symptoms of HSE ultimately being diagnosed with GBM or gliomatosis cerebri [3–8]. Several possible mechanisms of disease are consistent with the atypical progression of glioblastoma described in these cases. First, patients may have developed viral encephalitis and glioblastoma in the same place coincidentally, but given the relative rarity of these diseases and the time course of their discovery and development, this is an unlikely possibility. Alternatively, viral encephalitis may play a role in the formation of glioma. However, most studies suggests that viral encephalitis plays a role of tumor regulation rather than oncogenic role in the development of glioblastoma.[9–11]. Therefore, it's most likely that glioblastoma occurs at the first examination, but only involves the local cerebral cortex.

Several causes of the misdiagnosis of this case were analyzed, and the differences between GB and viral encephalitis can be summarized as follows: (1) epilepsy was the initial symptom of the patient and is a common clinical manifestation of encephalitis, while GB and other brain tumors are also prone to induce epilepsy, making it difficult to differentiate the two based only on clinical symptoms. Generally, encephalitis progresses rapidly, and the progression of tumors is relatively slow, but some glioma or gliomatosis may also show acute neurological symptoms similar to encephalitis symptoms [12–14]. Generally, viral encephalitis often has a history of fever, but this patient had no history of fever, and this

may be the main characteristic that distinguishes this case from encephalitis based on clinical symptoms. (2) On the first MR examination, the patient showed only cortical swelling and abnormal cortical signal without obvious vasculogenic edema and space-occupying effect, which is a common manifestation of viral encephalitis. This was the main cause of misdiagnosis during the first examination. The appearance of these imaging findings may have been related to invasive growth along the cerebral cortex in the early stage of GB. In the early stage of GB, the growth of the vascular network is weak, and the blood-brain barrier is not destroyed, and there is therefore no obvious edema or space-occupying effect. An MR plain scan of viral encephalitis usually shows high signal intensity on T2WI and FLAIR that involves the cortical and subcortical white matter, indicating local cytotoxic edema. Diffusion-weighted imaging (DWI) is the most sensitive sequence for detecting the acute phase of encephalitis, typically manifesting as high signal lesions with apparent diffusion coefficient (ADC) limited [15–17]. Although the patient showed a high signal on the DWI sequence, it was isointense on the FLAIR sequence, indicating that the abnormal signal was not caused by cytotoxic edema but by tumor cell infiltration, which did not accord with the imaging manifestation of encephalitis. This was the main point of discrimination between this case and viral encephalitis in routine imaging examination. This patient did not have a CT examination at the first visit, but in a CT scan, viral encephalitis should appear with low density, indicating local edema, while GB often appears with a slightly higher density, indicating locally dense tumor cells. (3) In this case, the symptoms of the patients significantly improved after treatment with antiepilepsy and antiviral drugs and the relief of brain edema, further confirming the diagnosis of viral encephalitis. However, it should be noted that although the relief of epileptic symptoms was achieved by antiepileptic drugs, these drugs did not inhibit the growth of the tumor cells.

The imaging manifestation of high signal intensity in the cerebral cortex on DWI and T2WI sequences is called a cortical "Ribbon sign" and is also known as a "lace sign". In addition to viral encephalitis, diffuse cortical hyperintensity on DWI and T2WI sequences should be distinguished from that observed in Creutzfeldt-Jakob disease, MELAS syndrome, epilepsy-mediated brain changes, autoimmune encephalitis and other diseases. Creutzfeldt-Jakob disease is caused by prion virus infection, which mainly manifests with progressive dementia, mental disorder, and muscle spasm [18]. The main manifestations of Creutzfeldt-Jakob disease on MR are a high signal intensity on T2WI and DWI in the cortex and thalamus. Typical MR manifestations include "ribbon sign" and "hockey sign" [19]. Mitochondrial encephalomyopathy is a multisystem disease. Typical MELAS syndrome mainly occurs in the cortex and subcortex. The deep white matter is not involved. It shows a high signal intensity on T2WI and DWI. An increase in the lactate peak in brain tissue can be found by MRS and is an important characteristic of MELAS syndrome [20]. In patients with a clear history of epilepsy, epilepsy-mediated brain changes also need to be considered. The main manifestations are high signal intensity on T2WI in the cortex, subcortex, basal ganglia, corpus callosum and cerebellum, and half of affected patients show high signal intensity on DWI [21]. The main feature of this disease is lesions that disappear quickly during short-term review. Autoimmune encephalitis refers to a class of encephalitis mediated by autoimmune mechanisms. Its pathogenesis is related to anti-neural antibodies. Its imaging manifestations are similar to those of encephalitis, but they generally also have inducing factors such as tumors and infections [22]. The

pathological basis of the above diseases is similar to that of encephalitis, and all of them involve cytotoxic edema of local brain tissues, so the lesions appear with low density on CT and high signal intensity on FLAIR sequences, while GB is a local tumor cell infiltration, and it therefore appears as high density on CT and iso-signal on FLAIR sequences, and this is the most important difference in imaging characteristics between cortical GB and the above lesions.

GB is highly malignant, it very easily relapses after surgery [23], so early detection of these lesions is particularly important. In this case, only the cortex was involved on MRI in the early stage of the tumor, making it easy to misdiagnose. Therefore, we speculate that when GB infiltrate only the cortex at the early stage after onset, there could be imaging findings similar to the "ribbon sign" in the cortex. Combined with our diagnostic experience in this case, if only abnormal cortical ribbon signals are found on MR, we should also consider the possibility of cortical GB in addition to encephalitis and other diseases. At this time, a multimodal MR examination should be performed and combined with CT examination. If necessary, brain biopsy should be performed to reduce the rate of misdiagnosis, reduce the possibility of delays, and achieve early diagnosis and treatment.

Abbreviations

GB (Glioblastoma) MRI(Magnetic Resonance Imaging) NAA(N-Acetyl Aspartate) ASL(Arterial Spin Labeling) CBF(cerebral blood flow) MRS(Magnetic Resonance spectroscopy) ADC(apparent diffusion coefficient) MELAS(Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes syndrome)

Declarations

Ethics approval and consent to participate

This study has been approved by the ethics committee of the Affiliated Hospital of Qingdao University.

Consent for publication

The patient's family member have signed the written informed consent and allowed the publication of this Case Report.

Availability of data and material

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JZ was a major contributor in writing the manuscript. CC, CD, LN Provided clinical history and laboratory examination data. XL was responsible for Article final verification and correspondence author. All authors read and approved the final manuscript.

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Figures

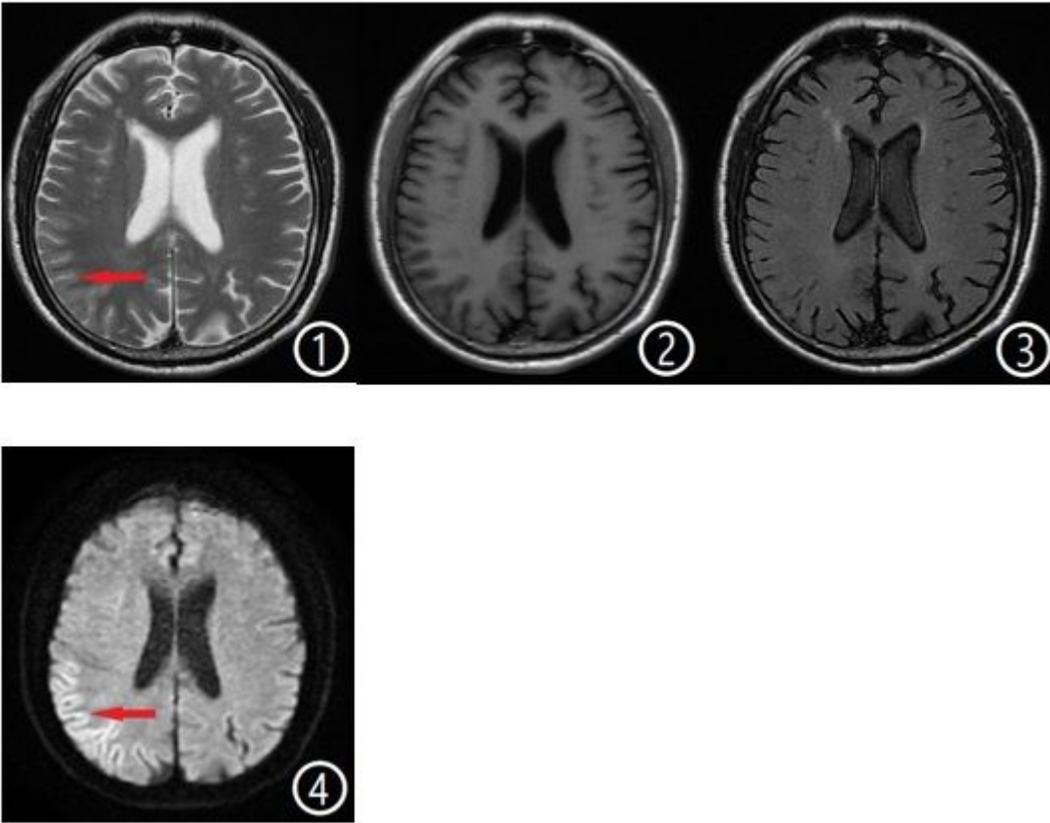


Figure 1

On the first examination, an MR plain scan showed swelling of the right parietal temporal gyrus and thickening of the local cerebral cortex, low signal intensity on T1WI, high signal intensity on T2WI, iso-signal on a FLAIR sequence, high signal intensity on a DWI sequence, and a ribbon-shaped lesion with a clear boundary (as shown by the red arrow).

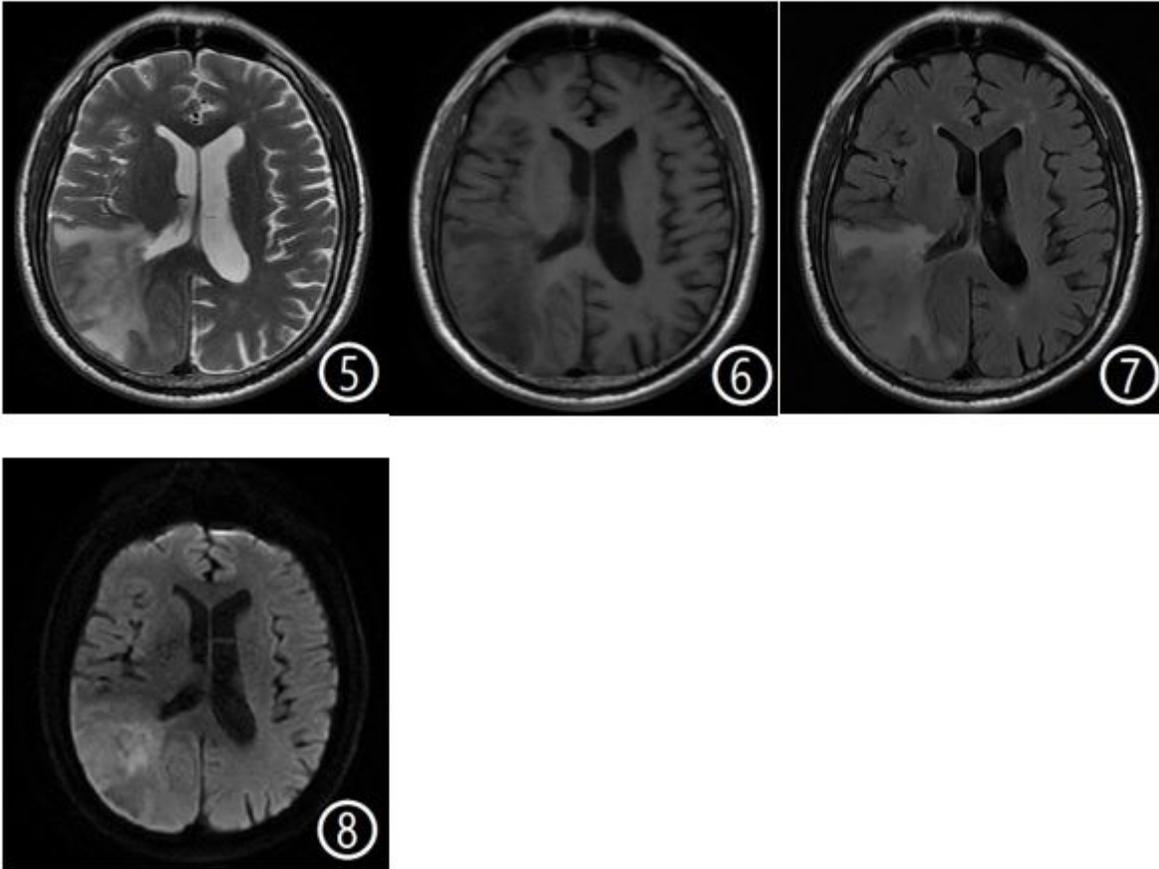


Figure 2

On MR plain scan, the mass in the right parietal-occipital temporal lobe showed low signal on T1 and high and low mixed signal on T2, and FLAIR and DWI showed high and low mixed signals. The boundary of the lesion was unclear, and a large area of edema was seen around it.

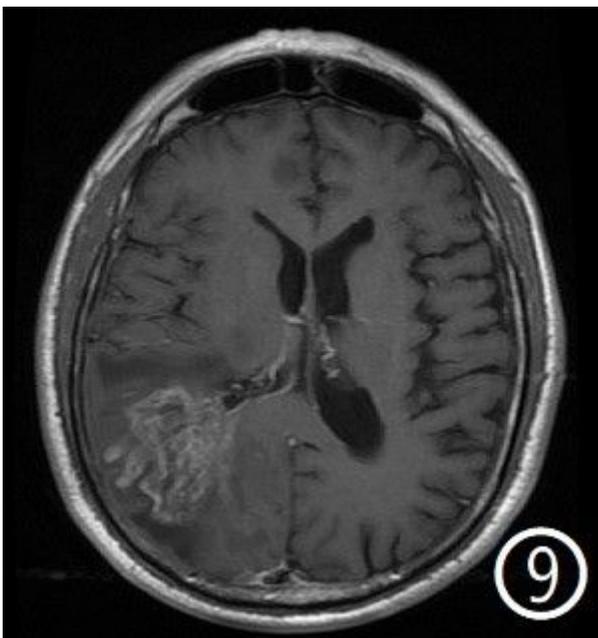


Figure 3

Contrast-enhanced MR showed inhomogeneous circular enhancement and no enhancement in the central necrotic area.

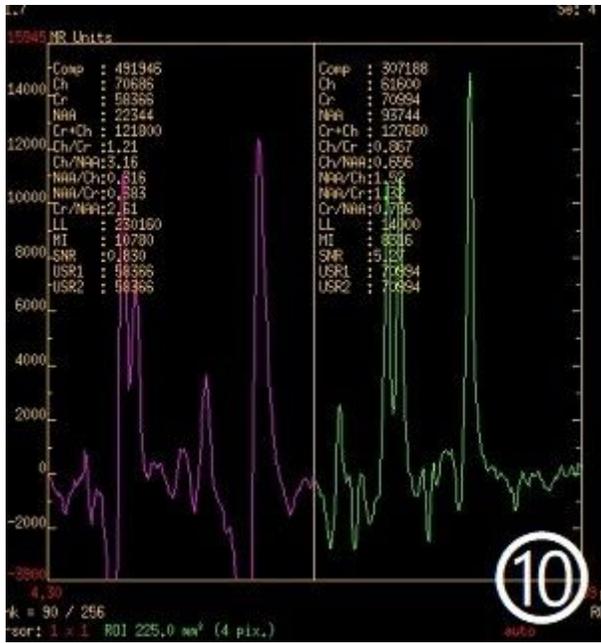


Figure 4

MRS showed that NAA was significantly lower in the lesion area than in the contralateral white matter, while Cho was significantly higher and Lac-Lip was significantly higher in the former than in the latter.

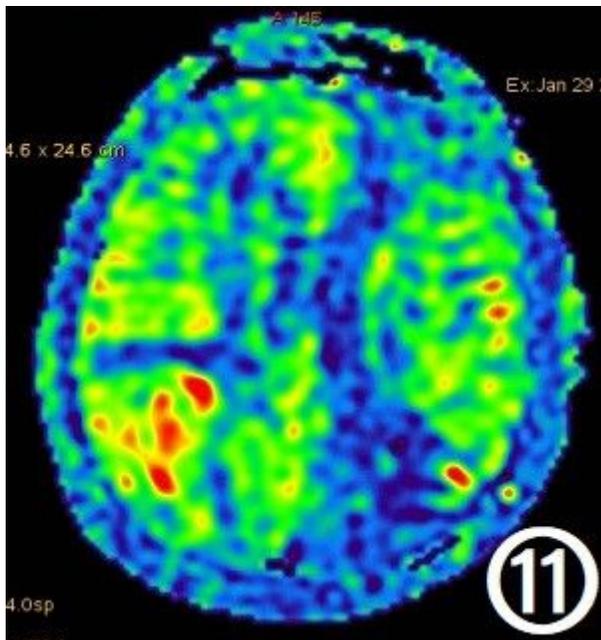


Figure 5

The CBF of the solid part of the lesion was significantly increased.

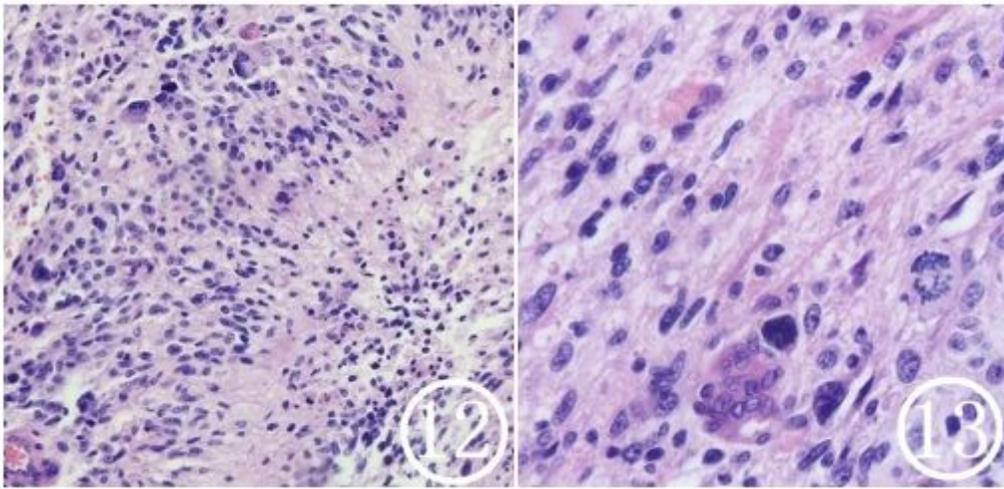


Figure 6

The pathological section of the right temporal occipital lobe lesion—glioblastoma (WHO grade IV)

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