



Cystic angiocentric glioma: a case report and literature review

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Abstract

Angiocentric glioma (AG) is a rare form of brain tumor characterized by cortical epileptogenic lesions that show angiocentric patterns upon histopathological examination. Cystoid degeneration is a rare radiological manifestation of this condition. We report a case involving the left eloquent cortical areas and review the clinical features of angiocentric glioma. A 10-year-old girl presented with a history of refractory drug-resistant epilepsy. Imaging revealed a cystic-solid neoplasm within the left frontal lobe. Surgical procedures were performed, and it was observed that the pathological manifestations were consistent with those of AG. Angiocentric glioma should be considered for diagnosis when the supratentorial cortical neoplasm contains a cystic component. The diagnosis of AG can be confirmed by histopathological examination. Gross total resection is the recommended strategy for controlling seizures elicited by this condition.

Keywords Angiocentric glioma · Seizure · Low-grade glioma · Pediatric epilepsy

Introduction

Angiocentric glioma (AG) was first reported in 2005 [5, 10]. Cerebral cortices are usually affected, and seizures occur quite often. Prominent therapeutic strategies include administration of anti-epileptic drugs and tumor resection. Here, we report a case that we came across.

Case report

A right-handed 10-year-old girl had a history of simple partial seizures followed by secondary generalized tonic-clonic seizures over the previous year. She had been treated with anti-epileptic drugs, such as oxcarbazepine and valproate, and traditional Chinese medicine. However, her seizures could not be controlled and occurred thrice a day, on an average. Results of the interictal physical examination were normal. A cranial computed tomography (CT) scan revealed a slightly hypodense lesion without calcification in the left frontoparietal lobe (Fig. 1a). Brain magnetic resonance imaging (MRI) revealed a cystic-solid, non-enhancing neoplasm

involving the cortical and subcortical white matter in the left frontal region. T1-weighted imaging (T1WI) showed a well-defined hypointense mass close to the left precentral gyrus, a low-intensity signal in the cystic area, and a slight hyperintensity deep in the lesion in the sagittal image (Fig. 1b). T2-weighted imaging (T2WI) showed hyperintensity (Fig. 1c). Fluid-attenuated inversion recovery (FLAIR) imaging revealed the lesion clearly with a size of 2.26 cm × 2.44 cm × 2.66 cm, a hyperintense solid component and hypointense cystic area, and a stalk-like neoplasm projecting toward the lateral ventricle (Fig. 1d, e). Apparent diffusion coefficient (ADC) showed no restricted diffusion (Fig. 1f). Post-contrast T1WI showed no enhancement within the neoplasm (Fig. 1g). No seizures occurred throughout the period of video electroencephalogram (EEG) monitoring that showed sharp wave and sharp-and-slow-wave complexes in the left parietal, posterior temporal, and central areas (Fig. 1h).

We made a U-shaped incision on the scalp in the left frontoparietal region and located the neoplasm, central sulcus, precentral gyrus, and postcentral gyrus using neuronavigation. The tumor was situated in the frontal precentral gyrus. Electrocorticography revealed that epileptic discharge was associated with the tumor, precentral gyrus, postcentral gyrus, and paracentral lobule. The electrophysiological findings coincided with those of neuroimaging. Therefore, we resected the tumor (3 cm × 2.5 cm × 1.5 cm) totally under a surgical microscope. The precentral gyrus, paracentral gyrus, and draining veins were unaffected.

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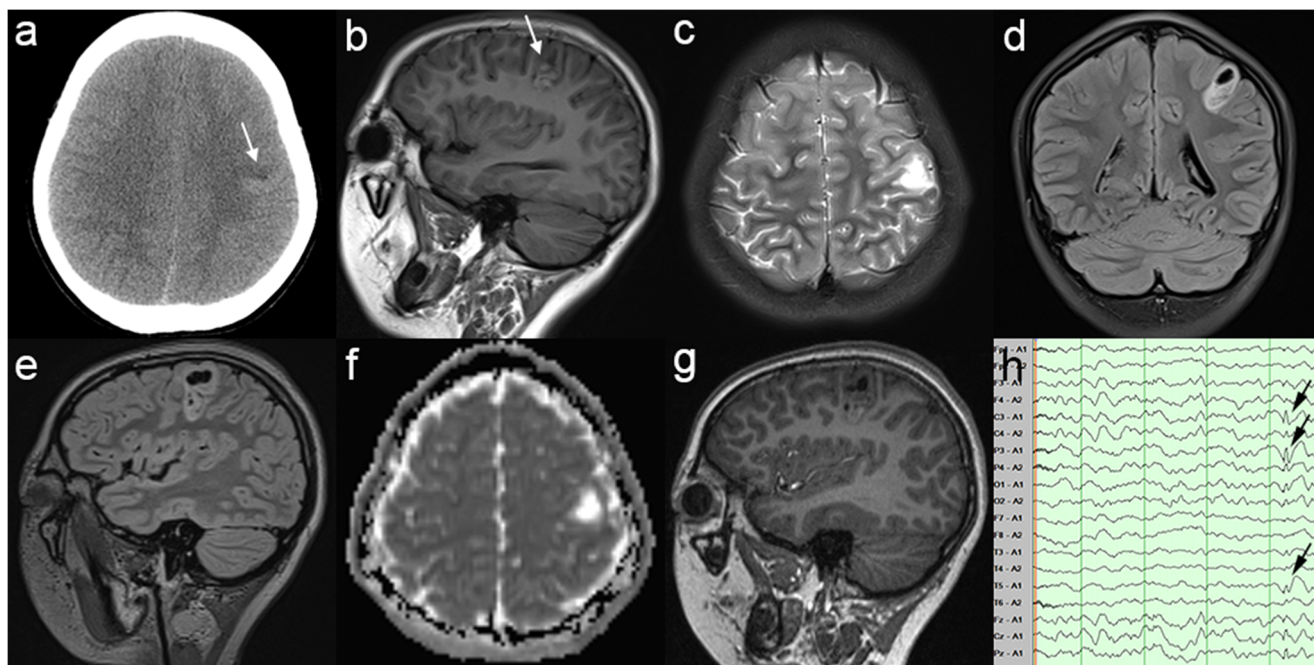


Fig. 1 Preoperative neuroimaging findings and EEG. **a** Axial CT revealing a hypodense lesion (white arrow). **b** Sagittal T1-weighted image revealing a predominantly hypointense lesion in the frontal lobe with a hyperintense component (white arrow). **c** T2-weighted axial image revealing no peripheral edema and significant mass effect. **d**, **e** Flair coronal, flair sagittal images revealing a cystic component within the lesion

and a stalk-like neoplasm projecting toward the lateral ventricle. **f** ADC axial image revealing no restricted diffusion. **g** Post-contrast axial image revealing no enhancement. **h** Interictal EEG revealing epileptiform discharges within the left parietal, posterior temporal, and central areas (black arrow)

Both histopathological and immunohistochemical findings confirmed the diagnosis of AG. High-density regions of tumor

nuclei consisted of multiple angiocentric patterns (Fig. 2a). Eosinophilic extracellular matrix with sparse nuclei

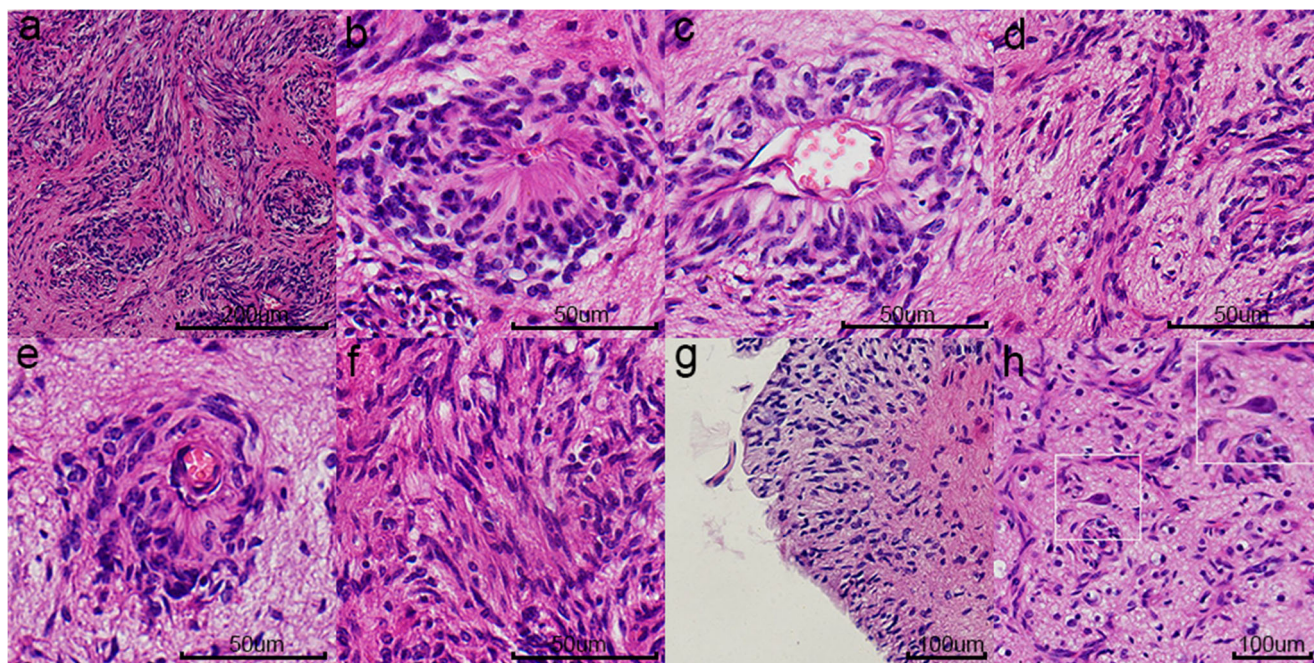


Fig. 2 Hematoxylin-eosin (H&E) findings. **a** Tumoral cells constitute multiple angiocentric patterns like pseudorosettes and schwannoma-like patterns (H&E, $\times 100$). **b** Monomorphic, elongated neoplastic cells surround a small vessel and present an angiocentric appearance (H&E, \times

400). **c** Actinomorphous arrangement (H&E, $\times 400$). **d** Longitudinal arrangement (H&E, $\times 400$). **e** Circumferential arrangement (H&E, $\times 400$). **f** Fasciculate arrangement (H&E, $\times 400$). **g** A palisade-like arrangement under pia matter (H&E, $\times 200$). **h** Tapped neuron (H&E, $\times 200$)

constituted the low-density regions (Fig. 2a). Monomorphic bipolar spindle-like cells were arranged around a small blood vessel and formed pseudorosettes with nuclear-free zones close to the central vessel (Fig. 2b). The nuclei were aligned in parallel with the neoplastic cells, and contained granular chromatin (Fig. 2b). Fusiform neoplastic cells were arranged radially, longitudinally, and toroidally around small and large blood vessels (Fig. 2c–e).

Tumor cells formed braided structures similar to those in schwannomas (Fig. 2f), and palisades under pia matter (Fig. 2g). Trapped neurons were also present among the tumor cells (Fig. 2h). Mitosis, necrosis, and microvascular proliferation were absent. The spindle-like cells had high levels of expression of glial fibrillary acidic protein (GFAP), S100 proteins, and vimentin (Fig. 3a–c), indicating a neuroglial origin. Epithelial membrane antigen (EMA) staining exhibited dot-like structures around the nuclei (Fig. 3d). The trapped neurons showed immunoreactivity for neuronal nuclei (NeuN) (Fig. 3e). Ki67 showed low levels of expression with a proliferation index of 1% (Fig. 3f).

On postoperative day 1, the girl could stretch the fingers of her right hand, but failed to flex them. We recommended long-term neurological rehabilitation in addition to hyperbaric oxygen treatment to improve the strength of the fingers in her right hand. Postoperative video-EEG did not detect epileptic waves (Fig. 3g). A 36-month follow-up brain MRI revealed that the lesion was successfully removed and showed no recurrence (Fig. 3h). The patient had been seizure-free without

taking anti-epileptic drugs and could stretch and flex the fingers of her right hand without difficulty. At the time of submission of this manuscript, she could successfully write with her right hand and had returned to normal life. Follow-ups with clinical and radiological investigations are ongoing.

Discussion

In 2005, Wang and Lellouch-Tubiana et al. [5, 10] reported for the first time about cases of brain tumors that were characterized by monomorphic, fusiform tumor cells aligning around small or large blood vessels. They named the newly discovered type of tumor as monomorphous AG or angiocentric neuroepithelial tumor. In 2007, the World Health Organization (WHO) classified the newly described tumor as a subtype of neuroepithelial tumors and named it AG (WHO grade I tumor) [6]. Sex-specific differences in tumor incidence rates have not been reported so far. Children and young adults are at the highest risk of developing this condition. However, the case of AG in elderly patients has also been reported [2]. These tumors are predominantly located in the frontal, temporal, and parietal lobes of the brain. Less common locations include the occipital lobe, insula, thalamus, and brainstem [3, 7, 11]. Supratentorial cortical AGs often cause seizures. Other presentations include symptoms, such as increased intracranial pressure, weakness of limbs, and paralysis of cranial nerve [7, 11].

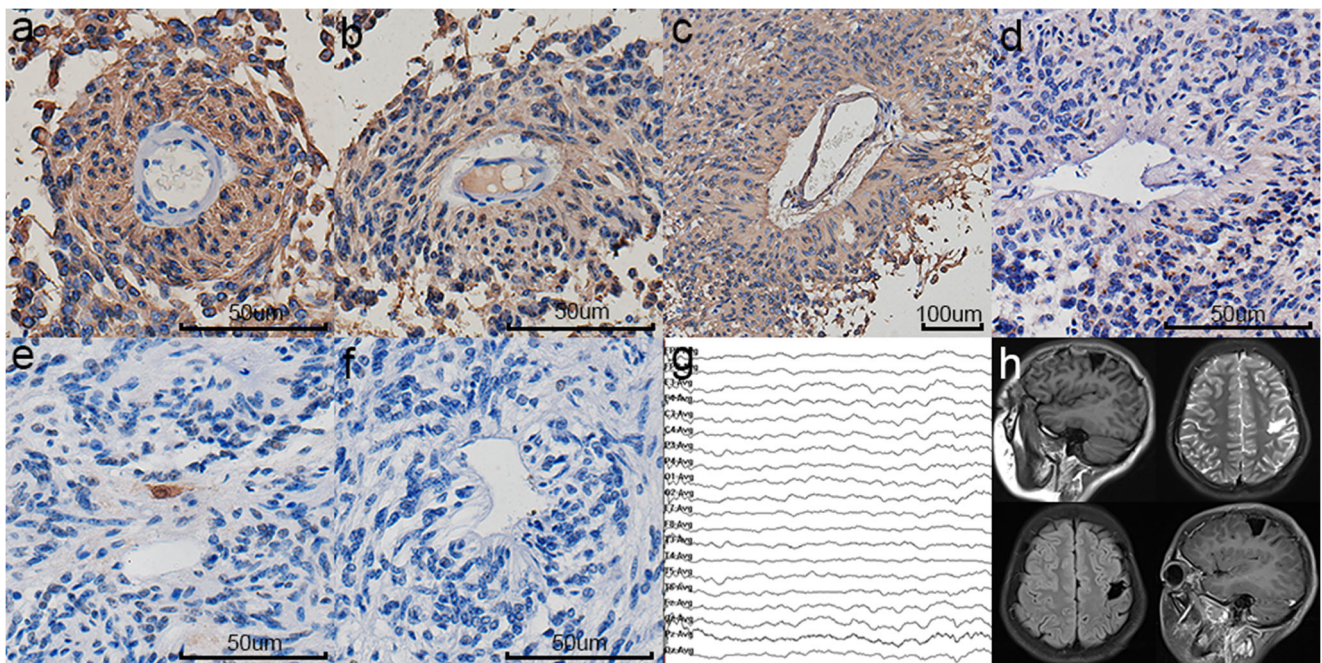


Fig. 3 Immunohistochemical findings of the lesion, postoperative EEG and MRI. **a** Strong immunoreactivity of GFAP ($\times 400$). **b** Strong immunoreactivity of S100 ($\times 400$). **c** Strong immunoreactivity of Vim ($\times 200$). **d** EMA presents dot-like positive around neoplastic nuclei (\times

400). **e** A neuronal component is positive for NeuN ($\times 400$). **f** Tumoral cells are weakly positive for Ki67(1%) ($\times 400$). **g** Postoperative interictal EEG demonstrates low waves and no epileptic discharges. **h** Postoperative MRI images show no tumor residual and no recurrence

Typically, AG is characterized by low-intensity signals on T1WI scans, high-intensity signals on T2WI/FLAIR scans, and non-enhancing neoplasms. Interestingly, a stalk-like shape projecting toward the ventricle is usually observed in FLAIR images. CT scans show hypodense or isodense regions. Our patient showed most of the aforementioned characteristics. Some AGs present hypointense T1 lesions with a ring-like hyperintense cortex. We observed hypointense T1 lesion with a slightly hyperintense part deep in the lesion in our case. Magnetic resonance spectroscopy demonstrates evaluated choline/phosphocreatine and choline/N-acetyl aspartate ratios as well as increased levels of myoinositol and glycine [12]. Some studies have reported a slight contrast enhancement in AGs [4]. To the best of our knowledge, few studies reported AGs with cystic degeneration and calcification [4, 8, 9]. Peripheral edema and mass effect are usually absent. Therefore, AGs should be differentiated from other epileptogenic lesions or tumors, such as dysembryoplastic neuroepithelial tumor, ganglioglioma, gangliocytoma, cortical ependymoma, pleomorphic xanthoastrocytoma, desmoplastic infantile ganglioglioma/astrocytoma, encephalomalacia, and focal cortical dysplasia.

The histopathology of AG is characterized by monomorphous bipolar fusiform cells and presents the following pathological features: (1) Angiocentric pattern: tumor cells align longitudinally, radially, or annularly around small or large blood vessels and form pseudorosettes similar to those of ependymoma. Elongated bipolar cells show nucleus-free zones close to the central vessels. The nuclei align parallel to the long axis of bipolar cells, possess granular chromatin, and show few or no mitotic divisions. Both microvascular proliferation and necrosis are rarely observed. (2) Fasciculate pattern: tumor cells show fascicular arrangement similar to that of schwannoma. (3) Palisade pattern: neoplastic cells under the pia mater line up and show a palisade appearance. (4) The tumor cells can trap neurons that are not neoplastic components. (5) AG can co-occur with adjacent cortical dysplasia. Glial biomarkers, including GFAP, vimentin, and S100 proteins show strong cytoplasmic immunoreactivity and outline the angiocentric patterns. EMA staining of ependymal biomarkers shows dot-like structures around the nuclei. Neuronal biomarkers are absent in the tumor, except in the trapped neurons. Ki67 was under 5%. In cases where malignant transformation or extracranial metastasis occurs, the proliferation index can go up to 25% or more [7, 9]. AG is frequently associated with a focal deletion in the long arm of chromosome 6. The resultant MYB-QKI fusion promotes the elevated expression of MYB gene and drives tumorigenesis [1].

Maximal tumor resection can relieve seizures and reduce the tumor burden to prevent tumor progression [8]. Since AG frequently affects the supratentorial cortex and subcortical white matter, neuronavigation can help neurosurgeons in

making incisions that reduce skin damage and bleeding. Electrooculography and a multi-modal technique can aid in locating the epileptic discharge scale and the neoplasm. For neoplasms involving the eloquent areas, multiple subpial transection or cortical thermocoagulation is recommended. Biopsy or partial resection may be required to confirm the pathological diagnosis and facilitate subsequent adjuvant therapy [11]. Despite being classified as WHO grade I tumor, McCracken et al. [7] reported a case of angiocentric glioma which transformed into anaplastic ependyma with an interval of nineteen months. Subsequent chemotherapy and radiotherapy were both performed, yet ineffective. Spinal cord multiple metastases occurred 10 months after the diagnosis of AG [9]. So, AG possesses a potential malignant trait. In view of the increased incidence of MYB-QKI fusion in AGs, gene-targeted therapy may be another choice [1].

Conclusion

Since AG is a rare epileptogenic glioma, a careful and informed analysis of the preoperative clinical presentations could contribute to accurate diagnosis. Histopathological examination is the “gold standard” for the diagnosis of AG. Resecting the neoplasm maximally can achieve control of seizures.

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Author contributions Qiqi Wang collected the data and drafted the manuscript. Yubo Xiong and Jun Chen analyzed the EEG. Qiang Shao prepared the figures and assessed the images. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Written consent was obtained from the patient and her legal guardian for this scientific publishing.

Abbreviations ADC, apparent diffusion coefficient; AG, angiocentric glioma; CT, computed tomography; EEG, electroencephalogram; EMA, epithelial membrane antigen; GFAP, glial fibrillary acidic protein; MRI, magnetic resonance imaging; NeuN, neuronal nuclei; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; Vim, vimentin; WHO, World Health Organization

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