Child's Nervous System
https://doi.org/10.1007/s00381-019-04445-0

CASE REPORT

Temporal lobe angiocentric glioma with oligodendroglioma-like areas: a rare association of an uncommon tumor. A case report with review of literature

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Received: 4 September 2018 / Accepted: 19 November 2019

Abstract

Background Angiocentric glioma (AG) is a relatively uncommon clinico-pathological entity that presents in childhood. Angiocentric glioma displays various histopathological features which resemble cortical ependymoma, astroblastoma, and pilomyxoid astrocytoma and schwannoma. The astrocytes in angiocentric glioma appear peculiarly elongated, bipolar in shape, and characteristically arranged around blood vessels. They resemble radial glia and tanycytes morphologically. Unlike ependymomas, AG is a diffusely infiltrating lesion and perivascular processes are often much thicker than those in classic ependymomas.

Case presentation AG usually present clinically as seizures, often as medically intractable epilepsy. In the indexed case, apart from unusual presentation with features of raised intra-cranial tension, an unusual histological picture of a more cellular oligodendroglioma like component was also seen.

Conclusion The appropriate diagnosis is critical as AG is usually slowly growing and treatable by surgical excision alone.

Keywords Angiocentric glioma · Hippocampal sclerosis · Temporal low-grade neuroepithelial tumor

Introduction

Angiocentric gliomas (AGs) are benign (WHO Grade I) tumors of mixed astrocytic and ependymal lineage [1–9]. AGs are a rare cause of medically refractory temporal lobe epilepsy (TLE); their association with other causes of TLE is further rare [2, 9–15]. We present a case of a young boy presenting with TLE and features of raised intra-cranial tension. Histopathologically, there was diffuse infiltration of the cortex by an angiocentric tumor with nodules of oligodendroglioma-like cells. We report this case due to its unusual presentation, unusual histomorphology, and hippocampal sclerosis-like dentate gyrus neuron loss.

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Case report

A 14-year-old boy presented with holocranial headache and complex partial seizure/déjà vu since 1 year. He also had vomiting and bilateral progressive painless diminution of vision since 1 month. His vision was 6/24 and 6/9 in the right and left eye respectively. Fundoscopy showed bilateral secondary optic atrophy. The patient underwent a contrast enhanced computed tomogram (CECT) which showed a well-defined, 6 × 6 × 7 cm, hypodense lesion in the right temporal lobe (Fig. 1a). On contrast enhanced magnetic resonance image (MRI), the lesion was T1 hypo-to-isointense and T2 hyperintense with heterogenous enhancement (Fig. 1b–e). The lesion extended inferiorly to the temporal base and superiorly to the thalamus (Fig. 1d). Angiogram was normal (Fig. 1e and g). MR spectroscopy (MRS) showed elevated choline and decreased NAA peak. A right anteromedial temporal resection (AMTR) with gross total resection (GTR) of tumor was done (Fig. 1h).

Histopathologically, the predominant histologic feature was angiocentric arrangement of oval to spindle-shaped tumor cells aligned radially and circumferentially around small- to medium-sized intra-cortical vessels. Microcyst formation was observed in most of the areas (Fig. 2a, b). However, there were no floating neurons. There was diffuse involvement of the

Published online: 02 January 2020

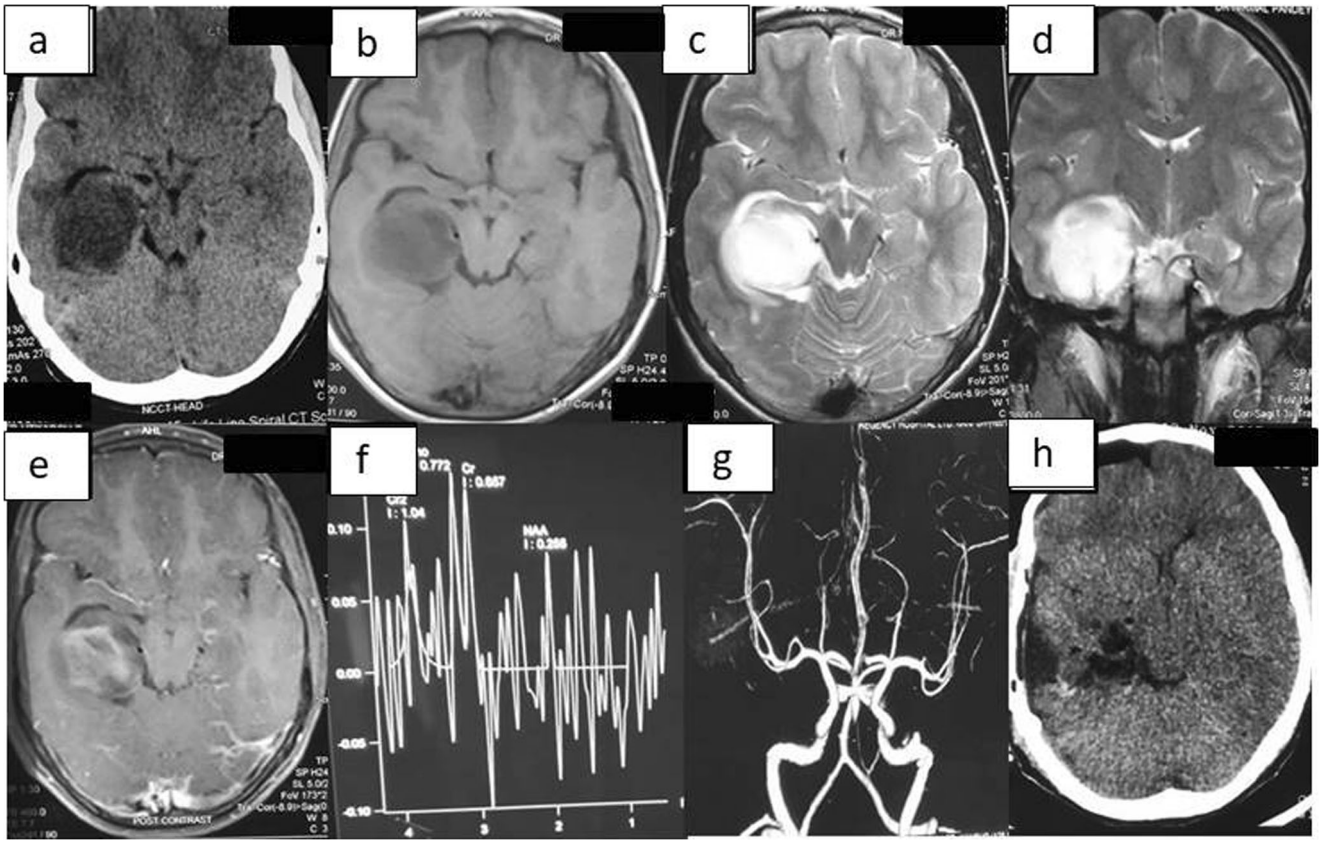

Fig. 1 **a** An axial non-contrast computed tomogram (NCCT) image showing a fairly well-defined hypodense lesion in the right medial temporal region with left temporal horn of the lateral ventricle compressed and pushed anteriorly and slightly laterally. There was no evidence hemorrhage. **b** T1-weighted axial MRI cut showing the same lesion was hypointense. **c,d** T2-weighted axial (**c**) and coronal (**d**) MRI showed that lesion was hyperintense with grade I peri-lesional edema. It was reaching the thalamus superiorly closely abutting the posterior limb of the internal capsule. **e** The tumor was heterogeneously enhancing. **f** MR spectroscopy showed a choline and NAA peak. **g** CT angiogram was essentially normal. **h** A post-operative NCCT head showed gross total excision of the tumor with a well formed surgical cavity

cortex with extension into the underlying white matter. Clusters of similar cells were present focally in the white matter. Mitotic figures were not discernible. Apart from perivascular pseudorosetting, foci of more cellular oligodendroglioma like component with peri-nuclear clearing were also present (Fig. 3a). The granule cell layer of the dentate gyrus showed patchy cell loss (Fig. 3c–e). Immunohistochemically, there was variable immunoreactivity for GFAP, S-100, and vimentin. Ki-67 index was low (less than 1%) (Fig. 2d,e). IDH 1 was negative. Though immunohistochemistry for EMA is non-contributory, the low-grade diffusely infiltrating glioma with striking perivascular arrangement of tumor cells was compatible with angiocentric glioma.

Discussion

AG was first described in 2005 by Wang and Lellouch-Tubiana independently [1, 2, 13, 15, 16]. Wang et al. described 8 cases of "monomorphous angiocentric gliomas" and Lellouch-Tubiana described 10 cases coining the term "angiocentric neuroepithelial tumors (ANET) [8, 11]. In 2007, WHO recognized these tumors as a separate entity viz. "angiocentric glioma" classifying these as "other neuroepithelial tumors" [2, 5, 6, 9, 13, 17, 18]. AGs are slow growing, superficial cortical tumors, mostly fronto-parietal in location, followed by temporal and occipital lobe [2, 3, 5, 8, 9, 14, 16]. Uncommon locations include brainstem, insula, and thalamus [2]. To date, under 90 cases have been reported and to the best of our knowledge, about 30 have been temporal in location [1, 19] (Table 1). Hippocampal sclerosis-like features are a rarity contributing to the uniqueness of our case. Only two cases have been previously reported to have hippocampal neuronal loss; 1 case each by Majores et al. in 2007 and Miyata et al. in 2011 [7, 20].

AGs commonly affect children and young adults (median age 17 years, range 2.3–70 years) irrespective of gender [1–5, 9, 14, 17, 19–21]. AGs are benign, epileptogenic, and clinically indolent [1, 8, 12]. The commonest presentation of these

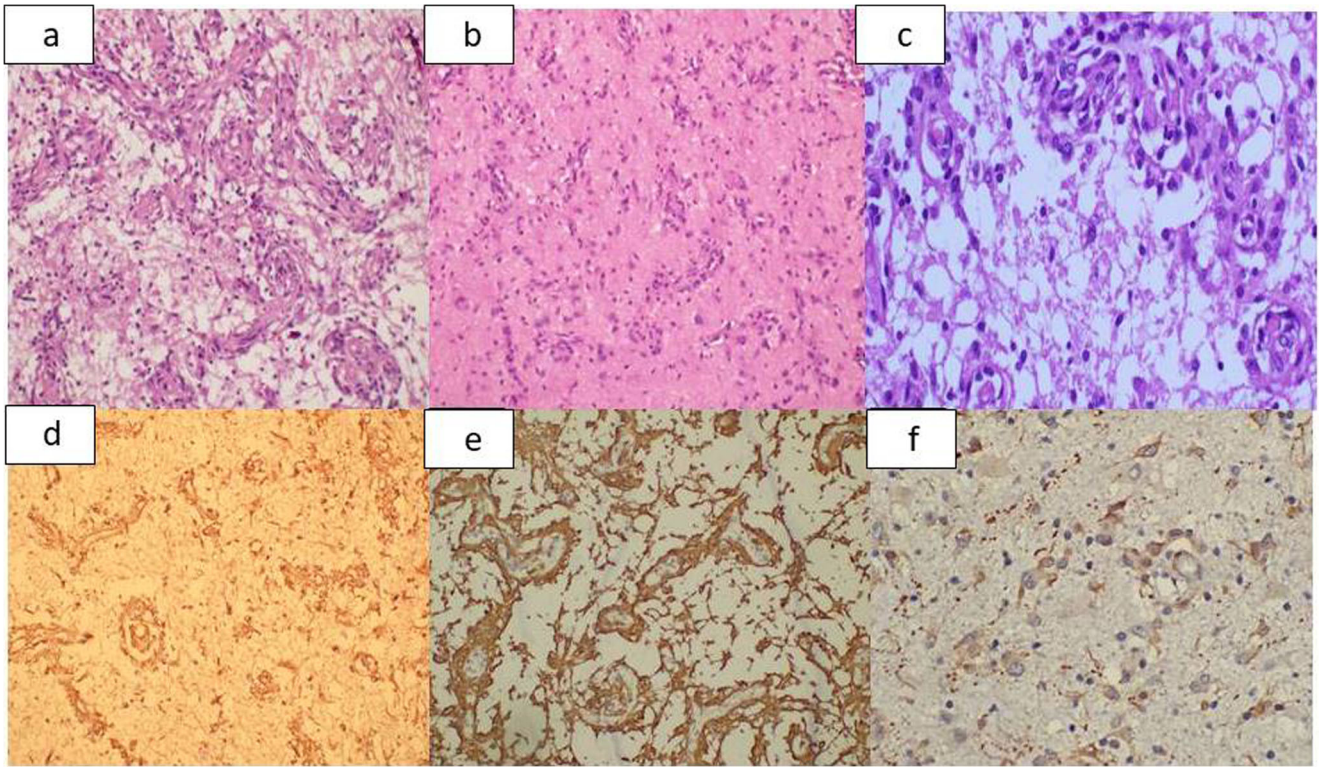

Fig. 2 **a**, **b** Low power view of H&E stained sections showing small round to oval cells diffusely infiltrating the cortex and adjacent white matter. There is striking angiocentric orientation of tumor cells and microcystic degeneration. The nuclear chromatin is bland (magnification × 20). **c** Higher magnification showing plump epithelial appearance of some the tumor cells (magnification × 40). **d**, **e** Tumor cells are strongly positive for GFAP and vimentin (magnification × 20). **f** Some of the tumor cells are positive for MAP 2(magnification × 20)

tumors is intractable seizures (≥ 90% patients) followed by headache, visual disturbances, and vomiting [1, 3, 6, 9, 11, 13, 14, 17–19]. In 2014, Blumcke et al. classified long-term epilepsy associated tumors (LEATs) and proposed reverting to the term "ANET" [2, 11, 22]. Contradictory to this, our patient had holocranial headache, vomiting, and bilateral secondary optic atrophy. Only two patients, one reported by Lellouch-Tubiana et al. in 2005 and one by Shakur et al. in 2007, presented with headache with hemiplegia and headache with difficulty in concentrating respectively [11, 18].

Radiologically, AGs are cortical although may involve subcortical white matter [5, 8, 14, 16]. On CT, these are well defined, heterogenous, and non-enhancing [1, 16]. On MRI, AGs appear heterointense on T1 images with an intrinsic rim-like hyperintensity [1, 6, 11]. They appear hyperintense on T2 images and are non-contrast enhancing [2, 14]. A stalk-like extension is usually seen from the tumor to the ventricle on T2 and FLAIR images [1–3, 11, 21]. MRS may show increased choline, myoinositol, and glycine or decreased NAA peaks [16]. Radiological differentials include DNET, ganglioglioma, low-grade astrocytomas, ependymoma, oligodendroglioma, and cortical malformations [1–3, 7, 11, 13, 16].

The histopathogenesis of AG is unclear. In 2016, Adamek et al. stated that a dual astrocytic and ependymal differentiation points towards the origin of AG from an early progenitor cells as does their co-occurrence with malformations of cortex-like focal cortical dysplasia and hippocampal sclerosis [2, 7, 11]. Histologically, AGs are cellular tumors composed of monomorphic spindle-shaped astrocytic bipolar cells arranged around the blood vessels radially, circumferentially, and longitudinally forming pseudorosettes and hence the name "angiocentric" [1, 5, 7, 8, 14, 20, 21]. The tumor cells show an infiltrative growth pattern (with sub-pial palisading) with entrapped normal neurons which, in adults, may show features of neuronal degeneration like neurofibrillary tangles and Aβ plaques [1, 2, 4, 5, 17, 19]. Features of ependymal differentiation like epithelioid cells and microvilli/microlumens may be seen on electron microscopy [2, 12, 17, 19, 20]. AG may show features resembling ependymoma, astroblastoma, and pilomyxoid astrocytoma. Miniature schwannoma-like areas have also been described [5, 8, 14, 20]. Micro-cystic changes were seen in our patient, and they being a rarity in AG [14, 20]. Nodular oligodendroglioma-like appearance is usually seen in LEATs like DNET/composite DNET. The presence of oligodendroglial component has never been reported until now. In 2015, Ni et al. published a series of 9 cases, of which 4 harbored atypical histological features viz. astroblastoma-like areas, cystic and myxoid changes, and

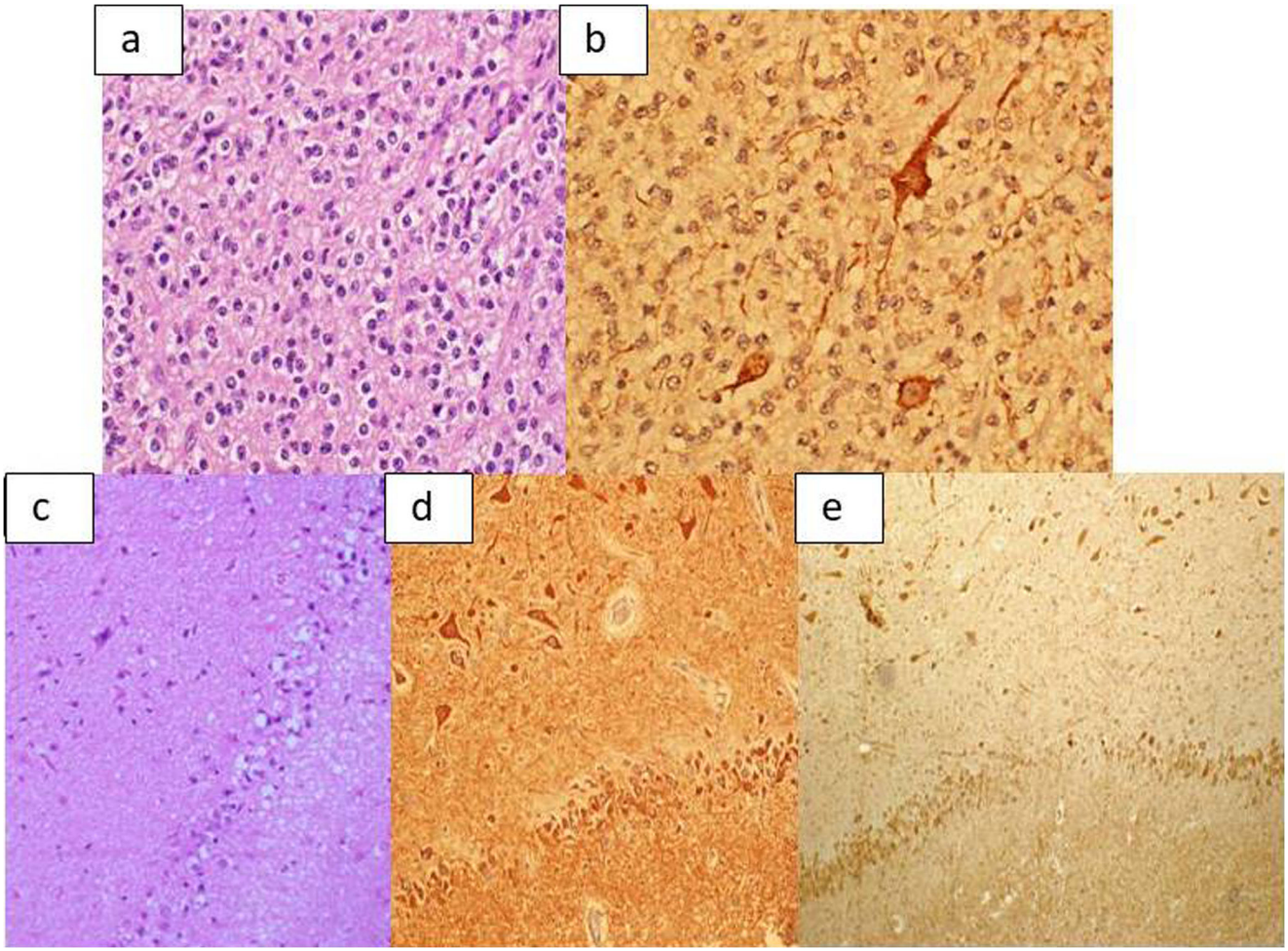

Fig. 3 **a** Sheets of oligodendroglioma-like cells with peri-nuclear clearing (magnification × 40). **b** Few neurofilament positive–entrapped mature neurons (magnification × 40). **c** H&E stain section showing focal loss of granule cell neurons in the dentate gyrus of hippocampus (magnification × 20). **d**, **e** Neurofilament- (**d**) and NeuN- (**e**) stained sections showing focus of granule cell loss (magnification × 20)

Table 1 Summary of reported cases of temporal angiocentric glioma and their salient features

Author	Age/sex	Presenting symptom	Symptom duration	Location	Extent of resection/ selective AH or AMTR performed	Histological evidence of hippocampal sclerosis*	Post-operative freedom from seizure
Chatterjee et al.[3]	22/F	Seizure	N/A	Right mesial temporal lobe	N/A; Yes	N/A	Yes
Grajkowska et al.[5]	15/F	Partial seizures	N/A	Right temporal lobe (middle)	GTR; No	-	Yes
Ni et al.[14]	1. 17/M	Seizure	4 years	Left temporal lobe	GTR; N/A	No	Yes
	2. 7/M	Seizure	16 years	Left temporal lobe	GTR; N/A	No	Yes
Alexandru et al.[13]	12/F	Complex partial seizure	N/A	Left fronto-temporal lobe	GTR; No	-	Yes
Liu et al.[15]	1. 22/F	Complex partial seizure	9 years	Left temporal lobe including amygdala	GTR; Yes	No	Yes
	2. 14/M	Complex partial seizure with secondary generalization	5 years	Right posterior- inferior temporal lobe	GTR; No	-	Yes
	3. 13/F	Generalized tonic spasms	9 years	Left amygdala	GTR; Yes	No	Yes
Koral et al.[6]	4/M	Developmental delay and seizure	Single episode of seizure	Right mesial temporal lobe	Partial resection; N/A	-	Yes
Miyata et al.[21]	1. 54/F	Complex partial seizure	10 years		GTR; Yes	*Yes*	No

Table 1 (continued)

Author	Age/sex	Presenting symptom	Symptom duration	Location	Extent of resection/ selective AH or AMTR performed	Histological evidence of hippocampal sclerosis*	Post-operative freedom from seizure
				Left amygdala and hippocampus			
	2. 37/M	Complex partial seizure	3 years	Left amygdala and uncus	GTR; Yes	No	Yes
Marburger et al.[18]	1. 15/M	Seizure, headache, visual disturbance	N/A	Temporal lobe	Partial resection; N/A	-	No
	2. 3/F	Seizure	N/A	Temporal lobe	GTR; N/A	-	Yes
Majores et al.[7]	46/M	Complexpartialseizures	N/A	Left Hippocampus	GTR; Yes	*Yes*	Yes
Rosenweig et al.[10]	28/M	Complex partial seizure with auditory hallucinations	7 years	Left superior temporal gyrus	GTR; No	-	Yes
Ma et al.[9]	25/F	Seizures	2 years	Right hippocampus	GTR; N/A	*N/A*	Yes
Shakur et al.[19]	1. 10/M	Headache, difficulty concentrating, visual disturbance	1 year	Left posterior temporal lobe	GTR; No	-	Yes
	2. 10/M	Complex partial Seizure	2 years	Left middle and inferior temporal gyrus lesion	GTR; No	-	Yes
	3. 13/F	Absence seizure	N/ A	Left anterior temporal lobe	GTR; No	-	Yes
Preusser et al.[12]	1. 6/M	Status epilepticus	Recent	Amygdala, hippocampus, para-hippocampal gyrus	Partial Resection; N/A	No	Yes
	2. 9/F	Psychomotor seizure	3 years	Inferior temporal gyrus	GTR; No	-	Yes
	3. 37/F	Complex partial seizure with secondary generalization	Childhood onset	Hippocampus and para-hippocampal gyrus	GTR; N/A	No	Yes
	4. 70/F	Complex partial seizure with secondary generalization	57 years	Hippocampus and para-hippocampal gyrus	GTR; N/A	No	Yes
Wang et al.[8]	1. 30/F	Seizure	25 years	Left anterior and medial temporal lobe	N/A	N/A	Yes
	2. 15/F	Seizure	4 years	Right medial temporal lobe	N/A	N/A	Yes
Lellouch-Tubiana et al.[11]	1. 5/F	Complex partial seizure	1 year	Left anterior temporal lobe	GTR; No	-	Yes
	2. 7/M	Headache,Vomiting, Hemiplegia	6 months	Left fronto-temporal lobe	GTR; No	-	Yes
	3. 10.5/ F	Complex partial seizure	5.5 years	Left mesial temporal lobe	GTR; N/A	*N/A*	Yes
Present case	14/M	Headache, Complex partial seizure, Deja vu	1 year	Right mesial temporal lobe	GTR; Yes	*Yes*	Yes

M, male; *F*, Female; *N/A*, not available; *GTR*, gross total resection; *Selective AH*, selective amygdalo-hippocampectomy; *AMTR*, antero-medial temporal resection

*In case of selective AH/AMTR was not done, then "-" refers to not applicable

ganglioglioma-like dysplastic neurons [14]. On immunohistochemistry, AGs are positive for GFAP, S-100, and EMA [1, 3, 4, 17, 20, 21]. EMA is peri-nuclear and cytoplasmic dot-like positive [2, 4, 5, 7, 9, 13, 20]. Necrosis, vascular proliferation, and mitoses are rare [1, 2, 9, 17, 21]. Recently genomic rearrangement in the form of MYB proto-oncogene fusion with QKI tumor suppressor gene has been described to be present in the majority [3, 4, 12, 23–25]. AGs are typically negative for IDH-1 and BRAF fusions [2, 4, 14, 23].

GTR is curative and key to seizure-free survival [1, 3, 9, 17]. Adjuvant radio-chemotherapy with Procarbazine, Vincristine, and Carmustine is advocated in partially resected and recurrent cases, especially those near eloquent regions [9, 21]. Only 1 mortality and degeneration to higher grade has been reported by Wang et al. in 2005, who operated twice on a 26-year-old male with a frontal AG [8]. The prognosis is good and seizures rare after GTR [7, 11, 13, 17, 18]. Recurrence is rare and occurs in partially resected tumors, time to recurrence ranging from 6 months–12 years [1, 7].

Compliance with ethical standards

Conflict of interest The authors declare that the article and its content were composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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