

Angiocentric Glioma: Report of a Rare Case Presenting with Psychosis

Abstract

Angiocentric glioma (AG), first described in 2005, was included as a distinct entity in the 2007 World Health Organization Classification of Tumors of the Central Nervous System. It is a very rare cerebrocortical tumor mainly affecting children and young adults with a history of intractable partial seizures. The histopathological features of this entity are perivascular arrangement of monomorphic, bipolar spindled cells with subpial aggregation of tumor cells and variable neuroparenchymal colonization. Of uncertain histogenesis, this is a stable/slowly growing tumor. Prognosis following total surgical resection is favorable. We describe an AG in a 16-year-old, intellectually disabled, male patient, with psychosis. This is a rare presentation with only one such case in literature. Patient's symptoms ameliorated following surgery.

Keywords: *Angiocentric glioma, low-grade glial tumor, mental retardation, perivascular pseudorosette, psychosis*

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Introduction

In 2005, Wang *et al.* described eight cases of a superficial cerebral tumor marked by an angiocentric growth pattern with features of both ependymal and astrocytic differentiation which they named "Monomorphous Angiocentric Glioma."^[1] Lellouch-Tubiana *et al.* described ten cases of a nearly identical tumor which they named "Angiocentric Neuroepithelial Tumor."^[2] These tumors were subsequently codified as a distinct clinicopathologic entity named angiocentric glioma (AG) in 2007 World Health Organization (WHO) Classification of Tumors of the Central Nervous System.^[3] AG is a rare neoplasm, and only 71 cases are reported till date, to the best of our knowledge. It typically presents in children and young adults (mean age 17 years) with intractable partial seizures and both genders are equally affected.^[3] The tumor is characterized by its typical angiocentric arrangement of monomorphic spindled cells and immunoreactivity for glial fibrillary acidic protein (GFAP), S-100, epithelial membrane antigen (EMA), and vimentin.^[3-5] We report a case of AG which presented with psychotic symptoms that ameliorated after surgery.

Case Report

A 16-year-old boy, born of a nonconsanguineous marriage, who had

delayed developmental and social milestones since birth presented with complaints of persistent bifrontal headache and vomiting since a week and an episode of generalized tonic-clonic convulsions 1½ months ago. The patient had first presented 2 years ago with irritability, fearfulness, sleep disturbances, auditory hallucinations, delusions of persecution, and suicidal attempts. While being worked up for the above, the right temporal space occupying lesion was found on magnetic resonance imaging (MRI) scan, and the patient was started on antipsychotics and anticonvulsants. The patient followed up erratically over the next 2 years and had little relief from his symptoms. Three months ago, the patient stopped all medications on his own, and he had a single episode of seizure as described above.

Recently, MRI showed a 1.7 cm × 1.2 cm solid cystic lesion, hyperintense on T1- and T2-weighted images, in the right medial temporal lobe within the parahippocampal gyrus, [Figure 1] with extensive cortical dysplasia suggestive of the right mesial temporal low-grade space occupying lesion. The patient underwent the right temporal craniotomy with total excision of the tumor.

Multiple gray-white fragmented tissue bits aggregating into 1.5 cm × 1 cm × 1 cm were received. The histopathologic examination showed small fragments of cerebral parenchyma with a diffusely permeating

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cortical-subcortical tumor of moderate cellularity with a fibrillary background. The tumor cells showed subpial aggregation and were arranged in sleeves around blood vessels [Figure 2a] with hyper and hypocellular areas reminiscent of a schwannoma [Figure 2b] prominent perivascular arrangement with pseudorosettes were seen [Figure 2c and d]. The tumor cells were monomorphic, elongate with spindle-shaped slender nuclei, and granular stippled chromatin [Figure 2d]. There was no evidence of necrosis, mitosis, or microvascular proliferation. The cells were immunoreactive for GFAP (clone GA 5) [Figure 2e] and S-100 (polyclonal) and were negative for synaptophysin and chromogranin. EMA (clone MC 5) showed dot positivity [Figure 2f]. All these antibodies are ready to use from Biogenex laboratory. MiB-1 labeling index was <1%. Based on the above morphology and immunohistochemistry, a diagnosis of AG was made. The adjacent normal parenchyma was not adequate to evaluate for features of cortical dysplasia.

At his 6 months follow-up visit to the Neurosurgery Outpatient Department, the patient was feeling well with reduction in his psychiatric symptoms and no episode of seizure after the surgery. The patient was continued on antipsychotics and anticonvulsant medications.

Discussion

AG is included in the category of “Other Gliomas” in the 2016 WHO Classification of Tumors of the Central Nervous System.^[3] It is a rare low-grade glial neoplasm with distinct clinicopathological features. To the best of our knowledge, seventy-one cases of AG [Table 1] have been reported till date.^[4-8] They are generally associated with long-standing drug resistant epilepsy, which was seen in 63 out of 71 cases. In literature, there are only eight cases with no history of seizures. These presented with only headache in one, headache with visual disturbance in 3, headaches with decrease hearing and vision in one, and dizziness in two cases. Cranial neuropathies with gait abnormality were seen in a case with posterior midbrain tumor and psychosis with a temporal lobe tumor, as seen in the present case, is

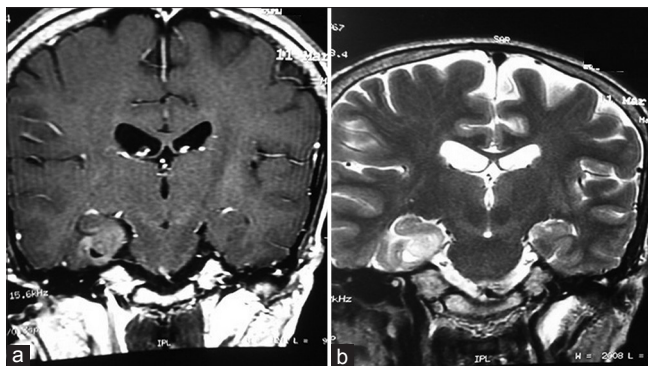


Figure 1: Magnetic resonance imaging showing (a) solid cystic lesion, hyperintense on T1 postcontrast and (b) T2 weighted images in the right medial temporal lobe within the parahippocampal gyrus

reported in only one case.^[6] This case was of 13-year-old adolescent who presented with auditory and visual hallucinations, persecutory delusions, and aggression. The patient’s symptoms remitted after the resection of the left temporal lobe, fusiform gyrus, uncus, amygdala, and hippocampus. Histological examination revealed AG.

The present patient was intellectually disabled, and he was evaluated only when he showed symptoms suggestive of psychosis, at which time the temporal SOL was found. The psychotic symptoms, especially hallucination and delusion, can probably be explained by the location, which is medial temporal lobe, i.e., the parahippocampal gyrus. Many human and primate studies have shown that parahippocampal gyrus has a multimodal association with psychosis and its volume correlates with the severity of symptoms.^[9,10]

Radiologically, AG is well-delineated solid, hyperintense on T2, non-enhancing cortical, or subcortical lesion and is described to form wedge-shaped lesions, which diffusely infiltrate the surface in a stemlike (stalklike) manner in the direction of the cerebral ventricle with focal enlargement of affected cortical gyrus.^[3]

The characteristic histology is monomorphic, bipolar spindled cells oriented about cortical blood vessels extend lengthwise along vascular axes and as radial pseudorosettes. In addition, cells often aggregate beneath the pia-arachnoid in horizontal streams or perpendicular, strikingly palisaded arrays. Nuclei are slender, with granular chromatin stippling. Unusual histological features documented are astroblastoma-like structures, cystic regions, myxoid change, presence of abnormal neurons, and high MiB1 labeling index (6%–10%). The clinical significance of these atypical features is as yet uncertain. The main differential diagnoses on microscopy include ependymoma and pilomyxoid astrocytoma.^[8] The presence of perivascular pseudorosettes and dot positivity on EMA mimics ependymal tumors;

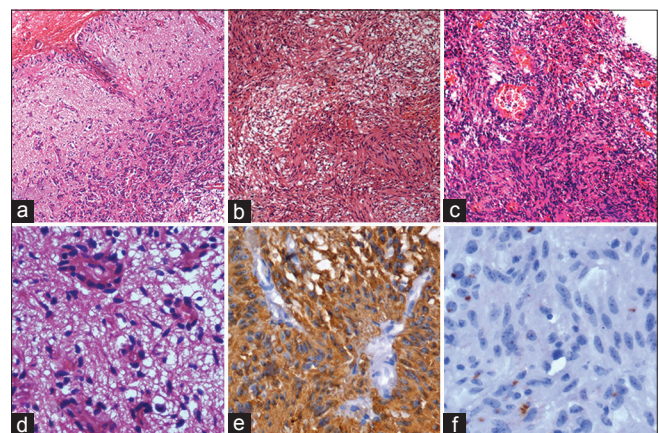


Figure 2: (a) Angiocentric glioma showing subpial aggregates of tumor cells (H and E, ×40). (b) Hypercellular and hypocellular areas (H and E, ×100). (c and d) Prominent perivascular arrangement of tumor cells. (e) Tumor cells are expressing glial fibrillary acidic protein. (f) Dot-like ethelial membrane antigen positivity in tumor cells

Table 1: Seventy-one cases of angiocentric glioma published in literature

Number	Journal	Age/ Gender (year)	Symptom	Location	Treatment	Follow up
1	Fulton <i>et al.</i> , J Child Neurol 2009;24(7):852-6	2	Refractory seizures	Right frontoparietal parasagittal	Lesionectomy	Seizure free at 14 months
2	Gyung-Jun <i>et al.</i> , J Korean Neurosurg Soc 2011;49:367-9	10/female	Dizziness, left otalgia, and gaze nystagmus	Right medial frontal lobe, high-signal intensity both in T1- and T2-weight images	Completely resection	Symptom free
3	Shakur <i>et al.</i> , J Neurosurg Pediatr 2009;3(3):197-202	10/male	History of headaches, difficulty concentrating, shortening attention span, decreasing visual acuity, and hearing loss	Left posterior temporal lobe	Left temporal craniotomy	Progression-free and asymptomatic at 24 months
4	Shakur <i>et al.</i> , J Neurosurg Pediatr 2009;3(3):197-202	10/male	Complex partial seizure	Nonenhancing left temporal cystic lesion (T1 hypointense, T2 hyperintense) 1.5 cm × 2.6 cm × 2.5 cm	Total resection of the left temporal lesion and the surrounding epileptogenic focus	Seizure free at 9 months
5	Shakur <i>et al.</i> , J Neurosurg Pediatr 2009;3(3):197-202	13/female	Absence seizures and headaches	Left anterior temporal lobe lesion (T1 hypointense, T2 hyperintense), 2.4 cm × 1.2 cm	Total resection of tumor	Seizure free at 6 months
6	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005 Oct; 64(10):875-81	3	Seizure	Occipital	Subtotal resection	No recurrence at 3 years
7	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-82	4	Seizure	Parietal	Total resection + radio + chemo	No recurrence at 4 years
8	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-83	12	Seizure	Inferior temporal	Partial resection	No recurrence at 2 years
9	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-84	14	Seizure	Postfrontal	Total resection	No recurrence at 2 years
10	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-85	15	Seizure	Amygdala	Total resection	No recurrence at 1 year
11	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-86	26	Seizure	Frontal	Partial resection	Recurrence and death
12	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-87	30	Seizure	Anterior medial temporal lobe	Total resection	NA
13	Wang <i>et al.</i> , J Neuropathol Exp Neurol 2005;64(10):875-88	37	Seizure	Frontal	NA	NA
14	Arsene <i>et al.</i> , Clinical Neuropathology 2008;27(6):391-5	20/male	Seizure	Temporal lobe	Total resection	Seizure free
15	Arsene <i>et al.</i> , Clinical Neuropathology 2008;27(6):391-5	55/male	Headache	Temporal and occipital	Total resection	Death 7 days

Contd...

Table 1: Contd...

Number	Journal	Age/ Gender (year)	Symptom	Location	Treatment	Follow up
16	Lum <i>et al.</i> , Neuropathology 2007;28(1):81-6	5/male	Intractable seizures	Cortex	Refractory to radiotherapy, hence resection of tumor	NA
17	Sugita <i>et al.</i> , Neuropathology 2008;28:516-20	6/male	Intractable partial seizures	Right occipitoparietal cortex high-signal intensity on T2-weighted image	Total resection	Seizure free at 9 months
18	Covington <i>et al.</i> , Pediatr Neurosurg 2009;45:429-33	5/female	Several cranial neuropathies and mild gait disturbance	Exophytic neoplasm arising from the posterior midbrain	Partial resection	No recurrence
19	Hu <i>et al.</i> , J Clin Neurosci 2010;17:917-18	NA	Dizziness	Frontal heterogeneous contrast enhancement	Total resection	No recurrence - 5 months
20	Ma <i>et al.</i> , Brain Pathol 2010;20:503-6	25/female	Epilepsy	Hippocampus	Total resection	Symptom free
21	Mott <i>et al.</i> , Diagn Cytopathol 2010;38:452-6	57/female	Seizure	Right frontal lobe	Radiotherapy	NA
22	Rosenzweig <i>et al.</i> , J Neuropsychiatry Clin Neurosci 2010;22:118-23	22/male	Refractory seizures, then auditory hallucinations	Left superior temporal gyrus, extending into posterior association areas	Near complete resection	No seizure or hallucinations
23	Marburger <i>et al.</i> , Arch Pathol Lab Med 2011;135:1037-41	10/female	Seizure	Left parieto-occipital	Total resection	Seizure free
24	Marburger <i>et al.</i> , Arch Pathol Lab Med 2011;135:1037-41	15/male	Seizures, visual disturbance, headache	Temporal cortex left	Subtotal resection	Tumor, seizure remained
25	Marburger <i>et al.</i> , Arch Pathol Lab Med 2011;135:1037-41	19/male	Seizure	Parietal cortex left	Total resection	NA
26	Marburger <i>et al.</i> , Arch Pathol Lab Med 2011;135:1037-41	3/female	Seizure	Left temporal cortex	Total resection	Seizure and tumor free
27	Marburger <i>et al.</i> , Arch Pathol Lab Med 2011;135:1037-41	15/male	Headache, visual disturbance	Right thalamic	Biopsy	
28	Pokharel <i>et al.</i> , Ann Clin Lab Sci 2011;41:257-61	3/male	Seizure	Right posterior parietal lobe, T2 hyperintense	Total resection	Seizure free
29	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-18	6	Seizure	Hippocampus	Partial resection	No progression - 4 years and 9 months
30	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-19	9	Seizure	Inferior temporal	Total resection	No tumor, 4 years and 8 months
31	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-20	15	Seizure	Precuneus	Total resection	No tumor - 5 years
32	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-21	16	Seizure	Precuneus	Total resection + radiotherapy	No tumor - 7 months
33	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-22	17	Seizure	Frontoparietal	Radiotherapy	No progression - 2 years
34	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-23	35	Seizure	Parietal	Near total resection	No progression - 6 months
35	Prusser <i>et al.</i> , Am J Surg Path 2007;31:1709-24	37	Seizure	Hippocampus	Total resection	No tumor - 1 year

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Table 1: Contd...

Number	Journal	Age/ Gender (year)	Symptom	Location	Treatment	Follow up
36	Prusser <i>et al.</i> , Am J Surg Pathol 2007;31:1709-25	70	Seizure	Hippocampus	Total resection	No tumor - 6 years and 11 months
37	Takada <i>et al.</i> , Neurol Med Chir 51:522-6	26/male	Refractory epilepsy	Right superior frontal gyrus, T2 hyperintense	Resection of the superior frontal gyrus including the tumor and the surrounding epileptic cortices	Seizure free on drug - 12
38	Li <i>et al.</i> , Brain Tumor Pathol 2012;29:68-72	4/female	Seizure	Right frontal lobe	NA	Free of tumor 6 years
39	Li <i>et al.</i> , Brain Tumor Pathol 2012;29:68-72	4/male	Seizure	Left frontal lobe	NA	NA
40	Li <i>et al.</i> , Brain Tumor Pathol 2012;29:68-72	9/male	Seizure	Right temporal lobe	NA	NA
41	Muhammed Tayyib <i>et al.</i> , Neurology Psychiatry and Brain Research 2013;19:197-200	13	Auditory and visual hallucinations, persecutory delusions, and aggression	Left temporal lobe	Resection with adjacent fusiform gyrus, uncus, amygdala, and hippocampus	Symptoms continued
42	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-6	7	Seizure	Frontotemporal	Total resection	NA
43	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-7	2.3	Seizure	Frontoparietal	Partial resection	Stable residual tumor - 3 years
44	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-8	10.5	Seizure	Medial temporal	Total resection	NA
45	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-9	6.5	Seizure	Parietal	Total resection	NA
46	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-90	12	Seizure	Frontal	Total resection	NA
47	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-91	14.5	Seizure	Orbitofrontal	Partial resection	Stable residual tumor 2 years
48	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-92	13.5	Seizure	Parietal	Total resection	NA
49	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-93	6.4	Seizure	Frontal	Partial resection	NA
50	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-94	15.5	Seizure	Premotor cortex	Partial resection	Stable residual tumor - 14 months
51	Lellouch <i>et al.</i> , Brain Pathol 2005;15:281-95	5/female	Seizure	Anterior temporal lobe	Total resection	NA
52	Chen <i>et al.</i> , Experimental And Therapeutic Medicine 2014;7:61-5	7/female	Refractory seizures	Right posterior parietal lobe, T2 hyperintense	Total resection	Seizure free, no tumor at 12 months
53	Shakur <i>et al.</i> , Journal of Neurosurgery 2009;3:197-202	10	Worsening headache and decreasing vision	Left temporal lobe, T2 hyperintense	Total resection	Symptom-free, 2 years
54	Shakur <i>et al.</i> , Journal of Neurosurgery 2009;3:197-203	10	Intractable seizure	Left temporal lobe, T2 hyperintense	Total resection	Seizure free at 9 months
55	Shakur <i>et al.</i> , Journal of Neurosurgery 2009;3:197-204	13	Intractable seizure	Left temporal lobe, T2 hyperintense	Total resection	Seizure free, at 6 months

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Table 1: Contd...

Number	Journal	Age/ Gender (year)	Symptom	Location	Treatment	Follow up
56	Majores <i>et al.</i> , Clinical Neuropath 2007;26:311-16	46	Seizures	Temp lobe	NA	Seizure free, at 2 years
57	Alexandru <i>et al.</i> , Perm J 2013;17(1):e100-e102	12/female	Seizures	Left frontotemporal	Total resection	Seizure free, at 3 months
58	Kumar <i>et al.</i> , Radiol Case Rep 2013;8(4):782	4/male	Seizure, limpiness on the right side		Left posterior frontal lobe	Seizure free on medication
59	Grajkowska <i>et al.</i> , Folia Neuropathologica 2014;52/3	15/female	Intractable seizure	Right temporal lobe	Total resection	Seizure free
60	Grajkowska <i>et al.</i> , Folia Neuropathologica 2014;52/4	14/male	Intractable seizure	Left parieto-occipital	Total resection	Seizure free
61	Cheng <i>et al.</i> , J Radiol Case Rep 2015 July; 9(7):1-9	25/male	Seizure	Right frontal region	Total resection	Recurrence free at 6 months
62	Erse <i>et al.</i> , Turkish J of Pathology 2014	21/male	Seizure with fever	Left frontal region	Completely resected	Recurrence-free at 4 years
63	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46		Seizure	NA	NA	NA
64	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
65	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
66	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
67	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
68	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
69	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
70	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA
71	Ni <i>et al.</i> , Neuropathology and Applied Neurology 2015;41:33-46	NA	Seizure	NA	NA	NA

NA – Not available

however, AG differs from ependymoma by its clinical presentation, cerebrocortical location and monomorphic spindle cells morphology with subpial aggregation and arrangement of tumor cells along the long axes of blood vessels.^[3,7] Pilomyxoid astrocytoma usually occurs at a very young age (median 10 months) and is most often located in the hypothalamic/chiasmatic region.^[3] It may histologically resemble AG due to the angiocentric arrangement of bipolar-spindled tumor cells, but it shows a prominent mucinous background and is not infiltrative.^[8]

A subset of AGs is associated with malformation of cortical development/focal cortical dysplasia.^[8] Cortical dysplasia was reported on MRI in the present case as well; however, the resected specimen showed very little normal cortex and cortical dysplasia could not be ascertained. Histogenesis of these tumors is unclear. Wang et al. suggested astrocytic and ependymal origin whereas Lellouch Tubiana et al. have proposed a dysembryoplastic process with origin from radial glia.^[2] Prognosis following gross total resection is very good with complete cessation of seizures.

A follow-up is available in 57 of 71 patients published in literature [Table 1], out of which 2 succumbed to death due to the disease. Of these 55 patients, 45 underwent a total resection and were free of symptoms without recurrence. The remaining 10 patients had stable residual disease, out of which 9 underwent partial resection, and one was not operated at all and was diagnosed on biopsy alone.^[3,4,7]

This case illustrates the classical morphology of AG and is unusual for its clinical presentation.

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Conflicts of interest

There are no conflicts of interest.

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