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Pediatric intracerebral anaplastic ganglioglioma : A Case Report

Anaplastic ganglioglioma (AGG) is an extremely rare aggressive, epileptogenic brain tumor. It is considered to be WHO grade III variant of ganglioglioma. Due to non-specific clinical manifestations and radiographic features, preoperative diagnosis of AGG may be very difficult at times. Frequently, it may be confused with either low grade ganglioglioma, dysembryoplastic neuroepithelial tumor (DNET) or high grade primary glial tumors. Here, we report a young girl presenting with headache and seizures preliminarily diagnosed as DNET but histopathologically proven as anaplastic ganglioglioma, along with a brief literature review.

Key Words: Anaplastic ganglioglioma, dysembryoplastic neuroepithelial tumor, ganglioglioma

Gangliogliomas are a rare mixed neuronal-glial tumor of the central nervous system. It makes up approximately 1.3% of all primary brain tumors. ^(9,3) Anaplastic ganglioglioma (AGG), is classified as WHO grade III, is a rare form of ganglioglioma with anaplastic features which most commonly affects children and young adults. This represents 1-5% of all gangliogliomas. ^(9,10,14)

Generally, it is located in the supratentorial region. It is thought to be highly epileptogenic and malignant, and frequently results in diffuse local and distant metastases within the craniospinal axis and overall shorter survival.

Pathologically, it consists of both neuronal and glial elements. These tumors are graded by the degree of malignancy in their glial portion. Radiological diagnosis is difficult due to the wide variation in its degree of solid and cystic components, contrast uptake, and calcification patterns. Its clinical course and optimal treatment have not been well understood to date.

Our present case is a young girl, presenting with headache and seizures, who successfully underwent craniotomy and gross total resection for right parietooccipital brain tumor at our institute; and surprisingly, it was reported as AGG (WHO grade III) on the histopathological examination.

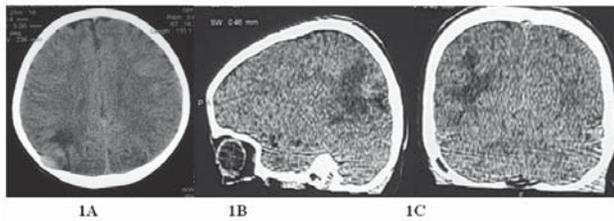


Figure 1: Preoperative CT scan of head revealing a small ill-defined lesion in lateral aspect of the right parietal lobe abutting the pial surface with presence of mild perilesional edema. Note the adjacent bony remodeling with thinning out of the inner table. A: Axial cuts, B: Sagittal and C: Coronal reconstruction.

Case Report

A 10-year-old right-handed girl presented to Neurosurgical Out-Patient Clinic of our institute with the chief complaints of right temporal unexplained headache, which was mild to moderate in intensity, occurring intermittently with occasional dizziness but was not preceded by nausea or vomiting for three months. In addition, she had five episodes of generalized seizures within one and half months. She was examined in a local hospital and prescribed antiepileptic drug (oral Phenytoin 50 mg thrice a day). Past history was nil significant. On neurological examination at presentation, her GCS was 15/15 with equal and reactive pupils; and all her cranial nerves were grossly intact. There was no weakness; and all her sensations were intact.

CT scan of head revealed a 2.0 x 2.0 cm ill-defined, mildly enhancing iso to hyperdense lesion in lateral aspect of the right parietal lobe abutting the pial surface. There was presence of mild perilesional cerebral edema. Adjacent bony remodeling was noted with thinning out of the inner table. (Fig1)

MRI of brain revealed approximately 2.2 x 2.0 cm T1 isointense and T2 and FLAIR heterogeneously hyperintense lesion in the right parietal lobe in the cortex and juxta cortical white matter with bulging of cortex and scalloping of inner table. The mass showed intense peripheral enhancement. Very minimal non-enhancing T2 and FLAIR high signal intensity was noted around the lesion, suggesting perilesional edema. The overall impression was neuronal tumor with differential diagnosis of dysplastic neuroepithelial tumor (DNET) and ganglioglioma. (Fig2) Awake EEG was reported to be normal without any epileptogenic foci or abnormal interictal pattern. There was no generalized sharp or spike and slow waves.

The patient was diagnosed as right parietooccipital brain tumor with high suspicion of dysembryoplastic neuroepithelial tumor (DNET); and underwent right

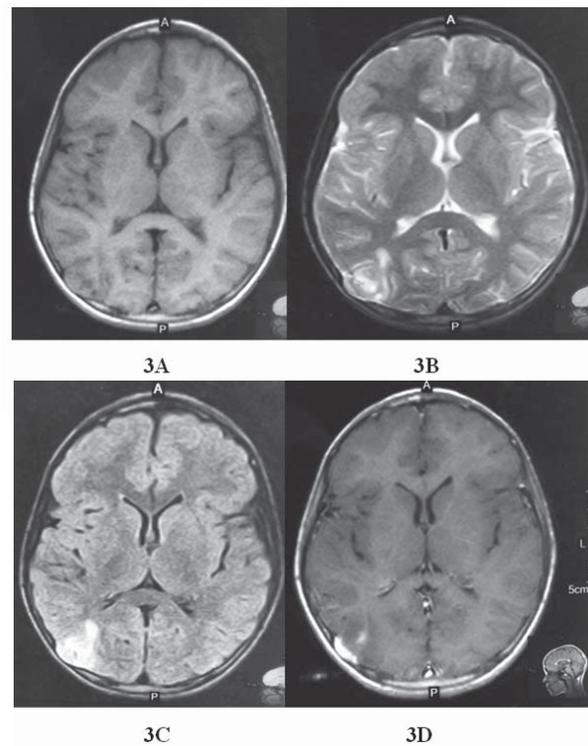


Figure 2: Preoperative MRI of brain depicting T1 isointense and T2 and FLAIR heterogeneously hyperintense lesion in the right parietal lobe in the cortex and juxta cortical white matter. Note the bulging of cortex and scalloping of inner table. The mass showed intense peripheral enhancement. Very minimal non-enhancing T2 and FLAIR high signal intensity was noted around the lesion, suggesting perilesional edema. A: T1-weighted, B: T2-weighted, C: FLAIR sequence D: contrast images.

parieto occipital craniotomy and gross total excision of the tumor. The patient was given general endotracheal anesthesia and kept on prone position. A Mitre skin flap was made, extending anterior from 1 cm in front of tragus toinion posteriorly, and right parietooccipital craniotomy was performed in a standard fashion. Dura was opened in a curvilinear shape. Microsurgical technique was employed to grossly resect the abnormal tissue in toto. Extended gross total lesionectomy which include resection of grossly abnormal tissue and surrounding gliotic tissue was done. The specimen was sent for histopathological examination. After thorough irrigation and hemostasis, the dura was closed in continuous water-tight fashion. The bone flap was put back in its original position, securing with minicranial plates and screws. The incision was closed in layers and skin approximated with staples.

Intraoperative finding was a 4 x 3 cm moderately vascular firm reddish-whitish glistening tumor with ill margin. (Fig3)



Figure 3: Intraoperative picture showing a 4 x 3 cm moderately vascular firm reddish-whitish glistening tumor with ill margin.

The postoperative course was uneventful; and the patient was discharged after staple removal on postoperative day 10 and continued on oral Phenytoin.

Histopathological report of surgical specimen revealed diffused proliferation of atypical cells showing moderate to marked pleomorphism revealing atypical astrocytes along the focal cells showing clearing resembling oligodendrocytes. In between the tumor cells, vascular proliferation was also noted. There was occasional presence of Mitosis. Necrosis was not seen. Scattered atypical and binucleated ganglion cells with round to oval, vesicular chromatin and prominent nucleoli were also noted. Adjacent transition to reactive glial tissue was seen, surrounding the tumor. The findings were consistent with anaplastic ganglioglioma, WHO Grade III. (Fig 4)

The patient was followed up one month after surgery and was advised for postoperative radio-chemotherapy.

Discussion

Gangliogliomas are rare mixed glioneuronal tumors which represent only less than 1% of all central nervous system (CNS) neoplasms. They contain a mixture of neoplastic glial and neuronal cells.⁸ These tumors are staged, according to the WHO classification as grades I and II, representing benign, slow-growing tumor while the remaining high grade group is composed of anaplastic gangliogliomas and ganglioblastomas (WHO grade III and IV).⁷

Anaplastic ganglioglioma, a rare form of mixed primary brain tumor, whether de novo or arising from a low-grade lesion, consist of both the neoplastic ganglionic and glial astrocyte cells.⁵ In AGGs, the anaplastic transformation most often occurs in the glial component.¹¹ Though the etiology and pathogenesis still remains unclear, it is said to originate from glioneuronal precursor.^{16,1} AGG is very rare

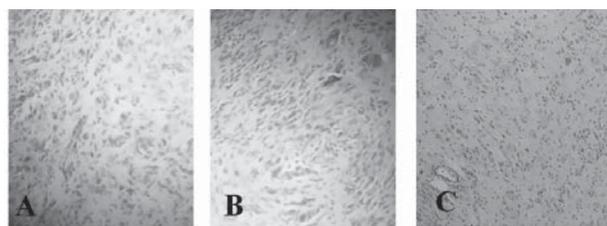


Figure 4: Photomicrography of H & E stain section consistent with anaplastic ganglioglioma. (A-C) shows diffuse proliferation of atypical cells showing moderate to marked pleomorphism. (A & B), Scattered atypical and binucleated ganglion cells with round to oval vesicular chromatin prominent nucleoli. Vascular proliferation in between the tumor cell.

and poorly characterized, which represents approximately 0.4 – 1.0% of all brain tumors. The incidence of AGG defined by a WHO grade III component with increased proliferative index, angiogenesis, and necrosis is very rare and estimated at 0.02 cases/million/year.¹² Up to 10%, the anaplastic transformation occurs in previously diagnosed benign ganglioglioma. It is said that most transformation occurs in the glial component; however, few have reported occurrence of transformation in the neuronal component as well.⁴ Though the ganglioglioma can occur anywhere throughout the CNS, they mostly occur in the supratentorial region, predominantly in the temporal lobe. The biological behavior of AGG is poorly understood due to their rarity and the current literature evidence is limited to case series or case reports. Though these tumors may affect anyone, it is more prevalent in children and young adult. They are also at higher risk for anaplastic transformation, which has also been associated with previous subtotal resection and radiotherapy. In pediatric population, there is a slight male predominance which is also more likely to have poorer prognosis. Most published series did not identify age as a separate prognostic factor; however, some authors reported that those with age more than or equal to 40 years was associated with a shorter overall survival. Generally, the common clinical manifestations of AGG may include progressive worsening headaches, nausea, seizures and other neurological deficits based on the location of the tumor. In our case, the patient presented with seizures only without any other neurological manifestations.

Imaging characteristics of gangliogliomas are varied and non-specific.^{16,6} Radiological characteristics of AGG were mostly a large unifocal tumor with intense annular contrast enhancement surrounding a central necrosis with mass effect and with an important perilesional vasogenic edema.

intracerebral anaplastic ganglioglioma

In majority of series or reported cases of AGG, on MR imaging, the tumors are typically isointense or hypointense on T1-weighted images, hyperintense on T2-weighted images and contrast enhancement is generally irregular. Similarly, in our case, it was isointense on T1 and heterogeneously hyperintense on T2 and FLAIR MRI sequences. MR spectroscopy has been previously shown to demonstrate peaks of glutamate, choline and myoinositol. Some studies have noted that MRS may reveal distinct but non-specific choline peaks which may differentiate these from benign conditions.²

AGG are clinically malignant aggressive tumor. It may assume the guises of low-grade ganglioglioma, DNET, oligodendroglioma, oligoastrocytoma, pilocytic astrocytoma, Taylor cortical dysplasia, neuroepithelial cyst and pleomorphic xanthoastrocytoma. Dysembryoplastic neuroepithelial tumor (DNET) a benign (WHO Grade I) slow growing mixed glioneuronal tumor of children and young adults, arising from either cortical or deep grey matter. In majority of cases, it is centered in the cortical grey matter, arises from secondary germinal layers, and is frequently associated with cortical dysplasia. Most commonly it is found in the temporal lobe. They characteristically cause intractable partial seizures. The key diagnostic features are well-demarcated, "bubbly" intracortical mass, often seen with minimal or no mass effect, slow growth with evidence of bone remodelling. It typically appears hypointense on T1WI, hyperintense on T2WI, and does not exhibit any enhancement. Spectroscopy study is non-specific, although lactate peak may be present. In our case, though it was located in the parietooccipital, the radiologic feature similar to that of DNET with isointensity in T1 and heterogeneous hyperintensity in T2 and FLAIR images, arising from the cortex and juxta cortical white matter with bubbly appearance and scalloping of inner table.

Due to the rarity of these anaplastic tumors, a standard treatment strategy for these entity is yet to be established. Both the treatment and prognosis of AGG is varied. In the largest evaluation of AGG outcomes using the SEER database, 5-year survival was reported as 63%.¹² The primary prognostic factor was resectability at presentation, with a greater than 25 % difference in overall survival at 2 years. The prognosis of AGG depends on the tumor grade and stage, the overall Karnofsky performance score and therapeutic response. Typically, the prognosis may need to be assessed on a case-by-case basis.

Though the standard treatment for AGG may include all three modalities-surgical excision, radio and chemotherapy; the main treatment is still the radical surgery with complete resection of entire tumor. In a study by Varlet et al (2004) of 40 malignant glioneuronal

tumors, the median survival was 44 months for cases undergoing gross total resection, but only 15 months for those with subtotal resection.⁽¹³⁾ While maximal safe resection is regarded as the primary treatment for AGG, the role of radiation and chemotherapy has not been established.

Conclusion

In summary, AGG is very rare tumors with a strong potential for distant metastasis, suggesting the need for more efficient systemic treatment strategy. The etiology and pathogenesis of this rare tumor remains unclear; however, patients with AGG benefit from surgical resection and definitive role of adjuvant radiotherapy remain to be defined.

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