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Case Report

Fetal subependymal giant cell astrocytoma: A case report and review of the literature

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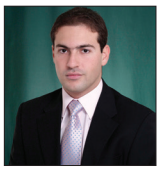

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Received : 08 January 19
Accepted : 04 February 20
Published : 25 February 20

DOI
10.25259/SNI_10_2019

Quick Response Code:

ABSTRACT

Background: Subependymal giant cell astrocytomas (SEGAs) appear approximately in 10% of patients with tuberous sclerosis. These tumors are most commonly diagnosed in childhood and adolescence, with *in utero* diagnosed SEGAs being an extremely rare entity.

Case Description: We present the case of a congenital SEGA detected in an antenatal ultrasound and further investigated with fetal magnetic resonance imaging (MRI) scans at 22 and 32 weeks of gestational age. At 9 days of age, the child underwent craniotomy and partial excision of the tumor, followed by a second more extensive operation 13 days later. The patient was subsequently administered mammalian target of rapamycin inhibitor (everolimus).

Conclusion: In the latest follow-up MRI, at the age of two, the SEGA remained unchanged. Management of these tumors in neonates is challenging, mainly due to high morbidity and mortality of surgical treatment in these ages.

Keywords: Congenital, *In utero* diagnosis, Subependymal giant cell astrocytoma, Tuberous sclerosis

INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder of high penetrance. It is estimated that this condition affects 1 child in 6000[1,5,10] and is characterized by the formation of hamartomas in multiple organs including the brain, eye, kidney, heart, and skin, as well as epilepsy and its comorbidities.[13] The intracranial lesions related to TSC are comprised cortical tubers, subependymal nodules, and subependymal giant cell astrocytomas (SEGAs). SEGAs are slowly growing tumors of glioneuronal origin that typically arises at the caudothalamic groove adjacent to the foramen of Monro.[13,14] They mainly affect children and young adolescents, although a few cases of neonatal SEGAs in TSC patients have also been reported.[12] Congenital SEGAs detected *in utero* are extremely rare.[2,4]

CASE REPORT

Case illustration

We present the rare case of a congenital SEGA detected by fetal magnetic resonance imaging (MRI).

This female was the first child of healthy parents with no known family history of turner syndrome (TS). Abnormal findings in an antenatal ultrasound were further investigated with fetal MRI scans at 22 [Figure 1] and 32 weeks of gestational age. The MRI scans showed a large mass in proximity to the left lateral ventricle involving the frontal and temporal horn and choroid plexus of the left lateral ventricle. The mass showed high signal at T1-weighed MRI scan and low signal at T2-weighed MRI scan. The initial antenatal diagnosis was subacute intracranial hematoma with a significant midline shift.

The girl was delivered by C-section at 38 weeks due to maternal hypertension. Apgar scores were 9 and 10 at 1 and 5 min, respectively, and the birth weight was 2690 g. Physical examination and routine hematology tests at admission were within normal values.

A postnatal ultrasound on day 2 showed a large lesion within the left lateral ventricle causing a midline shift to the right of 10 mm and mild dilatation of the third and right lateral ventricle. MRI on the same day [Figure 2] revealed a lobular tumor of 4 cm × 4.5 cm × 7 cm containing multiple vessel-like formations. The mass expanded through the third ventricle causing dilatation of both the right lateral ventricle and the remaining left ventricular system (frontal and occipital horns). The tumor showed marked and rather homogeneous enhancement after gadolinium administration while the part of the frontal lobe (straight gyrus) showed some peripheral enhancement indicative of local infiltration. A second smaller lesion of 4 mm was shown at the choroid plexus of the left lateral ventricle.

The patient was referred to the neurosurgical department of "Aghia Sofia" Children's Hospital under the diagnosis of choroid plexus papilloma. At 9 days of age, the child underwent craniotomy and partial excision of the tumor, followed by a second, more extensive operation 13 days later.

Postoperatively, the patient was admitted to the intensive care unit both times. She was extubated after 3 days and a few hours, respectively. The postoperative course was uneventful and neurological examination of the patient remained unremarkable.

Histological examination of the material obtained, showed findings suggestive of a SEGA and concurrent presence of cortical tubers, therefore, establishing the diagnosis of tuberous sclerosis.[8,13]

Following the diagnosis of TS, the patient was subjected to additional investigations by echocardiogram, renal ultrasound, skin examination, ophthalmologic examination, and electroencephalography. No other manifestations of TS were found at that point.

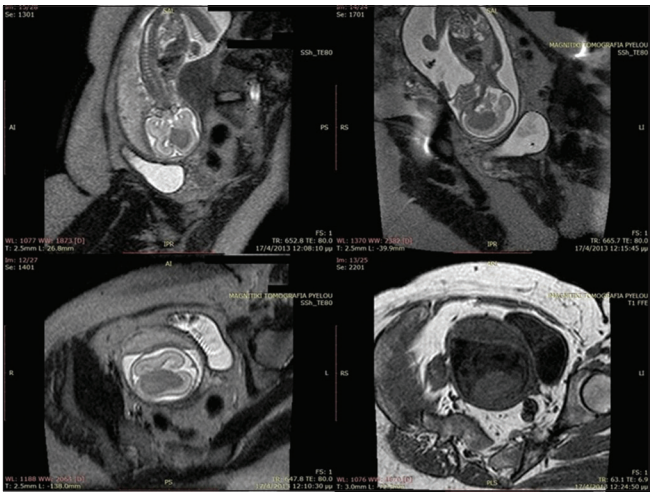

Figure 1: Fetal magnetic resonance imaging scans obtained at 22 weeks gestational age demonstrating a mass occupying the lateral ventricle. The mass is low signal in T2-weighted sequences and high signal in T1-weighted sequences.

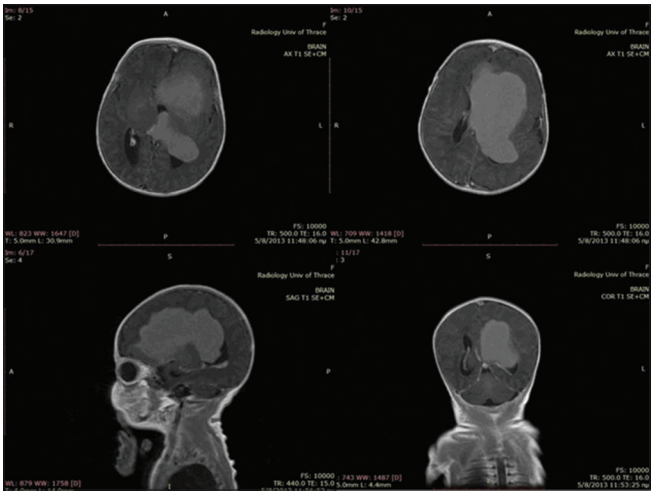

Figure 2: Magnetic resonance imaging scans with gadolinium showing marked and rather homogeneous enhancement after gadolinium administration while part of the frontal lobe (straight gyrus) showed some peripheral enhancement indicative of local infiltration. A second smaller lesion of 4 mm was shown at the choroid plexus of the left lateral ventricle.

During follow-up, seizures were noted for 2.5 months of age. An electroencephalogram showed the presence of single spike-wave.

A new effort to address the tumor by operation was performed at 4 months of age. Unfortunately, due to the infiltration of proximal structures (basal ganglia) and hemorrhagic nature of the lesion, total excision was not feasible. The patient was

subsequently administered mammalian target of rapamycin (mTOR) inhibitor (everolimus). Two months later, during follow-up, a small angiomyolipoma of the left kidney was found.

At 8 months of age, the patient was still receiving everolimus. Physical examination showed decreased mobility of the right hand. Atypical partial focal seizures appeared under treatment with vigabatrin, and the dose was modified. An MRI scan was obtained [Figure 3a]; partial regression of SEGA following treatment with everolimus was confirmed, which remained unchanged in 2-year follow-up [Figure 3b].

Pathology and immunohistochemical analysis

Pathological examination was carried out on hematoxylin and eosin stained paraffin-embedded tissue.

The tumor is composed of clusters of medium and large-sized polygonal and spindle-like eosinophilic cells. The nuclei of these cells contain prominent nucleoli. Their mitotic activity is very low. Among these cells, few gigantic neoplastic cells are noted with plump eosinophilic cytoplasm and either single or multiple nuclei without endonuclear vacuoles. Multiple psammoma bodies and calcium deposits are also present as well as a plethora of lymphocytes and macrophages [Figure 4].

Within the brain parenchyma, areas of distorted architecture are also identified in the form of cortical tubers.

Medium-sized vessels (both arteries and veins) are identified within the tumor borders. They showed signs of wall tumor infiltration.

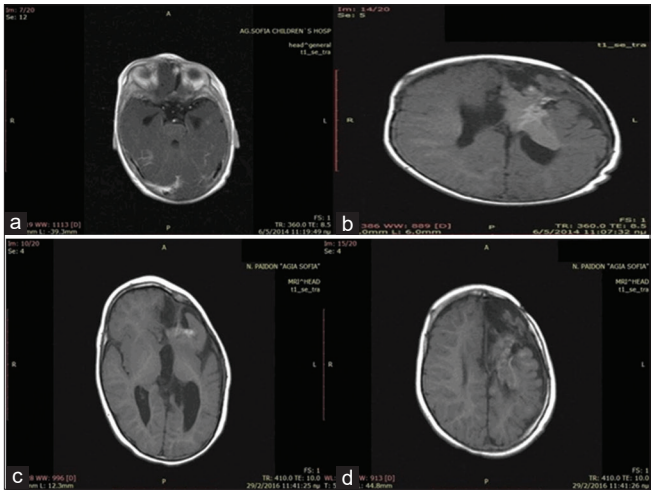

Figure 3: (a) Magnetic resonance imaging scans obtained at 8 months of age after two attempts to address the tumor surgically. The presence of deep-seated residual tumor is noted, as well as the appearance of cortical tubers. (b) Follow-up at 2-year postoperative does not show signs of recurrence.

Immunofluorescence analysis showed that glial markers, glial fibrillary acidic protein [Figure 5] and S100, were heterogeneously expressed (>30% of neoplastic cells), while neural stem cell marker Sox-2 also demonstrated significant nuclear expression concerning about 80% of neoplastic cells. β-tubulin was diffusely expressed (>60%). Markers for synaptophysin CD34, epithelial membrane antigen, CD 99, keratin 8-18, and myelin base protein were found negative.

Ki-67/MIB-1 and p-53 were found positive only in 2–5% and 5% of the giant spindle-shaped cells, respectively, while bcl-2 was not detected.

Immunohistochemistry was positive for markers of T (CD3) differentiation of lymphocytes. Macrophages and microglial cells showed marked expression of CD68/PG-M1 markers.

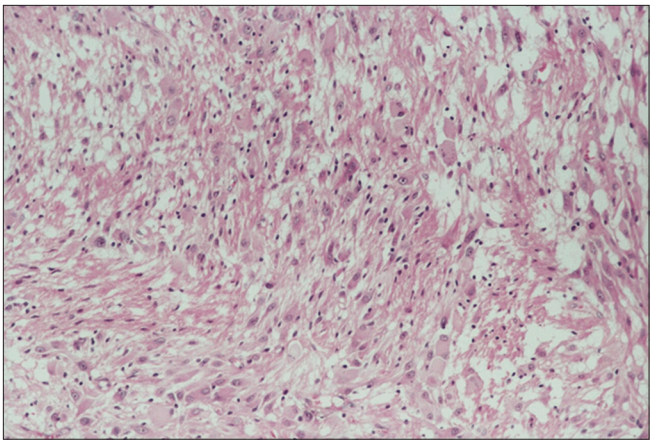

Figure 4: This cellular neoplasm consists of pleomorphic astrocytes in a fibrillar background. The large cells have pleomorphic nuclei with dispersed chromatin and prominent nucleoli, with occasional eosinophilic intranuclear inclusions and abundant eosinophilic cytoplasm.

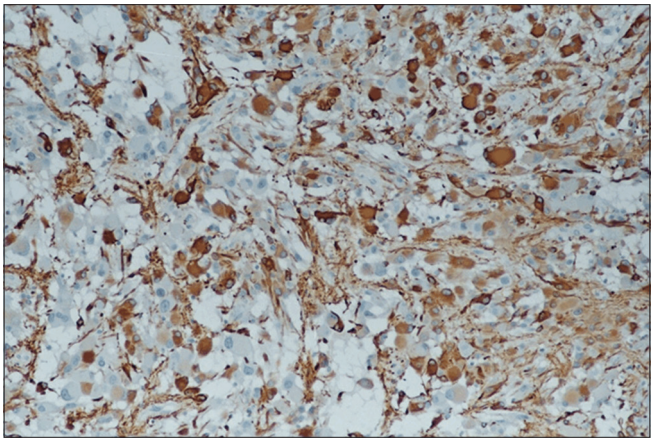

Figure 5: The large tumor cells are diffusely positive on glial fibrillary acidic protein immunostaining.

DISCUSSION

Patients who present primarily with SEGA only rarely seem to manifest the complete classic triad of adenoma sebaceum, seizure, and mental retardation, which characterizes tuberous sclerosis. In neonates with SEGA, especially, the classic triad is highly unlikely to be found. In addition, the fact that a sporadic presentation is rather common with approximately 85% of the cases being the result of new mutations (therefore no familial history of TS is usually obtained), makes the preoperative diagnosis extremely challenging.

Regarding this specific case report, the preoperative diagnosis was choroid plexus papilloma due to the atypical radiological findings of the tumor, such as hyperintensity on T1-weighted MRI and hypointensity on T2-weighted MRI, in reference to the cerebral cortex. Such an atypical presentation has been reported in neonates as a result of higher water concentration in the neonate's brain, calcification, and hypercellularity of the tumor.[3,9,15]

The tumor was located periventricularly, in proximity to the foramen of Monro, which is a characteristic location for SEGA.[13] It is not uncommon for the site of the lesion to be the only typical feature for the patient that presents with SEGA. Therefore, even in the absence of familial history, other manifestations of tuberous sclerosis and typical radiological findings, it is not an overstatement that perhaps every mass in proximity to the foramen of Monro should raise suspicion for SEGA.

Following the establishment of the diagnosis, the choice of therapeutic approach seems to be equally challenging. Most patients with congenital SEGA undergo early surgery, although most reports document relatively poor surgical outcomes in neonates with a significantly high-risk operative morbidity and mortality.[7,11,13]

The reason lies in the fact that in neonates, the particular tumor seems to acquire more aggressive clinical features while the perioperative risk for major brain surgery in neonates is significantly high. The presence of cardiac rhabdomyomas also contributes, being the cause of cardiac complications and severe intraoperative arrhythmia.

On the contrary, massive intratumoral or intraventricular hemorrhage and acute hydrocephalus can cause rapid deterioration in these patients. Furthermore, tumor excision is believed to aid in decreasing the risk of developmental abnormalities elicited by TS. With the increasing use of mTOR inhibitor, a place for pharmaceutical treatment arises, perhaps combined with surgical procedure.[6,13]

Nonetheless, with thorough preoperative evaluation and meticulous planning of the treatment strategy, it is possible that the multiple issues resulting in the treatment of SEGA and its underlying condition in this fragile group of patients can be successfully addressed.

Thanks to the continuous technological advances made in the area of imaging, it is certain that more cases of congenital SEGA will be addressed in future, and the unique characteristics of the particular astrocytoma, as well as the ambiguous nature of tuberous sclerosis, are expected to be an increasing cause of controversy.

CONCLUSION

Even though SEGA is considered to be a rare entity, every mass in the proximity to the foramen of Monro should raise concern and suspicion to neurosurgeons for a subependymal giant cell astrocytoma in pediatric patients. Finally, comprehensive preoperative analysis and meticulous planning of the treatment strategy should be discussed in a multidisciplinary team of pediatric specialists, such as neurosurgeons, neurologists, neuroradiologists, pediatricians, and oncologists.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Karagianni A, Karydakis P, Giakoumettis D, Nikas I, Sfakianos G, Themistocleous M. Fetal subependymal giant cell astrocytoma: A case report and review of the literature. Surg Neurol Int 2020;11:26.