Case Report

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Subependymal giant cell astrocytoma, report of a rare case

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ABSTRACT

Tuberous sclerosis complex (TSC) is a rare genetic disease that is inherited autosomal dominantly and may be associated with subependymal giant cell astrocytoma (SEGA) in 10-20% of cases. Different phenotypes are related to the form of lesions in different parts of the body, including skin, brain, kidneys, lungs, and heart. The age of the patient, the location of the tumor, and associated skin or neurological lesions may guide the pathologist for a definite diagnosis. Here we report a case of SEGA in an adolescent with TSC. Neurological clues including seizure and mental retardation, facial angiofibroma, renal mass, and histopathology examination of the brain tumor culminated in the diagnosis of TSC and SEGA.

Keywords: Subependymal giant cell astrocytoma, Tuberous sclerosis complex

INTRODUCTION:

Subependymal giant cell astrocytoma (SEGA) is a grade I glioma (WHO) consisting of neuroglial cells that grow slowly in the path of the caudothalamic groove. The tumor is located in the periventricular regions of the lateral ventricles and foramen of Monro, which has a good prognosis [1]. SEGA is one of the neurological lesions in patients with Tuberous Sclerosis Complex (TSC) that can occur since childhood. The prevalence is between 10% -20% and can be fatal [2]. TSC is a rare genetic disease that is inherited autosomal dominant in 1 in 6000 to 10000 births or is caused by a genetic mutation in two-thirds of patients. Different phenotypes are related to the form of lesions in different parts of the body, including skin, brain, kidneys, lungs, and heart [3]. Obstruction of the foramen of Monro caused by SEGA can develop hydrocephalus and ventricular enlargement, as well as seizures and focal neurological symptoms [4], which are probably caused by cortical tuber involvements [1]. Here we report a case of SEGA in an adolescent with TSC.

Case presentation:

A 16-year-old male adolescent was admitted due to headache, vertigo, malaise, nausea, and vomiting for 10 days with a recent increase in the severity of symptoms. The patient was unable to stand. He had a history of seizures since childhood. He was aphasic and mute, but agitated. He was mentally retarded and non-cooperative in physical examination. He had hydrocephalus but moved both limbs symmetrically. His last seizure was at the age of 12. Otherwise past medical and family history were negative. The patient's drug history consisted of phenytoin, levetiracetam, and dexamethasone. His vital signs were stable but he had an imbalance. Blood pressure was 100/60mmHg at the admission with a pulse rate of 110 beats/min, respiratory rate of 18/min, and temperature of 37.5oC. Skin lesions were present on the face (Figure 1). Glasgow coma scale (GCS) was 15/15. Neurologic exams were unremarkable. Heart and lung exams were normal. The clinical impression was a brain tumor. Ultrasound exam of the abdomen and pelvis was unremarkable except for a solid hypo-echo vascular mass in the middle part of the left kidney measured 37 x 40 mm with a recommendation for complementary Computed Tomography (CT) scan evaluation. Lab data was normal for PT, PTT, ESR, CBC, Urea, Cr, Na, K, Calcium, Po2, and BS at the time of admission. Serum Mg was 1.4 mg/dl (Child reference range: 1.5-2.3). Ophthalmologist consultation for papillae edema suggested tuberous sclerosis. The margin of the right disc was blurred but with no evidence of tumor lesions. Otherwise ophthalmologic exams of different segments of both eyes were unremarkable. Due to a decrease in consciousness level, the patient was a candidate for surgical removal of the tumor. Written informed consent was obtained from the patient's sister for surgery and a report of the case. Surgery was done on the tumor of the left lateral ventricle. In the operating room, the left frontotemporal incision, tumor resection, and extraction from the left lateral ventricle with duraplasty were done. The specimen sent to the pathology consisted of several creamy brown pieces measured 3.5 x 2.5 x 1 cm. The pathologist reported:

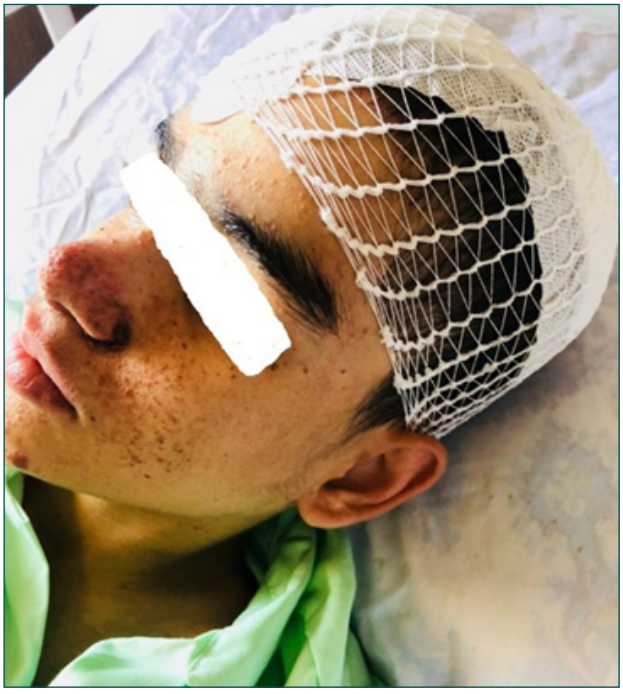

Figure 1. Facial angifibromas

"Subependymal giant cell astrocytoma, WHO, grade I" and recommended immunohistochemistry for EMA, P53, Ki-67, GFAP, TTF-1, S100, and NFP with clinic-radiologic correlation (Figure2 A-C). Only EMA and NFP were negative. Ki-67 was positive in less than 5% of tumor cells. White blood cells (WBCs) increased four days later after admission on the day of surgery to 24.5 x 103 / mm3 (Reference range: 4.0-10) with a differential count of Segment: 95.4%, lymphocyte: 2.8%, and monocyte: 1.8%. WBC decreased to 12.5 one day and 8.5, three days after surgery. Three days after surgery ESR was 26mm/hour (Male< 15). The patient was discharged in relatively good condition. One month later brain CT scan without contrast was done due to blurred vision. This imaging showed an ependymal-based mass measured 36 x 26 mm from the left lateral ventricle with foci of calcification. Also, calcified foci of the ventricular ependymal surface suggested subependymal hamartoma. Subcortical calcified hypodense areas suggestive of calcified tubers were noted. Expansion of the mass to foramen Monro and left frontal craniotomy with encephalomalacia of adjacent parenchyma was also mentioned. Subdural effusion in the left fronto-parieto-temporal region was present. The second surgery was done due to hydrocephaly. A shunt was indwelled between the ventricle and peritoneum. No further follow-up was available for the pathologist.

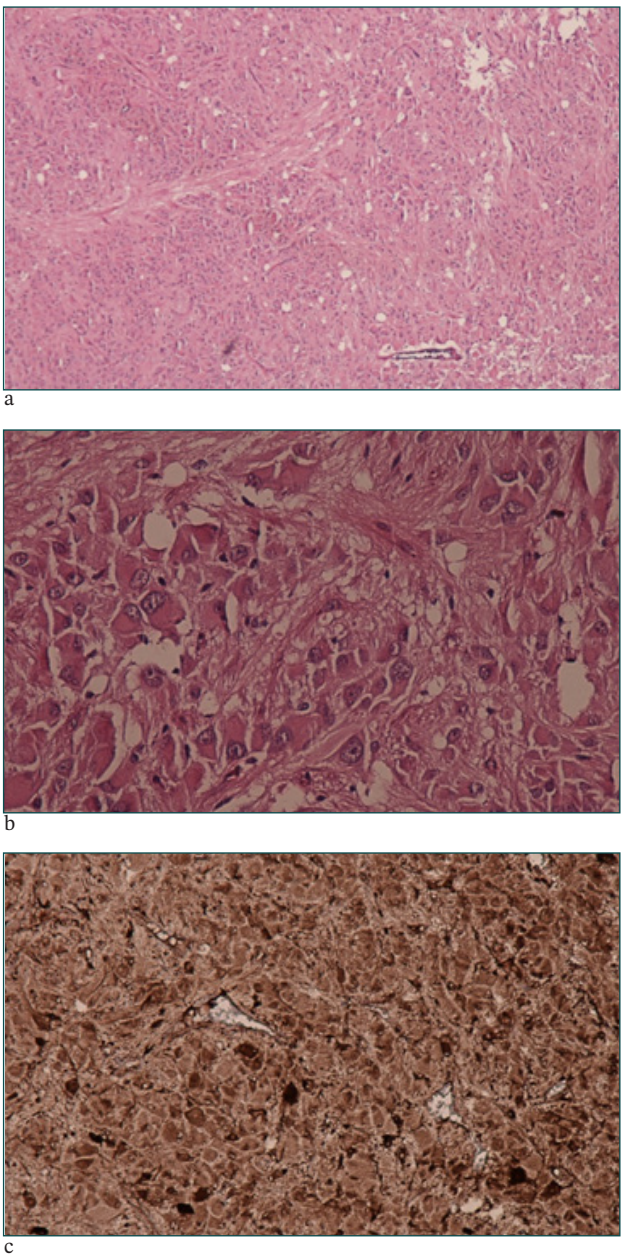

Figure 2. Subependymal giant cell astrocytoma. A, B- Cohesive nests of gemistiocyte-like cells. Hematoxylin-Eosin stain (A x40, Bx200 magnification). C-Positivity for GFAP. Immunohistochemistry stain (x100 magnification).

Discussion:

SEGA in most cases does not involve adults and is seen from birth to early adolescence [5]. The most common age of SEGA is under 20 years old [6], and its average age is 9 years. The coexistence of skin symptoms, seizures, and cognitive disorders creates a triad that is seen in a small number of SEGAs in TSC [7]. In this case, this triad has been seen.

Mutations in TSC1 and TSC2 genes, which encode hamartin and tuberin proteins, disrupt mTOR, resulting in disruption of cell cycle regulation and increased cell division, resulting in TSC. In most patients with TSC, the disease is confirmed by clinical diagnostic criteria and genetic testing. The clinical diagnostic criteria include 11 major and 6 minor. TSC has been confirmed in the presence of two major or one major and two minor criteria. Angiomyolipoma is a renal lesion that grows gradually from childhood and consists of abnormal blood vessels, immature smooth muscle, and fat cells can be seen as multiple lesions in both kidneys. SEGA and angiomyo-

lipoma are major criteria [3]. These two major criteria were probably present in this case for diagnosis of TSC. The two most common skin lesions in patients with TSC are hypopigmented patches and facial angiofibromas, with a prevalence of about 90% [3]. Bilateral reddish-brown papular lesions of different sizes, like sebaceous adenomas, are also seen on our patient`s face which is consistent with angiofibroma.

If mitosis, necrosis, and pleomorphism are seen in histopathology, because it is characteristic of malignant tumors, then the atypical type of SEGA is considered [8]. The location of brain lesions on CT scan and magnetic resonance (MR) imaging, along with knowing the patient`s age can help diagnose the type of lesion [4] . SEGA is diagnosed based on histopathology, clinical and radiological findings [9]. Tumors with giant cells and large neurons are in the differential diagnosis of SEGA in histologic analysis. These more aggressive tumors are gemistiocytic astrocytoma, glioblastoma multiforme, and ependymoma. In the first two, the cells have hairy projections, but cohesive cells are not present. Meanwhile, nuclear atypia, hyperchromasia, and mitosis are more easily seen. SEGA might have rosettes or rosette-like structures in common with ependymoma, but the cells in ependymoma are smaller with a small cytoplasmic volume [9]. Immunohistochemistry is of benefit in the confirmation of some cases of SEGA, albeit with considering clinical, location, radiology, and histopathology features. Glial fibrillary aciditic protein (GFAP) and S100 are positive in spindle cells but neurofilament (NF) and Synaptophysin are negative. Meanwhile, Ki-67 shows a low proliferation index [1]. Microtubule-associated protein 2 is also considered a positive marker [3]. In another study [6], Sadeghipour and colleagues stained 5 cases of SEGA with CD99 and found strong membranous positivity in all of them. They stated that the marker is negative in infiltrative glioma including gemistiocytic astrocytoma. CD99 was negative in another study [8] on a fetus with the diagnosis of SEGA. The only cure for SEGA is surgery [1]. Our patient`s symptoms also improved after surgery and there was a decrease in the number of WBC and inflammatory factors.

Conclusion:

SEGA is a WHO grade I brain tumor. It is mainly seen in periventricular regions of the lateral ventricles and foramen of Monro in the tuberous sclerosis complex. The age of the patient, the location of the tumor, and associated skin or neurological lesions may guide the pathologist for a definite diagnosis.

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Conflict of interest:

None

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