

Tuberous Sclerosis Complex Revealed by a Subependymal Giant Cell Astrocytoma: A Case Report and Literature Review

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Abstract

Introduction: Subependymal giant cell astrocytoma (SGCA) is an uncommon benign brain tumour, usually histologically low grade with slow evolution. frequently associated to tuberous sclerosis complex which is a phacomatosis due to genetic mutations affecting specific tumor suppressor genes. Radical surgery whenever possible is the cornerstone of treatment, mTor inhibitors are also effective in the case of associated TSC when surgical resection is impossible.

Presentation of case: We report herein the case of a 12-year-old Arabian child presented with symptoms of increased intracranial pressure without other neurological complaints. Brain imagine discovered tumor located in the right lateral ventricle with ventricular dilatation. Pathological examination of stereotaxic biopsy confirmed the diagnosis of SGCA. The child died by the complications of intracranial hypertension.

Discussion: Subependymal Giant cell astrocytoma is a rare benign tumor that originates from the wall of the lateral ventricles near the foramen of Monro, associated with the tuberous sclerosis complex or Bourneville's disease in 5 to 14%. The particularity of our case of SGCA, is the revealing aspect of TSC on the one hand, and the absence of typical cutaneous signs (present in 95% of TSC) and mental retardation on the other hand. The discovery of a huge renal mass suggestive of angiomyolipoma corroborated the diagnosis of TSC in our case.

Conclusion: Subependymal giant cell astrocytoma is a very rare benign tumor; so its diagnosis requires to realize a specific and orientated workup looking for other lesions associated with tuberous sclerosis complex.

Keywords: Subependymal giant cell astrocytoma; Tuberous sclerosis complex; Surgery; Targeted therapies

Introduction

Subependymal giant cell astrocytoma (SEGA, SGCA, or SGCT) is a rare benign brain tumor which histogenesis is not exactly understood. This tumor is usually histologically low grade, well circumscribed, and often calcified, with a slow evolution. It's frequently associated with the tuberous sclerosis complex (TSC) known as Bourneville's disease which is a phacomatosis due to genetic mutations affecting specific tumor suppressor genes. The prognosis of SEGA depends mainly on degree of hydrocephalus and intramural hemorrhage that can be caused, as well as the extent of visceral lesions in the case of associated TSC. The Treatment is based on complete surgery whenever possible, and the use of mTor inhibitors in the case of associated TSC when resection is impossible.

Case Presentation

A 12-year-old Arabian child, without medical history of mental retardation, psychologic disorders, or seizures. Presented to the department of pediatric emergencies with symptoms of increased intracranial pressure (headache, intermittent vomiting and visual troubles) without other neurological complaints. Physical exam found a conscious child, well oriented in time and space, without neck stiffness or fever. Brain CT scan showed an isodense tumor located in the right lateral ventricle with ventricular dilatation (Figure 1). In brain MRI the tumor was hyper-intense and heterogeneous in T1 sequence, centered by cystic component, with associated hydrocephalus (Figure 2). The child had benefited from an internal ventricular drain, with a stereotaxic biopsy. Histopathological study with immunohistochemistry showed a grade II astrocytoma AGFP (+), P100 (+) and NSE (+), confirming the diagnosis of giant cell astrocytoma (Figure 3). As part of the work-up

a body CT scan was performed showing a huge mass of the left kidney (Figure 4). Cardiologic and ophthalmologic exams were normal. The diagnosis of TSC was done, and the child received an mTOR inhibitor (pediatric form), but the evolution was marked by the aggravation of his intracranial pressure resulting in his death.

Discussion

Subependymal Giant cell astrocytoma is a rare benign tumor that originates from the wall of the lateral ventricles near the foramen of Monro, which often affects children and young adults, but congenital forms have been also described [1-6]. It's associated with the tuberous sclerosis complex or Bourneville's disease in 5% to 14%, a phacomatosis linked to the mutation of tumor suppressor genes TSC 1 and TSC2 localized respectively on the chromosomes 9 and 16, which is transmitted according to an autosomal dominant mode [7-12]. This mutation allows the activation of mTor pathway leading to the genesis of multiple and diffuses benign tumors in various organs [2,3]. The diagnosis of TSC is established on a set of criteria proposed by Gomez: 2 major criteria or a major criterium with 2 minor criteria suffice to make the diagnosis. The neurological involvement is dominated by giant cell subependymal

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Figure 1: Axial brain CT scan showing a tumour of the lateral right ventricle.



Figure 2: Axial T1 sequence MRI showing an hyperintense tumour with hydrocephalus.

(SEGA) astrocytoma [13-15], subependymal nodules (NSE) which are localized in ventricles and are benign tumors. Giant-cell ependymal astrocytoma (SEGA) is usually clinically manifested by signs of high intracranial pressure caused by obstructive hydrocephalus, epileptic seizures, and mental confusion, sometimes it can cause focal signs such as hemiparesis and cranial nerve VI palsy. These signs are difficult to detect in children with autism or severe mental retardation [3-5]. The ASCG may also reveal TSC as in our clinical case. Radiological features are not specific, in fact the morphology, intensity and signal of these intraventricular lesions vary from one case to another. But most often it is a tumor that is born from the wall of the lateral ventricle near the Monro hole, well limited, isodense enhances strongly after injection of the contrast medium, which associates with a ventricular dilation, sometimes calcified. The histopathological study confirms the diagnosis, histologically ASCG is made of a triple cell component distributed on a fibrillar background and the use of immunohistochemical staining allows to make a positive diagnosis because many markers like NSE (neuron-specific enolase), NF (neurofilament), NCAM (neuronal cell adhesion molecule) Substance P, S-100, and also glial fibrillary acidic protein (GFAP) are expressed in ASCG [16].

Among the particularities of our case is the absence of cutaneous lesions whereas cutaneous manifestation during TSC are present

in 95% in form of achromic macules as the earliest manifestations, followed by fibrous patches of the forehead, facial angiofibroma and periungual fibroids occurring usually later [3,4,7]. Paradoxically, our case presented with a giant kidney tumor, whereas renal involvement is frequent in adults but rare in children, it most often gives benign tumors called angiomyolipoma with an evolutive risk to renal failure [7,8]. The prognosis is dependent on complications of intracranial hypertension, intramural hemorrhage and associated visceral lesions. Treatment of ASCG is essentially based on extensive surgical exeresis, however, postoperative complications may occur including hydrocephaly, motor deficiency, hemorrhage and rarely infections. This surgical treatment must be done before the installation intracranial hypertension. The role of surgery is limited in the presence of extensive visceral lesions, hence the interest of targeted therapies which can slow down the progression of the disease [11,12,15]. In fact, mTor inhibitors (everolimus, sirolimus) have shown their activity in this sitting by allowing significant tumor size decrease for the treatment of ASCG if associated with TSC, with regrowth after cessation of therapy [17].

Conclusion

Subependymal giant cell astrocytoma is a very rare benign tumor; its diagnosis requires to realize a workup to rule out other lesions associated with tuberous sclerosis complex. Surgery when feasible is the cornerstone of the treatment, and targeted therapies are useful in the case of TSC. The prognosis is related much more to intracranial hypertension and the complications of surgery.

Ethical Approval

Not applicable

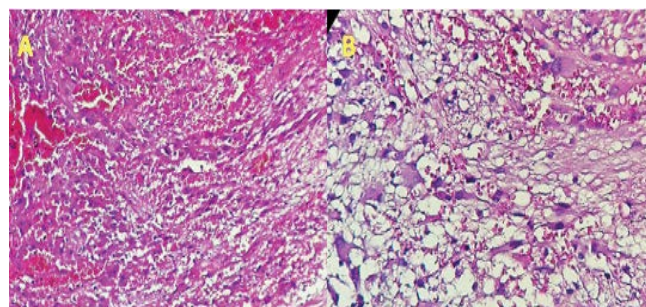


Figure 3: Histological features of SGCA.



Figure 4: Axial abdominal CT showing a huge left renal mass.

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Author Contribution

All authors contributed to the writing of this paper.

Conflicts of Interest

There are no conflicts of interest.

Research Registration Studies

Not applicable.

Patient Consent

Not applicable. This report does not contain any personal information that could lead to the identification of the patient.

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