**CASE REPORT**

Atypical Bourneville sclerosis without epilepsy and mental retardation: case report and literature review

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**Abstract**

Twenty-four-year-old woman without familiar detected signs of Bourneville’s disease or tuberous sclerosis complex (TSC) was diagnosed with this disease by casual discovery on cerebral magnetic resonance imaging (MRI) of an intraventricular tumor, after symptoms consist in headache, equilibrium disturbances, and progressive loss of vision. MRI shows an intracranial mass, 33/24/30 mm in size, localized at the level of third ventricle and lateral ventricles, with irregular shape, interesting the foramen of Monroe. There are also nodular areas of calcification and a supratentorial hydrocephalus involving the lateral ventricles and the posterior part of the third ventricle. The patients present facial angiofibromas, but from the classical triad of the disease, the epilepsy and mental retardation were absent, the patient never presented seizures. The total removal of the tumor (peace to peace) was performed surgically, the macroscopic features of resected tumor (20/10/10 mm) was of white-gray color, elastic consistency, localized in the both lateral ventricles (left>right) and into the third ventricle, traversing the foramen Monroe. The histopatological examination associated with specific localization of tumor and the facial angiofibromas are very suggestive for subependimargiant cell astrocytoma (SEGA). We have a rare case of atypical or incomplete TSC in which the epileptic seizures and the mental retardation are absent, the intelligence is normal, but occur some psychical symptoms: anxiety, sleeplessness, and autism or behavior disturbances. The evolution of this case was marked by complications because of postoperative hydrocephalus and multiple shunt insertions and revisions were performed after the tumor resection.

**Keywords:** tuberous sclerosis complex, astrocytoma, anxiety, atypical.

**Introduction**

The subependymal giant cell astrocytoma (SGCA) is a tumor localized in the cerebral ventricles. Characteristic for this tumor is the association with tuberous sclerosis, but rarely occur also solitary. Generally, is a benign type of astrocytoma, well circumscribed.

The incidence is 1:5800–1:10 000 live births [1].

Epilepsy has poor response to the therapy and occurs at 80–90% of patients, after Devlin er al. an sometimes at 93.2% of patients [2]. In conclusion, there are approximately 7–10% TSC cases without epilepsy and our case is included in this last percent, the patient being seizures free.

SGCA occur at approximately 10–15% patients with TSC [3]. Genetically transmutations were identified on two different genes: TSC1 (9q34) and TSC2 (16p13.3). The alterations into these two genes seem to be responsible from the occurrences of TSC.

Some authors concluded that TSC1 and TSC2 are equally responsible for the disease in familiarly cases with hereditary transmission [4]. Other studies show that TSC2 give more severe forms of TSC and the gene alterations in this type are more frequent [5].

To the molecular level, TSC1 produce hamartin and TSC2 tuberin, which are tumor suppressor genes. Inactivation of hamartin (TSC1) or tuberin (TSC2) lead to appearance of TSC [6]. Subsequent to the hamartin or tuberin inactivation, which result by specific genetically mutations, some organs of the body such kidneys, heart, lungs and skin have the risk to develop tumors.

Although TSC is an autosomal dominant disease, however 70% of cases results from a new mutation; in these cases, the parents or kindred are not affected by the disease.

Clinical presentation depends of number, location, type, size of lesions and the involved organ systems.

**Patient, Method and Results**

The patient, female, 24-year-old, was admitted in the hospital at neurosurgery for decease of vision, headache, vertigo and equilibrium disturbances with onset about one month ago, with an MRI performed in another service that shows intraventricular tumor.

Ophthalmological consult show papillary edema. Postoperative radiography of the chest reveals a degree of bilateral decreasing a lung’s transparency by opacities with mixed character and tendency to confluence.

Cardiological consult and ECG were normal.

Neurological consult shows: normal status of consciense GCS 15, without meningeval signs of irritation, cranial nerves without deficit, and no ataxia at neurological examination.
Magnetic resonance imaging (MRI) (Figure 1) describe an intraventricular tumor localized occupying the third ventricle and lateral ventricles left-right, affecting the foramen of Monroe, polylobated, with 33/24/30 mm in size. The tumor is spontaneous hyperdense with areas of hypodensity and inhomogeneous enhancement after contrast administration. The tumor presents also nodular areas of calcification at the level of right cerebellar hemisphere and subependimal, supratentorial internal hydrocephalus on the lateral ventricles and posterior part of the third ventricle.

Figure 1 – (a) Magnetic resonance imaging (MRI) frontal section; (b) MRI sagittal section; (c) MRI coronal section.

The majority of patients with TSC have subependymal nodules [7, 8] and 5–20% of TSC patients develop SEGA, which seem to be developed from the subependymal nodules [8, 9].

Cerebral angiography shows left intraventricular tumor, with low grade of vascularization, filled from left ACI, angiographic feature of internal hydrocephalus, poor injection of the left transverse sinus and of the 1/3 frontal of the superior sagittal sinus (Figure 2).

Figure 2 – Cerebral angiography of the left intraventricular tumor.

Preoperative abdominal ultrasound showed an increase in size of the liver, homogeneous appearance without dilated intrahepatic biliary ducts, gallbladder without gallstones, homogeneous spleen, normal pancreas, kidney without dilatation and no fluid in the peritoneum.

Psychological examination concluded a normal mental development; patient had higher education and works like economist at the time of admission. Patient’s functioning before admission was satisfactory.

Also, psychological examination revealed that patient was oriented, with no major disturbances of thought and perception. Was observed only a slight annoyance during the clinical interview with a spontaneous decreased attention, appeared in the same time with the installation of headaches, patient showing a slight decrease in final useful yield. Were found sleep disturbances, characterized by mixed insomnia. Anxiety accompanied clinical picture, Hamilton Anxiety Rating Scale (HAM-A) score was 19, indicate mild to moderate severity, Global Assessment of Functioning Scale (GAF) score 81–90 represent minimal symptoms at admission moment [10].

Surgical intervention consisted in quasi-total ablation (peace to peace) of intraventricular EPIC. Grossly examination shows a multi-fragmentation piece of 20/10/10 mm, white-gray elastic intraventricular located near the foramen Monroe.

Histopathological examination reveals a tumor with cell density average, apparently without cytoarchitecture drawings, except of incomplete tumor nodules. They are separated by fibrovascular stroma, with variable thickness. Tumor cells present mostly quasi-gemistocytic look, the rest looking elongated, fusiform. Cells with fusiform aspects appear in high-density areas, their appearance change probably due to the compression by the adjacent cells.

The tumor is mostly well defined, and without the majority of diffuse infiltrative character of astrocytomas. Occasionally has the small pocket of growth in the periphery that penetrates the periventricular brain parenchyma (Figures 4 and 5).
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Cells were larger than gemistocytes, but not really the kind of giant cell glioblastoma with giant cells or pleomorphic xanthoastrocytoma. The cytoplasm is eosinophilic with frosted glass appearance. The nucleus is pushed to the periphery and adopt an appearance resemble neuronal cells through vesicular and visible nucleus/nucleolus (Figure 6).

Amid uninucleate majority populations sometimes occur bi- and multi-nucleated cells. Fibrillar extensions originated in the opposite cell pole core thereby increasing neuronal appearance.

In Figure 7 are presented some groups of cells with ganglionary/ganglioid aspect. Described histological aspect and private location
are particularly suggestive for subependimal giant cell astrocytoma (SEGA) diagnosis.

The differential diagnosis is made with histologically tumor-like one side and on the other side with tumors that develop in this particular location. Among morphologically similar tumors should be excluded gemistocytic astrocytoma. This, however, does not develop intraventricular brain parenchyma, is diffuse infiltrative and gemistocytic astrocytes are smaller and have more tachychromatic nucleus and nucleolus much less obvious.

Figure 6 – Tumor’s cell type macro-gemistocytic showing vesicular nucleus and evident nucleoli with perivascular distribution (van Gieson staining, ×400).

Figure 7 – Groups of cells with ganglionary/ganglioid aspect (van Gieson staining, ×400).

Figure 8 – Cerebral CT scan postoperative images: (a) Intracranial hydrocephalus in the right occipital ventricular horn; (b) Cerebral CT-scan at 15 day after first intervention. The conversion of EVD in ventricular peritoneal drainage was realized with Medtronic valve level 1.5; (c) Cerebral CT-scan at 25 days after tumor resection – internal hydrocephalus. The ventricular peritoneal drainage was realized with Medtronic valve level 1.5 on the left side.

SEGA is a slow-growing tumor and evolves without any clinical manifestation until produce obstructive hydrocephalus [8, 9].

The best treatment for SEGA is the surgical resection; after resection, the rates of SEGA regrowth are low. In our case, quasi-total resection of the tumor was possible; the patient’s general and neurological status was undulating. Immediately postoperative, general status was good, the patient was vigil, mild motor deficit on the right arm, equal pupils, and photo-motor reflex bilaterally present.

In the day 7th postoperative, the general patient’s status decrease suddenly, she becomes somnolent, non-responsive. Cerebral computed tomography (CT)-scan (Figure 8a) performed in emergency shows acute intracranial hydrocephalus, which need surgical re-intervention in emergency with EVD (external ventricular drainage) in the right occipital ventricular horn. Postoperative, the patient was transferred in the intensive care unit (ICU). The patient’s general status was satisfactory, opened the eyes at nociception, spontaneous movement on both sides, without signs of meningeal irritation. During the next days, a meningeal syndrome occurs, which was remitted under therapy with Ciprofloxacin 600 mg per day.

At 8th day after the last intervention was realized the
conversion of EVD in ventricular peritoneal drainage with Medtronic valve level 1.5. The general status of the patients was marked by the occurrence of bronchopneumonia, which needs intensive therapy (Figure 8b).

After another 10 days (25 days after tumor resection) the general patient’s status was decreased and a CT-scan performed in emergency shows internal hydrocephalus. An emergency surgery was performed realize a ventricular peritoneal drainage with valve Medtronic level 1.5 on the left side (Figure 8c).

Postoperative, the patient was transferred in ICU. Subsequently the evolution was slow favorable, with spontaneously movements on both side, mild hemiparesis on the right arm, open the eyes spontaneously, expressive aphasia, surgical wounds cured normally, without fever.

Medication treatment of patients was with Ceftriaxonum 4 g per day, Nadroparinum one vial of 0.6 mg per day, Omeprazolum 20 mg per day, ACC two ampoules per day. The patient made recovery.

Discussion

TSC is known as an autosomal dominant inherited disease characterized by classical triad: epilepsy, mental retardation and facial adenofibromas. But, there are cases without epilepsy (about 10%) or mental retardation. However, most cases (70%) do not have parents affected by the disease, as is the case with our patient, implying that this patient there was a new genetic mutation in the genes TSC1 or TSC2.

It is widely accepted that the standard traditionally treatment of SEGA is the tumor resection [9, 11, 12].

Appropriate it would be to make total excision of the tumor because if remains a part of it, will continue to grow. In our case, it could make only subtotal ablation of the tumor.

The most common pathological brain lesions are cortical tubers, subependymal nodules (SENs), SGTS and abnormalities of white matter [3, 13].

It was found that cortical tubers are constantly in the brains with TSC. They would be the cause of epilepsy in TSC.

Cortical tubers are glial and neuronal cells proliferation with impairment of the cortical structure. SENs are present in most patients with TSC and SGCA occurring in 5–20% of TSC patients [8, 14, 15].

Typically, SEGA arise from SENs in the area of foramen Monroe, unilateral or bilateral [7, 8].

The best therapeutic solution is total tumor ablation. Recent studies suggested that mTOR inhibitors have a growing without being early or intermediate detected, prognosis remains reserved.

The absence of seizures or some significant mental disorders has made tumor grow in size without significant clinical signs.

The only overt manifestations were facial angiofibromas were not analyzed in the context of possible TSC, so the chance of surgery in these patients in the early stages of tumor development was practically zero. The patient required transfer in neuromotor rehabilitation ward because of significant postoperative neurological complications occurred.

Conclusions

Given the existence of such a case, with the minimum physical manifestations and the absence of any neurological symptom, clinicians must take into account that TSC can have atypical or incomplete picture. Performing a brain CT or MRI control by the family doctor, neurologist, psychiatrist if is suspected that a patient would have TSC, is encouraged. If the psychiatrist has to consult a patient with minor or mild manifestations of anxiety and insomnia to which may be added and particular cutaneous manifestations similar to those of TSC should suspected and exclude an organic cause brain, the more so if the symptoms are resistant to specific psychiatric therapy and occur in a young person without cardiac problems. A simple control brain CT may increase the chances of survival in such a case, knowing that the more brain tumor is larger, the vital risk and complications are higher.

References


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