Global Scientific JOURNALS

GSJ: Volume 7, Issue 11, November 2019, Online: ISSN 2320-9186

www.globalscientificjournal.com

A HYPERTENSIVE ENCEPHALOPATHY REVEALING A BOURNEVILLE TUBEROUS SCLEROSIS IN A INFANT

Djamila-Djahida Batouche [a*], Dalila Boumendil [a] ,Samia Benouaz [b] , Djillali Batouche [d] ,Nadia-Faiza Benatta[a], , Setti-Aouicha Zelmat[a], Kheireddine Kerboua [c]
a faculté de médecine Oran

b faculté de médecine SBA

c Laboratoire immunology Ouargla

d CHU Kremlin Bicetre

E-mail address: khedidjabatouche@yahoo.fr

Summary

Background-Tuberous sclerosis of Bourneville (TSB) is a rare genetic disease, transmitted in the autosomal dominant mode characterized by the development of benign tumors in different tissues: skin, kidney, heart, brain and eye. The classic triad in children includes skin spots, epilepsy and mental retardation.
Méthods-The authors report a clinical sticher of an infant admitted for lateralized convulsive seizures complicated by malignant arterial hypertension and whose etiological diagnosis of tuberous sclerosis of bourneville was made in a setting etiological assessment of a malignant arterial hypertension. complicated by convulsive encephalopathy.
Results- A . O 36 months old, the eldest of siblings of 02, of non-consanguineous parents. Psychomotor development was normal. A notion of epilepsy in the maternal uncle was reported in family history. The beginning of the symptomatology went back to the age of 07 months old ,by the occurrence of convulsions type syndrome WEST.02 days before admission, a state of convulsive illness motivated his transfer to the intensive care unit in May 2014. At admission: a stage IIa coma, a PA at 160 / 120 mmHg, an achromic skin placard of the sacral region, and the inner thighs.Pulmonary auscultation found some crackling rales at the two bases of the pulmonary field.An exploration report of the HTA found: on the abdomino - pelvic ultrasound a left nephromegaly. A renal scintigraphy with DMSA found a silent kidney on stenosis of the right renal artery. Blood creatinine, urine dosing of AMVs were unremarkable.Cerebral MRI revealed subependymal nodules along the lateral walls of the lateral ventricles The child was nephrectomized on the right. The histological study of the nephrectomized specimen revealed multiple angiomyolipomas in the cortex.The child was put out on day 25, under dual antihypertensive and anticonvulsant therapy.The death of the child occurred at home, 05 months following discharge of hospital, as part of a convulsive hypertensive encephalopathy refractory to treatment.
Conclusions- TSB is an autosomal dominant disorder.Its diagnosis is radiological clinico.The clinical manifestation is polymorphic. The prognosis is closely related to neurological manifestations. Vigabantrin treatment proves better control of convulsions.A multidisciplinary approach would improve the therapy and quality of life of patients.
Keywords
Infant, convulsive encephalopathy, malignant hypertension, achromic spots, cortical tubers, renal cysts,

Abréviations

Tuberous sclerosis of bourneville (TSB)

Cerebral magnetic resonance imaging (C MRI)

Hight Blood Pression (HBP)

Résumé :

Introduction -La sclérose tubéreuse de Bourneville (STB) est une maladie génétique rare, transmise sur le mode autosomique dominant caractérisée par le développement de tumeurs bénignes au niveau des différents tissus : la peau, le rein, le cœur, le cerveau et e l'œil. La triade classique chez l'enfant comprend des taches cutanées, l'épilepsie et le retard mental.

Méthode - Les auteurs rapportent une vignette clinique d'un nourrisson admis pour crises convulsives latéralisées, compliquées d'une hypertension artérielle maligne et dont le diagnostic étiologique d'une sclérose tubéreuse de bourneville a été posé dans un cadre du bilan étiologique d'une hypertension artérielle maligne compliquée d'encéphalopathie convulsivante.

Résultat -A . O âgé de 36 mois, l'ainé d'une fratrie de 02, issu de parents non consanguins. Le développement psychomoteur était normal. Une notion d'épilepsie chez l'oncle maternel était rapportée, dans les antécédents familiaux. Le début de la symptomatologie remontait à l'âge de 07 mois par la survenue de convulsions type syndrome de WEST.02 jours avant son admission , un état de mal convulsif a motivé son transfert en réanimation. en mai 2014.A son admission : un coma stade IIa, une PA à160 /120mmHg, un placard cutané achromique de la région sacrée, et la face interne des cuisses.

L'auscultation pulmonaire retrouvait quelques râles crépitants aux deux bases du champ pulmonaire. Un bilan d'exploration de l'HTA retrouvait : à l'echographie abdomino - pelvienne une néphromégalie gauche. Une scintigraphie rénale au DMSA a retrouvé un rein muet sur sténose de l'artère rénale droite.La créatinine sanguine , le dosage urinaire des VMA étaient sans particularité.

Une IRM cérébrale a révélé des nodules sous-épendymaires le long des parois externes des ventricules latéraux. L'enfant a été néphréctomisé à droite .L'étude histologique de la pièce néphréctomisée a révélé de multiples angiomyolipomes au niveau de la corticale .L'enfant était mis sortant à j25, sous bithérapie antihypertensive et anticonvulsivant.

Le décès de l'enfant est survenu à domicile, 05 mois après sa sortie du service , dans le cadre d'une encéphalopathie hypertensive convulsivante réfractaire au traitement.

Conclusion -La STB est une affection autosomique dominante.Son diagnostic est clinico radiologique .La manifestation clinique est polymorphe. Le pronostic est étroitement lié aux manifestations neurologiques. Un traitement par du vigabantrin s'avère contrôler mieux les convulsions.Une approche multidisciplinaire permettrait d'améliorer la thérapie et la qualité de vie des patients atteints.

Mots clés

Nourrisson, Encéphalopathie convulsivante, hypertension artérielle maligne, taches achromiques, tubers corticaux, kystes rénaux,

Background.

Tuberous sclerosis of Bourneville (TSB) is an autosomal dominant disease. belongs to the genetic group of phacomatoses. It leads to an increase in multi-systemic benign hamartomas, which mainly involve the skin, the brain, the kidneys, the heart, and the eyes, leading to symptomatology variation .The classic triad in children includes skin spots, epilepsy and mental retardation. The authors report a clinical sticker of an infant, admitted for lateralized convulsive seizures, complicated by malignant arterial hypertension and whose etiological diagnosis of TSB was made in a framework etiological assessment of a malignant arterial hypertension, complicated by convulsive encephalopathy in this infant.

Observation

A. O, a 36 months old, the oldest of 2 siblings, whose parents were non-consanguineous, was admitted to pediatric intensive care unit for convulsive hypertensive encephalopathy in May 2014. The pregnancy was followed and full terme. The delivery was normal. There was no indication of neonatal suffering. The Psychomotor development was normal. A case of a maternal uncle with epilepsy was reported in the family medical history.

The symptomatology began at 07 months of age, before his consultation, with the occurrence of seizures type lateralization of eyes, for which he was examined by paediatrician and treated by Phenobarbital , sodium valproate 25mg / kg / day, then Hydrocortisone 100mg / j, for suspicion of WEST syndrome .

A state of febrile seizure, followed by a post-critical coma was mentioned during the interrogation. This episode was treated as on ambulatory care. Evolution was marked by the occurrence of a right motor deficit, wich regressed after four months.

On the day of admission, the child experienced several seizures leading to his transfer to pediatric intensive care unit , in May 2014. At the pediatric intensive care unit, a comatose child stage 2a was found, with lateralization of the gaze on the right, reactive isocoric pupils. Reflexes of coughing and swallowing were also noticed. An respiratory rate at 32 C / min with 93% oxygen saturation in the open air. Blood Pression was 160/120 mm Hg. The heart rate was 140 bpm. Skin discoloration Time <3 Sec. A T° was at 39 °. Pleural pulmonary auscultation found a few crackles at the basal level, and cardiovascular auscultation confirmed tachycardia. Examination of the skin lining showed shagreen patch in the lumbosacral region. Also, there were achromic spots affecting the external genitalia and the inner thighs, as well as a lumbar formation 7 Cm in diameter suggestive of a lipoma.

There were café-au-lait spots on the lower eyelids. The rest of the somatic examination came with no particularity.

The evolution was marked by:

-Returning to consciousness, 05 minutes after a dose of midazolam at 0.2 mg / kg and Apyrexia with external cooling.

- Blood pressure raised to 200/150 mmHg, which prompted the health care team to treat the child by anti-hypertensive therapy like Nicardipine (loxen). The syringe pump was at a rate of 0.2 mg / kg / day, then doses in increments of 0.5m / Kg to 3mg / Kg / a day were increased to achieve a mean blood pressure of around 120 mmHg.

- Passage to the oral nicardipine after the stabilization of blood pressure in 28 hours.

The etiological assessment of these hypertensive seizures was based on:

- blood test of creatinine and urea returned without particularities.

- A dosage of Vanyl Manderic acid in search of a Pheochromocytoma and which returned normal
- Abdomino - pelvic ultrasound: objectified a left nephromegaly with multiple cysts and a discreet unobstructed pylocalic dilatation.
- Renal CT scan: revealed a diffuse form, with multiple cystic images and angiomyolipoma of the left kidney
- A DMSA renal scintigraphy showed no function of the right kidney with a silent kidney on stenosis of the right renal artery.
- Ophthalmological examination found bilateral papilledema with multiple retinal phages.
- A magnetic resonance imaging showed cortical (cortical tubers) and subcortical hyperdense lesions (in T1 weighting after gadolinium injection) : hypo-intense or without bilateral siege signal, associated with T2-weighted hyposignal subependymal nodules located along the lateral walls of the lateral ventricles, an aspect of phacomatosis like TSB .

Right nephrectomy was performed because the DMSA scintigraphy showed no function of this kidney. Histological examination revealed multiple cortical angiomyolipomas, segmental and focal glomerulosclerosis lesions.

The child continued intermittently convulsing, his mean arterial pressure was higher than 120 mmHg. sodium valproate at 25 mg / kg / day and nicardipine at 25 mg / day day were administered and put out in 25 days of hospitalization.

One week later, the child was readmitted for refractory epilepsy to initial therapy, prompting the health care team to increase the doses of sodium valproate to 40 mg / kg and the combination of Vigabatrin 50 mg / kg / day.

The child lost sight following his discharge of hospital . 05 months later, child's mother come back to hospital and inform that her child died at home, due to convulsions refractory to the prescribed treatment .

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Discussion

BTS is a congenital disorder of autosomal dominant inheritance, of a very high but incomplete penetrance and variable expressivity .Its occurs in 1 out of 6000 births. [1]

However, according to the authors, two-thirds of cases are sporadic, corresponding to a novo mutation uninfluenced by parental age. In one third of cases, the mutation is carried by one of the two parents. It is supported by two different genes TSC1 and TSC2 [2], carried respectively by chromosomes 9 and 16. Localized respectively on chromosome 9q34 and 16p13 and coding for two distinct proteins: Hamartine and Tuberin, which have an anti¬oncogenic role thanks to their complementary and interactive actions. [3] .The hamartomas target the cebtral Nervos System, the skin, the kidney, the

retina, the heart and the bone. The clinical expression of TSB is characterized by its polymorphism and variability from one subject to another. The diagnosis can come in the classic forms: epilepsy, mental retardation, cutaneous signs. But often, the expression is more discreet, and it is important to recognize, by using strict clinical criteria, the signs of the disease that can assert the TSB (Table 1)

Table 1: Diagnostic criteria for Tuberous sclerosis of Bourneville [4]

Major criteria	Angiofibroma
	Non-traumatic nail and periungeal fibroids
	Hypomelanic spots (more than three) shagreen patch
	Subependymal Nodule giant cell astrocytoma hamartomas
	Multiple retinal nodular
	Cardiac Rhabdomyoma (isolated or multiple)
	Pulmonary Lymphangiomyomatosis
	Renal Angiomyolipoma
Major criteria	Multiple holes in tooth enamel
	Hamartomatous rectal polyp
	Bone cyst
	Linear and radial anomalies of white matter migration
	Gingival fibroids
	Achromatic spot retinal
	Multiple renal cysts

A clearly identified TSB is defined by the existence of two major criteria or one major criterion and two minor criteria.

The diagnosis is probable in the presence of both a major and minor criteria. It is still possible when we observe one major criterion or two minor criteria [5].

Our patient had at least 02 major criteria and 01 minor criteria (cortical tubers, ependymal nodules, Hypomelanic spots ,renal cysts).

Neuroradiological signs are a key element to diagnosis. They are very frequent (more than 90%) and are part of the major and minor diagnostic criteria of TSB. Computed tomography reveals calcified subependymous nodules, which are along the external walls of the lateral ventricles. It also targets subcortical tubers in the form of sub-cortical hypodensities.

In children, cerebral Magnetic Resonance Imaging (MRI) of the head can show, in less than 10% of cases, that subependymal nodules that have evolved to a giant cell astrocytoma [6].

MRI from our observation has individualized the tubers in the form of hypersignals in T2 and hyposignals in T1.

Clinically, neurological manifestations mainly come in form of epilepsy and mental retardation, which are often the hallmarks of the disease. Seizures affect about 80% of patients [7].

They occur in the first year in more than two thirds of patients. Seizures often occur around the fourth or fifth month of life and are often focal, tonic or clonic. The evolution occurs in 50% of the cases towards the installation of West syndrome [8] .60% of them will have refractory epilepsy to the drugs. It has been demonstrated that the presence of refractory epilepsy and infantile spasms in the TSB were significantly associated with cognitive disorders and psychiatric disorders. In addition, any type of poorly controlled seizures is an important predictor of psychiatric disorders and, when epilepsy is refractory, it plays an aggravating role in neuropsychiatric disorders [8-12].

In our patient, West syndrome manifested itself at 07 months of age and was frequently followed by an increase, in frequency and severity of seizures, associated with a behavioral disorder in the form of extreme agitation described by the mother.

In the Maghreb countries, Chalabi and al [13] at Oran (Algeria) in university hospital , reported that 22 families were affected by this disease. The clinical and familial analysis made it possible to note the precocity of the signs, the appearance of epileptic seizures, partially complex in most cases, the frequency of a psychotic syndrome and the frequency of the inherited forms.

In Morocco , Chaouki and al report an observation of 11 children with TSB and whose first seizures occurred before the end of the first year of life in nine patients and, in two cases, in the first week of life. Five patients had West syndrome [14].

In some studies, from 17% to 68% of the cases of TSB, autistic disorders are observed without frequency differences between girls and boys [15, 16].These authors have suggested that periventricular calcifications that characterize TSB may have a role in the occurrence of autistic behaviors and several hypotheses that may trigger: epilepsy, mental retardation, anatomical lesions could be risk factors.

The cutaneous manifestations are the most frequent after the neurological manifestations, and come in the form of achromic spots and angiofibromas.[17].

The achromic spots, which occur in more than 90% of cases, are the most early manifestations of the first months in life. The pelts of shagreen patch, sitting at the level of the sacro-lumbar region, and appear between two years and five years and are seen in 30 to 50% of cases [18].

Finally, we can observe defects or holes in the dental enamel "pits" that can occur on the milk tooth as on the final teeth (incisors and canines in particular).These manifestations were absent in our patient. Other abnormalities such as angiofibromas on the face may appear in 3 to 4-year-old children and affect 50-75% of cases [19].

Renal damage can also be observed during the patient's childhood [19]. This kidney damage was revealed during the etiological review of our patient. In 75% of the cases, it was in the form of Angiomyolipomas, often multiple and bilateral, and in 25% of the cases, it was in the form of renal cysts.Angiomyolipomas are benign tumors and appear during the first years of life, the scalability which justifies regular monitoring as early as the second month. Renal cysts usually appear during childhood and have no evoluential potential.

In rare cases, multiple renal cysts may be responsible for high blood pressure or chronic renal failure [20]. Finally, the development of renal neoplastic lesions is possible in children but exceptional [21] . Our patient was admitted for convulsive encephalopathy with malignant hypertension and HBP was found in 30% of patients with renal localized TSB

Ophthalmological examination can help the diagnosis by highlighting retinal hamartomas According to our observation, ocular involvement is described in 50% of cases in the form of hamartoma or retinal phage [22].

Several authors have reported cardiac events related to cardiac Rhabdomyomas, which are present in 50 to 70% of patients but are rarely symptomatic. They may cause neonatal heart failure or, later, an obstructive problem, valvular dysfunction, arrhythmias, wolff-parkinson-white syndrome, and thromboembolic brain accidents.

They appear around 22-26 weeks of gestational age and can be detected by fetal ultrasound, which can help in prenatal diagnosis. They often regress completely during the first years of life [23,24].

Lungs and bones can be observed. During TSB Lymphangio -Leiomyomatosis is a rare lung disease that occurs in only 1% of cases, and almost exclusively in adult women. Bone damage often corresponds to cystic lesions and is usually asymptomatic [25]. These lesions were not observed in our patient.

Medical treatment remains symptomatic to control convulsive seizures, by anticonvulsant treatment that will be adapted to the types of seizures and epileptic syndromes. Vigabatrin is indicated in the treatment of West syndrome and appears to be effective in more than 80% of cases [26, 27].

Neurosurgical treatment may be discussed when the patient is on a drug-resistant epilepsy or has brain tumor, with better results if a single epileptogenic tuber is identified.

Our patient lost sight of and did not receive a neurosurgical intervention. His mother described a refractory epilepsy prior to his death that occurred at home, 5 months after the second hospitalization.

Study limitations

Our study has several limitations:

1. In this observation, we did not initially suspect a TSB, even if the patient had shown, when admitted to pediatric intensive care unit, the criteria that may indicate a TSB. Head Cerebral

MRI was carried out as part of an etiological assessment of HBP in this child. The MRI revealed to us a form of phacomatosis.

2. We did not ask a genetic examination of the parents, nor did we conduct a genetic study of our patient or his sister, due to the lack of technical platform at the hospital.

Conclusions

Tuberous sclerosis of Bourneville is a multi-systemic genetic disorder transmitted in a dominant fashion.The diagnosis of is a clinical radio diagnosis, based on major and minor criteria.

The prognosis is closely related to the neurological manifestations. The west syndrome and Convulsive encephalopathy are the dominant clinical form in children, complicated by a hypertensive crisis.

Treatment with Vigabantrin is found to better control the west syndrome.

An early and adapted multidisciplinary care would allow health care teams to preserve the cognitive functions of a large number of patients and improve the quality of their life.

Disclosure of interest

The authors declare that they have no competing interest.

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