Case Report

Rasmussen’s Epileptogenic Encephalitis in a Tropical Country

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Background: Encephalitis of Rasmussen is an inflammatory hemisphericopath of unknown etiology. It is a cause of drug-resistant epilepsy. Aim: To report two cases of Rasmussen’s encephalitis (RE) in a low-income setting. Clinical Observation: The cases concerned were that of an 8-year-old boy and a 4-year-old girl. The illness began with daily several seizures at the age of 28 months in the boy and 23 months for the girl. Epileptic seizures were generalized in the elder one and focal in the younger. The elder presented right hemiplegia with severe cognitive impairment. In the younger child, the expression of the language was disturbed, associated with right hemiparesis at 4/5. The electroencephalography recording showed background theta asymmetric rhythm associated with discharges of periodic lateralized epileptiform discharges (PLEDs) into the left hemisphere in the two cases. Brain imaging showed left hemisphere atrophy. The seizures had decreased in intensity after association of several anticonvulsant molecules over a period of 3–6 months. The diagnosis of RE was based on clinical, paraclinical, therapeutic, and evolution arguments. Conclusion: There was a delay to establish the diagnosis. Further studies are needed to evaluate rehabilitation capacities in children with RE before brain maturation.

Keywords: Cerebral imaging, encephalitis, epilepsy, Rasmussen

Introduction

Rasmussen’s encephalitis (RE) is a necrotizing epileptogenic and inflammatory hemisphericopath of unknown etiology described for the first time in 1950.[1] It leads to a gradual deterioration of motor and cognitive functions.[2] The incidence of the disease was 2.4 per 10 million children below 18 years.[1] The exact pathogenesis of RE is still unknown. Viral and autoimmune origins were suspected because of the histological features and focal inflammatory lesions.[4,5] In clinical terms, RE is characterized by neurological deficit and epileptic drug-resistant seizures.[6] The RE evolves in three phases defined by radio-clinical criteria parallel to the neuropathological lesions: a prodromal phase, an acute phase, and a residual phase.[7,8] Magnetic resonance imaging (MRI) of the brain is the gold standard for diagnostic evaluation and monitoring of RE.[9,10] Hemispherotomy improves cognitive function and the control of epileptic seizures.[11-13] We report two cases of RE presented in Togo.

Clinical Observation

Case 1

An 8-year-old boy presented in pediatrics unit for secondarily generalized focal epilepsy, right hemiplegia, and language disorders, which have been evolving since February 2014. In his antecedents, he was born on April 21, 2008 of a term pregnancy by vaginal delivery. He was resuscitated for neonatal life-threatening condition with Apgar score 7-8-9. Immunization coverage was up to date. Psychomotor development was normal until the age of 1 year. Parents did not have any chronic pathology. In the history of the disease, the child had generalized seizures (about one seizure per trimester) at the age of 1 month and febrile-impaired consciousness at 6 months of age. The onset of recurrent convulsions in a febrile context motivated the first hospitalization in January...
2010. Electroencephalography (EEG) was performed and lateralized epileptiform discharge directed to symptomatic focal epilepsy was observed. He was put on phenobarbital. The persistence of seizures motivated to change treatment to sodium valproate (30 mg/kg/day) and levetiracetam (10 mg/kg/day) and stopping phenobarbital. Epileptic seizures persisted with increasing frequency to over three seizures per day. The aggravation of epileptic seizures was correlated to high fever. Following the seizures, there was a motor deficit of the right hemi-body, disorders of language, and progressive worsening of character and behavior, which became disabling in October 2014.

Physical examination on November 20, 2016, showed a normal temperature, weight of 29 kg, and a height of 136 cm. Neurological examination showed that his intercritical consciousness was normal without meningeal signs. Walking and standing up were impossible. Spastic tetraplegia was observed with predominance on the right side with a muscular force rated 0/5 on the right and 3/5 on the left side. The osteotendinous reflexes were lively, polykinetic, and diffused to the four limbs. The signs of Babinski and Hoffmann were present and bilateral. The exploration of the superficial and deep sensibility was normal. Homonymous right lateral hemianopia was present. Examination of other cranial nerves was difficult because of cognitive disorders. The neuropsychological evaluation had objectified difficulties in capturing attention, a lack of response to the call of his name, a brief eyes follow-up of objects, a lack of concentration and alteration of comprehension, and a limitation of language to a few syllables.

Analyses assessment included biology, electroencephalogram, and medical imaging.

Lumbar puncture showed high protein level at 0.65 g/L. The search for inflammatory cells and antibodies and soluble antigens was not available. The EEG showed an asymmetry of the background rhythm with microvoltage in left hemisphere. Figures 1 and 2 show the EEG plots in longitudinal montage.

The brain scan showed atrophy of the left cerebral hemisphere, dilation of the Sylvian valley and the left lateral ventricular system, and enlargement of the left cortical furrows. No lesions of the posterior fossa and right cerebral hemisphere were observed. Figure 3 shows the computerized tomography (CT) scan sections of the patient. Brain MRI showed similar lesions with Evans ratio stage 4 [Figure 4].

Regarding the treatment, carbamazepine (300 mg twice daily) was associated to levetiracetam 1000 mg/day and sodium valproate. Corticosteroid therapy is not indicated at this stage of evolution, which corresponds to the clinical residual phase. We initiated functional rehabilitation.

At 6-week follow-up, we noted a decline in the frequency of seizures to one seizure per week under three anticonvulsant therapy. Cognitively, we noted a stabilization of symptoms. The language disorders worsened with complete alteration of the understanding and expression. Three months later, we observed a cessation of seizures with heavy motor, cognitive, and language sequelae.

Case 2
A 4-year-old girl presented with focal epilepsy and motor deficit of the right hemi-body. The onset of symptoms dated back to October 2014 and was marked by secondary general seizures in a febrile context, complicated by an alteration of consciousness for a month. On awakening, she developed cognitive and language disorders associated to right hemi-corporeal motor impairment. She received speech therapy and motor physiotherapy. She was put on phenobarbital at 50 mg dosage. Epileptic seizures persisted with increasing frequency (approximately 12 focal seizures per day).
Regarding the antecedents, the pregnancy was completed at term and without incident. Delivery was by cesarean section for severe oligoamnios and cephalic presentation. The Apgar score was 7-8-10 and the weight was 2900 g. On day 3, she was admitted to pediatric intensive care unit for neonatal infection. The evolution was favorable with discharge after 10 days under antibiotics. The vaccination status was up to date. Psychomotor development was normal until September 2014.

The physical examination of September 6, 2016, showed a fairly good general condition. The temperature was 37°C and weight was 15 kg for a size of 99 cm. The cranial perimeter was 49 cm and brachial circumference was 16 cm.

On the neurological level, her walk faltered to the right. Spastic right hemiparesis was noted with a muscular force rated at 4/5 on british medical council muscular testing. The osteotendinous reflexes were sharp on the right. The Babinski and Hoffmann signs were present on the right. Superficial hyperesthesia was observed on the right hemi-body associated to right lateral homonymous hemianopia and right hyposmia.

The neuropsychological assessment noted moderate language impairment with conservation of understanding, good oral mobility, and perfect repetition of vowels. However, a deformation of some consonants with velar | K | and | 9 |, liquids | I | and | R |, and fricative | Z | was observed. The active and passive lexicons were quite rich with some difficulty of access to the exit lexicon.

Paraclinical assessment included biology, EEG, and medical imaging. Cerebrospinal fluid reported a protein concentration of 0.50 g/L. The search of specific antibodies and inflammatory cells was inaccessible. The EEG showed an asymmetric theta background rhythm, associated with spike wave discharges and generalized polyspikes predominating on the left side such as periodic lateralized epileptiform discharges (PLEDs) [Figures 5 and 6]. The brain scan showed atrophy of the left cerebral hemisphere with dilatation of the Sylvian valley and enlargement of the cortical furrows [Figure 7]. The patient was started on sodium valproate and carbamazepine in a progressively effective dose. She received motor physiotherapy and speech therapy. At 6 weeks control, we had noted the persistence of three to ten (3-10) focal seizures a day. Cognition and language had the same disturbances. We stopped valproic acid and associated phenobarbital to carbamazepine and levetiracetam. Three months later, a reduction to five single focal seizures per day was observed, which reduced to three daily seizures at 6 months.

**Discussion**

This study reports two cases of RE. The study of these two cases cannot be generalized to the whole Togolese population. Some children may have drug-resistant epileptogenic encephalitis, but they have not been able to reach specialized neurological health facilities for many reasons. On the other hand, the rarity of this pathological entity makes this result useful for sharing with the scientific community. RE is a neurological disorder described in children with a median age of 6 years despite some reported cases in adolescents and young adults. The boy experienced a prodromal phase of the disease that began since the age of 1 month marked by epileptic seizures. The acute phase began in May 2014 and was followed by the residual phase with no signs of edema on MRI. The prodromal
phase was less marked in the girl. The antecedent of neonatal infection requiring hospitalization 3 days after birth is not “a priori” related to the RE diagnosed later. This clinical evolution in three phases is classic in the course of the disease but the prodromal phase is not always present. In both cases, they had experienced a perinatal fetal distress. This condition has long been evoked as the diagnosis of cerebral palsy, the first cause of epilepsy in children in resource-limited countries. The focal nature of epileptic seizures presented by children is suggestive of focal brain damage. The appearance of the hemi-corporeal motor deficit motivated the realization of the brain scan in children. For this purpose, the CT scan is the most accessible tool of the brain exploration in our region, where 90% of patients do not have access to specialized medical facilities and MRI. This lack of imaging may partly explain this low rate of reported cases of RE in the African countries. Although hemispheric atrophy is visible on CT scan at an advanced stage of the disease, this is not the case at an early stage when there is diffuse unilateral cerebral hypometabolism on functional MRI. The children were right handed before the onset of the disease. The dominant hemisphere is affected, so it seems obvious that the boy has more language disorders. The degree of severity may also be due to the age of onset of the disease, that is, at age 6 years, with insufficient cerebral maturation and hemispheric specialization, leaving little route for adaptation.

The opposite was observed in the girl with an onset of the disease at 22 months of age. Almost total recovery from language disorders was observed despite atrophy of the left hemisphere. We can evoke the probable hypothesis that the dominant hemisphere is on the left and there were some secondary phenomena of rehabilitation with passage of the language centers on the right. Functional MRI may confirm this hypothesis but was not accessible. In both the cases, the diagnosis was made on the basis of CT scan. Left hemisphere atrophy is evident, but contralateral hemisphere appears less obvious. The dilatation of the Sylvian valley observed on the cerebral scans is symptomatic of the lesions of the peri-Sylvian region, which is a predilection site for the attacks in RE. The ipsilateral atrophy of the head and tail of the caudate nucleus described as specific to the RE is less visible on the CT scan than on the MRI scan. In the only case reported in adolescents, the diagnosis was also made on the basis of CT scan. MRI was performed in boys to eliminate differential diagnoses. The quality of the MRI performed does not permit to describe accurately the structures affected in the basal ganglia. Functional MRI is not yet available in our hospital to diagnose the disease at an early stage. There was a mild contralateral atrophy on the child’s MRI that relates to gliosis in the context of drug-resistant epilepsy.

In both cases, the EEG showed an asymmetry in the background rhythm with a micro-left voltage, symptomatic of left hemisphere atrophy. Asymmetric background rhythm and PLEDs are EEG characteristics of RE. These abnormalities are more obvious as the disease progresses with a frequency of 70% between 3 and 6 years after the onset. The main etiologies of PLEDs are ischemic stroke (34%), infections (16%), tumors (13%), intracranial hemorrhage (9%), metabolic causes (6%), cerebral anoxia (5%), Creutzfeldt–Jakob disease (1%), and unknown causes (16%). The absence of EEG patterns of seizures on the left in the...
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girl with partial seizure confirms the random nature of these abnormalities in the surface EEG.[19]
The presence of behavioral disorders explains the difficulty in obtaining an interpretable EEG of rest.
The sedation of the epileptics to realize the EEG does not make it possible to do the different stimulations and thus reduces the chance of causing the appearance of the epileptic anomalies, although these are not specific of the RE.[5] All the criteria proposed by the European Commission in 2005 for the diagnosis of RE were obtained in the boy's condition. The absence of MRI does not allow making the diagnosis in the girl according to these European criteria. The absence of histopathological tests in our study is a limitation. Hemiconvulsion-hemiplegia-epilepsy (HHE) syndrome is a rare and severe complication of focal epilepsy in children under 4 years of age during febrile illness.[20,21] HHE syndrome is the most likely differential diagnosis for RE. This syndrome usually occurs before the age of 2 years, as the case of the girl, but in the HHE syndrome, hemiconvulsions preceding the motor deficit and epilepsy occur from 1 to 3 years.[15] Most children with HHE syndrome have some degree of cognitive impairment. Histopathological tests would formally eliminate the diagnosis of HHE syndrome but were inaccessible.
The treatment comes down in the management of seizures with habitual difficulties of observance in tropical countries.[16,22] RE is characterized by drug-resistant epilepsy and it is difficult to evaluate the response to treatment in case of poor compliance. It is therefore imperative to emphasize therapeutic education to improve adherence to treatment. The girl had benefited from functional rehabilitation during hospitalization for 6 months at the beginning of the illness. This rehabilitation could explain the good recovery of language and motor deficit leading to walk without help. The real impact of the absence of functional rehabilitation in the second child seems weak speech disorders. Other therapeutics were reported in the literature, such as immunotherapy and hemispherotomy, and have a real beneficial effect on the prognosis of the disease. The result is better when these treatments are given at an early stage of the disease.[23,24] Language recovery in the youngest child could also be an argument for early diagnosis and management in children.[25,26]

CONCLUSION

RE is a rare neurological disease and a cause of drug-resistant epilepsy. The diagnosis was made according to the European Commission 2005 criteria in acute and residual phases. The severity of this condition lies in the appearance of acute phase after brain maturation, but further studies are needed to test this hypothesis. All children with cerebral palsy should perform detailed neurological explorations to identify different causes. The CT scan helps to make the diagnosis at a late stage of the disease in our country, making the specific treatment difficult with heavy sequelae at this stage.

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Conflicts of interest

There are no conflicts of interest.

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