Management of two cases of Rasmussen's Encephalitis at the department of pediatric neurology at the FANN National Hospital in Dakar, (Senegal).

Prise en Charge de deux cas d'Encéphalite de Rasmussen au service de neurologie pédiatrique du Centre Hospitalier National de FANN de Dakar, (Sénégal).

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Abstract

Rasmussen encephalitis is a rare autoimmune disease first described in the late 50s. It diagnosis requires multidisciplinary participation around the neuropediatrician. The diagnosis is confirmed with the association of several features: clinic, EEG, brain imaging and pathology. The Bien et al., diagnosis criterias provide good clues to retain the diagnosis of RE in the absence of cerebral biopsy. Treatment options relay on antiepileptic drugs, immunomodulator therapy and surgery. We are doing a brief report of non-usual onset of Rasmussen encephalitis and the challenging treatment decision implied in a low equipped setting.

Keywords: Epileptic Encephalopathy - Paediatric Neurology - Rasmussen Encephalitis - Refractory Epilepsy - Sub-Saharan Africa.

Résumé

L'encéphalite de Rasmussen est une maladie auto-immune rare décrite pour la première fois à la fin des années 50. Son diagnostic nécessite une participation multidisciplinaire autour du neuropédiatre et il est confirmé par l'association de plusieurs éléments : les données cliniques, les données de l'EEG, l'imagerie cérébrale et la pathologie. Les critères diagnostic de Bien sont un outil efficace et pratique pour retenir le diagnostic d'encéphalite de Rasmussen en l'absence de biopsie cérébrale. Le traitement repose sur les antiépileptiques, les immunomodulateurs et la chirurgie. Dans cet article, nous présentons la prise en charge de deux cas d'encéphalite de Rasmussen dans un environnement à ressource limitées.

Mots-clés: Afrique Sub-saharienne - Encéphalite de Rasmussen - Encéphalopathie épileptique - Épilepsie réfractaire - Neurologie pédiatrique.

Introduction

Rasmussen encephalitis (RE) has first described in the late 50s by Theodore Rasmussen and Europeans diagnostics criterias was established by Bien et al. [1]. It is a progressive disease characterised by drug-resistant focal onset epilepsy, progressive hemicorporeal motor deficit and equally progressive cognitive decline with unihemispheric atrophy on brain imaging [2]. RE generally evolves in three phases with neurocognitives damages that become irreversible [3]. Various antiepileptic drugs (AEDs) have been used with a rather satisfactory response. On the other hand, it is classically described a superiority of immunomodulatory treatments in the management of neurocognitive deterioration [4]. From two cases, we present the challenges faced by neuropediatrician in the management of Rasmussen's encephalitis in low-incomes countries.

Observation

Case 1: A 14-year-old boy hospitalised at the children's hospital Albert Royer (CHAR), for status epilepticus (SE). Symptoms started four months before admission to CHAR with intense headaches of rapidly progressive onset in a febrile setting and generalized tonico-clonic seizures 48 hours later successfully treated with valproate acid (VPA) and Diazepam (DZP) in a regional hospital. Four months later he developed a true SE and has been transferred to CHAR. He has no previous medical or surgical history. On admission, he presented with a SE consisting of clonic seizures, of the left hemicorp with a Glasgow coma scale (GCS) of 6 out of 15, a more or less spastic motor deficit of the right hemicorp, sharp osteotendinous reflexes in all four limbs, epileptoid tremor in both feet without meningeal or cranial nerve involvement. The rest of the examination was unremarkable. A treatment based on VPA and DZP was commenced. An improvement was noted 48 hours later. The interictal time interval was several minutes longer and the GCS raised at 12 out of 15. Right hemiparesis was more marked with a predominantly crural motor deficit with a muscular bulk at 2 out of 5 on right lower limb and 4 out of 5 on the right upper limb according to the Medical Research Council scale. He had no cognitive impairment.

The brain CT-Scan showed a left hemicerebral atrophy marked by a cortical hemiatrophy and a left caudate nucleus head's atrophy (Figure 1).

The cerebro-spinal fluid (CSF) study was normal. The non-specific biological inflammatory assessment was unmarkable. Specific inflammatory assessment was not done due to financial issues.

The awake Video-EEG (Figure 2), showed a hemispheric asymmetry marked by a left hemispheric slowing with diffuse spike and spike-wave predominantly Rolandic right sometimes resulting on a true right hemispheric electrical SE. Permanent lower limb clonus at the video confirmed the electroclinical diagnosis of continuous partial epilepsy (CPE).

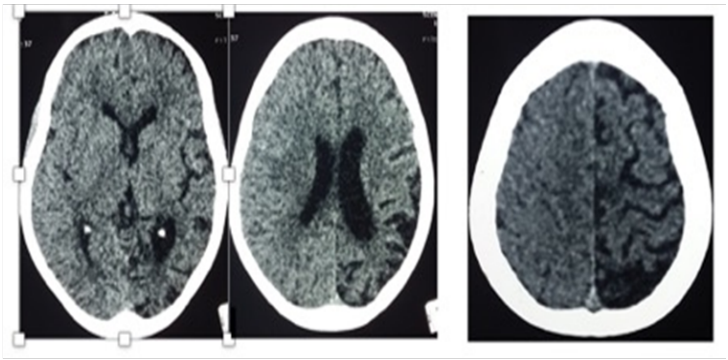
After 72 hours DZP was stopped and Phenobarbital (PB), initiated at 3mg/kg/d, associated with VPA at 30mg/Kg/d. The persisting CPE leaded the replacement of VPA by Carbamazepine (CBZ) at 600mg/d in association with PB and Clonazepam (CZP) at 1mg/d. The CPE markedly improved. A residual focal epilepsy without loss of consciousness remained. Social contact was very good, language was preserved in terms of expression and understanding. The motor deficit was persistent and had not worsened.

After ruling out hemiconvulsion-hemiplegia-epilepsy syndrome (HHS), unihemispheric vasculitis complicating viral encephalitis or autoimmune disease, cortical dysplasia

and inborn metabolic error, we retained the diagnosis of Rasmussen's encephalitis with atypical expression. The arguments in favour were CPE, cerebral hemiatrophy involving the caudate nucleus, EEG asymmetry with slowing in the atrophied hemisphere, unihemispheric electrical SE in the non-atrophied hemisphere.

Despite seizures were quite controlled with antiepileptic drugs, the patient unfortunately passed away two weeks after he has been discharged in a SUDEP while his seizure was quite well controlled.

Figure 1: Non-injection brain CT scan showing left cerebral hemiatrophy and LV dilatation witnessing caudate nucleus head's atrophy.



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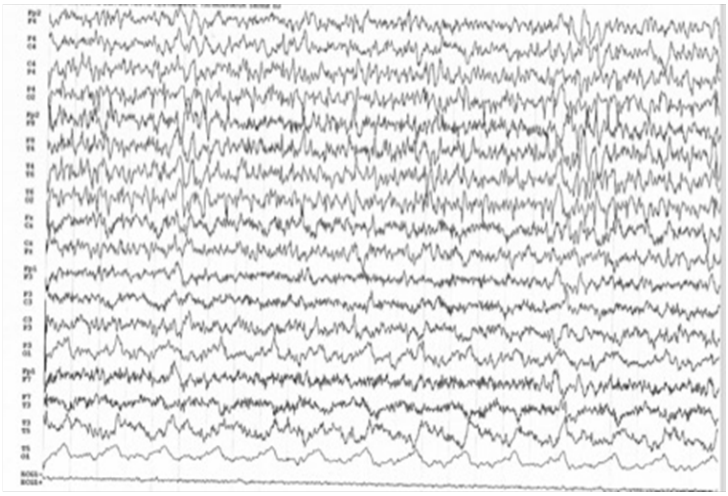

Figure2: EEG showing hemispheric asymmetry with left hemispheric slowing and right hemispheric diffused spike and spike-wave.

Case 3: A15-year-old adolescent, laterally right-handed and enrolled in the second year of secondary school with a need for academic support (AVS), was followed in pediatric neurology at the IP Ndiaye clinic of the Fann National Hospital in Dakar for inaugural seizures. There was no particular history. His first seizures appeared in 2010 at the age of ٥ years and were left hemicorporeal tonico-clonic. The initial workup, two EEGs, brain imaging (CT and MRI) and CSF analysis were unremarkable. After a second seizure, six months later, he was commenced on antiepileptic treatment (AET): Sodium Valproate (VPA) at ٢٠mg/Kg/d with excellent seizure control for about two years. After these two years an enrichment of the symptomatology with vegetative signs (rupture of contact, left clonic seizures and vomiting) was observed. A symptomatic focal epilepsy was evoked. VPA was replaced by Carbamazepine (CBZ). The occurrence of left hemicorporeal myoclonus predominating in the upper limb led to the replacement of CBZ by Lamotrigine (LMT) coupled with VPA, which resulted in a moderate improvement of the symptomatology. EEG performed in April2012 demonstrated a well-organized left hemisphere sleep pattern with an irritative slow focus and a disorganized sleep architecture that was almost devoid of physiological figures in the right hemisphere. The patient presented with subintrant seizures without contact break, with vegetative seizures and a reduction in the frequency and intensity of motor seizures motivating the initiation of Levetiracetam (LVM) and VPA. A secondary worsening of motor seizures occurred after three years. EEG performed in January 2019 demonstrated right unihemispheric slowing, with the presence of paroxysmal activity with a parietal onset generalizing concomitantly to three motor seizures on video. The MRI showed a right unihemispheric atrophy. A few weeks later he presented a SE followed with a progressive worsening of the symptomatology with seizures of polymorphic appearance, more often left hemicorporeal clonic without rupture of contact.

Cognitive examination revealed discreet heteroaggressiveness and an «unhappy» child.

RE was discussed. The parents requested a second opinion overseas in May 2019. There he had a SE one day after his arrival and has received oral AEDs.

An EEG-Video of 72 hours showed polymorphic seizures, sometimes purely straight, sometimes with inter-hemispheric diffusion. The starting point was always right hemispheric, either with posterior onset and temporal diffusion, or with temporal onset and rolandic diffusion. CSF protein electrophoresis reveals oligoclonal bands. CSF cytochemistry was normal. Amino acids, lactic acid to pyruvic acid ratio, antineuronal antibodies and anti TPO antibodies in CSF were negative. The plasma balance was normal except for a discreet increase in type I interferon two times the higher threshold. On psychomotor examination, ideomotor difficulties, difficulties in graphomotor gesture and normal oral language for age were noted. The diagnosis of RE was confirmed and a hemispherotomy was preferred to immunomodulatory treatment. The postoperative period was essentially marked by a sequelae of left hemiparesis allowing walking and a syndrome of hemineglect. Psychologically these signs had been extremely poorly experienced by the patient.

The control MRI was satisfactory with images of a right hemispherotomy scar (Figure 3).

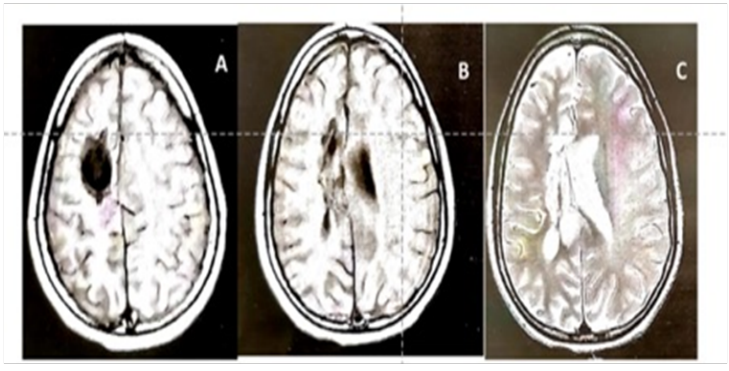

Figure 3: Post hemispherotomy control MRI showing the right cortical parietal and deep hemispherotomy sequel with moderate right unihemispheric atrophy: A and B sequence T1, C sequence T2.

Discussion

Diagnostic criteria: We reported two patients with Rasmussen's encephalitis whose clinical presentations as well in terms of age of onset, clinico-electrical manifestations, neuroimaging features and evolution pattern, were different from each other and from the classical description of this pathology. In our first case, the onset had initially led us consider a vascular cause, in fact some strokes are associated with convulsive seizures at the inaugural stage [5]. However, according to the criteria established by Bien et al. [6] we retain the diagnosis of RE. These criterias are very good diagnosis tool for work environment like ours in the absence of biopsy.

Clinical presentation and diagnosis : The first patient was likely to have bilateral RE which is certainly seldom but already described by Pareiso et al. [7]. We also considered a RE associated with another cerebral disease such as described by Prayson et al., [8]. In the absence of a brain biopsy, we relied on clinical, electrical and brain imaging features to retain the diagnosis of Rasmussen's encephalitis in our patients according to Bien's criterias [2].

Our patients had different clinical evolutions. In both cases, the linear and progressive evolution of the RE was not found. In fact Rasmussen's encephalitis is classically known to have three evolution phases [3,9]. The speed of cognitive decline is inversely proportional to age in general [9].

Treatment: Our patients were initially treated with first generation antiepileptic drugs with moderately acceptable results. As the main concern for of in the second case was refractory epilepsy rather than cognitive decline, the treatment option was the surgery according to Bien et Schramm guidelines [10]. In both of our patients, cognitive decline was not in the forefront and therefore seizure control was the top priority. However, the problem of lifetime lasting neurocognitive complications induced by the surgery as in our second case is then something to integrate with patients and families. This dilemma has been addressed by several authors especially in cases of bilateral involvement with mixed results on epilepsy [2,10]. Epilepsy surgery is not widely available in sub-Saharan African countries. Antiepileptic treatment and immunomodulatory treatment remain then the gold-standard in our context.

Conclusion

Our patients have benefited from medical anti-epileptic treatment with a hemispherotomy for the one. Control of the seizures and preservation of the cognitive functions were quite average in both cases. RE is a diagnosis of exclusion after multidisciplinary consultation. The Bien criterias established in 2005 are a reference for diagnosis, particularly in resource-limited settings. This has allowed for better management of patients before the stage of cognitive deterioration. The popularization of epilepsy surgery in low- and middle-income countries would be an invaluable advance in the management of these patients.

Authors contribution: Dr. Michel-Arnaud SAPHOU DAMON made the second observation, wrote the manuscript, collected data, made the bibliography and translate into English the manuscript. Pr NDIAYE Moustapha approved the manuscript and its bibliography after review. Pr DIOP SENE Marième Soda reviewed the manuscript and the bibliography. Dr. NDONG Marie Émilie Yande, Dr MBAYE Khalifa Ababacar made the first observation and reviewed the manuscript. Dr. SANTOS Mame Maïmouna Diaw reviewed the manuscript and the bibliography. All the author agreed this manuscript in its submitted version.

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References

1. Bien CG, Tiemeier H, Sassen R, Kuczaty S, Urbach H, von Lehe M, et al. Rasmussen encephalitis: Incidence and course under randomized therapy with tacrolimus or intravenous immunoglobulins: Rasmussen Encephalitis Incidence, Course. Epilepsia 2013; 54,3:543-50.
2. Bien CG. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: A European consensus statement. Brain 2005; 128,3:454-71.
3. Granata T, Andermann F. Rasmussen encephalitis. Handbook of Clinical Neurology 2013; 111:511-9.
4. Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. The Lancet Neurology 2014; 13,2:195-205.
5. Hassani YE, Ribaupierre SD, Sajadi A, Pereira VM, Rilliet B. Accidents vasculaires cérébraux hémorragiques spontanés chez l'enfant : étiologies et prise en charge. Revue Médicale Suisse 2010; 6.
6. Bien CG, Urbach H, Deckert M, Schramm J, Wiestler OD, Lassmann H, et al. Diagnosis and staging of Rasmussen's encephalitis by serial MRI and histopathology. Neurology 2002; 58,2:250-7.
7. Peariso K, Standridge SM, Hallinan BE, Leach JL, Miles L, Mangano FT, et al. Presentation, diagnosis and treatment of bilateral Rasmussen's encephalitis in a 12-year-old female. Epileptic Disorders 2013; 15,3:324-32.
8. Prayson RA. Dual Pathology in Rasmussen's Encephalitis: A Report of Coexistent Focal Cortical Dysplasia and Review of the Literature. Case Reports in Pathology 2012; 2012:1-4.
9. Bien CG, Widman G, Urbach H, Sassen R, Kuczaty S, Wiestler OD, et al. The natural history of Rasmussen's encephalitis. Brain 2002; 125,8:1751-9.
10. Bien CG, Schramm J. Treatment of Rasmussen encephalitis half a century after its initial description: Promising prospects and a dilemma. Epilepsy Research 2009; 86,2–3:101-12.