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Case Report

Headache maybe the initial symptom in Rasmussen's syndrome: A child case report

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ABSTRACT

Objective: The aim of this case report was to study that headache maybe the initial symptom in Rasmussen's syndrome (RS).
Introduction: Headache has not yet been reported as prodromal symptom.
Methods: We studied a case of RS in which the patient experienced a recurring headache for about one year prior to the onset of partial seizures.
Results: Magnetic resonance imaging (MRI) results were normal when the headache first occurred and showed left brain atrophy three years later. It was difficult to relieve the patient's headache, even once seizures were controlled.
Conclusions: This case demonstrates that the initial symptom of RS may involve only headache.

1. Introduction

Rasmussen syndrome (RS), also called Rasmussen's encephalitis, is a chronic T-cell-mediated disorder that usually affects one cerebral hemisphere, and that typically presents in childhood. In 2005, a panel of experts established formal RS diagnostic criteria [1]. The nonspecific prodromal period lasts for about 7 months (range: 0 months to 8 years) and may involve mild signs and symptoms, typically including low frequent focal onset seizures and rarely mild hemiparesis. In the subsequent acute phase, which lasts for about 8 months (range, 4–8 months), frequent focal onset seizures occur, sometimes presenting with epilepsia partialis continua (EPC), accompanied by progressive cortical dysfunction. Finally, patients in the residual stage exhibit stable neurologic deficits and continuation of seizures [1]. However, some cases involve atypical features, manifesting absence or delayed-onset seizures, and dual pathology, suggesting that focal onset seizures are not necessary for RS diagnosis [2].

We reported a case of RS in a child who presented with the initial onset of headache, and who later was admitted to the hospital several times with the chief complaint of headache, even after her seizures were controlled.

2. Case report

A nine-year-old girl with normal development presented with a headache and a feeling like her whole head was expanded without localizing characteristics, unaccompanied by nausea or vomiting, and having no obvious etiology about five years ago. The headache was mild and could remit spontaneously, but repeat about five times, each time with a duration of about 15 days. Magnetic resonance imaging (MRI) results were normal at this time.

One year after the onset of headache, this patient experienced a headache that lasted for several hours, with a 2-minute generalized tonic–clonic seizure beginning about 3 h after the onset of headache. After this incident, the patient frequently experienced focal motor seizures involving the right lower limb without losing consciousness. Electroencephalograph (EEG) confirmed the presence of epileptiform discharge with increased slow waves in the whole brain without focal abnormalities. Epilepsy was diagnosed, and levetiracetam (about 20 mg/kg/d, twice a day) was prescribed.

The patient's symptoms showed no improvement after taking oral levetiracetam for about two months. At this time, the patient was admitted to the hospital for detailed laboratory and ancillary testing. Brain MRI revealed abnormal signal foci in the left frontal cortex, and EEG showed diffuse slowing with epileptiform discharge in the left hemisphere. Lumbar puncture revealed normal cerebral spinal fluid (CSF) cell count, protein, glucose, chloride, and cryptococcal meningitides. Blood test results were normal for ceruloplasmin, lactic acid, ammonia, immunoglobulins (IgA, IgM, IgG), rheumatoid factor (RF), antistreptolysin O (ASO), C-reactive protein, autoantibody to nuclear

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antigen (ANA), extractable nuclear antigen (ENA), and autoantibody to double-stranded DNA (anti-dsDNA) were negative.

Rasmussen syndrome (RS) was diagnosed according to the diagnostic criteria (Part A) [1]. The patient received IV methylprednisolone (25 mg/kg/d) pulse therapy for three days and intravenous immunoglobin (IVIG, 400 mg/kg/d) for five days. The patient also received oral prednisone (1 mg/kg/d, three times a day), carbamazepine (10 mg/kg/d, twice a day), and phenobarbital (10 mg/kg/d, three times a day) for seizures, and oxycodone–acetaminophen (oxycodone 5 mg with acetaminophen 325 mg per tablet, one tablet three times a day as needed) for headache. After about five months, the seizures stopped, and the patient's parents discontinued the patient's antiseizure medication without consent from the doctors. After approximately half a year without headache and focal seizures, the headache and focal seizures resumed. The headache was moderate in intensity and hard to be tolerated at times. Ibuprofen had been tried and did not work. Occasional skin rash developed when the patient was treated with carbamazepine, and this was a reason for the discontinuation of treatment. The patient was then prescribed sodium valproate sustained release tablets (20 mg/kg/d) and oxycodone–acetaminophen (one tablet three times a day as needed), with follow-up every three months, and with blood concentration of sodium valproate maintained at around 90 μg/ml. Three years after the onset of headache, brain MRI (Fig. 1a) showed atrophy of the left frontal temporal lobe and deep gray matter, large patchy hypointensities on T1 and increased T2 signals, and bilateral ventricular enlargement.

The headache disappeared and the patient was seizure-free for about 2 years and 6 months, at which time the treatment with sodium valproate and oxycodone–acetaminophen was stopped. After about 6 months without symptoms, the headache resumed, and the patient was hospitalized again. The headache was mild to moderate and could be tolerable, and only localized in the left unilateral head region. At this time, the patient also showed gait instability. Brain MRI (Fig. 1b) revealed atrophy of the left cerebral hemisphere, with this space occupied by abnormal T1 and T2 signals, as well as enlargement of the third and fourth ventricles and the left ventricle. Physical examination showed clear consciousness; dysarthria; defects in calculation ability; weakness of the right lower limb; decreased grip strength of the right hand; slightly enhanced muscular tone of the right limbs; and normal movement, strength, and muscular tone in the left limbs. The patient's right Babinski sign was positive, and the left one was negative. A consulted neurosurgeon advised that the patient was not an optimal candidate for surgical treatment. Because of concerns regarding side effects of corticosteroids, IVIG (400 mg/kg/d) was administered for 5 days with the informed consent of her parents. The headaches eased, but dyskinesia in the right limbs remained, and oral oxycodone–acetaminophen was administered again.

3. Discussion

In RS, the initial damage to the brain is mediated by T cells and microglia, and there may be a window for treatment if RS is diagnosed early enough. Inflammatory processes observable with MRI can support an RS diagnosis [2], and early diagnosis may be easier in typical cases that closely align with the diagnostic criteria. On the other hand, diagnosis remains challenging in some atypical cases, as there are not yet diagnostic biomarkers available.

In our present case, the patient suffered from headaches for about one year prior to her first focal seizure. Headaches without functional loss are very common among children and are often due to migraines in the absence of abnormalities upon ancillary testing [3]. Thus, a diagnosis of RS was not suspected in our case during the first year. We cannot confirm that the headaches in our case were specifically symptoms of RS, but some pathogenic factors for RS may also stimulate headaches. It is possible that some cases of RS may have the same pathogenesis as some headaches, and that analyzing headaches in RS may represent a new route to clarifying RS pathogenesis.

The headache could appear and disappear without treatment at the start, and then became a concomitant symptom when the patient was diagnosed with epilepsy. When the headache relapsed the third time, it was hard to tolerated, and then oxycodone–acetaminophen was prescribed. Oxycodone–acetaminophen (oxycodone 5 mg with acetaminophen

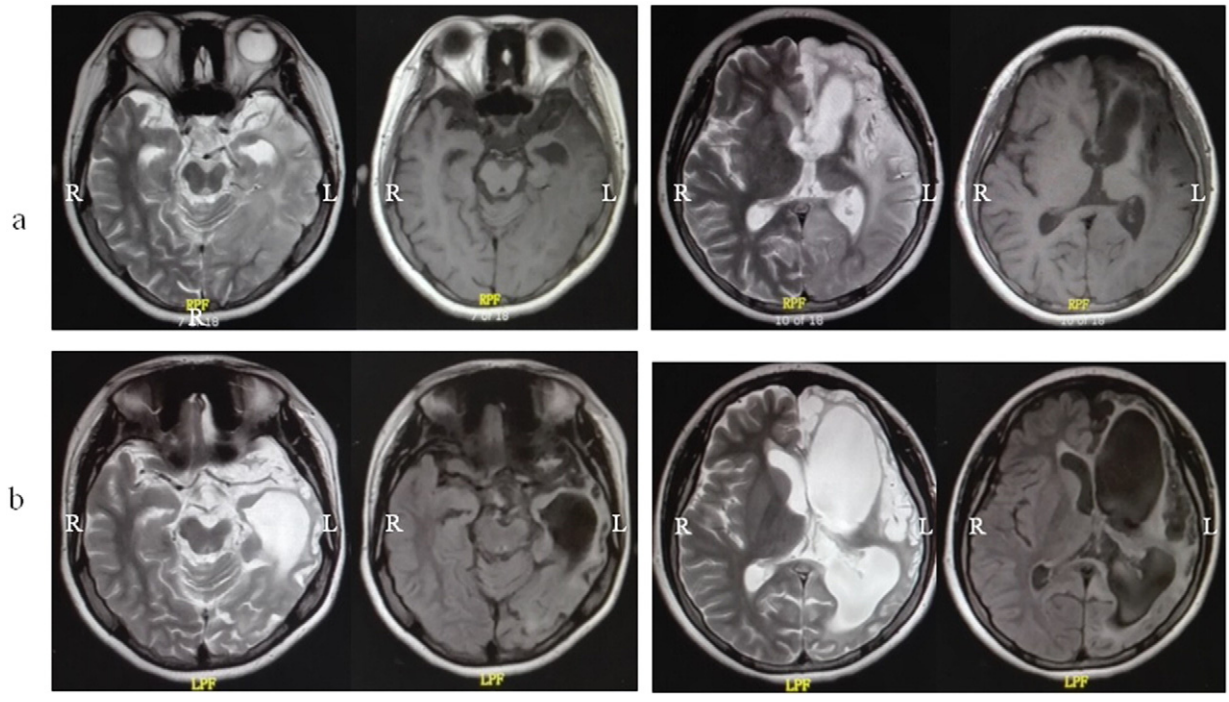

Fig. 1. The brain MRI images. (a) Brain MRI after three years after the onset of headache and two years after the onset of partial seizures reveals atrophy of the left frontal temporal lobe and deep gray matter, with large patchy abnormalities on T1 and T2 sequences with bilateral ventricular enlargement. (b) Brain MRI after five years after the onset of headache and four years after the onset of focal seizures shows atrophy of the left cerebral hemisphere, with this space occupied by T1 and T2 signal lesions with enlargement of the third and fourth ventricles and left ventricle.

325 mg per tablet) has multimodal analgesia through a combination of an opioid (oxycodone) with a nonopioid (acetaminophen) component . The intensity and frequency of headache were decreased, and the patient was headache free after about two weeks.

Immunomodulatory treatments, such as corticosteroids and/or IVIG, appear to slow but not halt disease progression, without substantially changing the eventual outcome. During the first year in our case, headaches without any concomitant symptoms could be relieved by rest, like migraines, and did not show any specific characteristics indicating their cause. Thus, these headaches could not be identified as prodromal symptoms of RS at that time. Only once seizures occurred during the headaches did we consider that RS and the headache were symptoms of the same disease. From then on, headaches and focal seizures were due to the same complaints and, over time, the headache could no longer be relieved without medication. In the final stage, the headache changed to only involve the side of brain injury. Based on the evolution of the headache with the disease progression, we conclude that the initial headache was a presenting symptom of RS.

Here, we reported an RS case that started with repetitive headaches, adding to the current body of knowledge about RS. Rasmussen syndrome (RS) without seizures is considered a potentially under-recognized cause of progressive unilateral neurological deficits in childhood [4]. Thus, it is important to diagnose atypical cases, even if we can presently only delay but not halt RS progression. This requires recognizing early possible signs and making follow-up observations. In our case, follow-up was inadequate for the first two years because the patient's parents did not understand the natural history of the disease process. Regular follow-up was performed only after confirmation of cerebral lesions identified on brain MRI.

Because of the outcome of RS, in cases involving differential diagnoses of headaches, it is important to consider some rare diseases, such as RS. We think that follow-up for headache patients is important to verify the cause or diagnosis. In our experience, we suggest that repeated brain MRI and EEG examinations should be considered to re-evaluate the headache causes even when the examinations were normal previously. In addition to re-evaluating patients with ancillary testing when new symptoms arise such as with new onset seizures.

Atypical RS is hard to diagnosed immediately. Our single case cannot serve as an example of what is typical, but our observations suggest that the initial syndrome of RS may involve only headache. Though while RS is not presently curable, we hope to help promote early diagnosis and prompt treatment to delay disease progression.

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