Rasmussen Encephalitis: In a Two and a Half Year Old Infant Presenting at a Tertiary Care Hospital in Karachi.

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Abstract

Rasmussen Encephalitis is a rare, acquired chronic inflammatory disorder of unknown etiology, usually affecting one brain hemisphere. It is a childhood disorder characterized by unilateral atrophy associated with focal seizures, motor deficits and cognitive decline. Here we present a case of a two and half year old boy with a two day history of fever, seizures and unresponsiveness. After 24 hours of presentation to the emergency department of the Abbasi Shaheed Hospital, patient regained consciousness and a repeat neurological evaluation revealed left sided hemiplagia and aphasia. Magnetic resonance imaging (MRI) T2-weighted images revealed abnormal signal intensity in right parieto-occipital subcortical white matter associated with swelling and effacement of adjacent sulci. The electroencephalogram however done in a seizure-free state was normal. He was managed with neuroprotective modalities and antiepileptics, initially followed by physiotherapy which showed progressive improvement. This case is notable as it is a rare form of encephalitis and an emphasis should be laid on excluding the case on the basis of diagnostic criteria and neuroimaging. We aim to review the clinical presentation, diagnostic modalities and current treatment and also to highlight the treatment trials underway.

Keywords: Rasmussen encephalitis, focal epilepsy, childhood, epilepsia partialis continua
(ASH & KMDC 20(1):65;2015).

Introduction

Rasmussen encephalitis (RE) is a relentlessly rare, progressive disorder of childhood with a presentation of about 6 years of age in a previously healthy child. Its onset is marked by focal or secondarily generalized seizures and may later progress to hemiparesis, hemidystonia, and cognitive impairment[1]. First reported by Theodore Rasmussen in 1958, Rasmussen Encephalitis is a rare disorder which is now being progressively more recognized[2].

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The disease is conceived as sporadic, since no hereditary evidence has been found. The previously reported viral etiology is now replaced with humoral factors involving antibody mediated mechanism against antiglutamate receptor (GluR3) subtype 3 and GluR∈2 or NMDA receptor 2B (NR2B)[3,4]. The diagnostic criteria proposed by European consensus panel emphasizes on neuroimaging comprising of MRI and EEG to exclude other differentials. The use of long term immunotherapy with corticosteroids, intravenous immunoglobulins, plasmapheresis and the T-cell inactivating drugs; Tacrolimus and Azathioprine has been reported so far[5]. This case is presented so that RE should not be missed in the differential diagnosis of a child presenting with fever, focal seizures, and loss of consciousness hemiplagia and aphasia with history of normal developmental milestones.

Case Report

A two and a half year old boy presented to the emergency department with fever for two days and sudden onset of focal seizures involving left leg and left sided facial twitching followed by unresponsiveness. Later on he regained consciousness with GCS 15/15 but had weakness in left side of the body and was unable to walk or sit. He developed epilepsia partialis continua (EPC) of the left leg despite of taking antiepileptics (Phenytoin, Phenobarbitone and Levetericetam). He became aphasic but was able to swallow. His perinatal period and developmental milestones had been normal. On examination, the left lower limb showed remarkably decreased tone and power (1/5).

Routine blood and cerebrospinal fluid investigations and metabolic tests were within normal limits. Magnetic resonance imaging (MRI) as shown in Fig.1 a-d, revealed hyper intensity in the right parieto-occipital subcortical area of the cerebrum on T2-weighted (T2W) and fluid-attenuated inversion recovery (FLAIR) images. Atrophy of the right frontal lobe of cerebrum was also noted. Magnetic resonance angiography (MRA) was reported normal thus vasculitic lesion was excluded. EEG however done in a state of controlled seizures was inconclusive. Based on above findings the diagnosis of Rasmussen encephalitis was considered.

Our patient had no relevant past surgical and medical history. His perinatal period and developmental milestones were normal. Before developing the symptoms he used to run and climb up stairs using alternate steps. He would follow commands and talk two to three word sentences.

The patient was managed with antiepileptics and a short course of corticosteroids. Gradually his seizures were controlled and an improvement in power of left lower limb noted. However he was discharged home with a residual focal deficit of left upper limb and inability to walk, sit and talk. He is on continuous follow-up and compliant with anti-epileptics and physiotherapy. A gradual improvement in his activities is noted. He is now able to sit without support after 4 months.

Discussion

Though RE has long been identified as a chronic inflammatory disorder, its etiology still remains unknown. Histopathological examinations of brain by open biopsy characteristically show T-cell domination in the multifocal encephalitis with activated microglia and reactive gliosis. However, CSF standard tests are not sufficient for the diagnosis of RE[6]. Initially a viral etiology was hypothesized by Rasmussen based on the constituents of immune reactions in the brain but this hypothesis was rejected because so far all attempts to identify a pathogenic viral agent have been inconclusive[7].

Later the role of autoantibodies against glutamate receptors were identified, nonetheless additional studies have illustrated that GluR antibodies are not present in all RE patients, and the pathogenic role of elevated GluR∈ autoantibodies in RE remains unclear[7,4]. Recent studies suggest a role of cytotoxic T cell mediated damage of the neurons[8].

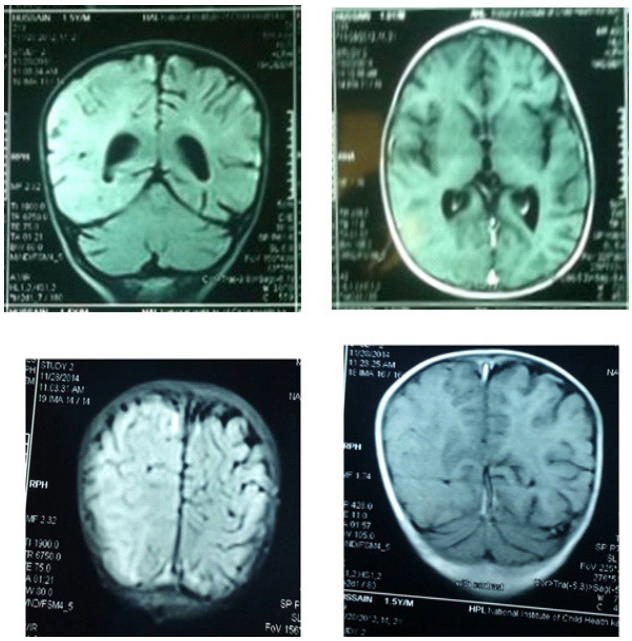
Rasmussen encephalitis is characterized by a classical clinical picture of intractable focal epilepsy, epilepsia partialis continua (EPC, and other forms of status epilepticus) accompanied by successive hemiparesis and cognitive decline owing to the progressive loss of tissue in the involved hemisphere. The typical disease progression can be described in three stages[7]. Initially, the 'prodromal stage' (median duration 7.1 months) is characterized by a relatively low seizure frequency and rarely some degree of hemiparesis[8]. The patient then enters the 'acute stage' of the disease (median duration 8 months). It is characterized by frequent seizures, mostly simple partial motor seizures and often in the form of EPC. It is also manifested by hemiparesis, hemianopia, cognitive decline and aphasia if the dominant hemisphere is involved[4]. The initial MRI scans performed at this stage showed that the inflammatory lesions in all the patients had a monofocal onset. It is in this stage that most of the hemispheric loss occurs. After this stage, the patients enter in the 'residual stage' with a stable neurological deficit. It is characterized by

Table 1. Rasmussen Encephalitis diagnostic criteria suggested by European Consortium[7].

Part A	
(1) Clinical	Focal seizures (with or without epilepsia partialis continua) and unilateral cortical deficit(s)
(2) EEG	Unihemispheric slowing with or without epileptiform activity and unilateral seizure onset
(3) MRI	Unihemispheric focal cortical atrophy and at least one of the following:
	Gray or white matter T2-weighted/ FLAIR hyperintense signal
	Hyperintense signal or atrophy of the ipsilateral caudate head
Part B	
(1) Clinical	Epilepsia partialis continua or progressive unilateral cortical deficit(s)
(2) MRI	Progressive unihemispheric focal cortical atrophy
(3) Histopathology	T-cell-dominated encephalitis with activated microglial cells (typically, but not necessarily forming nodules) and reactive astrogliosis
	Numerous parenchymal macrophages, B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE

Source: From the European Consortium (Bien *et al.* 2005).

Fig 1a-d: MRI images revealing abnormal signal intensity in right parieto-occipital subcortical white matter associated with swelling and effacement of adjacent sulci.



decreased frequency of seizures and permanent hemiparesis[8].

The clinical features of RE are nonspecific, particularly at the beginning of the disease. This makes the diagnosis a major issue at the initial stages[9]. Our patient presented at an early age with a relatively milder form of seizure activity and disabilities. No etiological factors were identified in our patient and all the differentials such as Multiple sclerosis (MS), mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS), as well as cerebral vasculitis were considered and ruled out by history, clinical examination and investigations.

In the vast majority of patients, EEG finding are characteristic of disorganized background and sleep activity in the involved hemisphere. Other epileptic abnormalities include; focal slow activity, multifocal ictal disharges and subclinical ictal discharges[4]. Magnetic Resonance Imaging is considered not only the main diagnostic modality but also helps in assessment of disease progression. T2/FLAIR hyper intense signal is detected in cortical or sub cortical regions and an ipsilateral atrophy of the head of the caudate nucleus is a typical accompanying feature of hemispheric atrophy, and indicates an early sign. Serial MRIs done reveals white matter hypersensitivity, cortical swellings and progressive atrophy of the affected hemisphere[2,8]. In our patient we found similar findings in MRI as mentioned above, involving the right cerebral hemisphere however the EEG findings were inconclusive.

Based on the criteria suggested by the European consortium[7] as shown in (Table 1.) our patient fulfilled the clinical and MRI requirements but EEG was normal. However EEG was done at a stage when patient was seizure free for days and was on antiepileptics. Rapidly increasing frequency and severity of simple focal (usually motor) seizures, postictal deficits, together, with a lack of evidence of any neuroanatomic abnormalities on MRI should indicate RE[7]. Hence RE was considered in our patient.

The use of antiepileptics in RE aims to control the seizures and improve the motor deficit. EPC seem to be refractory to antiepileptic however the antiepileptics are targeted to prevent severe episodes of seizures rather to eliminate the seizures completely. There had been trials as evidenced by case reports on the use of Botulinum toxin, Methylprednisolobe pulse therapy and Plaspheresis and Rituximab infusions to control the intractable seizures[10].

Considering the immunological etiology a long-term immunosuppressive therapy had been implemented to control the primary causes of the disease such as corticosteroids, intravenous immunoglobulins, plasmapheresis or protein. A immunoabsorption and inactivating drugs for T cell inactivation such as Tacrolimus and Azathioprine[11].

Hemispherectomy is reserved for patient having uncontrolled seizures despite above mentioned measures and is the definitive treatment to make a patient seizure free. However homonymous hemianopia and hemiplegia are inevitable[12].

Conclusion

We have reported a rare case of RE in a child who presented focal seizures, hemiplegia and aphasia with cerebral atrophy localized to a single hemisphere. His symptoms were managed with antiepileptic and a short course of corticosteroids and he showed a gradual improvement. More published cases regarding this rare disorder may help us to diagnose and manage the childhood onset of the disease timely and appropriately.

It is important to consider Rasmussen's Encephalitis - a rare disorder in the differential diagnosis of encephalitis as the treatment and prognosis of the child depends on its correct diagnosis.

Conflict of interest

Author has no conflict of interest and no funding/grant from any organization.

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