

Rasmussen's Encephalitis: A Rare Cause of Intractable Seizures

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ABSTRACT

Rasmussen's encephalitis (RE) is a rare chronic progressive inflammatory disease of the brain that results in difficult-to-control seizures (mostly focal: *epilepsia partialis continua*), cognitive decline and progressive loss of neurological function including speech, motor skills with eventual paralysis of one half of the body (hemiparesis) and encephalitis. It is a disease that usually affects a single hemisphere and presents commonly at an early age. It poses a lot of challenges, both in diagnosis as well as treatment. We report a case consistent with the findings of RE in a 4.5-year male child, who presented with status epilepticus; and was diagnosed as a case of RE on clinical and radiological findings.

Key Words: *Rasmussen's encephalitis, Inflammatory disease, Seizures, Cognitive decline, Hemiparesis.*

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INTRODUCTION

Rasmussen's encephalitis (RE) is a chronic inflammatory disease that involves the brain tissue resulting in unilateral atrophy. It was first described by Rasmussen *et al.* in 1958.¹ Clinically, this disease presents with drug-resistant focal seizures, progressive motor weakness as well as worsening of motor and cognitive functions.^{1,2} It is commonly seen in children, 10 years and under, with the average age of onset being six years.³ It is uncommon in adults, accounting for around 10% of the total cases. Diagnosis of RE is challenging and requires both clinical history and peculiar radiologic findings. Here, we report a case consistent with findings of RE in a 4.5-year male child, who presented with status epilepticus; and was diagnosed as a case of RE on clinical and radiological findings.

CASE REPORT

A 4.5-year male child, known case of epilepsy for the last seven months, born at 38 completed weeks of gestation, *via* uncomplicated vaginal delivery, vaccinated, 2nd in birth order among four siblings, presented in status epilepticus involving the left side of the body. He had history of weakness of left side of the body for the last seven months, when he started having seizures involving either left upper limb or lower limb or both, initially 2-3 times per day and then increasing to 8-10 episodes per day, lasting 10-15 minutes, for which he was started on valproic acid (20 mg/kg/day).

The seizures did not improve, although the frequency reduced to 5-6 episodes/day. No workup was done previously for his symptoms and now the child landed in Emergency Room (ER) in status epilepticus, which was managed according to guidelines, but the child continued to have left-sided tonic-clonic seizures, 3-4 times per day, while on phenytoin (8 mg/kg/day) and valproate (40 mg/kg/day). On physical examination, the patient was found to be alert but aphasic and disoriented in time and space. He also had exaggerated deep tendon reflexes on the left side (biceps, triceps, brachioradialis, knee, and ankle) and left-sided up-going plantar response. Pupils were bilaterally reactive and equal in size and shape. The facial nerve was intact. The rest of the cranial nerves could not be assessed as the child did not comply.

Blood counts and serum electrolytes were within the normal range. Cerebrospinal fluid (CSF) analysis showed normal cell counts with slightly raised protein levels (96 mg/dl). Computed tomography (CT) brain showed unilateral edema involving the right cerebral hemisphere. Electroencephalogram (EEG) showed a severe degree of diffuse encephalopathy with inter-hemispheric asymmetrical background rhythm comprising of 1-3 Hz delta wave activity, as shown in Figure 1. Magnetic resonance imaging (MRI) brain with contrast (Figures 2, 3, and 4) reported that right cerebral hemisphere and right basal ganglia appear edematous and hyperintense on T2-WI and fluid attenuated inversion recovery (FLAIR) sequence as compared to the left side, showing restricted diffusion on diffusion weighted imaging (DWI) and post-contrast enhancement. Bilateral cerebellar hemispheres and brainstem along with all the ventricular system appeared normal.

He was started on levetiracetam at the dose of 20 mg/kg/dose, BD, along with steroids (3 IV boluses of methylprednisolone at 400 mg/m²/day on alternate days), which lowered the frequency

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of seizures to 2-3/day. However, cognitive abilities and aphasia did not improve. He was discharged on levetiracetam (20 mg/kg/dose×BD) and valproate (60 mg/kg/day divided in 2 doses) and called for follow-up after four weeks.

The patient did not arrive for follow-up on the specified date. His parents were contacted telephonically and they reported that the child still experiences seizures, which occur 2-3 times per day; however, the duration is reduced (15-20 seconds). There is no loss of consciousness and the episodes vary between tonic and clonic, involving only left half of the body. As reported by the parents, the aphasia and hemiparesis involving the left side of body was still persistent. They were called for follow-up EEG, but they refused due to COVID-19 pandemic and lockdown situation.

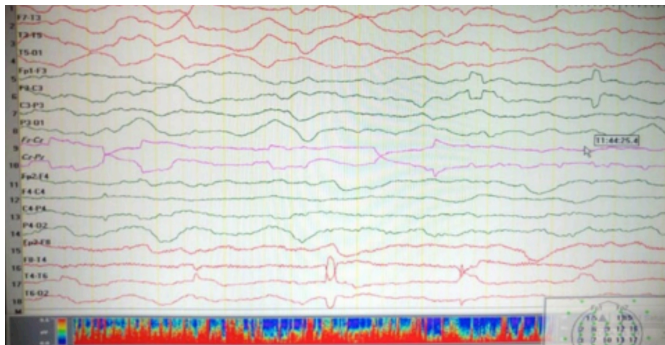


Figure 1: EEG of the case showing severe diffuse encephalopathy.

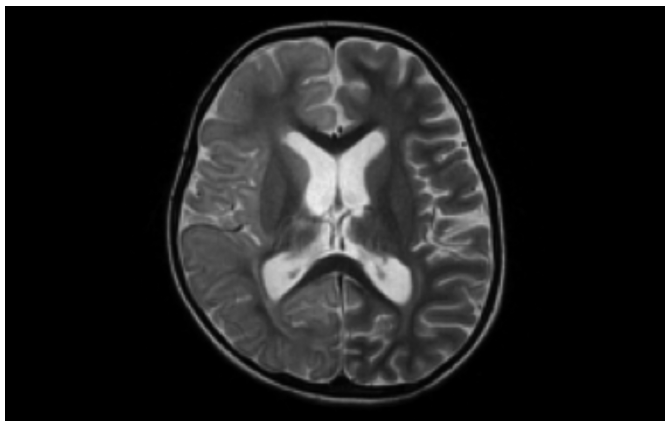


Figure 2: MRI brain showing T2WI images of the case.

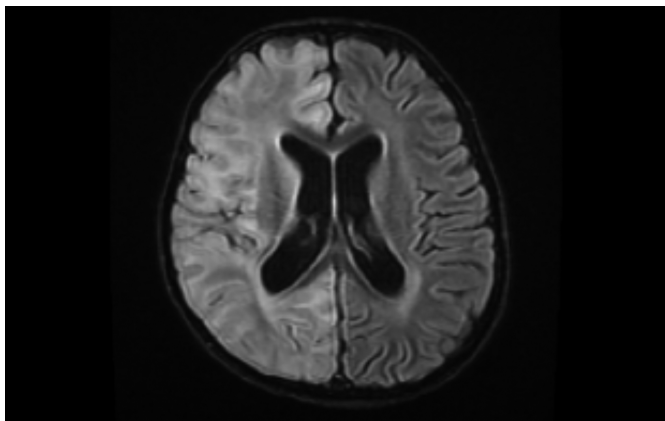


Figure 3: MRI brain: T2 FLAIR images showing right-sided hyperintensity in the region of the cerebral hemisphere and basal ganglia with post-contrast enhancement.

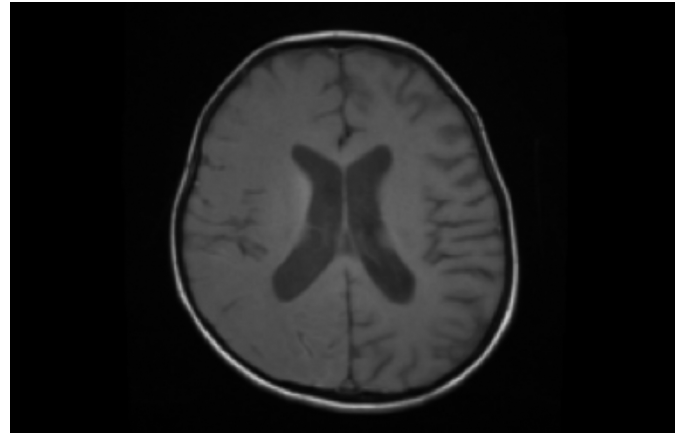


Figure 4: MRI brain showing T1 image of the case with edematous right cerebral hemisphere and basal ganglia region with loss of pattern in sulci and gyri. The ventricles appear normal.

DISCUSSION

Our case presented with a clinical history consistent with the diagnosis of RE; although the MRI brain did not show cortical atrophy, which might be because the child presented in the early stages of the disease.

Various theories have been put forth explaining the etiology of RE, including cell-mediated immunity, more precisely T-cell immunoreaction against neurons and astrocytes.⁴ It is further supported by a recent study that suggests that cytotoxic T cells may be directed against a viral protein present in both neurons and astrocytes.⁵ On the contrary, another school of thought supports autoimmune pathology. In 1994, Rogers *et al.* found the role of antibodies against glutamate receptor (GluR3). Other triggers like herpes simplex virus and cytomegalovirus have also shown association.⁶ Rasmussen *et al.* postulated it to be because of an infective process.¹

Diagnosis of RE is commonly based on the typical clinical, radiological, and pathological features. Clinical presentation is variable, according to anatomical site and age at presentation, including focal or continuous seizures, neurological deficits, aphasia, and cognitive defects. There is a clinical staging called the MNI (Montreal Neurological Institute) staging.⁷ Stage 1 is a prodromal stage with low seizure frequency and mild hemiparesis. Stage 2 is defined as the acute phase of the disease, with a rapid increase in seizure frequency (to > 10/day) accompanied by the development or deterioration of a hemiparesis until the completion of neurological deterioration. Stage 3 is defined as a rather stable state, with a fixed hemiparesis and a seizure frequency lower than stage 2. Our patient presented in stage 2 of the disease, and later progressed to stage 3 as there was fixed hemiparesis and reduced frequency of seizures.

The specific MRI features suggestive of the disease are seen as hyperintense T2/FLAIR signals from areas of the cerebral cortex.⁸ Serial MRI studies have demonstrated a spectrum of changes ranging from an apparently normal image at onset to cortical atrophy of a specific focus or an entire lobe in the late stage. One case with bilateral cerebral involvement on EEG and

MRI has also been reported.⁹ CT and MRI studies in our case showed evidence of left cerebral hyperintense signals suggesting stage 2 disease.⁸

Pathological appearances of RE are also variable, according to the severity of the disease. Macroscopic features in reported cases operated within the first 2 years of disease onset show subtle changes such as slight discoloration and granularity, along with focal thinning of the cortex, although severe cases may show gyral atrophy with widespread hemiatrophy and ventricular dilatation.¹⁰ Although brain biopsy is needed for confirmation of the diagnosis, parents did not give consent for the procedure.

Treatment of RE is challenging and is typically tailored to control seizures and arrest disease progression. Seizures in these patients are mostly resistant to antiepileptic drug therapy with no standard therapy yet approved despite a trial of multiple combinations. Seizures were controlled with levetiracetam and corticosteroids in our patient. Intravenous immunoglobulins (IVIG) and plasma exchange have all been tried in adult-onset RE in different studies, but none have shown consistent results to allow approval.¹¹ IVIG and plasma exchange was not available in our setup and the parents could not bear the heavy cost. Surgery has been pivotal in the control of seizure activity since 1950. Hemispherectomy, both anatomic and functional, is highly effective in achieving seizure control; and currently, it offers the only means to halt disease progression. The postsurgical seizure freedom rates range between 62.5% to 85%, but hemiparesis and language dysfunction are its complications.¹² Parents of our patient refused to undergo surgery, considering the risks involved; and consented to manage the child on medical therapy.

PATIENT'S CONSENT:

Informed consent was obtained from the patient's parents regarding data collection and publication.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MBM: Concept, data collection, compilation and writing the whole manuscript along with patient follow-up and approval of the final form of manuscript to be published.

AF: Data collection, literature search and review of manuscript with advice about important changes.

MHH: Concept, and final compilation of the manuscript with scientific and intellectual changes with advice about the

manuscript, and approval of the final form of manuscript.

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