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Case Report

Diagnostic misdirection in posterior-onset Rasmussen's encephalitis: A case report☆,☆☆

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ABSTRACT

Rasmussen's encephalitis (RE) is a rare, chronic, and progressive inflammatory brain disorder, characterized by drug-resistant seizures, cognitive decline, and unihemispheric atrophy. Focal neurological deficits and focal motor seizures are typically the initial manifestations. However, we encountered an exceptionally rare case where occipital seizures were the sole presenting feature. This unusual presentation poses unique diagnostic and therapeutic challenges, stemming from its posterior seizure onset and atypical clinical profile, complicating recognition and effective management. We report the case of an 11-year-old boy with no prior medical or familial history of epilepsy. Born to nonconsanguineous parents, his prenatal, perinatal, and early developmental milestones were unremarkable. The patient exhibited normal psychomotor development until 5 years prior to presentation, when occipital drug-resistant visual seizures began. Clinical, imaging, and electrophysiological findings revealed posterior-onset seizures and unilateral hemispheric atrophy consistent with Rasmussen's encephalitis. Posterior-Onset seizures can present as the exclusive initial manifestation of Rasmussen's encephalitis. This case highlights the importance of considering this diagnosis in patients with newly diagnosed drug-resistant visual seizures particularly when accompanied by cognitive decline.

Background

Rasmussen's encephalitis (RE) is a rare, severe, immune-mediated brain disorder first described by neurosurgeon Theodore Rasmussen and colleagues in the late 1950s [1]. It is characterized by unilateral brain atrophy, progressive neurological decline, and refractory seizures [2]. The typical clinical course, defined over the past century, generally begins at

Abbreviations: EEG, electroencephalography; IVIG, intravenous immunoglobulin; MRI, magnetic resonance imaging; PET, positron emission tomography; RE, Rasmussen's encephalitis.

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a median age of 6 years [3]. In some cases, a prodromal phase marked by mild hemiparesis or infrequent seizures may precede the acute stage by several years [3]. Although rare, non-motor seizures have been reported as manifestations of RE, with only one documented case of posterior-onset RE published to date [4].

Despite decades of research, the exact etiopathogenesis of RE remains poorly understood, although it is defined pathologically by T-cell-predominant encephalitis [5]. This has prompted the use of various immunotherapies. However, their efficacy remains limited, and hemispherectomy often becomes the definitive treatment for seizure control [6]. The 2005 European consensus on the pathogenesis, diagnosis, and treatment of RE remains the established guideline for clinical evaluation [2,7]. Nevertheless, the variable clinical features and incomplete understanding of RE, prompt the reporting of this extremely uncommon presentation.

Here, we present a rare case of RE with several atypical features, including a sensory visual seizure onset, gradual progression to hemispheric atrophy, and fairly good seizure control achieved through a combination of antiepileptic drugs and immunomodulatory therapy without the need for hemispherectomy.

Case presentation

An 11-year-old Caucasian boy with no prior medical or familial history of epilepsy was born to nonconsanguineous parents. His prenatal, perinatal, and developmental milestones were unremarkable. At the age of 6, he presented with stereotyped paroxysmal visual phenomenas described as colorful objects in the left visual hemifield. These episodes were associated with pallor, headache, and hypersomnolence lasting a few seconds to 2 minutes. He was started on valproic acid. These episodes remained isolated for one year until, at age 7, he experienced a left hemibody tonic-clonic seizure with postictal weakness, prompting the addition of levetiracetam. By 2020, his seizures had worsened, presenting as frequent visual hallucinations followed by loss of consciousness, oral and manual automatisms, left hemibody dystonia, and occasional progression to bilateral tonic-clonic seizures. This clinical worsening was accompanied by psychomotor regression and declining academic performance. A brain MRI performed at this stage showed no abnormalities, and clobazam was added to his treatment. Over the next 2 years, his seizures became resistant to a combination of 3 anti-seizure medications (ASMs): carbamazepine, levetiracetam, and clobazam. The seizures persisted with the same semiology, occurring twice per week. At admission to our unit, on November 2023, the patient was alert and interactive, with neurological examination revealing a discreet left hemiparesis, asymmetry in muscle tone, but no sensory deficits or reflex asymmetry. Extensive diagnostic testing was conducted. Cerebrospinal fluid analysis showed 1 WBC/mm3 with normal glucose, protein, and lactate levels, as were thyroid function tests, autoimmune antibody screening (antinuclear anti-body), complement levels, and viral serologies (VZV, CMV, hepatitis B and C). Onconeural markers were also negative. Despite treatment, interictal electroencephalography (EEG) revealed repetitive slow-wave discharges originating in the occipital region and spreading to the right side (Fig. 1). The perictal EEG revealed occipital background slowing with diffuse delta waves progressing centrally, followed by rhythmic acceleration (Fig. 2). A repeat brain MRI revealed a right hemispheric cerebral atrophy (Fig. 3), subsequently confirmed by PET scan, which demonstrated a diffuse hypometabolism in the right frontal, parietal, temporal and occipital lobes, as well as within the ipsilateral basal ganglia (Fig. 4). Given the combination of drug-resistant epilepsy, gradual cognitive decline, and progressive radiological abnormalities, the diagnosis of Rasmussen's encephalitis was established. Differential diagnoses, including other causes of encephalitis, small vessel CNS vasculitis, and systemic inflammatory conditions with CNS involvement, were excluded. The patient received immunomodulatory therapy, including 5 days of intravenous methylprednisolone 500 mg daily, followed by intravenous immunoglobulin (IVIG) 2 g/kg over 5 days. The patient's clinical course stabilized. Currently, his daily function remains good, with a reduction in seizure frequency to one episode every 2 weeks on topiramate, levetiracetam and carbamazepine.

Discussion

Rasmussen's encephalitis (RE) is a rare neurological disorder characterized by progressive inflammation and atrophy of one cerebral hemisphere, leading to drug-resistant focal seizures, unilateral motor deficits, and cognitive decline [1]. First described in 1958 by Theodore Rasmussen and colleagues, its course is divided into 3 stages: a prodromal phase with infrequent seizures, an acute stage marked by rapid neurological deterioration and frequent seizures, and a residual stage with persistent deficits and reduced seizure frequency [8]. The pathophysiology of RE is thought to involve an autoimmune process triggered by an initial insult, leading to T-cell-mediated cytotoxicity against neuronal and glial components [9]. This chronic immune activation results in cortical inflammation, neuronal loss, and progressive atrophy [9]. Glutamate receptor (GluR3) autoantibodies and persistent cytotoxic T-cell activity have been implicated as key contributors, although their exact roles remain an area of ongoing research [10,11].

While the patient eventually met the diagnostic criteria for RE as the disease progressed, several atypical features were observed. Notably, the patient's seizure semiology, along with electroencephalographic and radiographic findings, initially pointed to occipital lobe involvement—a rare feature in childhood-onset RE. Occipital involvement is more typically associated with atypical adolescent- or adult-onset forms [12]. It is less frequently affected compared to the frontal lobe, the most common site of pathology in RE [9]. Our review identified only one other reported case of posterior-onset RE in a 6-year-old boy, characterized by atypical features such as posterior-predominant seizure onset, progression to severe choreoathetosis, and ipsilateral cerebellar atrophy. This patient also developed autoimmune disorders, including psoriasis and uveitis, highlighting the variability in RE's clinical presentation [4].

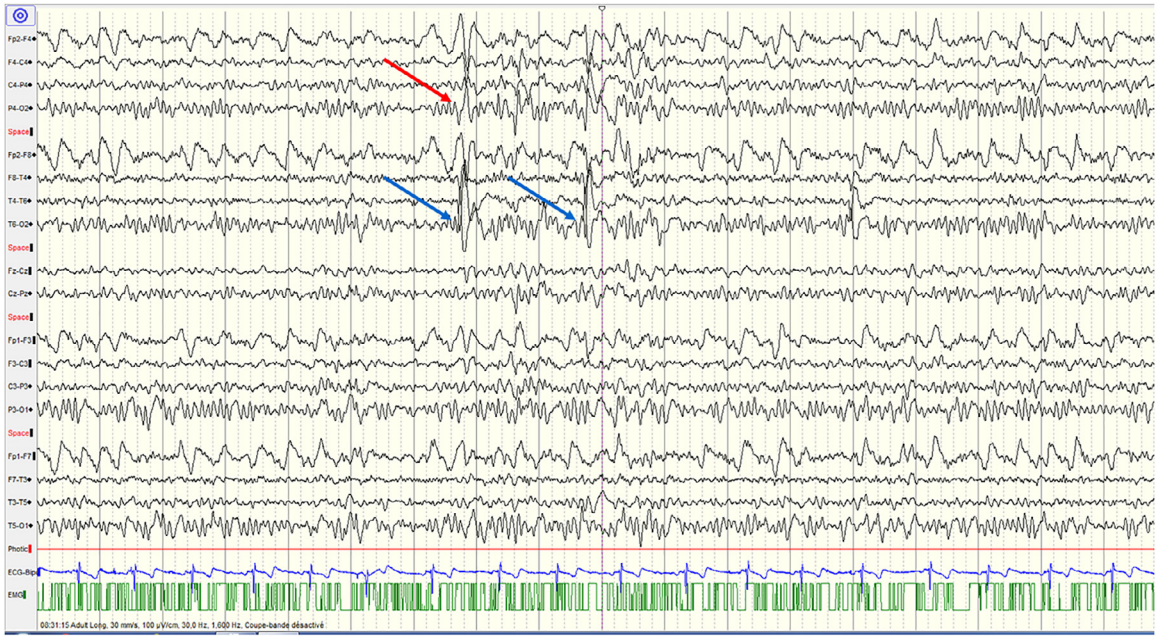

Fig. 1 – Interictal EEG findings. This is an A-P longitudinal bipolar montage. It shows repetitive slow-wave discharges originating in the occipital region (blue arrow), with diffusion toward the rest of the right cortex (red arrow).

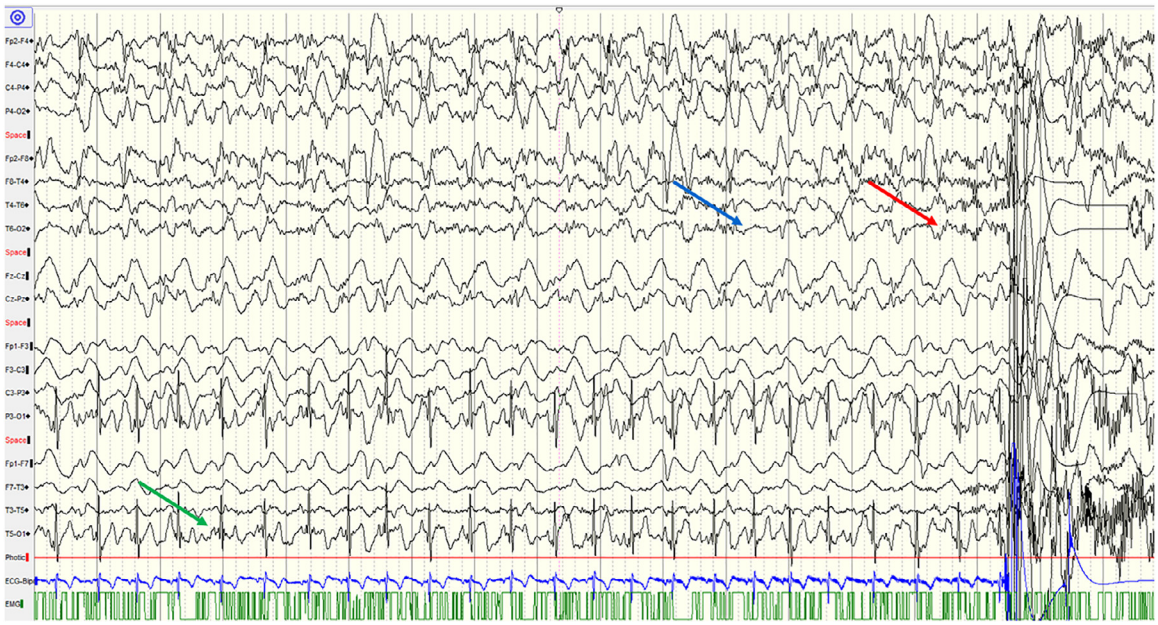

Fig. 2 – Perictal EEG findings. This A-P longitudinal bipolar montage showing slowing of the occipital background rhythm, represented by diffuse delta waves extending toward the central regions (blue arrow), followed by an acceleration of rhythm suggestive of ictal progression (red arrow). An ECG artifact is observed in the T5-O1 channel (green arrow).

Our patient also exhibited a prolonged prodromal phase of focal epilepsy before progressing to a clinical profile consistent with RE. Specifically, a 3-year gap was noted between the initial visual seizures and the onset of motor regression, with a 5-year delay between the first visual seizures and the detection of cerebral hemiatrophy. Typically, untreated pediatric cases of RE evolve rapidly within the first year of epilepsy onset, manifesting with hemiparesis, hemianopia, and cognitive decline. While a delayed progression from seizure onset to the fulfillment of diagnostic criteria is well-documented in adolescent and adult RE cases, it is relatively uncommon in younger children [13]. This case highlights the significance of early recognition, as prior to the emergence of seizures, the patient lacked the neurobehavioral

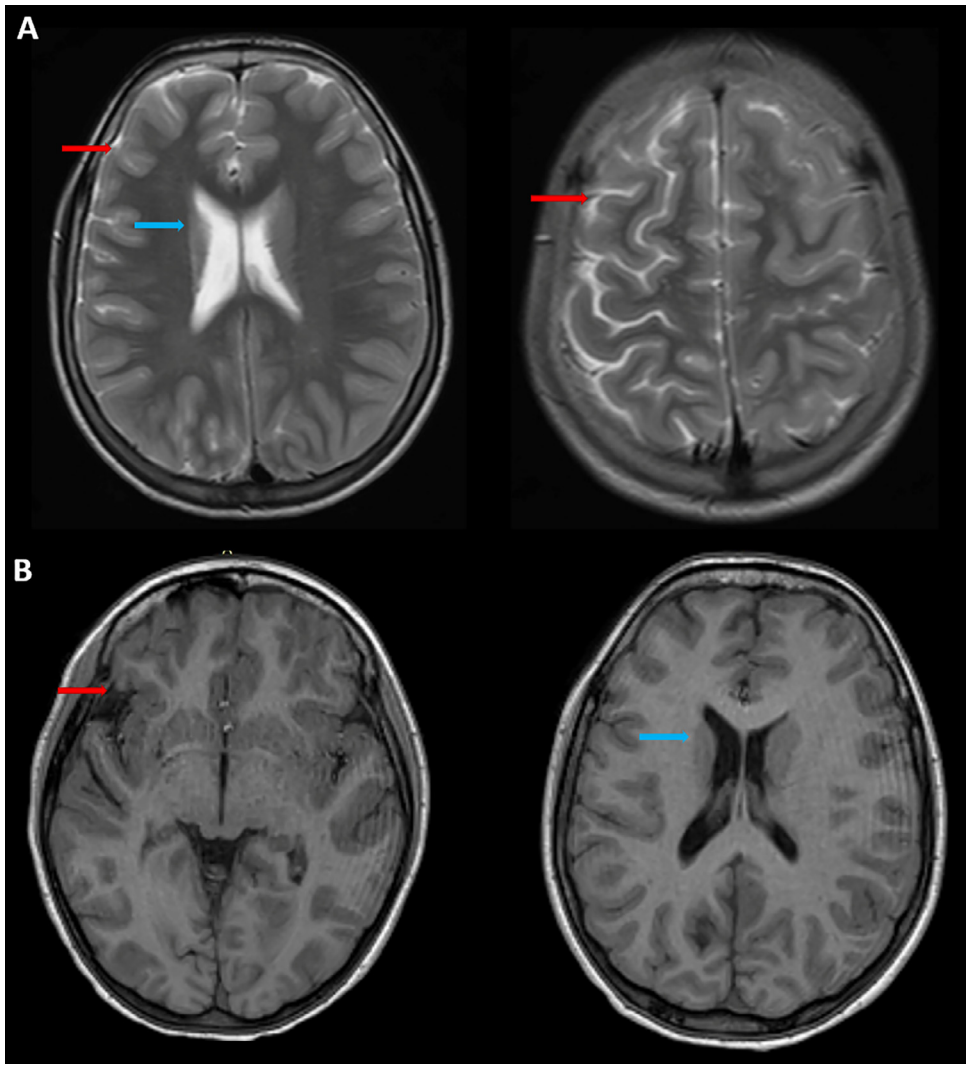

Fig. 3 – Axial T2-weighted brain MRI (A) reveals exaggerated right hemispheric gyri, indicative of right hemispheric atrophy (red arrow), accompanied by subtle retraction of the ipsilateral lateral ventricle (blue arrow). Axial T1-weighted sequence (B) further demonstrates the enlargement of the sylvian fissure (red arrow) along with atrophy of the ipsilateral caudate head (blue arrow).

deficits often detected through standardized assessments in early RE.

During the course of his illness, the patient developed left hemiparesis and an evolving seizure semiology, transitioning from occipital-origin seizures to drug-resistant seizures with a broader right hemispheric involvement. This progression underscores the dynamic nature of seizure onset zones in RE. Electroencephalographic findings in RE patients are highly variable and often correlate with the stage of disease progression. Unlike most reported cases of RE, this patient demonstrated relatively well-controlled epilepsy with a combination of antiepileptic drugs and immunomodulatory therapy with no need for hemispherotomy. Interestingly, the absence of background rhythm slowing may provide insight into the reduced pharmacoresistance observed, suggesting a potential link between specific electrophysiological findings and treatment responsiveness in RE. Furthermore, the patient did not present with continuous partial seizures, a challenging complication often encountered in the management of this disease. While no specific EEG pattern is pathognomonic for RE, certain changes, such as the development of persistent high-amplitude delta activity in the affected hemisphere, may emerge within months of seizure onset [8]. These findings highlight the critical need for serial EEG evaluations, including long-term monitoring, as symptoms evolve to refine diagnostic accuracy and guide management.

While the observed reduction in seizure frequency following intravenous immunoglobulin (IVIG) therapy in this patient is encouraging, it is likely to be temporary. Immunotherapy in RE primarily aims to slow disease progression, mitigating cortical atrophy and motor deficits rather than providing lasting seizure control. This aligns with findings from the only randomized controlled trial in RE, which demonstrated that both IVIG and tacrolimus could delay clinical deterio-

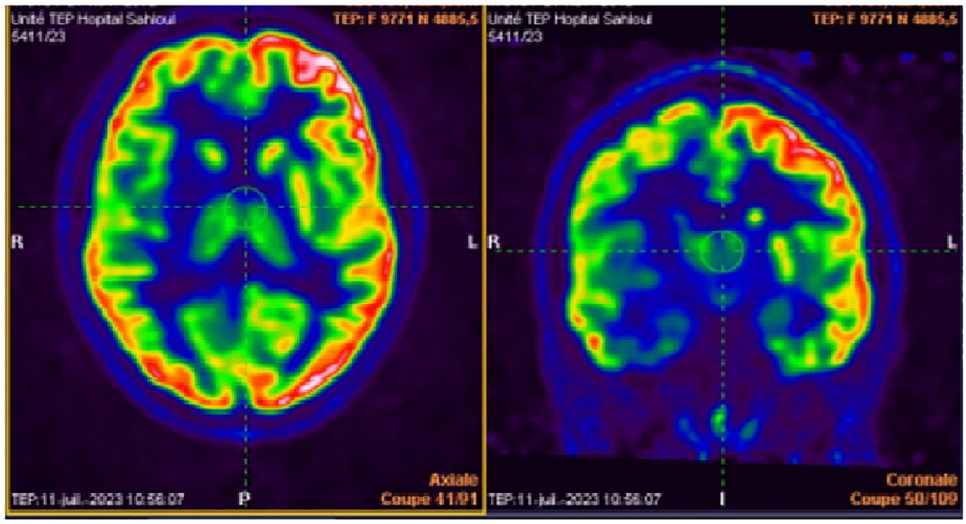

Fig. 4 – FDG-PET scan demonstrating diffuse, unilateral diffuse hypometabolism in the right frontal, parietal, temporal and occipital lobes, corresponding to the areas of atrophy observed on MRI, as well as within the ipsilateral basal ganglia.

ration without significantly reducing seizure frequency [14]. Consequently, definitive treatment with hemispherectomy remains the standard of care in most cases, particularly as drug-resistant seizures persist despite immunotherapy [15].

The broad range of atypical presentations reported in the literature and illustrated in this case further emphasizes the complexity of this rare disease. Awareness of such variability is crucial for early identification and timely management. Future directions in RE management necessitate large-scale, multicenter trials to explore novel immunotherapeutic targets, especially in the early stages of the disease.

Conclusion

Rasmussen's encephalitis can present with atypical features, such as posterior seizure onset and a prolonged prodromal phase. These uncommon presentations contribute to diagnostic challenges and delayed treatment initiation. Due to its rarity and clinical variability, further studies are needed to deepen our understanding of the pathophysiological mechanisms, refine diagnostic criteria, and optimize therapeutic strategies for this debilitating condition.

Registration of research studies

Not applicable.

Ethical approval

The institution (Fattouma Bourguiba University Hospital) exempts the case report from ethical approval.

Provenance and peer review

Not commissioned, externally peer reviewed.

Patient consent

Written, informed consent was obtained from the patient and their legal representative for the publication of this case report, including relevant clinical details and any accompanying images. The patient has been given the opportunity to review the manuscript and understands that the information will be published while maintaining confidentiality. A signed consent form is securely retained by the authors and can be provided to the journal's editorial board upon request.

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