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## RASMUSSEN ENCEPHALITIS: RESPONSE TO EARLY IMMUNOTHERAPY IN A CASE OF IMMUNE-MEDIATED ENCEPHALITIS

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**Background.** Rasmussen encephalitis (RE) is a severe immune-mediated neurologic disease characterized by unihemispheric inflammation, progressive neurologic deficits, and intractable focal epilepsy. Functional hemispherectomy is considered to be the only effective intervention for this devastating disease.<sup>1,2</sup>

Reports on immunotherapy use in RE, including steroids, IV immunoglobulin, and tacrolimus, have been published.<sup>2–4</sup> These therapies may lead to “arrest” of the disease in patients with pharmacoresistant epilepsy in whom motor function is not impaired enough to be offered a functional hemispherectomy.<sup>2–4</sup> Information regarding the effect of early and aggressive immunotherapy on cognitive function, MRI disease activity, and seizure control in this population is limited. Here we present a case of a child satisfying 2005 Bien diagnostic criteria for RE in whom disease control and motor and cognitive preservation was achieved using early aggressive immunotherapy.

**Classification of evidence.** This article provides Class IV evidence. This is a single observational study without controls.

**Case report.** A 6-year-old boy with an unremarkable past medical history experienced a sudden onset of focal seizures that gradually increased in frequency up to 20 times/day. His seizures were characterized by behavioral arrest, eyelid fluttering, and staring, followed by eye deviation upward and left hand twitching. The neurologic examination at the time of admission was normal, and his developmental history was normal.

EEG showed (1) right hemispheric slowing and interictal discharges, (2) right hemispheric ictal events (figure 1E), and (3) generalized spike and slow wave discharges. MRI of the brain showed right frontal and parietal cortical-subcortical T2/fluid-attenuated inversion recovery (FLAIR) hyperintensities (figure 1A).

Oligoclonal bands (OB) were present in the CSF but not in the serum, with normal CSF white blood cell

count and protein. A comprehensive infectious and rheumatologic (rheumatoid factor, complement c3, c4 NMDA receptor antibody [CSF/serum], extractable nuclear antigen, cytoplasmic antineutrophil cytoplasmic antibody, peripheral antineutrophil cytoplasmic antibody, anticardiolipin antibody) workup was negative except for antinuclear antibodies (ANA, 1:640).

Biopsy (figure 1D) performed on the parietal lobe lesion revealed reactive T lymphocytes (positive for CD 45, 3, and 8 staining) throughout the cortex in distinct clusters, frequently around vessels. Cortical gliosis with large astrocytes and perivascular microglial nodules were present. There was no evidence of demyelination, vasculitis, or viral inclusions.

Based on the predominance of T cells on biopsy, methylprednisolone 30 mg/kg for 3 days and 7 monthly cycles of cyclophosphamide (750 mg/m<sup>2</sup>) were administered, followed by a slow steroid taper. Following this, oral mycophenolate mofetil (MMF, 600 mg/m<sup>2</sup>) was started. MRI 1 year later showed resolution of inflammatory changes and mild right parietal volume loss (figure 1B). Steroids were discontinued; the child was seizure-free and continued on MMF and levetiracetam.

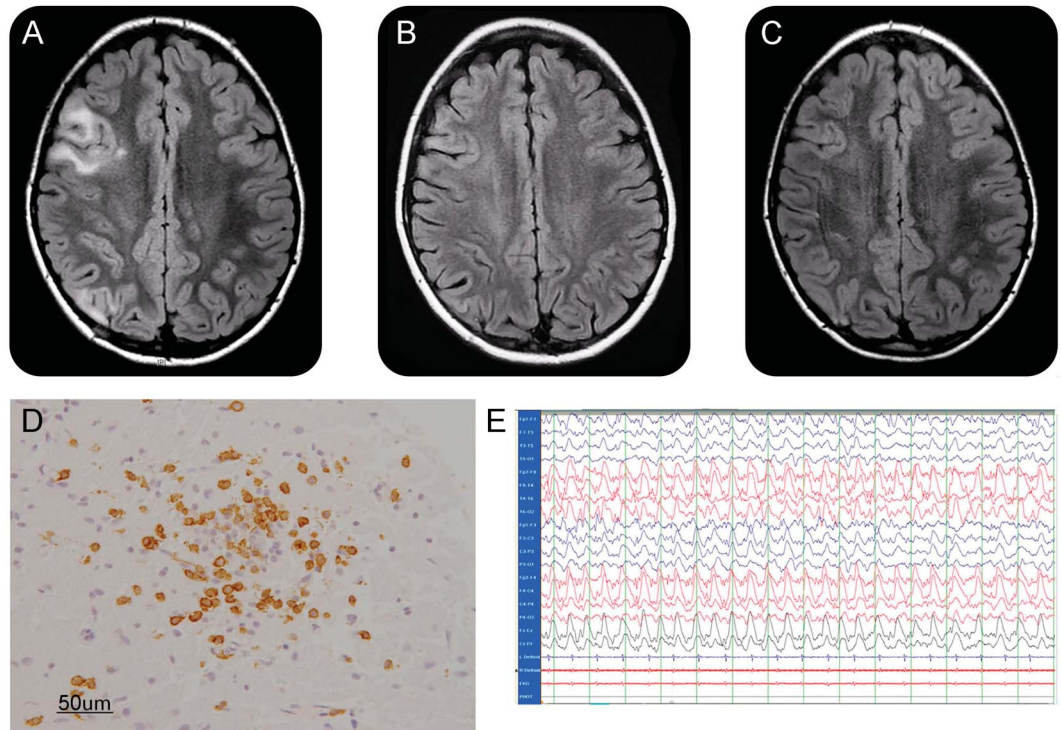
Unfortunately, within 3 months of steroid withdrawal, seizures of the same semiology recurred. EEG performed at this time showed (1) right frontal and temporal and (2) 3–4 Hz generalized spike-wave ictal events and interictal discharges. MRI of the brain showed no new T2/FLAIR hyperintensities or abnormal enhancement (figure 1C). Repeat CSF workup was positive for OB. Serum ANA was 1:640, with no other serum or CSF autoantibody positivity and no involvement of other organs.

The child received methylprednisolone 30 mg/kg for 3 days followed by a steroid wean, and lacosamide was introduced. The child has been off of steroids for 6 months and has remained seizure-free on MMF (600 mg/m<sup>2</sup>), levetiracetam, and lacosamide (figure e-1 at [Neurology.org/nn](http://Neurology.org/nn)). He is cognitively intact and making progress in school and continues to have a normal neurologic examination. No serious side effects from any of the medications were observed.

**Discussion.** This child met clinical, electrographic, pathologic, and MRI diagnostic criteria for RE, although the evolution of the case was atypical.<sup>1</sup>

Supplemental data  
at [Neurology.org/nn](http://Neurology.org/nn)

**Figure 1** MRI, pathology, and EEG findings



(A) Axial fluid-attenuated inversion recovery (FLAIR) MRI sequences of the brain showing right frontal and parietal cortical-subcortical hyperintensities at onset. (B) Axial FLAIR sequences 1 year later after therapy showing regression of the lesions. (C) Axial FLAIR sequences at the time of seizure recurrence after steroid withdrawal showing no new lesions. (D) Biopsy of the right parietal lesion with immunohistochemistry for CD8 showing a cortical cluster of inflammatory cells consisting primarily of cytotoxic T cells. (E) EEG showing right hemispheric ictal episode.

Effective immunosuppression was initiated soon after seizure onset and biopsy. In the 2 years of follow-up since presentation, he has experienced no cognitive or motor decline/deficit and is functioning at an age-appropriate level.

Search for a specific biologic marker for RE has been elusive, although specific antibodies and OB in the CSF have been described in some cases.<sup>1</sup> In this case, OB were found in the CSF but not in the serum. Persistent ANA positivity was seen, but specific ANA were not identified. ANA and antineuronal antibodies have been described in association with epilepsy,<sup>5,6</sup> but the significance of ANA in this child's disease remains unknown.

This child had EEG evidence for generalized and focal seizures. Whether this finding is due to dual pathology is unclear. The underlying inflammatory state may have triggered both seizure types.

The relatively short follow-up of this patient suggests the need for caution in interpreting these results. However, recent data suggest a potential treatment window early in the context of the initial T-cell-mediated injury to the brain in RE.<sup>7</sup> Larger studies with longer follow-up are necessary to confirm our findings.

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