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Case report

Immunoglobulin-responsive refractory epilepsy – 3 cases with a similar EEG pattern

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1. Introduction

Autoimmune epilepsies are a heterogeneous group of recently described refractory epilepsies. They have been characterized by a variety of clinical, serological and radiological features. A range of anti-neuronal antibodies, which are usually found in limbic encephalitis, including antibodies to GAD,[1–4] VGKC-complex antibodies,[5–11] NMDA-R,[12–14] amongst others, have been associated with some of these disorders. Other, antibody negative epilepsy patients had radiological features of central nervous system inflammation, inflammatory infiltrates histologically or high CSF white cell counts and oligoclonal bands.[11] Immune therapy, including steroids and IVIg, has been used in these cases and resulted in clinical improvement. Best outcomes were associated with a short duration of the underlying illness.[5,12] Long-term immune therapy has often been utilized in these cases.

In this article, we describe a small cohort of patients who had a rapid, sustained response to a short course of IVIg, despite limited serological and radiological evidence for an underlying autoimmune process. This response was independent of the varying seizure phenotypes. Interestingly, all 3 patients shared a certain EEG pattern.

2. Case 1

A 17 year old right handed girl, with a diagnosis of juvenile myoclonic epilepsy, was transferred in super-refractory status epilepticus of 3 days duration. Seizure semiology comprised ongoing episodes of alternating left and right sided facial jerking, eye deviation to the right, unresponsiveness and audible shallow breaths. These focal episodes frequently evolved to generalized tonic-clonic seizures. Despite escalating treatment in an ICU setting with intubation and anaesthetic agents, using high doses of LTG, LEV, TPM, VPA, PHT, clobazam, midazolam, magnesium and propofol infusions, she had ongoing seizures after 11 days.

EEG showed alternating left and right hemispheric epileptiform discharges with simultaneous contralateral frontal spike wave activity (Fig. 1a).

Because of the hemispheric emphasis of the epileptiform discharges, reminiscent of Rasmussen's encephalitis, a treatment attempt with IVIg, at a dose of 0.4 g/kg/day for 5 days, was undertaken. Twelve hours after the first dose of IVIg, the seizures had terminated clinically, but she remained confused and drowsy. An EEG at this stage showed generalized slowing (Fig. 1b). An MRI performed at this point was normal. By Day 15, the patient had made a full recovery and was sitting in bed doing her homework. Her EEG had completely normalized (Fig. 1c). Anti-thyroid antibodies (serum collected prior to initiation of IVIG) returned as mildly positive (Table 1).

She was discharged a week later and followed up in the clinic at 1, 3, 6 and 15 months. Repeat MRI head and EEG at 3 months post discharge were normal. No further IVIg has been administered. Her current AED regimen has been reduced to monotherapy with LTG 100 mg BD. No further seizures have been reported by the patient or her family.

Prior to this episode, she was thought to have a generalized epilepsy syndrome on the basis of a positive family history (the parents are first cousins and there is a history of epilepsy in the maternal grandmother), a history of absences and upper limb

Abbreviations: ACTH, adrenocorticotrophic hormone; AEDs, antiepileptic drugs; CSF, cerebrospinal fluid; CT, computer tomography; DZP, diazepam; EEG, electroencephalogram; FDG-PET, flurodecarboxyglucose – positron emission tomography; GAD, glutamic acid decarboxylase; GGE, genetic generalized epilepsy; IVIg, intravenous immunoglobulins; LEV, levetiracetam; LTG, lamotrigine; MRI, magnetic resonance tomography; NMDA-R, N-methyl-di-aspartase receptor; OxC, oxcarbazepine; PB, phenobarbitone; PHT, phenytoin; RE, Rasmussen's encephalitis; SIADH, syndrome of inappropriate antidiuretic hormone secretion; TPM, topiramate; VGB, vigabatrin; VGKC, voltage-gated potassium channel; VPA, valproic acid.

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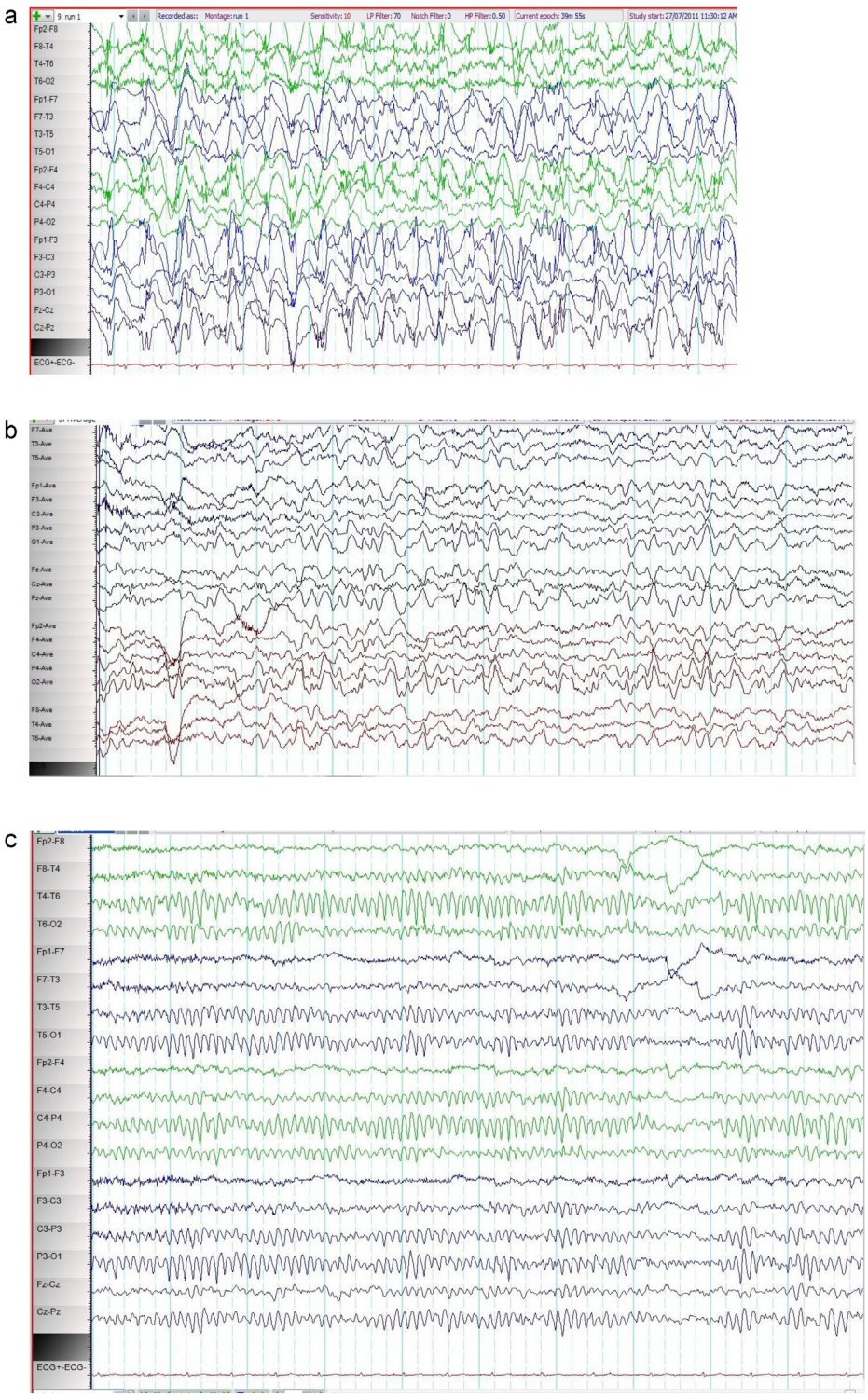

Fig. 1. (a) Case 1 – EEG, day 9 of super-refractory status epilepticus. Bipolar 10-20 montage of ongoing left hemispheric and bi-frontal polyspike and 2.5–3 Hz spike-wave epileptiform discharges. (b) Case 1 – EEG 12 h post IVIg – referential average montage showing generalized slowing. (c) Case 1 – EEG post 5 days IVIg. Return of normal trace.

myoclonus and a routine interictal EEG showing a burst of 4 Hz generalized spike and polyspike and wave activity.

She had a past history of three admissions, at the ages of 6 months, 9 months and 2 years, to intensive care units with refractory status epilepticus (including one episode of epilepsia partialis continua aged 2 years old). Each episode lasted between 2 and 15 days. Ictal EEGs were reported to show continuous 4–5 Hz spike and polyspike and wave activity, which on various admissions occurred either independently over both hemispheres or unilaterally over either the right or left hemisphere. Treatment was reported to have been difficult and required midazolam infusions, nitrazepam, paraldehyde, PB, PHT and ACTH in various combinations.

Maintenance therapy initially consisted of VGB and PHT with poor control. Later, after addition of LTG, the patient became seizure-free for 5 years on monotherapy.