Seizure 39 (2016) 1–4

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Clinical letter

Successful treatment of super-refractory tonic status epilepticus with rufinamide: First clinical report

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ARTICLE INFO

Article history:
Received 5 March 2016
Received in revised form 24 March 2016
Accepted 7 April 2016

1. Introduction

Rufinamide (RUF) is a novel antiepileptic agent that has entered clinical use within the last 10 years, thought to act through modulation of sodium channel activity [1].

Based on evidence from several independent randomised controlled trials (RCTs), RUF is used as an adjunctive agent in the treatment of Lennox–Gastaut syndrome (LGS) [2]. LGS is an epileptic encephalopathy syndrome, typically with onset in childhood, characterised by the presence of multiple seizure types including tonic, atonic and atypical absence seizures, and electroencephalography (EEG) showing slow spike-waves during waking, and fast rhythmic activity during sleep, as well as psychomotor delay and personality disorders.

In addition to its use in LGS, RUF has shown some efficacy in other refractory epilepsy syndromes in both children and adults [3], though retention rates appear highest in LGS [4].

We are not aware of any prior experience of the use of RUF in status epilepticus. Here we present a case in which RUF was used as an adjunctive agent to treat super-refractory tonic status epilepticus, in a young adult male with an unusual epilepsy syndrome sharing some features with LGS.

2. Case study

A 24-year old man with mild autistic spectrum disorder and learning disability presented with a recurrence of tonic seizures. He had previously had similar seizures at the age of 7, which came under rapid control on carbamazepine and valproate. These were withdrawn at the age of 10, and since then he had been seizure free without treatment.

Seizures consisted of sudden tonic abduction and extension of the arms into a "crucifix" posture associated with loss of awareness, lasting between 3 and 10 s, followed by very rapid recovery of awareness. Within days of recurrence, with no identified precipitant, the seizures rapidly escalated until they were occurring every 1–2 min, more than 95% of the time. He was admitted initially to a neurology ward, and after 2 weeks with little progress to a neurological intensive care unit. Magnetic resonance brain imaging showed no structural abnormality, cerebrospinal fluid results were unremarkable and cytogenetics showed no chromosomal abnormality. Antineuronal antibody screening was also subsequently confirmed as negative.

Benzodiazepines, phenobarbitone and levetiracetam had no impact. Valproate was partially successful at high doses (up to 4.8 g/day), but led to a hyperammonaemic encephalopathy. Burst suppression was eventually achieved only with a combination of ketamine, propofol and barbiturate with hypothermia. Subsequent trials with high doses of topiramate, lacosamide, phenobarbitone and further benzodiazepines were of no benefit, with seizure recurrence on multiple attempts at withdrawal of anaesthetic agents over a 4 week period.

As the electro-clinical picture included features reminiscent of LGS (Fig. 1), after informed discussion with the patient's family, RUF was rapidly titrated up to a total dose of 3 g/day over 10 days. Seizures abated completely for several days despite withdrawal of all sedation, with no apparent adverse effects. There were no significant changes in clinical observations, haematinics or biochemistry beyond improvements in his seizure frequency and responsiveness over this period.

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http://dx.doi.org/10.1016/j.seizure.2016.04.003

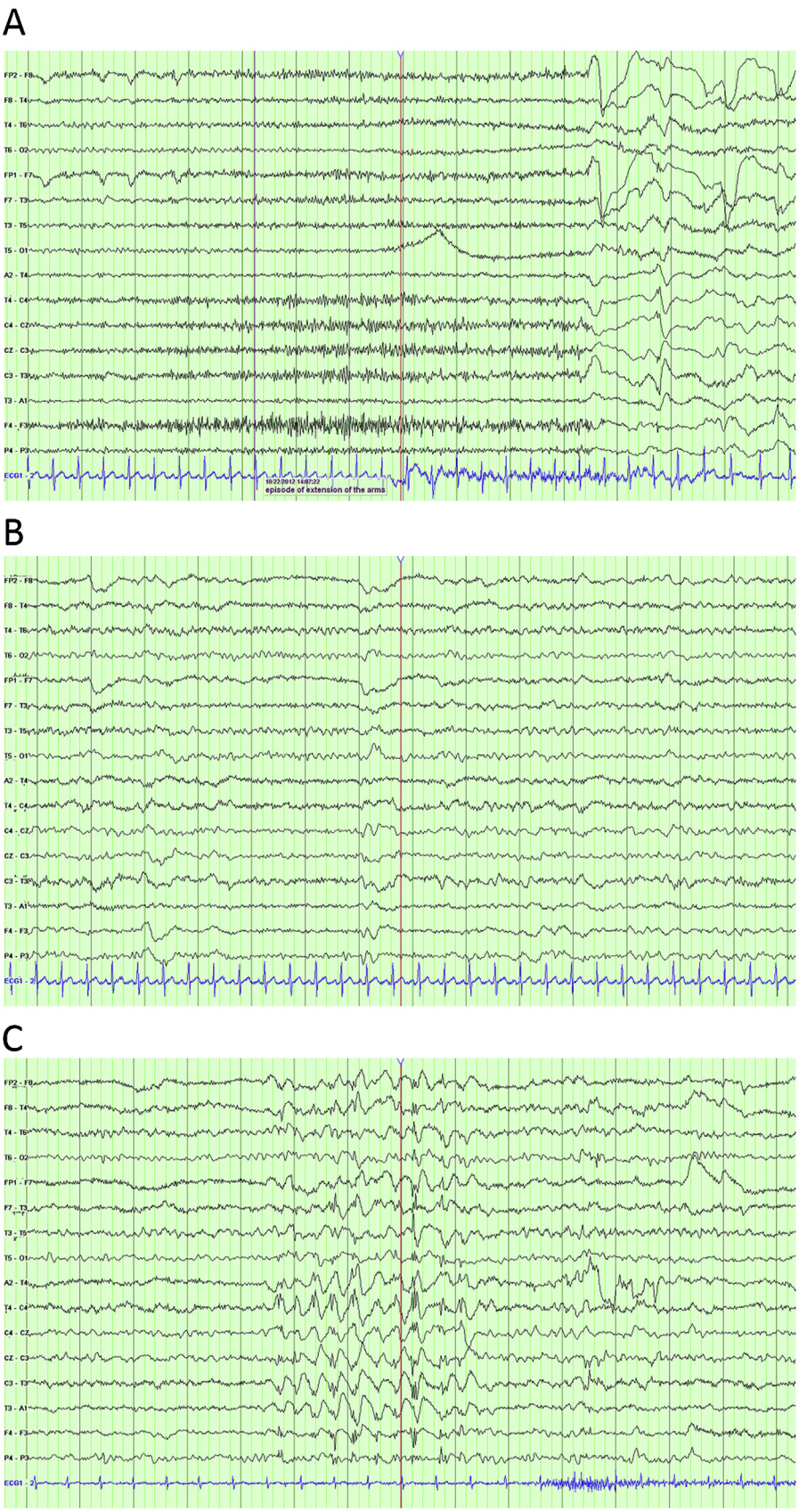

Fig. 1. Electroencephalography (EEG). (A) Ictal EEG. Tonic seizure starts at the purple line. Fast rhythmical activity (21 Hz) precedes clinical onset, followed by slow activity (2.5–4 Hz) with anterior emphasis. (B) Inter-ictal EEG 1. Mild excess of slow wave activity with intermittent irregular temporal theta. (C) Inter-ictal EEG 2. Excess of slow wave activity in background. Fairly frequent bursts of spikes/polyspikes and slow wave complexes, without clinical accompaniment.