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Short communication

Epilepsy of infancy with migrating focal seizures: Six patients treated with bromide

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ABSTRACT

Purpose: We present six patients with epilepsy of infancy with migrating focal seizures (EIMFS) and provide a comprehensive evaluation of potassium bromide therapy.
Method: Between February 1, 2007 and July 31, 2012, six patients who met the diagnostic criteria of EIMFS were treated with potassium bromide. Potassium bromide was added to other antiepileptic drugs (AEDs) in doses ranging from 30 to 80 mg/kg/day. Plasma bromide concentration was monitored. A therapeutic bromide concentration between 75 and 125 mg/dL was considered to be ideal.
Results: Four of six children responded well to bromide. One of these patients became seizure free, but remained severely mentally impaired. Two boys, currently 4 and 6 years of age, respectively, have monthly seizures as well as axial hypotonia and severe language impairment. The fourth child responded well to bromide, having only weekly seizures and moderate psychomotor retardation. The patient who became seizure free improved visual contact and head control. In the other three patients with good control, the seizures became focal without secondary generalization and status epilepticus and hospital admission was not required. The remaining two patients did not respond well to bromide. Adverse effects were seen in three cases: vomiting in one, drowsiness in another, and acneiform eruption in the face in the remaining patient. Adverse effects resolved with dose reduction.
Conclusion: Early treatment with bromides should be considered in EIMFS to control the seizures and status epilepticus and to avoid progressive cognitive impairment. Potassium bromide is an old AED. Plasma concentration monitoring should be considered.

1. Introduction

Epilepsy of infancy with migrating focal seizures (EIMFS) is a well-defined and rare epileptic syndrome characterized by an onset of multifocal seizures before 6 months of age and a typical ictal electroencephalography (EEG) pattern consisting of seizures that arise independently and sequentially from both hemispheres.[1] The seizures are refractory to antiepileptic drugs (AEDs) and cause subsequent severe mental retardation.[1,2]

Several reports have focused on seizure control or reduction with the use of different AEDs, such as levetiracetam, adrenocorticotropic hormone (ACTH), benzodiazepines, stiripentol, and rufinamide, and potassium bromide alone or in combinations with variable results.[3–5] Triple bromides have also been used in the treatment of refractory epilepsy, but in the literature we did not find any important differences between these two forms of bromides in terms of efficacy and tolerability.

Recently, EIMFS has been described related to different genes in sporadic and familial cases.[6] These findings suggest a genetic heterogeneity.

Here, we present six patients with EIMFS and provide a comprehensive evaluation of potassium bromide therapy.

2. Methods

Between February 1, 2007, and July 31, 2012, six patients who met the diagnostic criteria of EIMFS were treated with potassium bromide. We used potassium bromide as this was the formula we found in Argentina. The charts of all patients were analyzed

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considering response to therapy – especially to potassium bromide – and final outcome.

All patients underwent brain computed tomography (CT) scan and magnetic resonance imaging (MRI) as well as EEG recordings, neurometabolic tests, and karyotyping. No genetic markers associated with EIMFS were investigated in any of the patients.

All patients had received more than one of the conventional and new AEDs, before bromide was introduced: Carbamazepine was used in six patients, valproic acid in five, phenobarbital in four, diphenylhydantoin in four, clobazam in four, clonazepam in three, levetiracetam in four, topiramate in four, zonisamide in three, lamotrigine in three, ACTH in three, the ketogenic diet in one, and rufinamide in one. Bromide was added to levetiracetam and topiramate in two patients, to zonisamide and clonazepam in one, to valproic acid and clobazam in one, to levetiracetam and rufinamide in one, and to lamotrigine and clobazam in the remaining one. No AEDs were withdrawn after the introduction of bromide. The average dose of bromide was 65 mg/kg/day (range, 30–80 mg/kg/day). The starting dose was 10 mg/kg/day divided into two or three doses. No protocol was used to adjust the doses. Due to its exceptionally long half-life, plasma bromide concentration was monitored to prevent toxicity. The dose was titrated over one to two months and bromide levels were monitored every 3–4 months. A therapeutic bromide concentration of between 75 and 125 mg/dL was considered to be ideal. The effectiveness of the maintenance dose was evaluated based on the quality of life of the patients and their families. The parents of one patient did not accept to increase the dose of bromides.

3. Results

3.1. General characteristics

A total of six patients (four boys and two girls) were identified between 2005 and 2012 at the Garrahan Hospital of Buenos Aires. In all patients, the neurological examination showed hypotonia after the seizures became refractory, but there were no other neurological abnormalities. The initial head circumferences of the children were normal for age.

At onset, brain CT scans and MRIs were normal in all patients. Subsequent repetitive MRIs showed mild ventricular enlargement in one, and a moderate degree of the same finding in five. In one, the MRIs showed unilateral mesial temporal sclerosis. Electroretinogram and visual and auditory evoked potentials were normal in all cases, but somatosensory evoked potentials, performed before bromide initiation, showed increased amplitude and prolonged latency in the cortical component in two patients. No etiologies were found.

3.2. Electroclinical findings

The mean and median ages at the time of the first seizure were 45 days and 30 days, respectively (range, 15–60 days). Three electroclinical patterns were recognized according to seizure frequency, recurrence, and topography: (1) Alternating simple focal motor seizures at onset with an ictal EEG pattern that was characterized by recurrence of rhythmic focal spikes or rhythmic

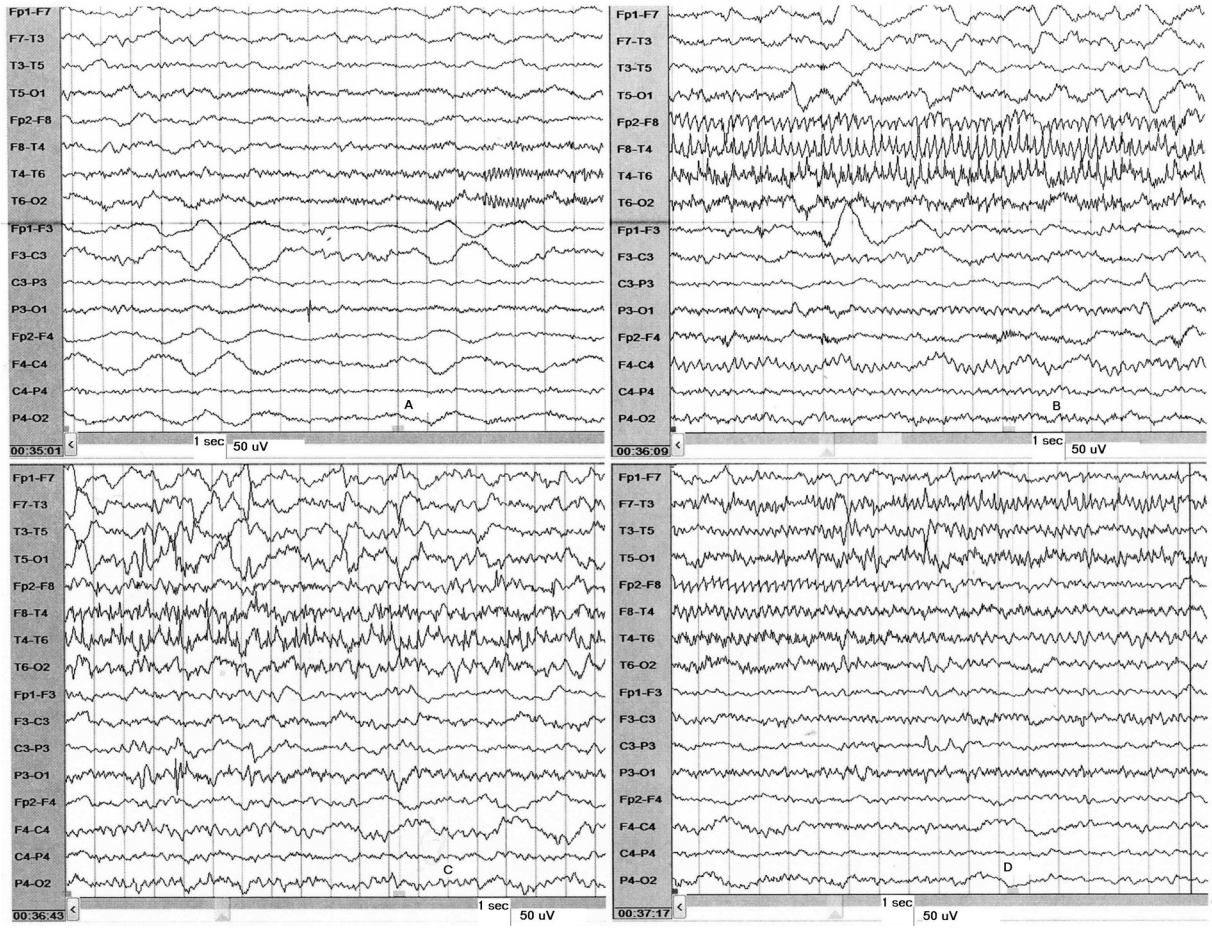

Fig. 1. A 2-month-20-day-old girl with seizure onset with right posterior temporal theta rhythms. B and C: 68 and 94 s after onset, respectively, the ictal EEG recording shows theta rhythms propagating to the anterior regions of the same hemisphere. D: Two minutes and 16 s after onset, rhythmic theta activity appears in the left hemisphere.