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Clinical Observations

Potassium Bromide for Treatment of Malignant Migrating Partial Seizures in Infancy

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ABSTRACT

BACKGROUND: The syndrome of malignant migrating partial seizures in infancy is a rare epileptic syndrome with a devastating course characterized by early onset of continuous pharmacoresistent multifocal seizures arising from multiple independent sites of both hemispheres with unknown etiology. **PATIENT:** A 2-month-old boy with the characteristic clinical and electroencephalograph pattern of migrating partial seizures in infancy was treated with potassium bromide. His seizures were unresponsive to the conventional and new generation antiepileptic drugs. **RESULTS:** The seizure frequency was reduced markedly with potassium bromide. **CONCLUSIONS:** Potassium bromide, an old antiepileptic drug, is useful in the treatment of malignant migrating partial seizures in infancy.

Keywords: malignant migrating partial seizures in infancy, potassium bromide, refractory epilepsy

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Introduction

The syndrome of malignant migrating partial seizures in infancy (MMPSI) is a rare entity described first in 1995 by Coppola et al.[1] The syndrome is characterized by early onset of continuous multifocal seizures arising from multiple independent sites in both cerebral hemispheres with unknown etiology. The prognosis is poor, with a marked developmental regression.[1] The seizures are markedly pharmacoresistent. A few reports focused on seizure control or reduction with the use of different antiepileptic drugs including potassium bromide, stiripentol, levetiracetam, clonazepam, and rufinamide or their combinations with various success rates.[2–7] Among them, potassium bromide is an old antiepileptic drug whose use has declined because of adverse effects. However, bromides continued to be used in refractory cases in specialized epileptology instutions.[8] The main adverse effects involve the central nervous system, gastrointestinal system, and skin.[9,10] Drowsiness and acneiform eruptions are the most common and well-known adverse effects.[11] Here we present a 2-month-old boy with refractory migrating focal seizures whose seizures were almost controlled with potassium bromide treatment.

Case Report

A 2-month-old boy was referred to our hospital with seizures. He was born normally to nonconsanguineous parents at 39 weeks' gestation after an uneventful pregnancy. His mother first noticed clonic jerks of the right arm 1 week ago; these jerks then migrated to the left arm, then to the legs. After that, she noticed eyelid twitches and jerks of his mouth to one side. At first, these jerks lasted a few seconds, and then they lasted longer and appeared simultaneously. The seizure frequency increased and the jerks occurred in clusters several times daily. The family history revealed epilepsy in the patient's uncle. On admission he had a mild drop; otherwise, the neurologic examination was normal. He was given phenobarbital. However, the seizures continued in an increasing manner. Routine hematologic, biochemical, and blood gas analyses were normal.

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TABLE 1.
Potassium bromide in the treatment of MMPSI in the literature

	Age	Dosage mg/dL	Response	Side Effects
Okuda et al., 2000	14 months, M	110	Complete control of seizures in 3 weeks	Not observed
Coppola et al., 2007	7 months, F	80	Complete control of seizures in 3 weeks	Not observed
Caraballo et al., 2008	6 months, 2 years	124-600	A girl, seizure-free at 3 years of age; a 3-year-old boy, only rare subclinical frontotemporal seizures during sleep	Not observed
Nabatame et al., 2010	3 months, M	80	Decrease in seizures within a week	Erythematous papules leading to discontinuation of therapy
Djuric et al., 2011	2 months, F; 4 months, M	80	Decrease in seizures >50% additional with stiripentol and levetiracetam	Not observed
Fasulo et al., 2012	6 months, F	Not mentioned	Almost seizure-free	Not observed

Urine organic acid and tandem mass analyses revealed no abnormality. Plasma biotinidase activity, ammonium, lactic acid, pyruvic acid levels and cerebrospinal fluid/blood glucose ratio and cerebrospinal fluid amino acid profile were all normal. His brain magnetic resonance imaging findings revealed no pathology. His initial electroencephalograph (EEG) recordings were normal. Further prolonged EEG recordings were performed during hospitalization. Seizure frequency increased and the seizures appeared in clusters; a subsequent EEG a month later showed independent focal spikes on the left and right temporoparietooccipital region and a slow background activity on the left temporoparietooccipital region accompanied. The diagnosis of MMPSI was considered by the clinical characteristics and EEG patterns.

He was given vitamin B6 intravenously as well as topiramate, clonazepam, levetiracetam, clobazam, and vigabatrin in various combinations. All these antiepileptic drugs were started at low doses and titrated to the recommended doses. However, they failed to stop the seizures and the status epilepticus. He was hospitalized three times for status epilepticus. His seizures were highly pharmacoresistent, unresponsive to intravenous phenytoin, levetiracetam, and midazolam infusion. Only thiopental infusion in the intensive care unit led to seizure control. However, as the infusion dosage was reduced gradually, his seizures started either with arm or leg jerks, twitches of the eyelids, jerks of the mouth to one side, or tongue jerks migrating to the whole body from one body part to the other leading to a generalized tonic-clonic status epilepticus. He was intubated when needed. Then he was given potassium bromide with a starting dose of 50 mg/kg. The dosage was increased up to 80 mg/kg in 2 weeks gradually while phenobarbital dosage was decreased. Three weeks later, the seizures stopped and he was discharged seizure-free after 4 months of hospitalization and periods of recurrent and refractory status epilepticus. On discharge, he had marked axial hypotonia, an absence of visual contact, and poor head control. His head circumference was below the third percentile at age 7 months. He was fed by nasogastric tube. At the 3 months during the follow-up course, there was no improvement in the stage of encephalopathy and the seizures continued as clonic jerks of the legs or arms with a frequency of 1 to 3 seizures weekly, but never leading to a generalized tonic-clonic status epilepticus and a need for hospitalization.

Discussion

MMPSI is a rare syndrome with a devastating course. The seizures are markedly pharmacoresistent and progressive deterioration of psychomotor development is inevitable. Our patient had clinical and electrographic characteristics fulfilling the clinical criteria for MMPSI including continuous migrating polymorphous focal seizures combined with multifocal EEG patterns. Potassium bromide, an old antiepileptic drug, led to a significant seizure reduction in our patient with MMPSI.

Potassium bromide is a water-soluble salt that is rapidly and nearly completely absorbed in the upper intestine and distributed in the extracellular space. It is excreted by the kidneys and has a very long half-life, which has been estimated at 8-14 days in adults and 6-8 days in children. In two experimental epilepsy models, Meierkord et al[12] showed that potassium bromide's anticonvulsive action might be related with increased γ-aminobutyric acidergic inhibition rather than by an altered acid-base status.

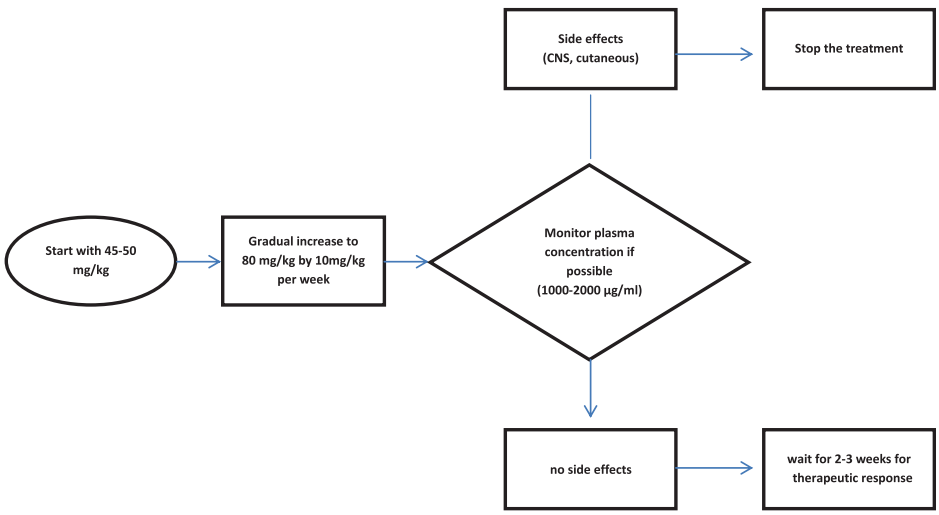

FIGURE 1.
Summary of potassium bromide usage.

There is little experience with potassium bromide in treatment of patients with MMPSI. Okuda et al.[2] and Coppola et al.[3] reported sustained seizure control with potassium bromide in their patients aged 7-14 months old. Both authors' patients showed neurological improvement after cessation of seizures without adverse effects. On the other hand, Nabateme et al.[13] reported gradual decrease in seizure frequency with bromide therapy; however, the therapy was discontinued because of side effects including apneic episodes and skin rashes. Two patients were also reported by Caraballo et al.[14] to respond well at unusually high doses of 124-600 mg/kg daily. Potassium bromide trials in the literature are shown in Table 1.

We started potassium bromide therapy in our patient with 50 mg/kg per day divided in two oral doses and gradually increased the dosage up to 80 mg/kg according to earlier reports.[2–4] The therapeutic response was achieved after 2 weeks and no side effects were observed. The patient was discharged seizure-free. We propose a flowchart for potassium bromide therapy shown in Figure 1.

In conclusion, potassium bromide therapy should be considered in MMPSI patients whose seizures are refractory to the conventional and new-generation antiepileptic drugs and in the treatment of refractory and recurrent status epilepticus, as in our case. However, further studies are required to evaluate the efficacy and tolerability of this old antiepileptic drug.

References

1. Coppola G, Plouin P, Chiron C, Robain O, Dulac O. Migrating partial seizures in infancy: a malignant disorder with developmental arrest. *Epilepsia*. 1995;36:1017-1024.
2. Okuda K, Yasuhara A, Kamei A, Araki A, Kitamura N, Kobayashi Y. Successful control with bromide of two patients with malignant migrating partial seizures in infancy. *Brain Dev*. 2000;22:56-59.
3. Coppola G, Operto FF, Auriccio G, D'Amicco A, Fortunato D, Pascotto A. Temporal lobe dual pathology in malignant migrating partial seizures in infancy. *Epileptic Disord*. 2007;28:145-148.
4. Djuric M, Kravljanac R, Kovacevic G, Martic J. The efficacy of bromides, stiripentol and levetiracetam in two patients with malignant migrating partial seizures in infancy. *Epileptic Disord*. 2011;13:22-26.
5. Vendrame M, Poduri A, Loddenkemper T, Kluger G, Coppola G, Kothare VS. Treatment of malignant migrating partial epilepsy of infancy with rufinamide: report of five cases. *Epileptic Disord*. 2011; 13:18-21.
6. Fasulo L, Saucedo S, Cáceres L, Solis S, Caraballo R. Migrating focal seizures during infancy: a case report and pathologic study. *Pediatric Neurol*. 2012;46:182-184.
7. Merdariu D, Delanoë C, Mafoudi N, Bellavoine V, Auvin S. Malignant partial seizures of infancy controlled by stiripentol and clonazepam. *Brain Dev*. 2013;35:177-180.
8. Dreyer R. Die pharmacotherapy der Epilepsien. In: Kisker KP, Meyer IE, eds. *Psychiatrie der Gegenwar*. Berlin, Germany: Springer Verlag; 1972:Volume 2.
9. Korinthenberg R, Burkart P, Woelfle C, Moenting JS, Ernst JP. Pharmacology, efficacy, and tolerability of potassium bromide in childhood epilepsy. *J Child Neurol*. 2007;22:414-418.
10. May Th, Giuccioli D, Rambeck B. Einfluss von bromid-dosis und physiologischen faktoren auf die steady-statekonzentration von bromide bei 139 patienten. In: Scheffner D, ed. *Epilepsie 91*. Reinbek, Germany: Einhorn Verlag; 1992.
11. Browne TR, Ascanape JS. Diones, paraldehyde, phenacemide, bromides, and sulthiame. In: Engel Jr J, Pedley TA, eds. *Epilepsy: A Comprehensive Textbook*. Philadelphia, PA: Lippincott-Raven; 1997.
12. Meierkord H, Grunig F, Gutschmidt U, et al. Sodium bromide effects on different patterns of epileptiform activity, extracellular ph changes and GABAergic inhibition. *Naunyn Schmiedebergs Arch Pharmacol*. 2000;361:25-32.
13. Nabateme S, Saito Y, Sakuma H, et al. Bromoderma in a patient with migrating partial seizures in infancy. *Epilepsy Res*. 2010;91:283-288.
14. Caraballo RH, Fontana E, Darra F, et al. Migrating focal seizures in infancy: analysis of the electroclinical patterns in 17 patients. *J Child Neurol*. 2008;23:497-506.