Epilepsy & Behavior Reports 12 (2019) 100329

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

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

Case Report

Adolescent-onset absence epilepsy years after resolution of childhood epilepsy with myoclonic-atonic seizures

Sarah H. Berth, Eric H. Kossoff *

Johns Hopkins Hospital, Department of Neurology, Sheikh Zayed Tower, Room 6005, 1800 Orleans Street, Baltimore, MD 21287, United States of America

ARTICLE INFO

Article history:
Received 20 May 2019
Received in revised form 7 June 2019
Accepted 27 June 2019
Available online 22 July 2019

Keywords:
Doose
Epilepsy
Astatic
Atonic
Absence
Valproic acid

ABSTRACT

We present a case series of three boys with childhood epilepsy with myoclonic–atonic seizures (EMAS) who achieved complete remission during childhood only to develop absence seizures during early adolescence. In all three cases, the recurrent seizures resolved again with antiseizure drugs, and two are currently medication-free for a second time.

1. Introduction

Doose syndrome (DS), otherwise known as epilepsy with myoclonic-atonic seizures (EMAS) and previously myoclonic-astatic epilepsy, is a seizure syndrome of young childhood associated with prominent myoclonic and astatic seizures [1]. EEG findings include bursts of 2- to 5-Hz spike and polyspike and wave complexes, with normal sleep architecture and posterior basic rhythm. EMAS typically presents with a peak onset between the ages of 3–4 years, with a range of 7 months and 6 years of age [1]. Antiseizure drugs reported to be the most effective for EMAS include ethosuximide, lamotrigine, and valproic acid, although levetiracetam is also widely used [2]. Certain antiseizure drugs may cause paradoxical worsening, including carbamazepine, oxcarbazepine, phenytoin, and vigabatrin. The ketogenic diet has been shown to be highly efficacious, and reports have suggested that it could be even considered as a first line therapy in these patients [3]. Close to two-thirds of patients achieve seizure remission, within 5–6 years of onset [4,5].

The long-term outcomes from EMAS are not widely described. Although most patients will achieve remission, it is not clear how many will have recurrence years later. Additionally, it is known that other epilepsy syndromes can remit, only to have other seizure types or even different syndromes occur months to years later [6–10].

We report a case series of three patients with EMAS that underwent seizure remission for ≥4 years as children, who then developed what appeared to be a different syndrome with both absence seizures and generalized tonic–clonic seizures during early adolescence. These three children were not as difficult to control during this second epilepsy syndrome, and two are currently not receiving treatment for a second time.

1.1. Case 1

A previously normal 3-year-old boy presented after a single generalized tonic–clonic (GTC) seizure, followed by the onset of atonic seizures that occurred up to 40 times per day. EEG revealed polyspike and wave bursts with a normal background suggestive of EMAS (Fig. 1A). MRI was normal, and genetic testing showed a SCN1A mutation with transversion of nucleotide 1091 from serine to threonine. He was treated with zonisamide and clonazepam which were ineffective, then valproic acid led to immediate seizure freedom within several days. At the age of 5.5 years, after he was seizure-free for 2 years with a normal EEG, his valproic acid was discontinued.

At the age of 9 years, his family began noticing staring spells at home and school that gradually increased in frequency to daily over a several month period. Hyperventilation in the clinic induced a classic absence seizure and an EEG revealed 3-Hz spike and wave discharges, shifting at times from left to right maximal, only with hyperventilation (Fig. 1B). He was restarted on valproic acid at 20 mg/kg/day divided twice daily, and seizures stopped immediately, similar to the previous use of valproic acid when he was younger. After 2 years of seizure freedom

* Corresponding author at: Johns Hopkins Hospital, Department of Neurology, Suite 2158-200 North Wolfe St, Baltimore, MD 21287, United States of America.
E-mail addresses: sberth1@jhmi.edu (S.H. Berth), ekossoff@jhmi.edu (E.H. Kossoff).

https://doi.org/10.1016/j.ebr.2019.100329

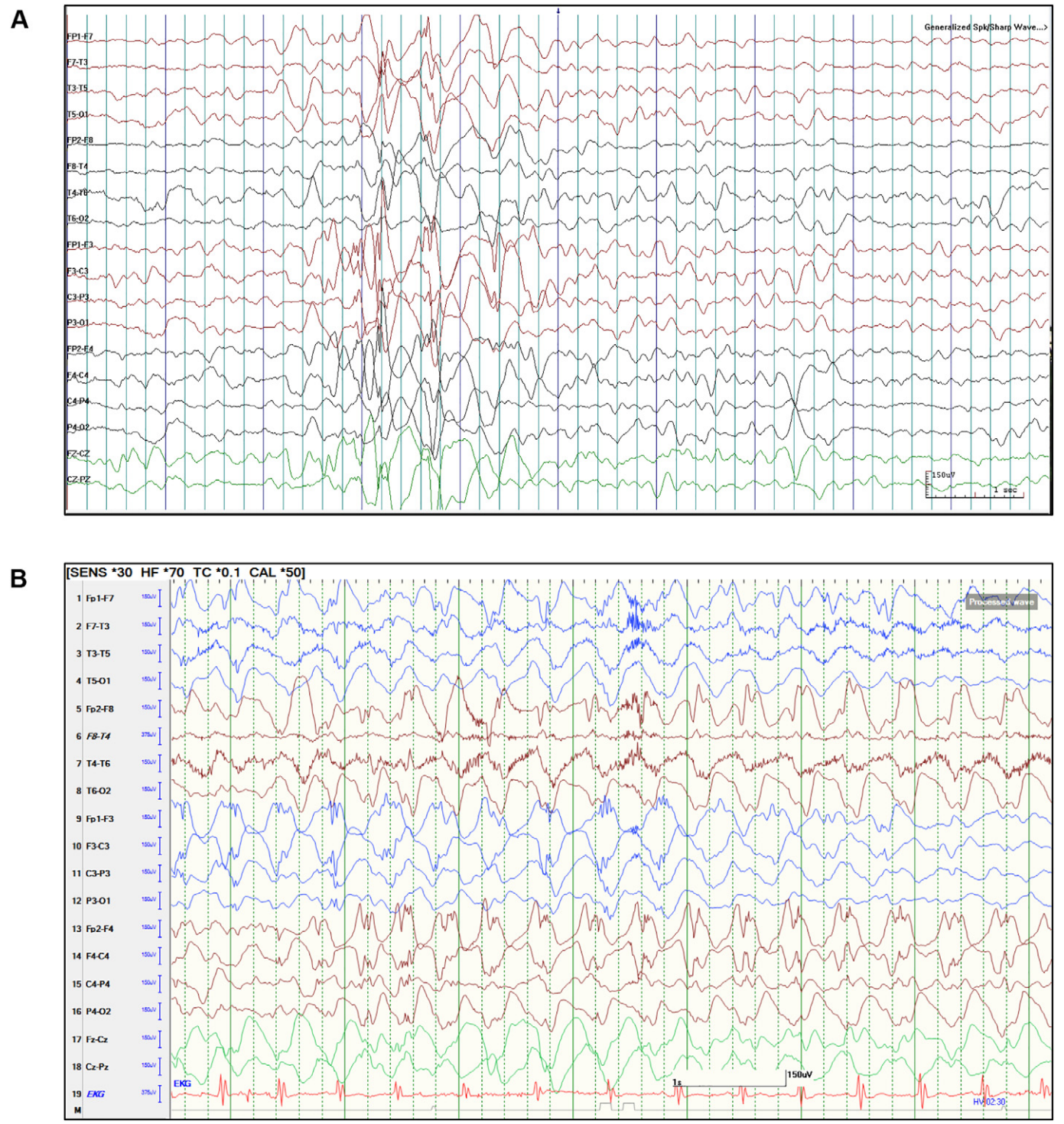

Fig. 1. EEG tracings from Case 1 demonstrate an electrographic change in seizures in the same patient. **(A)** Bipolar montage from EEG at age 3 shows bursts of spike and wave and polyspike and wave complexes, consistent with EMAS. His seizures went into remission with valproic acid, and valproic acid stopped. At the age of 9 he developed new absence seizures, with EEG showing shifting asymmetry of 3 Hz spike and wave complexes only induced by hyperventilation **(B)**.

(age 12 years), his EEG had normalized, and his valproic acid was again discontinued carefully. One year later, he remains seizure-free.

1.2. Case 2

A previously normal 3-year-old boy developed sporadic convulsions and 3–12 atonic seizures daily over several months. Brain MRI was unremarkable, and an EEG revealed generalized polyspike and wave bursts suggestive of EMAS. He was unsuccessfully treated with phenytoin, oxcarbazepine, zonisamide, lorazepam, and lamotrigine. His seizures were ultimately completely controlled at the age of 5 years with a combination of levetiracetam and zonisamide. After 4 years of seizure control, his antiseizure drugs were stopped. Two years later, at the age of 11 years, he began having staring spells and an EEG revealed bursts of 3–4 Hz spike-and-slow –wave discharges (not triggered by hyperventilation). Levetiracetam was restarted but ineffective, and following a

convulsion, clobazam was added. Seizures remained unchanged for an additional 3 months until valproic acid at 15 mg/kg/day was added. All seizures stopped within days and levetiracetam and clobazam were gradually discontinued. After 2 years of treatment with valproic acid monotherapy, at the age of 14 years, his EEG normalized, and he was weaned off of valproic acid. He has remained seizure-free for the past year.

1.3. Case 3

A previously normal 3-year-old boy began having GTCs, drop seizures, and myoclonic seizures, with a frequency that increased over three months up to 50 total seizures per day. An EEG showed generalized spike and sharp wave bursts consistent with a clinical diangosis of EMAS, and an MRI of the brain was normal. Genetic testing revealed a variant of uncertain significance (HNRNPU gene, seen in his father who does not have epilepsy). He was placed on levetiracetam then oxcarbazepine, both without benefit. At 4 years of age, the ketogenic diet was initiated, and after 91 days his seizures stopped, and he was taken off of both antiseizure medications. The ketogenic diet was maintained for 21 months; his EEG normalized, and he was transitioned back to regular foods.

At the age of 12 years, after 8 years of seizure freedom, he then began having hours of "confusion and slowed thoughts", which were occurring about every 4 weeks. After 6 months, he had two GTCs and a subsequent EEG showed 4 Hz spike-and-slow wave bursts (not triggered by hyperventilation). He was placed on lamotrigine, but continued to have seizures until ethosuximide at 10 mg/kg/day was added in combination at the age of 14 years. Seizures immediately stopped, an EEG revealed only scattered 1-second bursts of generalized epileptiform discharges, and lamotrigine was discontinued 6 months later. Since then, he has not had any additional seizures and remains on ethosuximide monotherapy at age 15 years.

2. Discussion

In this case series, three boys with EMAS were completely seizure-free (2 with antiseizure drugs, one with the KD), underwent seizure remission, and then developed a new seizure syndrome during adolescence suggestive of absence epilepsy. Not surprisingly, when absence seizures began at ages 9–12 years after resolution of EMAS, families were very concerned; however, these seizures rapidly responded to valproic acid or ethosuximide. Two patients are currently now off antiseizure medications for a second time after apparent remission, with the third likely to discontinue medication in approximately one year. Of note, the EEG may have been normalized due to the use of valproic acid in patients 1 and 2; these parents were counseled about this, and their antiseizure drug wean performed slowly and carefully. Additionally, as some generalized epilepsies may have prolonged periods of apparent remission, these patients will continue to be followed carefully.

To our knowledge, this evolution into absence seizures following remission has not been previously reported in EMAS. Oguni in 2002 reported recurrence of generalized tonic–clonic seizures in 14% of his patients after 3–17 years that were "controlled easily" [5]. Most series report a favorable prognosis and remission in the majority of cases [2–5,11]. Although absence seizures may coexist at the time of atonic seizures, they are not typically seen independently and certainly not expected to occur years later after apparent remission.

The absence seizures were well-controlled with antiseizure drugs known to be effective for EMAS: ethosuximide and valproic acid. In two of three, lamotrigine was not effective (either for EMAS or absence epilepsy). With this small number of patients, it is premature to claim this antiseizure regimen is ideal; however, we would consider valproic acid early for both the EMAS as well as the absence epilepsy.

3. Conclusion

To our knowledge, this is the first report of recurrence of absence seizures during adolescence in patients with EMAS after apparent remission. The similarities in age of onset, EEG findings, gender, recurrence, treatment response, and excellent prognosis are striking. This may represent a subset of EMAS, with the classic atonic seizures presenting in childhood evolving into an atypical course involving absence seizures years later during adolescence. This may alternatively represent a coincidental second epilepsy syndrome unrelated to EMAS, which has been reported to occur for other epilepsy syndromes such as benign epilepsy with centrotemporal spikes.

Ethical statement

We wish to confirm that this work has been carried out in accordance with the Declaration of Helsinki.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose related to this manuscript.

References

[1] Tang S, Pal DK. Dissecting the genetic basis of myoclonic-astatic epilepsy. Epilepsia 2012;53:1303–13.
[2] Nickels K, Thibert R, Rau S, Demarest S, Wirrell E, Kossoff EH, et al. How do we diagnose and treat epilepsy with myoclonic-atonic seizures (Doose syndrome)? Results of the pediatric epilepsy research consortium survey. Epilepsy Res 2018;144:14–9.
[3] Kelley SA, Kossoff EH. Doose syndrome (myoclonic-astatic epilepsy): 40 years of progress. Dev Med Child Neurol 2010;52:988–93.
[4] Kaminska A, Ickowicz A, Plouin P, Bru MF, Dellatolas G, Dulac O. Delineation of cryptogenic Lennox-Gastaut syndrome and myoclonic astatic epilepsy using multiple correspondence analysis. Epilepsy Res 1999;36:15–29.
[5] Oguni H, Tanaka T, Hayashi K, Funatsuka M, Sakauchi M, Shirakawa S, et al. Treatment and long-term prognosis of myoclonic-astatic epilepsy of early childhood. Neuropediatrics 2002;33:122–32.
[6] Camfield PR, Camfield CS. Intractable seizures after a lengthy remission in childhood-onset epilepsy. Epilepsia 2017;58:2048–52.
[7] Datta AN, Wallbank L, Wong PKH. Co-existence of Rolandic and 3 Hz spike-wave discharges on EEG in children with epilepsy. Can J Neurol Sci 2019;46:64–70.
[8] Sarkis RA, Loddenkemper T, Burgess RC, Wyllie E. Childhood absence epilepsy in patients with benign focal epileptiform discharges. Pediatr Neurol 2009;41:428–34.
[9] Gambardella A, Aguglia U, Guerrini R, Morelli F, Zappia M, Quattrone A. Sequential occurrence of benign partial epilepsy and childhood absence epilepsy in three patients. Brain Dev 1996;18:212–5.
[10] Dimova PS, Daskalov DS. Coincidence of Rolandic and absence features: rare, but not impossible. J Child Neurol 2002;17:838–46.
[11] Stephani U. The natural history of myoclonic astatic epilepsy (Doose syndrome) and Lennox Gastaut syndrome. Epilepsia 2006;47(Suppl. 2):53–5.