


CASE REPORT

Open Access



Focal seizures during adrenocorticotrophic hormone therapy in a school-aged boy: a case report

Yoshitaka Ota¹, Shuichi Shimakawa^{2*} , Hikaru Tsuda-Kitahara², Miho Fukui², Mitsuru Kashiwagi¹ and Akira Ashida²

Abstract

Background: Adrenocorticotrophic hormone therapy for infantile spasms, including West syndrome, has been previously reported to induce seizures. We present the findings for a school-aged child with epilepsy who developed new focal seizures during adrenocorticotrophic hormone therapy.

Case presentation: The Japanese patient had posttraumatic epilepsy and developed intractable focal seizures at the age of 13 years. Adrenocorticotrophic hormone therapy was administered when the patient was 14 years of age. On day 10 of treatment, he developed new focal seizures, which were characterized by left arm contractions followed by movements of touching things with his right hand and writhing and rocking his body left and right and back and forth as automatisms. The focal seizures clustered for 40 minutes and disappeared after suppository administration of 10 mg diazepam. These focal seizures did not reoccur after more than 2 years of follow-up.

Conclusion: Adrenocorticotrophic hormone-induced seizures can occur in children older than previously reported, and can occur in children with intractable seizures other than epileptic spasms.

Keywords: Hemiconvulsion–hemiplegia–epilepsy syndrome, Posttraumatic epilepsy, ACTH treatment, ACTH-induced seizures

Background

Adrenocorticotrophic hormone (ACTH) therapy for infantile spasms, including West syndrome, has been reported to potentially induce seizures [1–4]. These ACTH-induced seizures are characterized as new seizures that develop during ACTH therapy and cease after discontinuation of ACTH therapy. However, ACTH-induced seizures have not been described in patients with seizures other than epileptic spasms, patients without a history of epileptic spasms, and patients aged over 1 year.

Here, we report the findings of a school-aged child who developed ACTH-induced seizures. The findings presented in this case demonstrate that ACTH-induced seizures can occur in older patients with intractable seizures other than epileptic spasms.

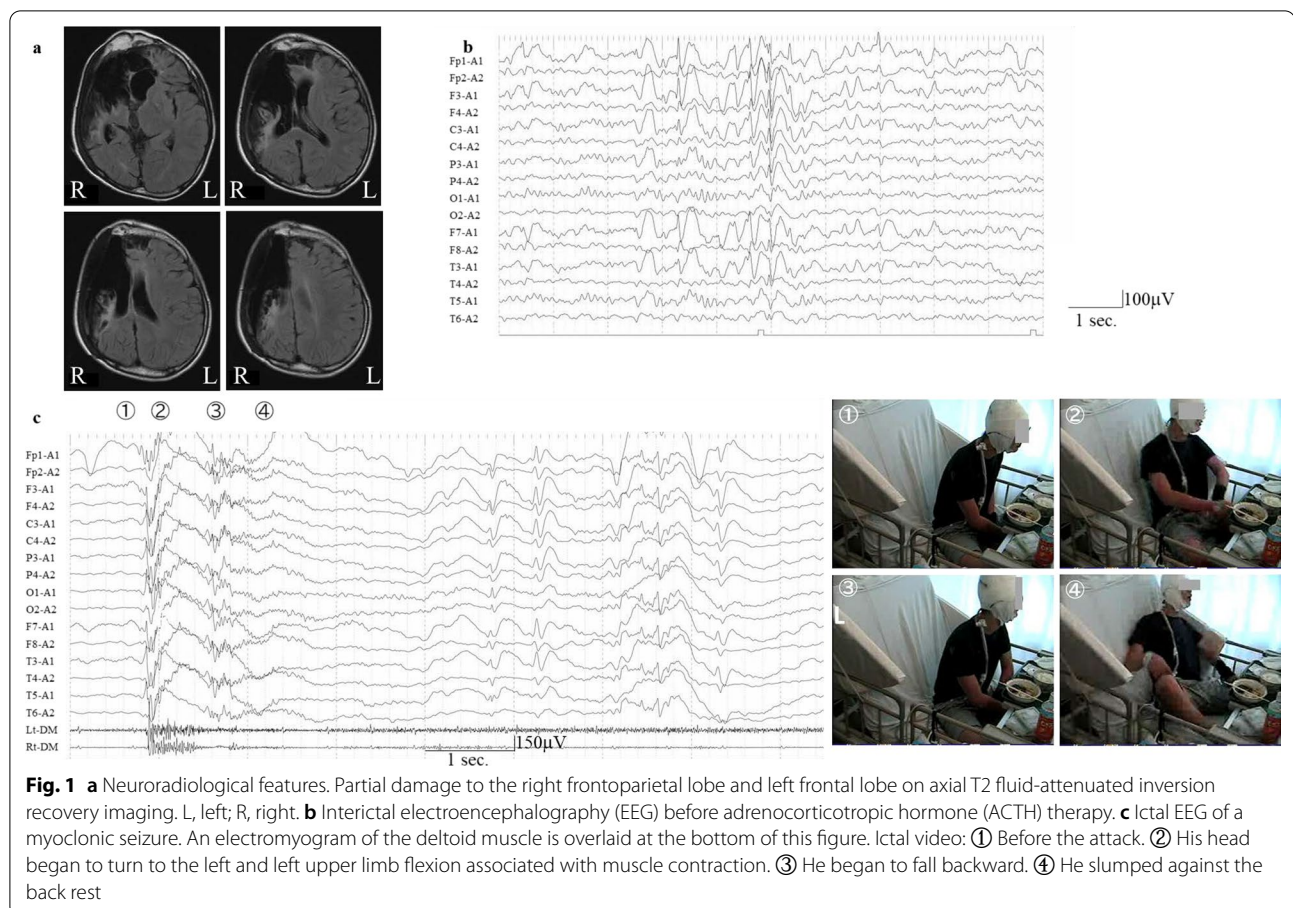
Case presentation

The patient was a 14-year-old Japanese boy who sustained a traumatic brain injury during a motor vehicle accident at the age of 6 years. The physical sequelae of this injury included partial damage to the right frontoparietal lobe and left frontal lobe, right enophthalmos, left hemiplegia, and loss of vision in the right eye (Fig. 1a). He developed unconsciousness following generalized seizures at the age of 10 years and was diagnosed with secondarily generalized tonic–clonic

*Correspondence: shuichi.shimakawa@ompu.ac.jp

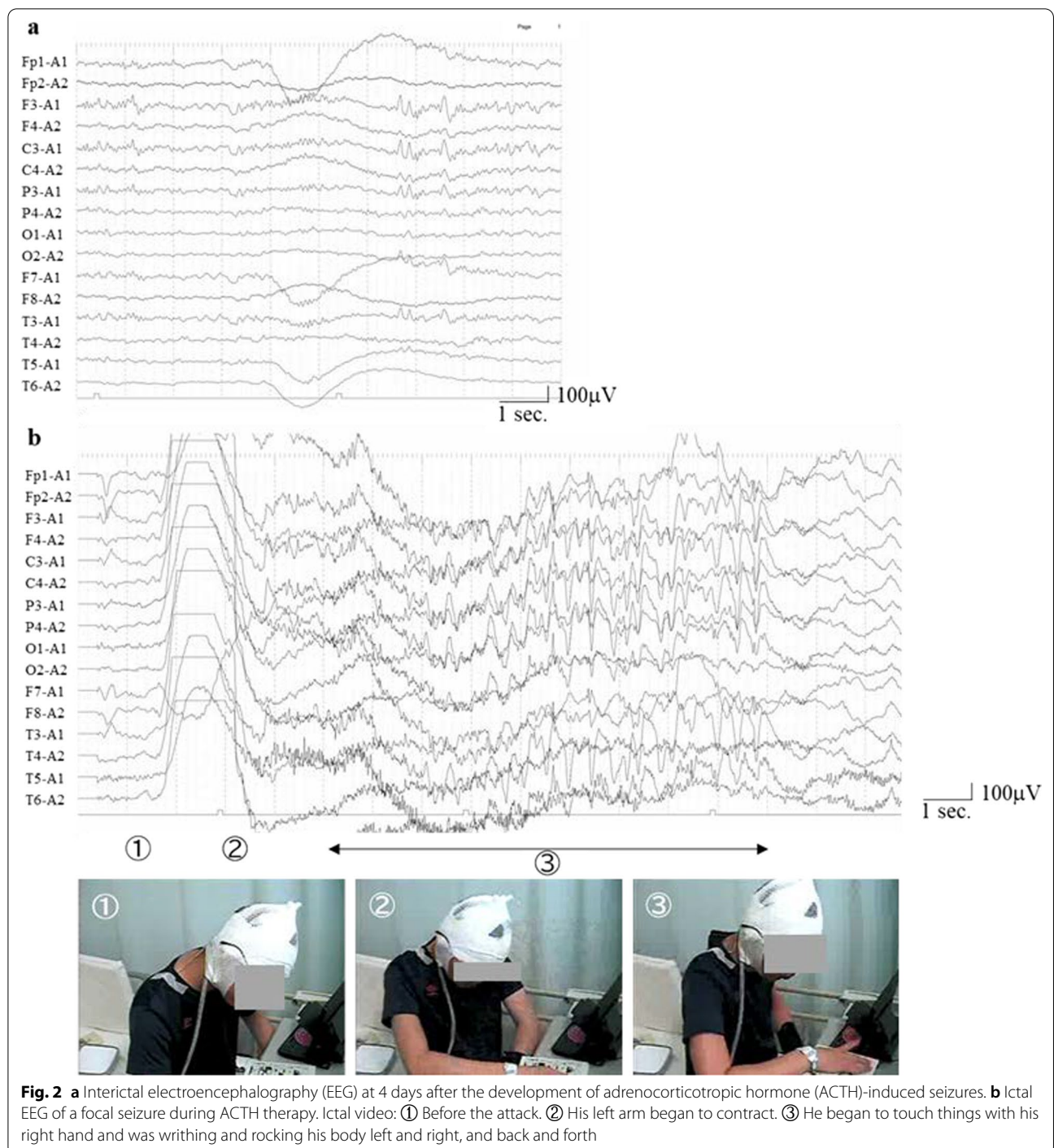
² Department of Pediatrics, Osaka Medical and Pharmaceutical University Hospital, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan
Full list of author information is available at the end of the article





seizures. His seizures were not stopped by levetiracetam, sodium valproate, lamotrigine, clobazam, zonisamide, perampanel, phenobarbital, clonazepam, or lacosamide treatment. The frequency of seizures was recorded monthly. At 13 years of age, when carbamazepine was administered, brief muscle contractions of the upper limb occurred, and these seizures continued after carbamazepine was discontinued. Interictal electroencephalography (EEG) showed high-amplitude spikes or spikes and waves located in the left frontal pole to the frontal region (Fig. 1b). On video EEG monitoring, the ictal EEG revealed generalized rhythmic spike bursts preceded by a spike wave in the left hemisphere, followed by slow-wave bursts with left hemisphere dominance corresponding to his habitual seizures, which were characterized by turning his head to the left and left upper limb flexion along with muscle contraction in a sitting position after a fall backward and unawareness lasting 5 seconds (Fig. 1c). The seizures were diagnosed as focal seizures. In addition to the aforementioned drugs, oral administration of rufinamide and clorazepate did not reduce seizure frequency. After obtaining informed consent, ACTH therapy (synthetic ACTH, a

zinc hydroxide suspension of tetracosactide acetate; Cortrosyn-Z [Daiichi-Sankyo, Japan]) was initiated at 10 months after video EEG monitoring. ACTH was administered as daily intramuscular injections (0.0125 mg/kg) for 2 weeks and was then gradually tapered off over 1 week. On day 10 of ACTH therapy, although his habitual seizures before ACTH therapy disappeared transiently, he developed new focal seizures characterized by left arm contractions followed by movements of touching things with his right hand and writhing and rocking his body left and right and back and forth as automatisms. On video EEG monitoring, the ictal EEG of the newly developing focal seizures showed generalized low-voltage fast waves followed by high voltage in the left hemisphere only, which was then followed by high-voltage slow-wave bursts with left hemisphere dominance (Fig. 2b). The focal seizures clustered for 40 minutes and disappeared after suppository administration of 10 mg diazepam. Interictal EEG at 4 days after the development of the new seizures showed spikes located in the left frontal region (Fig. 2a). These focal seizures did not reoccur after more than 2 years of follow-up. No new lesions were identified on brain



computed tomography after the onset of focal seizures. On day 10 of ACTH therapy, his habitual seizures before ACTH therapy disappeared transiently; however, they reoccurred on day 14 after ACTH therapy and subsequently returned to daily frequency.

Discussion and conclusion

As a paradoxical effect of ACTH therapy, new seizures can appear over the course of therapy, and are known as ACTH-induced seizures. In previous reports, patients with West syndrome were shown to develop ACTH-induced seizures; however, ACTH-induced seizures have not been previously reported in school-aged children.

In the case described in this study, ictal EEG during the ACTH-induced seizure revealed a spike wave in the left hemisphere preceded by a burst of electromyographic activity followed by generalized rhythmic spike bursts. The patient's ictal symptoms were characterized by turning his head to left and left upper limb flexion. Because the interictal and ictal EEG showed focal epileptiform discharges and ictal symptoms also showed lateralizing signs of motor symptoms, his seizures were diagnosed as focal motor seizures [5]. In previous studies, patients with West syndrome have been reported to develop ACTH-induced seizures; however, ACTH-induced seizures have not been previously reported in school-aged children with focal seizures (Table 1). Our findings suggest that ACTH-induced seizures can occur in school-aged children with epilepsy and focal seizures.

As described in our previous report [4], the focal seizure in our case was suggested to be an ACTH-induced seizure for the following reasons: (1) the seizures, which were different from the patient's habitual seizures, only appeared during ACTH therapy; (2) no new epileptic focus was revealed by EEG or brain imaging; (3) the seizures induced by ACTH therapy occurred on days 9–11 of consecutive ACTH injections (Table 1) [4]. In our case, the new seizures that occurred during ACTH therapy disappeared after a single dose of diazepam, suggesting that the seizures appeared only during ACTH therapy

and were new epileptic seizures in the narrow sense. The findings suggest that ACTH-induced seizures can occur in school-aged children and in children with intractable seizures other than epileptic spasms.

The pathophysiology of ACTH-induced seizures remains unknown. Because ACTH-induced seizures developed in a patient with intractable posttraumatic epilepsy, these patients may share similar electrical and clinical characteristics. Both multifocal spikes on interictal EEG and multiple epileptic seizure types, which may reflect a hyperexcitable state and decreased seizure threshold, were found in these patients. Hypsarrhythmia has been observed in many patients with West syndrome, and these patients are likely to have other seizures. Among patients with infantile spasms, 39.1% have been reported to have partial seizures [6], and it is possible to transition from West syndrome to Lennox–Gastaut syndrome. One report suggested that patients with intractable posttraumatic epilepsy may have multiple epileptogenic foci because of poor surgical treatment results [7]. ACTH is a powerful therapeutic agent and may exert various central nervous system effects in infants and children. However, a state of hyperexcitability and a decreased seizure threshold may contribute to the development of ACTH-induced seizures.

In our case, ACTH therapy was used to treat intractable focal seizures. In a previous report, ACTH therapy was

Table 1 The characteristics of seizures induced by adrenocorticotrophic hormone

	Number of cases	Age/sex	Onset of ACTH-induced seizure after ACTH injection	Day of epileptic spasm cessation before or after ACTH discontinuous	Seizure type induced by ACTH	Drug during ACTH therapy	Ictal EEG of ACTH-induced seizure	Interictal EEG during appearance of ACTH-induced seizure
Kanayama et al. [1]	SWS = 1	7 mo/F	11th day	Day 15 after ACTH	Tonic seizure	none	15–20 c/s, 50–100- μ V fast-wave bursts	N.D.
Otani et al. [2]	SWS = 1	5 mo/F	9th day	Day 14 after ACTH	Tonic seizure	PB, CZP	15–20 c/s, 50–100- μ V fast-wave burst	Fast wave burst intermingled with Hyps.
Tokuyama et al. [3]	CWS = 1	5 mo/M	9th day	Day 7 after ACTH	Partial seizure	None	N.D.	N.D.
Fukui et al. [4]	CWS = 1	6 mo/M	10th day	Day 24 after ACTH	Partial seizure	VPA	P4 high-voltage slow \rightarrow generalized	P3, P4 spikes
Our case	Posttraumatic epilepsy	14 y.o./M	10th day	Day 11 before ACTH	Partial seizure	RUF, CLZP, LTG	Generalized low-voltage fast-wave \rightarrow left hemisphere \rightarrow high-voltage slow	F3, C3 spikes

CLZP clorazepate, C3 left central region, CWS cryptogenic West syndrome, CZP clonazepam, EEG electroencephalography, F female, Hyps hypsarrhythmia, F3 left frontal region, LTG lamotrigine, M male, mo month, ND no data, P3 left parietal region, P4 right parietal region, PB phenobarbital, RUF rufinamide, SWS symptomatic West syndrome, VPA sodium valproate

effective in older patients with intractable epilepsy other than spasms [8]. The author did not describe ACTH-induced seizures; therefore, their prevalence might not be high. However, ACTH-induced seizures may need to be considered when ACTH is used to treat these patients.

In conclusion, ACTH-induced seizures can occur in children older than previously reported, and can occur in children with intractable seizures other than epileptic spasms.

Abbreviations

ACTH: Adrenocorticotrophic hormone; EEG: Electroencephalography.

Acknowledgements

We would like to thank Editage (www.editage.com) for English language editing.

Author contributions

YO treated the patient as a pediatric resident and prepared this paper. SS treated the patient as a pediatric neurologist and prepared this paper. HT-K and MF treated the patient as pediatric neurologists. Professor AA and MK provided accurate advice for the patient's treatment and this paper. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical committee of Osaka Medica and Pharmaceutical University Hospital (approval number: 2020-109).

Consent for publication

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Pediatrics, Hirakata Municipal Hospital, Hirakata, Osaka, Japan.

²Department of Pediatrics, Osaka Medical and Pharmaceutical University Hospital, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan.

Received: 22 February 2022 Accepted: 26 April 2022

Published online: 24 May 2022

References

- Kanayama M, Ishikawa T, Tauchi A, Kobayashi M, Takasaka Y, Shibata H. ACTH-induced seizures in an infant with West syndrome. *Brain Dev.* 1989;11:329–31.
- Otani K, Tagawa T, Futagi Y, Okamoto N, Yabuuchi H. Induced microseizures in West syndrome. *Brain Dev.* 1991;13:196–9.
- Tokuyama M, Akiba Y, Ishihara C, Matsuyama G, Norikazu S, Tateno A, et al. ACTH-induced postural seizures in an infant with West syndrome. *J Med Soc Toho.* 2009;56:21–6.
- Fukui M, Shimakawa S, Tanabe T, Nomura S, Kashiwagi M, Azumakawa K, et al. Partial seizures during ACTH therapy in a cryptogenic West syndrome patient. *Brain Dev.* 2014;36:80–3.
- Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: position paper of the ILAE Commission for Classification and Terminology. *Epilepsia.* 2017;58:512–21.
- Ohtsuka Y, Murashima I, Asano T, Oka E, Ohtahara S. Partial seizures in West syndrome. *Epilepsia.* 1996;37:1060–7.
- Marks DA, Kim J, Spencer DD, Spencer SS. Seizure localization and pathology following head injury in patients with uncontrolled epilepsy. *Neurology.* 1995;45:2051–7.
- Okumura A, Tsuji T, Kato T, Natsume J, Negoro T, Watanabe K. ACTH therapy for generalized seizures other than spasms. *Seizure.* 2006;15:469–75.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

