CASE REPORT

Repeated seizures in an elderly patient with alcohol dependence and mild cognitive impairment

Nobuyoshi Ishii, Takeshi Terao, Yasuo Araki, Koji Hatano

Department of Neuropsychiatry,
Oita University Faculty of
Medicine, Yufu, Oita, Japan

Correspondence to
Professor Takeshi Terao,
terao@oita-u.ac.jp

SUMMARY

A 69-year-old man with alcohol dependence and mild cognitive impairment (MCI) suffered from repeated tonic-clonic seizures. The seizures typically occurred several hours after his last alcohol intake at home (early withdrawal seizure) and 22 days after his last intake of alcohol (14 days after the last dose of diazepam substituting for alcohol: late withdrawal seizure) on the ward. Psychiatrists in charge of this patient found it difficult to attribute his seizures to alcohol withdrawal syndrome (AWS) because of the atypical onset. The patient responded to diazepam resumption and valproate combination. This case highlights the need to always consider AWS as a possible cause of seizures and to gradually decrease diazepam as a substitute for alcohol. Moreover, in this patient, MCI may have induced vulnerability in the brain for AWS and the patients' older age might have decreased liver function leading to delayed onset of the seizures after diazepam withdrawal.

BACKGROUND

Seizures are often observed as a symptom of alcohol withdrawal syndrome (AWS). Seizures are usually within 24–48 h¹ more specifically 6–48 h² of consumption of their last drink. This patient repeatedly had seizures several hours after his last drink of alcohol at home, and after admission 22 days after his alcohol intake. The present case was presented to show that it is important to always suspect AWS as a cause of seizures and to gradually decrease diazepam substitution for alcohol in order to prevent withdrawal seizures in a patient with alcohol dependence.

CASE PRESENTATION

A 69-year-old man was admitted to the psychiatric ward of our university hospital. He had been a bus driver and, after retirement, was working as a farmer from home. He had no history of epilepsy or psychiatric illness. At the age of 64, he noticed forgetfulness and consulted a doctor with the result that there were no abnormal organic findings. Three years later, his forgetfulness became gradually worse and he came to our hospital. At that time, Mini-Mental State Examination (MMSE) scores and Hamilton Depression Rating Scale scores were 25 and 6, respectively. Although he was not depressed, he worried about his two sons' divorce. Sulpiride 150 mg/day and donepezil 3–5 mg/day were administered. He was drinking alcohol almost every day and the alcohol consumption was increased up to 135 g/day of ethanol equivalents.

At the age of 68, the patient developed tonic-clonic seizures occurring four times during last year. In addition, he was behaving strangely during sleep. Although clonazepam 1 mg/day and valproate 400 mg/day were added, he was often found wandering in the evening at home with amnesia. He was subsequently involved in a road traffic accident in his car and it was decided that he should be admitted to our hospital.

In the morning of admission, the patient was drinking alcohol at home. On admission, he was found to have mild cognitive impairment and memory disturbance (MMSE=24). He had no visual or auditory hallucinations. His serum protein was slightly low (6.2 g/dL) and γ -GTP was relatively high (85.1 IU/L). To prevent AWS, diazepam 10 mg/day was administered with donepezil 5 mg/day. Owing to the absence of any symptom of AWS, diazepam was gradually decreased and 2.5 mg/day was discontinued 8 days after admission. However, 22 days after admission (ie, 14 days after diazepam discontinuation) he suffered from tonic-clonic seizures and delirium, which were treated by venous infusion of 20 mg of diazepam and his seizures subsided. Later, he could not recall most of the episode.

INVESTIGATIONS

During alert consciousness, the Alzheimer's Disease Assessment Scale score was 10.7 (mild cognitive impairment). Also, Wechsler Memory Scale-Revised scores were 67 in verbal memory, 39 in visual memory, 106 in general memory, 40 in attention/concentration and 43 in delayed recall and Behavioural Assessment of the Dysexecutive Syndrome score adjusted by age was 84 (borderline executive function).

MRI of the brain showed slight cortical atrophy. One day and 2 weeks after the seizures on the ward, EEG showed no paroxysmal pattern. Six days after the seizure in the ward, a cerebrospinal fluid examination revealed no abnormalities. Single-photon emission CT showed gradually decreased blood perfusion from 1 year before admission (cerebral blood flow (CBF): left 39.1, right 38.1 mL/100 g/min), during hospitalisation (CBF: left 38.2, right 37.9 mL/100 g/min) and to 1 year after discharge (CBF: left 35.5, right 35.4 mL/100 g/min).

DIFFERENTIAL DIAGNOSIS

Intrinsic seizures (ie, epilepsy).

CrossMark

To cite: Ishii N, Terao T, Araki Y, et al. *BMJ Case Rep*. Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201575

Provoked seizures induced by organic brain diseases such as brain tumour, encephalitis and degenerative brain disease and physical diseases.

TREATMENT

Two days after the seizures, valproate 600 mg/day was added to diazepam 10 mg/day and donepezil 5 mg/day. Six days after the seizures in the ward, diazepam was decreased from 10 to 5 mg/day. Moreover, 17 days after the seizures, diazepam was decreased from 5 to 2.5 mg/day, and 24 days after the seizures, diazepam 2.5 mg/day was discontinued. Although the patient had no further seizures on the ward, he was drinking alcohol again at home when on leave from our hospital. For alcohol dependence, topiramate was added.

OUTCOME AND FOLLOW-UP

Two months after admission, the patient was discharged. Again, he was drinking alcohol and suffered from seizures during sleep twice at 2 and 6 months after discharge. Topiramate was discontinued due to bradycardia. Throughout the year following the last seizure, while treated with valproate 600 mg/day and donepezil 5 mg/day, the patient had no further seizures.

DISCUSSION

The patient's history of regular and excessive alcohol drinking before admission, the drinking behaviour on leave and after discharge strongly confirms the diagnosis of alcohol dependence. He had tonic-clonic seizures before admission, during hospitalisation and after discharge. Taken together, it appears that alcohol withdrawal may have induced tonic-clonic seizures during sleep before admission and after discharge at home where returned to his previous drinking habits.

As for the episode of tonic-clonic seizures and delirium on the ward; this occurred 22 days after admission (ie, 22 days after discontinuation of alcohol) which is atypical because, when seizures occur, they generally happen within 24–48 h³ of withdrawal. In our case, the seizures may have been induced by early discontinuation (only 8 days of administration) of diazepam substituting a large quantity of alcohol (135 g/day of ethanol) because the duration of diazepam administration (8 days) was not enough long to offset AWS in this patient. Taking the long half-lives of diazepam (34.7 h) and desmethyldiazepam (103.1 h)⁴ into consideration, 14 days would have reduced desmethyldiazepam levels to approximately 1/8 which could have induced tonic-clonic seizures and delirium as benzodiazepine withdrawal symptoms (or rebound of AWS) in this patient. Moreover, mild cognitive impairment may have increased the patient's vulnerability for alcohol and/or diazepam

withdrawal in the brain because this patient developed tonic-clonic seizures in parallel with the increased forgetfulness. Also his older age itself may have decreased liver function for metabolising diazepam and further delayed the onset of the seizures because the slower the metabolism, the higher the bioavailability of a drug, so more diazepam/metabolites would be available for longer.

As for pharmacotherapy, it should be noted that valproate may be useful when withdrawing diazepam to prevent AWS seizures because throughout the year following his last seizure, while receiving valproate 600 mg/day and donepezil 5 mg/day, he had no further seizures.

Learning points

- ▶ It is important to always suspect alcohol withdrawal syndrome as a cause of seizures.
- ▶ It is important to gradually decrease diazepam when substituting for alcohol in order to prevent withdrawal seizures in a patient with alcohol dependence.
- ▶ Valproate may be useful to successfully withdraw diazepam and to prevent alcohol-withdrawal syndrome seizures.
- ▶ Mild cognitive impairment may increase vulnerability for alcohol and/or diazepam withdrawal in the brain.
- ▶ Age itself may decrease liver function to metabolise diazepam and further delay the onset of the seizures.

Contributors NI and TT designed the case report and wrote the protocol. TT and KH collected the clinical data of the patient and managed the literature searches and analyses. All authors discussed the results and drew a conclusion. NI wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 McKeon A, Frye MA, Delanty N. The alcohol withdrawal syndrome. *J Neurol Neurosurg Psychiatry* 2008;79:854–62.
- 2 Hughes JR. Alcoholic withdrawal seizures. *Epilepsy Behav* 2009;15:92–7.
- 3 Nejad SH, Schaefer PW, Bajwa EK, et al. Case 39-2012: a 55-year-old man with alcoholism, recurrent seizures, and agitation. *N Eng J Med* 2012;367:2428–34.
- 4 Wan J, Xia H, He N, et al. The elimination of diazepam in Chinese subjects is dependent on the mephenytoin oxidation phenotype. *Br J Clin Pharmacol* 1996;42:471–4.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow