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Recurrent alcohol-induced seizures in a patient with chronic alcohol abuse

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ABSTRACT – Seizures related to alcohol are a common finding, and are usually attributed to alcohol withdrawal, or to a neurotoxic effect of ethanol leading to seizures that are unrelated to acute alcohol consumption or withdrawal. However, there is also evidence for a third kind of alcohol-related seizure: alcohol-induced seizures. We describe a 36-year-old patient who, during the years from 1996–2006, was admitted 27 times with alcohol-induced seizures that occurred during alcohol consumption. Excluding one documented withdrawal seizure, serum ethanol levels at admission were 3.24 ± 0.67%. There were no seizures that were unrelated to alcohol consumption. This case report supports the evidence of a seizure-provoking effect of ethanol that should be considered in the diagnosis and treatment of patients with alcohol-dependency and seizures.

Key words: epilepsy, alcohol, seizures

Seizures related to alcohol are a common cause for emergency department admissions. The prevalence of seizures in alcohol-dependent patients is about triple that in the general population (Hillbom *et al.* 2003) and alcohol abuse was found in 41-49% of adult patients admitted for seizures (Earnest and Yarnell 1976, Hillbom 1980).

The most common cause of alcohol-related seizures is alcohol withdrawal. This type of seizure occurs 6-48 hours after cessation of alcohol consumption (Earnest and Yarnell 1976, Hillbom *et al.* 2003). However, alcohol abuse may cause seizures that occur independently of the timing of alcohol consumption or withdrawal (Devetag *et al.* 1983, Alldredge and Lowenstein 1993, Bartolomei *et al.* 1997, Bartolomei 2004). There is also evidence for alcohol-induced seizures or "convulsive inebriation", even though the existence of alcohol-induced seizures as a separate entity is still controversial (Yamane and Katoh 1981, Devetag *et al.* 1983, Bartolomei *et al.* 1997).

We report a case that lends support to the existence of this entity.

Case report

A 36-year-old patient was admitted to our neurological department 27 times with recurrent alcohol-induced generalized tonic-clonic seizures between 1996 and 2006. In three cases, generalized tonic-clonic seizures were observed by the emergency medical services, on two occasions there were subsequent generalized tonic-clonic seizures at the emergency department. On the other occasions, sei-

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zures were reported by laypersons. In six cases, the patient was found unconscious or somnolent, probably postictally. On several occasions, the patient had bitten his tongue, injured himself or passed urine. He was usually somnolent at the time of admission and presented with an odour of alcohol and cerebellar symptoms such as dysarthria, ataxia, atactic walking pattern and intentional tremor. There were no signs of delirium tremens. The patient has been a regular heavy drinker since the age of 16, with occasional exacerbations. Concomitant diseases included a perinatal brain injury, leading to a mild, right-sided hemiparesis and complex extrapyramidal and cerebellar syndrome. In addition, he suffered from reflux oesophagitis.

Only one documented alcohol withdrawal seizure occurred (ethanol level of 0.1%, following 12 to 24 hours of alcohol abstinence). Excluding this seizure, the mean ethanol level at the time of admission was 3.24 ± 0.67% (range: 1.2-4.3% *[figure 1]*). On eight occasions, no blood ethanol levels were available, but clinical signs of alcohol intoxication had been documented. CDT was taken on several occasions between 1999 and 2006 and ranged from 11.2 to 15.1% (normal range: < 2.5%). Liver enzymes tended to be slightly above the normal range; CK was elevated on several occasions (304 + 415 U/L). Electrolytes, leucocytes, CRP and blood glucose were within the normal range at all admissions.

A drug-screen was performed during one of the admissions for generalized tonic-clonic seizures and on 12 other occasions during 1998 and 2006: it was always negative. However, in 1990, the patient was admitted after intoxication with benzodiazepines. Carbamazepine levels were below the normal range on four occasions and within the normal range on one occasion.

Several EEGs taken after admissions in 1996, 1998, 2001 and 2005 showed normal results. A CT scan revealed cortical atrophy, but no focal lesions.

On three occasions, the patient received 1-2.5 mg lorazepam; he received 2 mg diazepam twice and 1 mg clonazepam on one occasion. Antiepileptic drugs were started several times, but were never taken regularly.

Discussion

To address the complexity of seizures related to alcohol, a classification was proposed by Mattson (1990). According to this classification, alcohol-related seizures can be caused by alcohol withdrawal, but also by acute cerebral or medical disorders including metabolic disturbances, drug abuse, infections, trauma or coincidental disorders. In addition, seizures may be attributed to coincidental, symptomatic epilepsy or latent epilepsy unmasked by alcoholism or alcohol use. The classification also includes controversial relationships between alcohol and seizures: epilepsy due to neuronal damage caused by alcohol, epilepsy due to a kindled effect of repeated withdrawal seizures, and seizures induced by a direct effect of alcohol.

Seizures induced by a direct effect of alcohol (convulsive inebriation) have been described in an earlier study as a very rare condition, which was found only in two out of the 1431 alcohol-dependent patients studied (Devetag *et al.* 1983), and these two cases were not described further. There are very few other reports of convulsive inebriation in humans (Yamane and Katoh, 1981, Bartolomei *et al.* 1997). In one study, eight patients with alcohol-induced seizures were reported. All patients had generalized tonic-clonic or secondary generalized complex partial seizures, six patients had normal EEG findings and four had brain atrophy as shown by a CT scan (Bartolomei *et al.* 1997), and thus showed results similar to those presented here. Unfortunately, ethanol levels were not documented and, in addition, all eight patients reported seizures unrelated to acute alcohol intake. The authors concluded that alcohol-induced seizures should not be considered a separate entity.

In our patient, there was a clear correlation between ethanol levels and the occurrence of seizures. The patient was admitted 26 times for generalized tonic-clonic

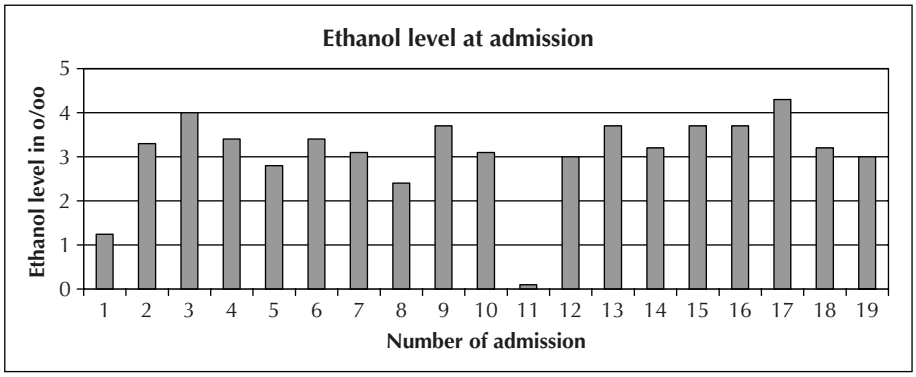

Figure 1. Ethanol levels as ‰ at each admission due to seizures.

seizures that occurred during the time of drunkenness with one additional admission for a withdrawal seizure. He had no documented seizures that were unrelated to acute intoxication or withdrawal, supporting the hypothesis of seizures induced by a direct effect of alcohol.

Even though the patient had also suffered a perinatal brain injury, which might have rendered the patient more vulnerable to alcohol-induced seizures, the strong association between ethanol level and seizures leads to the assumption that the seizures were induced by the high ethanol level. Furthermore, the post-ictal EEG of the patient presented here was normal, which is a common finding in alcohol-related seizures, whereas abnormal EEG findings suggest epilepsy or symptomatic seizures unrelated to alcohol (Sand *et al.* 2002). One might argue that the tonic-clinic seizures could have been caused by concomitant drug abuse, a toxic level of carbamazepine, hypoglycaemia or electrolyte imbalances. However, drug screens were always negative during the time period reported and carbamazepine levels were usually below or within the normal range. In addition, electrolytes and blood glucose levels were within the normal range.

The effects of ethanol on cortical excitability are mediated by diverse compensatory changes in the glutamatergic and GABAergic transmitter systems (Davis and Wu 2001, Hillbom *et al.* 2003, Rogawski 2005), leading to an inhibiting effect of ethanol and a lowered seizure threshold after alcohol withdrawal. However, the seizure-provoking effect of ethanol in our patient and a few patients reported in earlier studies can not really be explained by these mechanisms. The direct seizure-inducing, excitatory effects of ethanol evoking alcohol-induced seizures have previously been attributed to disturbances in microcirculation, hypomagnesemia or other electrolyte imbalances (Yamane and Katoh 1981, Hillbom *et al.* 2003). Serum levels of magnesium were never tested in our patient, but other electrolyte levels were normal.

Disturbances in the microcirculation can neither be confirmed nor denied as the cause of seizures related to alcohol abuse in the patient presented here.

Based on electroencephalogram and evoked-response findings, another theory suggests that ethanol has a biphasic effect on the nervous system, which might be due to differential sensitivity of neurons to ethanol or to a different functional structure of neurons (Kalant 1975, Hari 1979). In the light of these studies, alcohol-induced seizures in our patient might be due to a different excitation-inhibition balance at the receptor or cell level, possibly as a consequence of the perinatal brain damage.

In conclusion, there is clinical evidence of a seizure-provoking effect of ethanol, leading to convulsive inebriation seen in the patient presented here. This condition appears to be rare, but should be taken into account when treating alcohol-dependent patients with seizures. The pathophysiology of alcohol-induced seizures remains unclear and studies on the mechanisms underlying this clinical finding are warranted. □

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