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CLINICAL FEATURES

Central Pontine and Extrapontine Myelinolysis After Alcohol Withdrawal

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Abstract — Central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) are well-recognized syndromes that are related to various conditions such as rapid correction of hyponatremia and chronic alcoholism. We report a very case of a patient with dysarthria, dysphagia and psychiatric symptoms including abnormal behavior starting after alcohol withdrawal, with radiological evidence of CPM and EPM. There was little improvement in the dysarthria or psychiatric symptoms in the first month.

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INTRODUCTION

Central pontine myelinolysis (CPM) was described by Adams and colleagues in 1959 as a disease affecting alcoholics and the malnourished (Adams *et al*., 1959). In ∼10% patients, CPM is associated with extrapontine myelinolysis (EPM), and this may generate Parkinson symptoms (Wright *et al*., 1979) and psychotic features (Lim and Krystal, 2007).

Although the cause and pathogenesis of CPM and EPM remain unclear, many studies have implicated the rapid correction of hyponatremia as the major factor associated with CPM, due to exposing the pontine glia and extrapontine glia to osmotic stress (Ashrafian and Davey, 2001). There are many reports to date of CPM or EPM caused by other factors except hyponatremia, and there has been only one case reported about CPM after alcohol withdrawal with a relatively good prognosis (Korn-Lubetzki *et al*., 2002).

We describe here a case of CPM that also displayed EPM without hyponatremia after alcohol withdrawal in a chronic alcoholic, and this resulted in a transient progressive course and a poor prognosis.

CASE REPORT

A 47-year-old man was admitted to the hospital with complaints of progressive dysphagia and dysarthria for a week, and this occurred just 2 days after he stopped drinking. His medical history was unremarkable. He had smoked 20 cigarettes daily for 20 years and had abused alcohol, two bottles of spirits daily, for several years.

On the first neurologic examination, he was alert and well oriented and had no extraocular movement limitation, nystagmus, cerebellar dysfunction or gait disturbance. He only displayed bulbar palsy and dysarthria. A full blood count, electrolyte studies that included sodium, potassium, calcium, phosphate and magnesium, renal function tests, thyroid function tests and Wilson's disease-related laboratory findings were all within the normal ranges, except for a slightly abnormal liver function tests.

At admission, the MRI T2 weighted image and diffusion image showed symmetric high signal intensity on the bilateral basal ganglia and central pontine area. Because of his dysphagia, he was kept on a Lavin tube and was treated with conservative care, including a thiamine supplement.

Two days after the admission, he showed violent behavior, agitation and irritability, getting angry on the slightest provocation without any mental changes or Parkinson symptoms or aggravation of his dysarthria. At first, we considered his symptoms to be alcohol withdrawal psychosis and started antipsychotics to control him, but his symptoms worsened. We performed MRI again 5 days after he developed psychiatric symptoms. The second MRI showed extended lesions in the bilateral basal ganglia and pons, as compared with the previous MRI.

Ten days after his admission, we performed neuropsychological tests and the results revealed preserved memory, language and visuospatial function, except for minimal frontal lobe dysfunction.

Since steroid administration has proved beneficial in several previous cases, we started steroid pulse therapy that was continued for 3 days and we maintained his conservative management with atypical antipsychotics for his psychiatric symptoms. While his dysphagia was slightly improved to some degree, his dysarthria and prominent psychiatric symptoms showed little improvement for 1 month. Follow-up MRI after 1 month showed no significant changes (Fig. 1).

DISCUSSION

We describe here a patient who had psychotic features and bulbar symptoms after alcohol withdrawal. He was eventually diagnosed as suffering with CPM and EPM. He showed no electrolyte imbalance, hyponatremia or abnormal osmolarity, not only at the time of his admission, but also after the admission when his psychotic symptoms developed. Compared with the previous case reported as CPM after alcohol withdrawal (Korn-Lubetzki *et al*., 2002), the distinctive features of our case were the psychotic features with a transient progressive course and poor recovery. This was consistent with developing CPM and EPM seen on the serial MRIs.

The medical conditions associated with CPM are known to include dialysis, liver failure and transplantation, advanced

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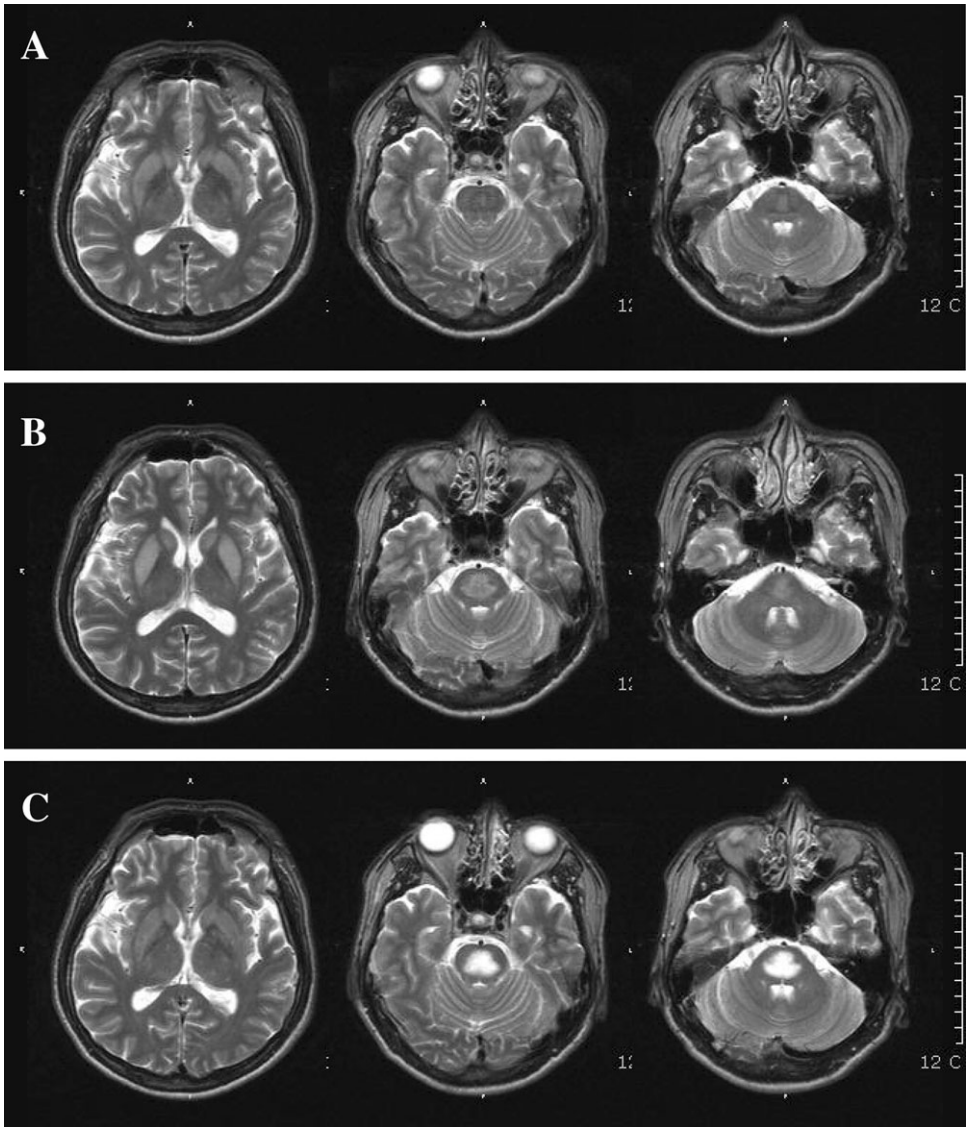

Fig. 1. T2 weighted axial MRI of the patient. On the initial MRI (**A**), there are hyperintensities involving the bilateral basal ganglia and pons. The MRI (**B**) performed 5 days after the development of psychiatric symptoms showed extension of the previous lesions. The MRI taken after 1 month (**C**) revealed no recovery or resolution.

lymphoma, carcinoma, cachexia from various causes, severe bacterial infections, dehydration and electrolyte disturbance, acute hemorrhagic pancreatitis, chronic alcoholism and pellagra (Laureno and Karp, 1997; Ashrafian and Davey, 2001; Martin, 2004). Chronic alcohol abuse appears to be a particular risk factor for CPM and EPM; it has been reported that chronic alcoholics may be asymptomatic or have relatively few symptoms, with a better outcome of their CPM and EPM than in cases associated with an acute correction of hyponatremia (Mochizuki *et al*., 2003). In other words, like the asymptomatic CPM and EPM in chronic alcoholics, the involvement of the basal ganglia is not always revealed, namely Parkinson symptoms and cognitive dysfunction. We cannot explain the reason and mechanism of the poor prognosis in this case, although we could predict a poor prognosis from the serial MRIs.

The mechanisms of CPM and EPM are poorly understood, but the proposed mechanisms include osmotic injury to the vascular endothelial cells and this causes the release of myelinotoxic factors, the production of vasogenic edema and/or brain dehydration. This then causes separation of the axon from its myelin sheath with resultant injury to the oligodendrocytes, particularly at the interface of the gray and white matter. Chronic alcoholics may not be able to maintain protective cerebral mechanisms against osmotic stress, as well as suffering from the direct toxicity of alcohol (Norenberg, 1983). Further, the excess production of free radicals and the deranged nitric oxide metabolic effects in alcoholics may favor apoptosis of brain neurons (Norenberg, 1983; Lohr, 1994; Ashrafian and Davey, 2001). Abnormality of the basal ganglia is known to cause various cognitive dysfunctions and abnormal behavior

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via the involvement of the corticostriatothalamic or cortical–subcortical circuit through the basal ganglia (Carlsson, 1988), while the role of pontine pathology for cognitive function and personality remains unclear. One possible hypothesis is that disruption of the corticopontine networks may cause symptoms, and another hypothesis involves the interruption of the neurotransmitter pathways that emerge from the brainstem, possibly the dopaminergic and cholinergic pathways, which impacts on cognitive functioning (Norenberg, 1983).

Based on the relatively preserved cognitive function and the lack of Parkinson symptoms, our patient's behavior cannot be simply postulated as being related to the basal ganglia lesions. Taken together, the widespread changes and synergic effects involving the basal ganglia and pontine areas with involvement of several neurotransmitter systems underlie the emergence of psychotic symptoms in patients with CPM and EPM (Papapetropoulos and Mash, 2005).

In addition, when CPM and EPM occur in chronic alcoholics, the differential diagnosis should include alcoholic psychosis or Wernicke's encephalopathy. It was not difficult to distinguish our case from Wernicke's encephalopathy in that there was no oculomotor abnormality, nystagmus, ataxia or confusion, and no improvement with thiamine supplementation was observed, plus the lack of signal changes in the mamillary bodies and the periaquiductal area on MRI. It was also possible to distinguish our case from alcoholic psychosis in view of the absence of visual hallucinations, intact orientation and the unusual time course unlike alcoholic psychosis in which the peak symptoms occur within 2–4 days after alcohol withdrawal.

In conclusion, from this case we learned that alcohol withdrawal itself may induce CPM and EPM in chronic alcoholics, and its prognosis may be poor and irreversible. CPM and EPM need to be included in the differential diagnosis of patients who manifest new psychotic symptoms after alcohol withdrawal.

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