Posterior Reversible Encephalopathy Syndrome Triggerred By Alcohol Withdrawal

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SUMMARY

Introduction: Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity characterized by headache, altered mental status, epileptic seizures, visual disturbances and typically transient changes in posterior cerebral circulation areas. This article presents a case report of a patient with alcohol withdrawal accompanied by PRES.

Case presentation: A 53-year-old male patient was presented to the Emergency Department with visual hallucinations and meaningless speech. History from his relatives revealed that he consumed alcohol for about 35 years with the last consumption 3 days ago. Neurological examination revealed limited cooperation and disorientation to person, place and time. This speech was incoherent and no localizing sign was observed. Cranial magnetic resonance imaging (MRI) revealed bilateral hyperintense areas in medial occipital cortices and in the subcortical white matter extending partly into the parietal region. Treatment for alcohol withdrawal was started. Signs and symptoms regressed on the 7th day of the treatment as well as the lesions on the MRI.

Discussion: The clinical presentation, characteristic MRI features together with the reversible nature of the syndrome suggest the diagnosis of PRES. The precise pathophysiological mechanism of PRES still remains unclear. Hypertension, clinical conditions associated with impaired cerebral autoregulation as well as alcohol use which increases the levels of reactive oxygen species and nitric oxide, may lead to the disruption of endothelial cells and blood-brain barrier breakdown. We suggest that chronic alcoholism and alcohol withdrawal might have caused endothelial dysfunction leading to PRES in our patient.

Keywords: Posterior leukoencephalopathy syndrome, alcohol withdrawal, alcoholism

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity characterized by headache, altered mental status, epileptic seizures, visual disturbances and typically transient changes in the posterior cerebral circulation areas (Hinchey et al. 1996). Besides the well-known etiologies of PRES, recent reports showed that various factors such as hypertension, eclampsia/pre-eclampsia, sepsis, immunosuppressive agents, chemotherapy, collagen vascular disease and renal failure were associated with PRES (Stevens and Heran 2012). Interestingly, only a few case reports have linked chronic alcoholism and alcohol withdrawal with PRES (Ishikawa et al. 2013, Kim et al. 2014, Kimura et al. 2010, McKinney et al. 2007). This article presents a case report that links PRES with history of alcohol withdrawal.

CASE PRESENTATION

A 53-year-old male patient was admitted to our clinic with visual hallucinations (insects on the walls, fire and dust in the house) and meaningless speech. His medical history given

Received: 15.08.2016- **Accepted**: 09.01.2017

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doi: 10.5080/u18397

by this family revealed a large amount of alcohol consumption in the last 3 days. Furthermore, they reported that he has been drinking daily for over 35 years (at least 70 cl of wine or beer everyday) but was on alcohol-free periods of maximum 2 weeks. Besides alcohol addiction, he was a smoker for 40 years with an average of 40 cigarettes per day. He had no premorbid psychiatric and medical history, or substance addiction. There was no family history of psychiatric and neurological disorder. He was never admitted to a health care facility due to alcohol withdrawal.

Upon admission, his physical examination revealed a blood pressure of 150/90 mmHg, a heart rate of 99 bpm, and a temperature of 37.1°C with sweating. No other significant pathological findings were found. A neurological examine revealed limited cooperation, agitation, speaking irrelevantly, visual hallucinations and disorientation to person, place, and time. Furthermore, the patient had postural tremor on both hands. His neurological symptoms were not consistent with Wernicke's encephalopathy such as ataxia and/or ophthalmoparesis. The cerebellar, sensory, visual acuity and visual field examinations were not evaluated due to the limited cooperation of the patient. The electrocardiogram showed a normal sinus rhythm. Hemoglobin, total leucocyte count, electrolytes, urea, creatinine, bilirubin, alkaline phosphatase, ammonia, total protein, albumin, lipase, amylase, mean corpuscular volume, folic acid, vitamin B12 were within normal levels. Upon admission, plasma levels of aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyltranspeptidase were 306 U/L, 139 U/L, and 138 U/L, respectively.

Delirium tremens was determined on admission. A cranial magnetic resonance imaging (MRI) was performed in order to rule out hepatic encephalopathy and Wernicke's encephalopathy. Fluid-attenuated inversion recovery (FLAIR) sequences revealed hyperintense areas in the medial cortex of bilateral occipital lobes and the subcortical white matter extending partly into the parietal region (Figure-1). These findings indicated PRES. To avoid alcohol withdrawal symptoms, the patient received intravenous (IV) hydration (isotonic liquid), IV thiamine (100 mg, 1 day) and 15 mg of diazepam daily (intravenously the first day and orally the following 5 days). Epileptic seizures were not observed during the follow-up period. An electroencephalography was not performed. After the treatment of alcohol withdrawal, his high blood pressure level (150/90 mmHg) returned to normal without any antihypertensive treatment the neurological symptoms improved and the lesions on a follow up MRI were significantly regressed. (Figure-2).

Magnetic resonance imaging in posterior reversible encephalopathy syndrome.

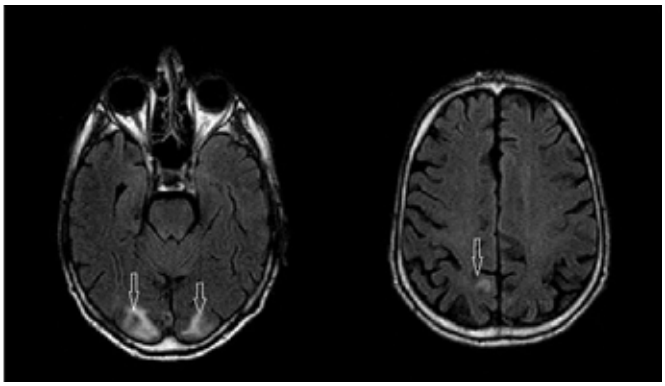

Figure 1. FLAIR sequences axial MRI revealed hyperintense areas in medial cortex of bilateral occipital lobes and the subcortical white matter extending partly into parietal region (indicated by arrow).

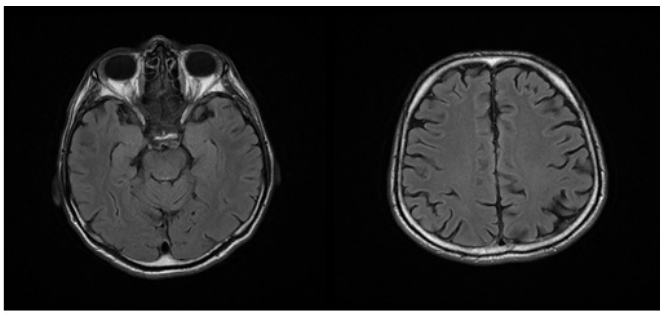

Figure 2. The lesions are observed to regress on a control FLAIR sequences axial MRI.

DISCUSSION

Posterior reversible encephalopathy syndrome was first defined by Hinchey et al. (1996). Although many etiological factors have been reported, its precise pathophysiological mechanism still remains unclear. Hypertension, which has been associated with impaired cerebral auto-regulation, as well as other clinical conditions and medications that may lead to endothelial injury i.e. immunosuppressive agents, systemic lupus erythematosus, hemolytic uremic syndrome and thrombotic thrombocytopenic purpura, have been defined as etiological factors that can lead to PRES (Bartynski and Boardman 2008). The patient discussed in this report was not exposed to any medication or had any systemic diseases.

The neurological symptoms of PRES manifest acutely or sub acutely (Fugate and Rabinstein 2015). Consciousness impairment is usually present, and the severity may vary from confusion to coma (Legrielet al. 2011). Focal findings such as generalized tonic-clonic seizures, headache, visual disturbance, hemiparesis or aphasia may accompany varying rates in patients (Fugate and Rabinstein 2015). However, none

of the symptoms is mandatory for the diagnosis of PRES (Granataet al. 2015).

Visual disturbances in PRES include visual field deficits, decreased visual acuity, cortical blindness, or visual hallucination (Fugate and Rabinstein 2015). Our patient had visual hallucinations; such as insects on the walls, fire and dust in the house. Visual hallucination may be a symptom of delirium tremens, but also occurs in patients with PRES (Legriel et al. 2011).

The pathophysiology of PRES remains still controversial. There are two main hypothesis. The first hypothesis states that impaired cerebral auto regulation is responsible for an increase in cerebral blood flow, whereas the second hypothesis states involve endothelial dysfunction with cerebral hypoperfusion (Legriel et al. 2011). Rabinstein et al. (2012) reported that the development of PRES could not be explained solely on the basis of severe acute hypertension or sudden blood pressure fluctuations, but that endothelial dysfunction probably contributed to the pathogenesis. In our case report, blood pressure was elevated at admission, but not as high as in the hypertensive crisis or hypertensive encephalopathy. Previously, reports have shown that PRES can be associated with elevated blood pressure level (Fugate and Rabinstein 2015). Chronic alcohol abuse causes increased reactive oxygen species and nitric oxide in brain endothelial cells (Kim et al. 2014). Furthermore, oxidative stress can cause disruption of endothelial cells lead to blood–brain barrier (B-BB) breakdown (Kim et al. 2014, Kimura et al. 2010). Previously reports on chronic alcoholism and/or alcohol withdrawal with PRES showed that PRES lesions were mostly located in the posterior cerebral circulation areas on cranial MRI, which is similar with our MRI findings (Ishikawa et al. 2013, Kim et al. 2014, Kimura et al. 2010, McKinney et al. 2007). However, in most cases the blood pressure was high at admission (Kim et al. 2014, Kimura et al. 2010). This evidence suggests that in our case report mainly endothelial dysfunction is associated with the pathophysiology of PRES due to chronic alcoholism and alcohol withdrawal. Subsequently B-BB is disconnected or damaged, providing vasogenic edema especially in patients with high blood pressure. When alcohol withdrawal happens, a transient increase in blood pressure can be occurred. After alcohol withdrawal, the channels of N-methyl-D-aspartate receptors are suddenly opened, leading to neuronal depolarization and increased firing. The hypothalamic–pituitary–adrenal system is activated, leading to increased levels of cortisol and catecholamine (Ceccanti et al. 2006), which can result in an increase in blood pressure. Consequently, we consider that both the transient increase in blood pressure and the endothelial dysfunction are associated factors for the development of PRES in our case.

Typical MRI findings in PRES are symmetric reversible T2 high-signal intensities, which are located in the occipital and parietal lobes leading to subcortical vasogenic edema (Granata et al. 2015). FLAIR sequence is much more sensitive for PRES lesions (Fugate and Rabinstein 2015). Diffusion weighted image (DWI) scans and apparent diffusion coefficient (ADC) mapping are noteworthy to differentiate vasogenic edema from cytotoxic edema (Granata et al. 2015). Ischemic lesions, followed by cytotoxic edema are seen as hyperintense on DWI, whereas PRES lesions are hypointense (Granataet al. 2015).

The characteristic radiological findings of PRES are categorized into 3 models, i.e. parieto-occipital model, hemispheric border-zone model and superior frontal sulcus model (Fugate andRabinstein 2015). . These models are considerable to establish the diagnosis of PRES since 70% of patients have at least one of these described features (Fugate and Rabinstein 2015). However, present categorization does not elucidate the type and severity of the clinical signs and PRES lesions can also be present in the basal ganglia or brainstem (Granataet al. 2015). Our case is categorized as a parieoto-occipital model.

The importance of cranial MRI in the diagnosis of PRES is indisputable. If a patient is a chronic alcohol user, undergoes alcohol withdrawal and has a cranial MRI, could that classify him for PRES? The answer to this question cannot be answered yet because indications of neuroimaging in the patients with chronic alcoholism or alcohol withdrawal are still lacking (Jesse et al. 2016, Galvin et al. 2010, Geibprasert et al. 2010, Niciuand Mason 2014, Zuccoliet al. 2010). Neuroimaging is recommended in cases with alcohol withdrawal, when status epilepticus (SE) or convulsion occurs (Jesse et al. 2016). It is essential to describe the findings of brain imaging associated with SE or convulsion. The most encountered abnormalities are hyperperfusion, cortical hyperintensities and low apparent diffusion coefficient (Jesse et al. 2016). The MRI findings were not related with epilepsy since our patient had no convulsion. Encephalopathies associated with alcohol such as Wernicke encephalopathy, Marchiava-Bignami disease, hepatic encephalopathy and osmotic demyelination syndrome, have specific characteristic features on an MRI (Geibprasert et al. 2010, Zuccoliet al. 2010). Typically, medial thalamus, mamillary body, tectal andperiaqueductal gray matter are the areas involved in Wernicke encephalopathy, while corpus callosum is mostly affected in Marchiava-Bignamidisease. The lesions are hyperintensive on T2 and FLAIR weighted images in both diseases (Geibprasert et al.2010, Zuccoli et al.

2010). MRI findings are variable according to stage of hepatic encephalopathy, however mostly T1hyperintensity due to manganese accumulation in basal ganglia is seen (Roviraet al. 2008). Osmotic demyelination syndrome occurs usually after the acute improvement of hyponatremia and neuroradiologicaly mostly pons but also thalamus, basal ganglia, cerebellum and cerebral cortex can be involved (Geibprasert et al. 2010, Zuccoli et al. 2010).

Taken together the results of the MRI, clinical signs and resolution of autonomic symptoms and lesions after treatment, we considered that our patient has PRES. Wernicke encephalopathy was excluded because there was no ataxia and ophthalmoparesis and no involvement in the medial thalamus, mammillary body, tectal and periaqueductal gray matter (Galvin et al. 2010, Geibprasert et al. 2010, Zuccoli et al. 2010). Hepatic encephalopathy was not considered since there was no hepatic insufficiency in his medical history; no clinical signs of rigidity, flapping tremor, hyper or hyporefleksia, hepatomegaly; no basal ganglia involvement on cranial MRI and no laboratory findings related to liver insufficiency. (Roviraet al. 2008). Furthermore, we excluded Marchiava-Bignami disease because our patient did not demonstrated muscle rigidity, convulsions and corpus callosum involvement (Geibprasert et al. 2010, Zuccoliet al. 2010). Osmotic demyelination syndrome was not considered due to the lack of hyponatremia. (Geibprasert et al. 2010, Zuccoli et al. 2010).

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