

Association of central pontin myelinolysis and extra-pontin myelinolysis in diabetic patient

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Abstract

Central pontin myelinolysis and extra-pontin myelinolysis (CPM/EPM) implies the clinical picture after rapid recovery of hyponatremia or hyponatremia alone. SPM/EPM picture can occur without hyponatremia. Findings such as dysarthria, dysphagia, tetraparesia/plegia accompanies the clinical table. Our case was also diabetic, but there were no electrolyte imbalance in admission. The presence of diarrhea in medical history of the patient might indicate a short-term undetected electrolyte imbalance. In our diabetic case that has borderline metabolic status and lack of any detected electrolyte imbalance, we decided to present SPM/EPM table together with literature information.

INTRODUCTION

Central pontin myelinolysis and extra-pontin myelinolysis (CPM/EPM) implies the clinical picture after rapid recovery of hyponatremia or hyponatremia alone [1,2,3]. Again underlying alcoholism and malnutrition are among the most common causes [4,5]. Generally due to the underlying cause, a clinical table occurs characterized with acute or subacute onset tetraparesia/plegia, pseudobulbar syndromes. The pathology of the disease is characterized with loss of myeline in pontin or extra-pontin region.

We present this case as a SPM/EPM occurred on diabetes mellitus basis without hyponatremia or hypokalemia.

CASE

Male patient, 48 years old with right hand dominance admitted to the neurology outpatient clinic with complaints such as progressive weakness in legs and arms for last 20 days, difficulty in swallowing, speech disorders and sleep tendency. The case had unregular type 2 diabetes mellitus for approximately 15 years. On this account, patient was often hospitalized due to diabetic ketoacidosis. The patient was hospitalized for unconsciousness resulting from diabetic ketoacidosis 40 days ago and he had diarrhea lasting nearly one week after discharge. The patient admitted to our hospital for progressive unconsciousness which developed in

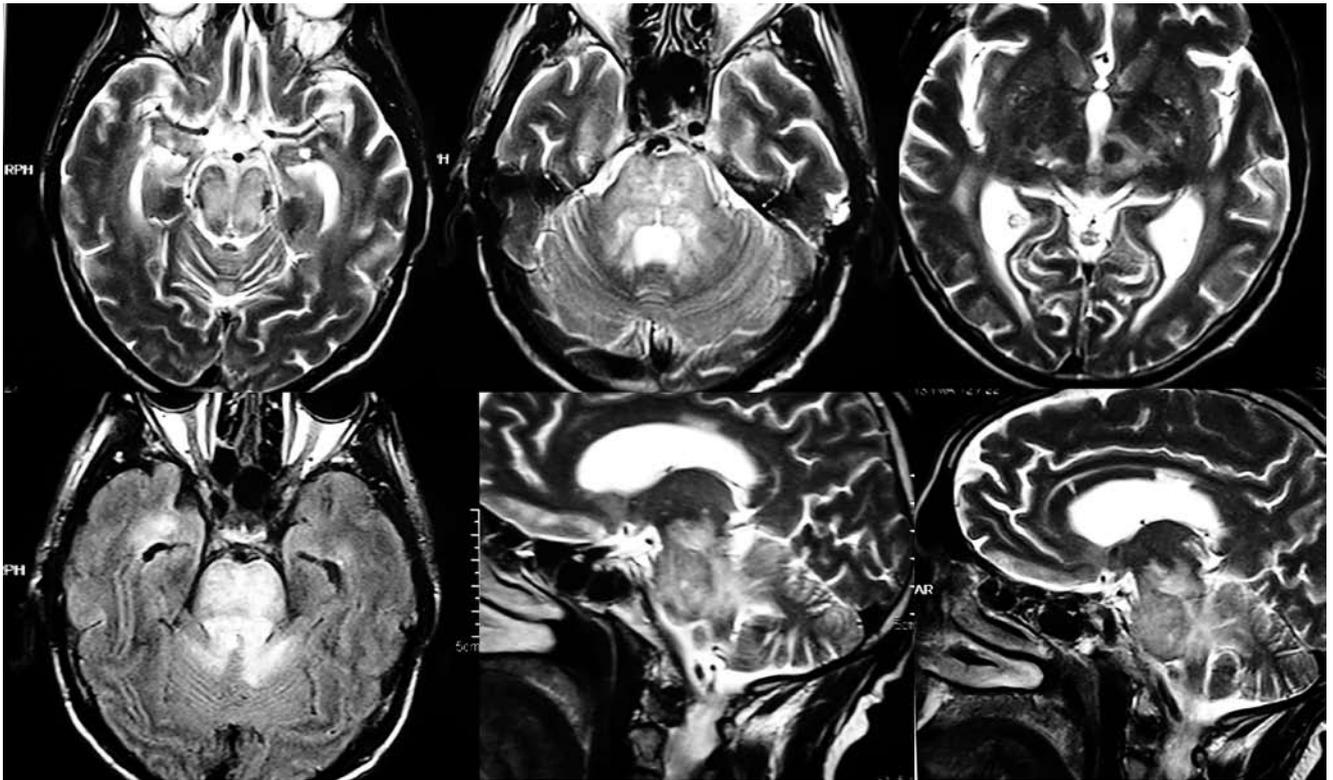


Figure 1. Cranial nerve MRI imaging

last several days and extremity weakness subsequent to improvement of diarrhea without any treatment.

In brief history of the case, he had no particular features other than type 2 diabetes mellitus and diabetic nephropathy. He was not drinking. He had no medication other than NPH insulin and oral antidiabetics.

In physical examination of the case, arterial pressure value was 170/80 mmHg, body temperature was 36.7 °C and his respiration was hypopneic and it was 25 breath per minute. In neurological examination, his consciousness was lethargic, speech was disarthric and saliva discharged from his mouth and nose. In cranial nerve examination, light reflex was bilaterally decreased, gag reflex could not be received and function of looking upwards was partially limited. Motor examination revealed that strength of the muscles in both extremity scored 4–5 and that he could stand only by assistance. He had no sign suggesting cerebellar pathology. DTR was decreased in all of the four extremities and there were no pathologic reflexes.

In cranial nerve MRI imaging of the case, findings compatible with demyelination were observed; findings showed that demyelination was present in pons, both of the cerebellum, middle cerebellar peduncle, mesencephalon and it was spreading to diencephalic region and partially to lateral ventricle and findings were iso-hypointense in T1 images, hyperintense in T2 images and significant signal increase in FLAIR sequences; however, in images, nucleus accumbens was reserved (Figure 1). In MR Spectroscopy, decrease in

N-acetyl-aspartate peak values and increase in choline peak values were observed.

Kinase was 38 U/L (range 29–200), AST was 24 U/L (range 5–34), ALT was 24 U/L (range 0–55), leukocyte count was 10 400/μl, erythrocyte count was 3 830 000/μl, hemoglobin value was 11.2 g/dL, hematocrite level was 34.2 and ketone in urine was negative. Levels of vitamin B12 and folate were within normal ranges. In CSF examination, the appearance was clear, leukocyte count was 2/mm³, protein 64 mg/dL, IgG index was 0.79 and oligoclonal band was negative. No pathological cells were detected.

The case was started pulse methylprednisolone medication subsequently to the hospitalization. In 10th day of the medication, his consciousness status started to improve. However, there was no improvement in bulbar findings.

DISCUSSION

Central pontin myelinolysis, first defined by Adams et al in 1959, were found to be often associated with alcoholism and malnutrition and it has been reported that ¾ of the SPM/EPM cases were developed secondary to the alcoholism. In some cases, rapidly improving hyponatremia had drawn attention [1–4]. In examination of the cases, it is observed that SPM/EPM can occur due to alcoholism, malnutrition, long-term diuretic administration, psychogenic polydipsia, burns, subsequent to the hepatic transplantation, post-operative period of pituitary surgery and following the glisine infusion (in increasing

order) [6]. The numbers of the published reports related with diabetes mellitus are relatively low [7,8]. Hypopotassemia are regarded among the causes [9,10].

Clinical picture can include a wide spectrum of symptoms ranging from slight unconsciousness to coma. Various symptoms could be observed due to the underlying cause such as dysphagia or dysarthria in involvement of corticobulbar fibers, para/tetraparesia or plegia in corticospinal fiber involvement, oculomotor findings in mesencephalic involvement and mutism, Parkinsonism, catatony, dystoni or tremor according to the involvement site of the extra-pontin (cerebellum, external capsule, putamen, thalamus, corpus callosum, serebral cortex or subcortex). In some cases locked-in syndrome might also be observed.

Immediate correction of the hyponatremia often underlies the pathophysiology of the disease [2,3,5,6]. In post-mortem histological evaluations, loss of oligodendrocytes were observed in demyelinating fields; but axons were reserved. There is vascular involvement and no inflammation is observed [11]. Osmotic damage hypothesis presented by Norenberg is the most widespread one [12]. Increase in pinocytic activity due to disintegration of the blood-brain barrier is observed and liquid transportation from endothelial cells is detected. Vasogenic edema and intracellular/intramyelinic edema is added on the clinical picture. Oligodendrocyte degeneration is observed due to the swelling of the myelin sheath. In later stages, endothelial hyperplasia and neovascularization might appear. Again, in several studies, it is reported that activated microglia and following release of cytokines subsequent to the disintegration of the blood-brain barrier increased the demyelination [13].

Whereas among the other imaging studies used in diagnosis, computerized tomography (CT) can demonstrate the lesion, magnetic resonance imaging (MRI) is superior in demonstrating the lesions. In involvement sites, T1 hypo-intense and T2 hyperintense lesions draw attention. In differential diagnosis multiple sclerosis, acute demyelinating encephalomyelitis, Marchiafava-Bignami disease should be considered. In early imaging studies, lesion might rarely be missed, but it might be detected in repeated studies. In MRI examination due to involvement of the pontin, "bat wing" image can be observed. Whereas electrolyte imbalance such as hyponatremia or hypopotassemia due to the root cause in laboratory examinations, normal levels can be detected in some cases. Alterations might be detected in parameters which can cause osmotic stress.

The basic principal of the treatment is prevention. Particularly for the patients with metabolic alterations, immediate changes in electrolyte status should be avoided. There are some recommendations for correction of the hyponatremia [6]. The generally accepted view is that correction of the hyponatremia should not exceed 10 mEq/L in first 24 hours and 21 mEq/L in 48 hours [2,3]. There is no generally accepted view for correction of the hypopotassemia. There is no study on treatment of

SPM/EPM after it occurred. Supportive treatment is advised. In small case series, intravenous immunoglobulin and thyrotropin releasing hormone were used.

We could not detect any electrolyte imbalance in our case. His clinical presentation included progressive unconsciousness, bulbar findings and tetraparesia. Previous diarrhea episode might have caused an electrolyte imbalance of which we could not detect. Due to the unregular diabetic control, he had brief history of intermittent hospitalization and treatment. In chronic patients whose clinical picture is similar to that of our patient who has balanced metabolic status, additional contributory factors such as diarrhea can cause SPM/EPM especially in conditions where compatibility with therapy is weak. Sometimes, recurrent hypoglycemic episodes can be presented by cognitive deficiency without causing the SPM/EPM table [14]. On this account, diabetic patient should be subjected routine controls in regular intervals not only for neuropathy, nephropathy, retinopathy but also for neuropathy and clinicians should suspect the SPM/EPM even in smallest metabolic imbalance.

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