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CASE REPORT

Pontine lesion in hyperglycemic crises: Relevance to osmotic demyelination syndrome and posterior reversible encephalopathy syndrome

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ABSTRACT

We herein describe a case of type 1 diabetes that presented with a pontine lesion during two hyperglycemic crises accompanied by marked fluctuations in serum osmotic pressure and blood pressure. Magnetic resonance imaging showed swollen pons with osmotic demyelination syndrome characteristics accompanying cytotoxic edema at the first crisis. The involvement of vasogenic edema was also assumed in the second crisis. Neurological symptoms were milder than magnetic resonance imaging findings. The patient recovered after 7 days without sequelae in both crises. Based on these findings, a pontine lesion needs to be considered in patients with poorly controlled diabetes showing rapid metabolic and blood pressure changes, as observed in hyperglycemic crises. Cytotoxic edema leading to osmotic demyelination syndrome and vasogenic edema caused by vascular endothelial cell damage might both be involved in the pathogenesis of a pontine lesion.

INTRODUCTION

Central pontine myelinolysis was initially described in alcoholic-malnourished patients and is now associated with the rapid correction of hyponatremia. Similar lesions have been detected in areas other than the pons and are called osmotic demyelination syndrome (ODS)[1].

ODS has been reported under conditions other than the rapid correction of hyponatremia, suggesting that myelinolysis is a more generalized injury pattern caused by fluctuations in extracellular fluid osmolality[2]. Diabetes mellitus is a risk factor for ODS[2]. Cases of ODS have been reported in poorly controlled diabetes mellitus[3–7].

The Na-K-ATPase pump system and the production of organic osmolytes allow cells to adapt to changes in extracellular osmotic pressure. Patients with poorly controlled diabetes cannot respond to rapid osmotic changes due to intracellular metabolic disturbances, which ultimately result in cytotoxic edema and the demyelination of oligodendrocytes[2]. Other than typical ODS patients, atypical pontine lesions have been reported in patients with diabetes[8,9].

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We present a case of type 1 diabetes that developed a pontine lesion during two hyperglycemic crises. Clinical and magnetic resonance imaging (MRI) findings were suggestive of the pathogenesis of a pontine lesion.

CASE REPORT

A 39-year-old man with type 1 diabetes for 10 years who received irregular insulin treatments presented with impaired consciousness after excessive intake of soft drinks. His consciousness level was E3V4M6 on the Glasgow coma scale; other than disorientation, there were no apparent neurological abnormalities. Blood pressure, heart rate, body temperature and body mass index were 204/128 mmHg, 103 b.p.m, 37.6°C and 21.9 kg/m^2, respectively. Metabolic control had been poor for years, as shown by a blood glucose level of 569 mg/dL and glycated hemoglobin of 9.9%. Serum creatinine, sodium and potassium levels were 2.95 mg/dL, 128 mEq/L and 3.9 mEq/L, respectively, and serum osmolality was 310 mOsm/L. An arterial gas analysis did not show metabolic acidosis. Urine was positive for ketone bodies. Fluid-attenuated inversion recovery (FLAIR) MRI showed swelling of the pons with hyperintense signals sparing the marginal area (Figure 1, upper row).

Diffusion-weighed imaging showed a small, restricted diffusion area in the pons with a reduced apparent diffusion coefficient, indicating cytotoxic edema (Figure 1, upper row). Collectively, these results suggested a demyelinating process, namely, ODS. After fluid and insulin replacement, consciousness was restored within 1 week.

Four months after the first hospitalization, the patient was admitted with disturbed consciousness. His consciousness level was E4V1M4 with snoring-like respiration, conjugated eye deviation to the left, and hypokinesia of the right upper and lower extremities. Blood pressure, heart rate and body temperature were 157/131 mmHg, 113 b.p.m. and 36.1°C, respectively. His blood glucose level was 1,056 mg/dL, total ketone body level was 6,658 μmol/L, and serum creatinine, sodium and potassium levels were 5.88 mg/dL, 120 mEq/L and 6.8 mEq/L, respectively, and serum osmolality was 357 mOsm/L. Arterial gas analyses showed metabolic acidosis: pH 7.167, PCO_2 27.0 mmHg, PO_2 127.2 mmHg and HOC_3^- 9.4 mEq/L. Hyperintense signals extending from the swollen pons to the cerebellar peduncle were observed on FLAIR images, diffusion-weighed imaging showed no abnormalities and apparent diffusion coefficient was slightly increased, indicating vasogenic edema (Figure 1, middle row). A cerebrospinal fluid examination showed a normal protein content, no oligoclonal bands and an elevated myelin basic protein level of 198 pg/mL (reference ≤102). Anti-nuclear and anti-aquaporin 4 antibody levels were negative. Neurological symptoms resolved without sequelae after 1 week.

In the 4-week follow up after the second crisis, the swelling of the pons was attenuated; however, hyperintense signals were still observed on FLAIR images (Figure 1, lower row).

DISCUSSION

In the first hospitalization, MRI findings suggested a demyelination process in the pons[1,2]. ODS was attributed to significant fluctuations in serum osmolality caused by irregular insulin treatments and excessive intake of soft drinks. In the second admission with ketoacidosis, more severe neurological symptoms were accompanied by an enlarged pontine lesion. MRI findings showed a brainstem variant of posterior reversible encephalopathy syndrome (PRES)[10], which involves vasogenic edema. However, elevated myelin basic protein in the cerebrospinal fluid and a prolonged high-intensity signal on FLAIR images persisting for >1 month suggest a demyelinating process[1,2].

Previous studies reported that patients with poorly controlled diabetes developed pontine lesions consistent with ODS under various conditions[3–7]. These patients showed marked fluctuations in blood glucose levels, indicating the perturbation of

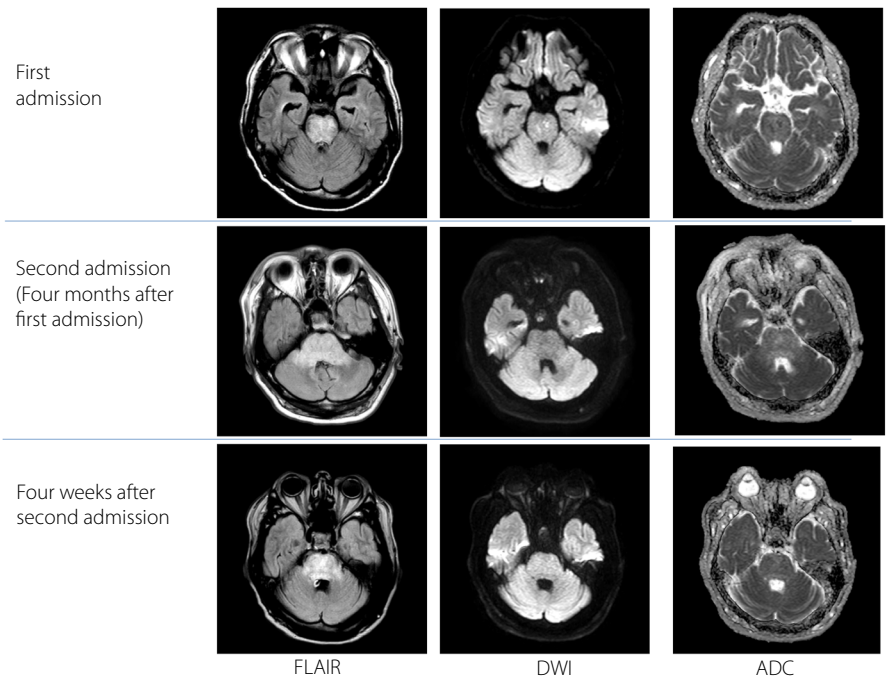

Figure 1 | Magnetic resonance imaging of the brain. Upper row, the first admission. Fluid-attenuated inversion recovery imaging showed swelling of the pons with hyperintense signals sparing the marginal area. Diffusion-weighed imaging showed a small, restricted diffusion area in the pons with a reduced apparent diffusion coefficient, indicating cytotoxic edema. Middle row, the second admission (4 months after the first admission). Hyperintense signal in swollen pons was observed on fluid-attenuated inversion recovery image, with slightly increased apparent diffusion coefficient, indicating vasogenic edema. Lower row, 4 weeks after the second admission. Left column, fluid-attenuated inversion recovery image (FLAIR); middle column, diffusion-weighed imaging (DWI); right column, apparent diffusion coefficient image (ADC).

serum osmolality. In the present case, a demyelinating process and vasogenic edema were both present in brainstem lesions. Both insufficient cellular adaptation to fluctuations in serum osmolality and inadequate vascular endothelial cell adaptation to rapidly elevated blood pressure seem to contribute to the pontine lesion formation.

Reversible brainstem lesions in diabetes patients might be diagnosed as ODS when marked osmotic changes are suspected, and have been categorized as brainstem variants of PRES in patients with elevated blood pressure[8]. PRES refers to reversible vasogenic brain edema caused by the breakdown of the blood–brain barrier due to endothelial cell injury[10]. Although FLAIR imaging and apparent diffusion coefficient suggested vasogenic edema in the present case, particularly in the second crisis, prolonged MRI changes were not compatible with PRES alone. Furthermore, MRI changes in ODS persist for months[1,2]. The abrupt exacerbation of blood glucose and blood pressure might occur in patients with poorly controlled diabetes in hyperglycemic crises. The clinical course and MRI findings of the present case indicated the coexistence of the pathogenesis of both ODS and PRES, resulting in a prolonged brainstem abnormality on MRI.

Similar pontine lesions might not be rare in hyperglycemic crises, particularly in patients with neurological symptoms. Evaluations of brain MRI will provide insights into the pathophysiology of pontine lesions and their clinical meaning.

DISCLOSURE

The authors declare no conflict of interest.
Approval of the research protocol: N/A.
Informed consent: The patient provided written informed consent for the publication of this report.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

REFERENCES

1. King JD, Rosner MH. Osmotic demyelination syndrome. *Am J Med Sci* 2010; 339: 561–567.
2. Kumar S, Fowler M, Gonzalez-Toledo E, *et al*. Central pontine myelinolysis, an update. *Neurol Res* 2006; 28: 360–366.
3. Casey E, Evans A, Krentz A, *et al*. Central pontine myelinolysis. An unusual complication of diabetes. *Diabetes Care* 1999; 22: 998–1000.
4. Saini M, Mamauag MJ, Singh R. Central pontine myelinolysis: a rare presentation secondary to hyperglycaemia. *Singapore Med J* 2015; 56: e71–e73.
5. Tajitsu M, Yamada T, Cao X, *et al*. Osmotic demyelination syndrome complicating diabetes with anti-glutamic acid decarboxylase antibodies and Graves' disease: a case report. *J Diabetes Investig* 2016; 7: 130–131.
6. Sharma C, Kumawat BL, Panchal M, *et al*. Osmotic demyelination syndrome in type 1 diabetes in the absence of dyselectrolytaemia: an overlooked complication? *BMJ Case Rep* 2017; 2017: bcr2016219148.
7. Pliquett RU, Noll A, Ibe R, *et al*. Hyperglycemia-related central pontine demyelinization after a binge-eating attack in a patient with type-2 diabetes: a case report. *BMC Endocr Disord* 2018; 18: 18.
8. Ichikawa H, Murakami H, Katoh H, *et al*. Central pontine lesions observed with MRI in four diabetic patients. *Intern Med* 2008; 47: 1425–1430.
9. Shimizu Y, Kozawa J, Hayakawa T, *et al*. Asymptomatic pontine lesion and diabetic amyotrophy after rapid improvement of poor glycemic control in a patient with type 1 diabetes. *Intern Med* 2019; 58: 3433–3439.
10. Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. *Lancet Neurol* 2015; 14: 914–925.