CASE REPORT

Posterior Reversible Encephalopathy Syndrome Complicating Diabetic Ketoacidosis

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Background: Posterior reversible encephalopathy syndrome (PRES) is a benign disorder of reversible subcortical vasogenic cerebral edema. **Case characteristics**: A 13-yr-old girl presented 4 days after complete recovery from diabetic ketoacidosis with symptoms of headache, altered sensorium, seizures, and visual loss. There was no hypertension or biochemical abnormalities identified. MRI brain showed hyperintense areas in subcortical and periventricular white matter of bilateral fronto-parieto-occipetal lobes, with possible diagnosis of normotensive PRES. **Outcome**: Full recovery without sequelae, following neuro-protection and expectant treatment. **Message**: Identifying PRES in diabetic ketoacidosis assists appropriate treatment and prognostication.

Key words: *Hypertension, Leukoencephalopathy, Outcome, Seizures*.

Reversible posterior leukoencephalopathy syndrome (PRES) is a clinicoradiological entity characterized by headaches, altered mental status, seizures, and visual loss and is associated with white matter vasogenic edema predominantly affecting the posterior occipital and parietal lobes of the brain [1]. Many possible triggers including hypertension, impaired renal function, immunosuppressive therapies and various inflammatory conditions were seen [2], but it can occur with many diverse clinical entities. The diagnosis can be made clinically and is reinforced by characteristic changes observed on MRI brain. Typical MRI findings include reversible, symmetrical, posterior subcortical vasogenic edema [1]. If recognized and treated promptly, the rapid-onset symptoms and radiologic features usually fully resolve within days to weeks. [3]

Case Report

A previously well 13-year-old girl presented with DKA as a first presentation of Type 1 diabetes mellitus (T1DM). Initially she was managed in a different hospital and found to have blood glucose of 510 mg/dL, severe dehydration, heart rate of 140/minute, saturation 90% in air, blood pressure 100/70 mmHg with peripheral perfusion of 2 secs and metabolic acidosis. Over the course of 12 hours in the referring hospital, she had received 2800 mL of fluids. She had urine output at 5 mL/kg/hr. Cerebral odema was suspected in view of deteriorating Glasgow coma scale, CO_2 retention and persisting severe acidosis. She received a dose of mannitol, intubated, ventilated and transferred to our centre. CT brain reported normal and cerebral edema was ruled out. She was extubated within 24 hours and recovered from DKA within 48 hours but found to have lower limb weakness and hypotonia with grade 3 power. No obvious identifiable cause was found for weakness except for raised creatine phosphokinase (742 U/L) which normalised within a week. She is the only child and mother is known case of Dermatosclerosis.

Biochemistry on day 1 indicated severe intravascular fluid depletion with serum sodium (Na) 162 mmol/l, serum potassium (K) 2.3 mmol/l, serum creatinine (Cr) 1.2 mg/dL and blood urea 32 mg/dL; all of these normalized by 3 days. On day 5, she was discharged on basal bolus insulin regimen with blood pressure recorded 119/70 mmHg and blood glucose 226 mg/dL.

She presented again to triage 4 days post-discharge with complaints of being drowsy, blurring of vision, headache and two episodes of seizures lasting for 30 seconds, described as vacant stare with eyes rolled up, increased tone of all four limbs, twitching of angle of mouth and right eye, with blood glucose 109 mg/dL, pulse

rate 112/min and BP 127/80 mmHg (90th centile) at presentation. She received 20 mg/kg (PE) loading dose of fosphenytoin. She remained drowsy and confused with heart rate 98/min, peripheral pulses feeble, respiratory rate 16/min with poor respiratory efforts, SpO_2 87% on room air and 98% on 3L oxygen. Hence she was electively intubated, VBG and biochemistry post intubation showed pH 7.3, PCO_2 58 mmHg, bicarbonate 28.5 mmol/l, Na 144 mmol/L, K 3.5 mmol/L, Cl 85 meq/L and Cr 0.5 mg/dL. MRI brain showed hyperintense areas in subcortical white matter of bilateral parieto-occipital lobes and no diffusion restriction ***(Fig.* 1***)*** with possible diagnosis of PRES. She got extubated after 3 days, blood pressure remained around 124/80 mmHg, vasculitis profile and infection screening (CSF, blood, urine cultures) was negative. Over the following two weeks, her lower limb weakness and vision disturbances improved completely. At last follow-up, two years after discharge, she remains well without any neurological symptoms and her HbA1C has been less than 6% (43 mmol/mol).

DISCUSSION

The child developed progressive encephalopathy, cortical blindness and seizures, typical of PRES and the same supported by characteristic appearances on MRI. As anticipated her clinical deficits improved rapidly with expectant management. The pathophysiology in PRES is the vasogenic oedema which has a favorable outcome when compared to osmotic cerebral edema seen in DKA [4]. Osmotic edema occurs during the course of DKA and is a leading cause of morbidity and mortality in children with type 1 diabetes [5], whereas vasogenic odema is usually seen after recovery from DKA as in our case.

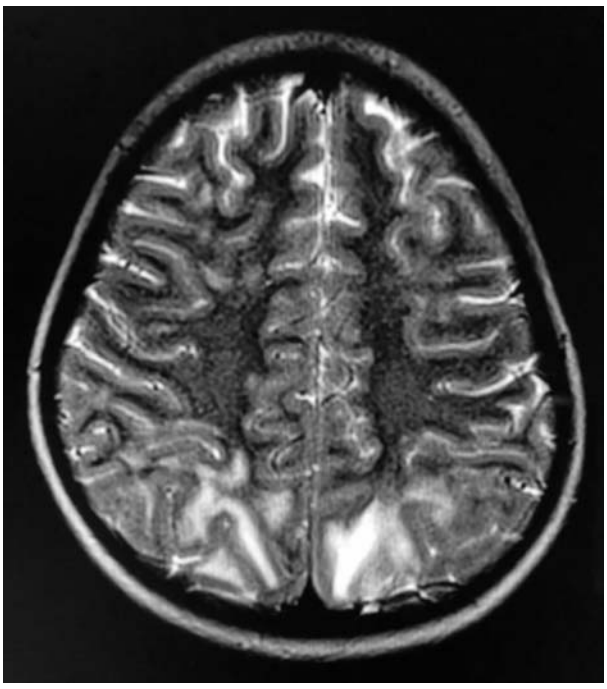

FIG. 1 *MRI brain T2 sequence showing hyperintense areas in subcortical white matter of bilateral occipital lobes.*

The underlying pathogenesis of PRES is not fully understood, but is thought to be caused by endothelial damage or dysfunction caused by excessive circulating inflammatory cytokines [4,6]. This is important because DKA is associated with increased serum proinflammatory cytokines [7], shown to up regulate expression of vascular endothelial growth factor and may therefore increase vascular permeability in PRES [4,8].

Hypertension and BP flctuations are recognized as potential triggers in PRES [1,2] but cases have been reported with normotensive PRES as well [3]. Electrolyte disturbances may have been contributory.

Hypertension and blood pressure fluctuations were not noticed in this child, unlike a common finding in the cases reported previously. Electrolyte disturbances such as hypokalaemia, hypernatremia in our case may have been contributory. The brain edema frequently involves, parieto-occipital pattern; though, it may also involve more anterior regions [4]. Nearly, half of the patients who develop PRES have a history of autoimmune diseases (*e.g.* systemic lupus erythematosus, hypothyroidism, Crohn's disease) [4], but there has been a recent report associated with onset of T1DM complicated by DKA [9]. Our case could be the second one reported showing association of PRES following DKA in children. Development of PRES in this patient was likely to be multifactorial and may have been potentiated by the metabolic effects of DKA and postulated indirect effects of electrolyte disturbances on vascular permeability.

Since PRES is often unsuspected by clinicians, recognizing the characteristic image findings by radiologists is key in diagnosing this syndrome and should guide the clinicians in preventing and minimizing deleterious work-ups or therapies unless there is atypical presentation. One can expect an excellent clinical outcome within few days.

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