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Case Report

Diabetic Keto Acidosis with Myocardial Dysfunction and Posterior Reversible Encephalopathy Syndrome

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Abstract

Acute neurological symptoms occur secondary to cerebral edema and it is the most frequently described complication in children with diabetic ketoacidosis (DKA). Reversible visual loss can occur in children following posterior reversible encephalopathy syndrome (PRES) and this is an unusual complication in children with DKA. We present a 6-year-old girl with new onset DKA who developed irritability, seizures, lethargy and blindness following recovery of ketoacidosis. Initial CT scan revealed hypodense areas predominantly in occipital region. Sequential magnetic resonance (MR) imaging revealed extensive hyper intense areas involving almost all lobes. Following neuroprotective measures and symptomatic therapy, child had complete neurological recovery.

Keywords: *Diabetic Ketoacidosis (DKA); Posterior Reversible Encephalopathy Syndrome (PRES); Magnetic Resonance (MR)*

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity presenting with acute neurological symptoms (seizures, encephalopathy, headache and visual disturbance) in the setting of renal failure, hypertension and auto-immune disorder. Though pathophysiological changes are not fully understood in PRES, endothelial injury related to blood pressure changes or the direct effects of cytokines on endothelium causes disruption of blood-brain barrier resulting in subcortical vasogenic brain edema [1]. The diagnosis is clinical and confirmed by typical MRI findings in the parieto-occipital region of both cerebral hemispheres [2]. Early recognition and prompt treatment results in complete resolution and full neurological recovery within days to weeks [3].

Case Report

Previously healthy 6-year-old girl presented with fever, vomiting, lethargy and breathlessness for 3 days. At the emergency room she was pain responsive with GCS of 9, heart rate of 150/min, respiratory rate of 60/min with compensated shock (capillary refill time > 2 sec, +++/+ pulses, BP 100/40 mm Hg). Shock was managed with 40 ml/kg of normal saline and dopamine infusion at 10 mcg/kg/min. DKA was diagnosed with a blood sugar of 581 mg/dl, wide anion gap metabolic acidosis and ketonuria. Arterial blood gases revealed a pH of 6.8, PCO_2 of 21 mm Hg, PO_2 of 72 mm Hg and bicarbonate of 3.3 mmol/L and anion gap of 36. She was started on DKA protocol (ISPAD regimen) with normal saline and insulin infusion. Investigations revealed total count of 12,800 cells/mm^3, haemoglobin of 11.2 g/dL, platelet of 2.24 lakhs/mm^3, urea was 65 mg/dL and creatinine was 1.1 mg/dL with lactate of 2.1 mmol/L (normal 0.8 - 1.5 mmol/L). Sodium was 130 mEq/L and potassium was 5.6 mEq/L. Coagulation profile and alanine and aspartate transaminases were Normal. Child regained normal sensorium by 24 hours of treatment. She was tachypneic with oxygen saturation of 88% on room air and this increased to 96% with supplemental oxygen through non-rebreathing mask. Chest radiograph revealed left lower lobe pneumonia. C-reactive protein (CRP) at admission was 48 mg/L. Child was started on inj ceftriaxone. Ultrasonogram of abdomen showed bilateral enlarged kidneys with grade I renal parenchymal disease. After 24 hours of fluids and insulin infusion, pH was 7.36 with bicarbonate of 15mEq/L and her GCS was 15.

She had persistence of tachypnea and increasing renal parameters (Table 1). On day 3 of ICU stay, she developed myocardial dysfunction with gallop rhythm and echo revealed an ejection fraction (EF) of 42% with moderate LV dysfunction. Troponin T was raised (0.067 ng/ml; normal < 0.03 ng/ml) and CPK level was 113 U/L (normal 0 - 250 U/l). Fluids were restricted to two-third of maintenance along with furosemide infusion at a dose of 2 mg/kg/day and dobutamine infusion at 10 µg/kg/min. She was started on heated humidified high

flow nasal oxygen therapy at 1.5 L/kg flow and 30% FiO_2. Evaluation revealed hypocalcemia (total 8.8 mg/dl iCa of 0.8 mmol/L) with magnesium of 1.6mg/dL (normal 1.5 - 2.3 mg/dL), 25 (OH) Vit D of 32 ng/mL (sufficiency > 30 ng/mL). Fluid balance in the preceding 48 hrs was stable. Myocardial dysfunction resolved by day 5 after correction with IV calcium. Her left ventricular function improved with ejection fraction of 62% and dobutamine infusion was stopped at 48 hours. She had abdominal pain by day 7 and on evaluation had elevated serum amylase (557 U/L; normal 30 - 100 U/L) and lipase (1695 U/L; normal 145 - 216 U/L) triglycerides was 194 mg/dl, LDH was 650 u/L, with normal electrolytes and renal parameters. CT abdomen revealed bulky pancreas. Her symptoms of acute pancreatitis resolved by 72 hours with conservative management.

Parameters/Day	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 10
Urea (mg/dL)	90	99	107	123	115	109	70	37
Creatinine (mg/dL)	1.9	2.0	2.4	2.4	1.9	1.6	1.1	0.7

Table 1: *Serial renal parameters.*

On 10th day of hospital stay she was irritable and developed generalised tonic clonic seizures. Seizures were controlled with IV midazolam and IV phenytoin. She had persistent elevation of blood pressures (blood pressure of 160/112 mm Hg -stage 2 hypertension). At 6 hours of seizures she was lethargic and complained of total blindness of both eyes with no other neurological deficit. Fundus examination revealed clear media with normal disc and vessels with changes in retinal pigment epithelium (RPE) suggestive of acute hypertensive choroidopathy. Basic metabolic parameters were normal (CBG 156 mg/dL, Sodium 135 mEq/L, ionised Calcium 1.2 mmol/L). CT brain revealed bilateral fronto-parieto-occipital white matter hypodensity suggestive of posterior reversible encephalopathy syndrome (PRES) (Figure 1). MRI of brain revealed multiple bilateral parenchymal bleeds with extensive bilateral white matter edema suggestive of PRES (Figure 2). Blood pressure was controlled using nifedipine and methyldopa. After 5 days of visual loss, she started gradual recovery of vision. She was on antihypertensives for 10 days and stopped before discharge. Her HbA1c level was 9.1. Child was discharged after a hospital stay of 30 days and at discharge, child had normal 6/6 vision with no neurological symptoms and is currently under follow-up for diabetic control.

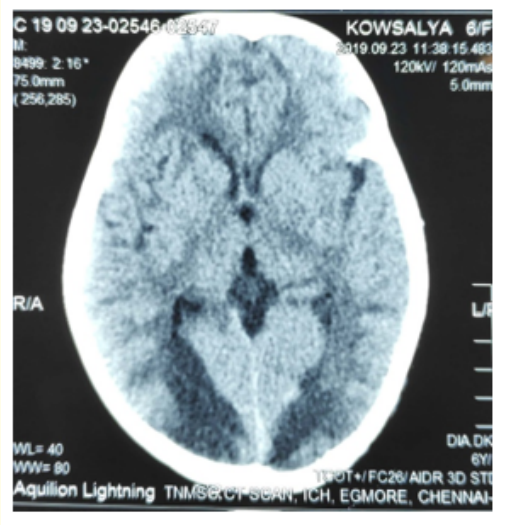

Figure 1: *CT Brain showing bilateral fronto-parieto-occipital white matter hypodensity.*

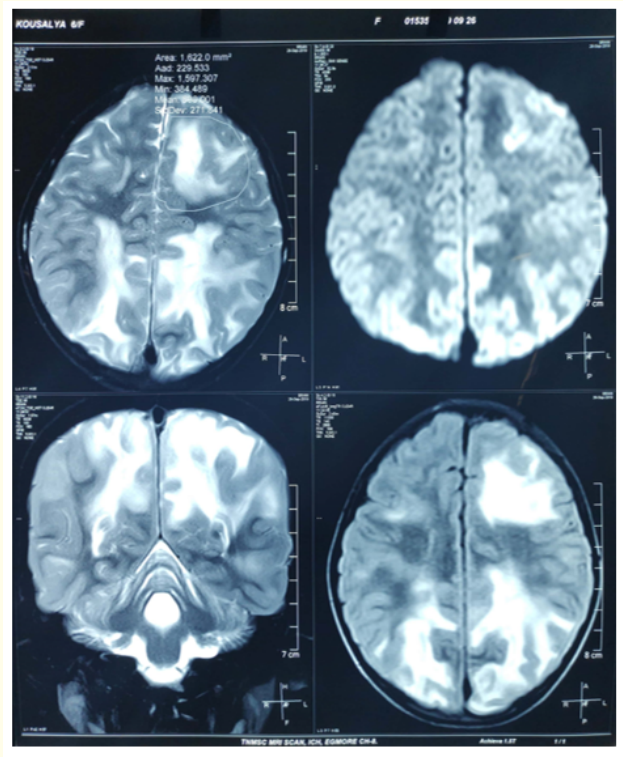

Figure 2: *MRI of brain T2 sequence showing hyperintense areas involving fronto-parieto-occipital region suggestive of extensive bilateral white matter edema.*

Discussion

Diabetic keto acidosis (DKA) is the commonest metabolic emergency in children with diabetes. Myocardial dysfunction is rarely reported in children with DKA. It may occur secondary to cardiac, pulmonary, metabolic or haemodynamic abnormalities. Severe acidosis, hypophosphataemia, hypokalemia, hypocalcaemia and hypomagnesaemia have been shown to contribute to poor myocardial performance and/or arrhythmias [4]. In this child, hypocalcemia could have contributed to myocardial dysfunction and it resolved following correction of the same.

The incidence of pancreatitis seems to be higher in adults than in children with DKA [5]. Significant but nonspecific elevations of amylase can be seen in DKA. Elevated lipase, traditionally thought to be more specific for pancreatitis, may also accompany DKA and does not necessarily denote concomitant pancreatic inflammation. Studies on pancreatic enzyme elevation in DKA suggest that pancreatic enzyme should be interpreted with caution if the child presents with abdominal symptoms or recur after correction of acidosis [6,7]. However, the acute pancreatic inflammation subsided with conservative management in this child.

Following recovery from DKA child developed hypertension, seizures and visual loss, typical of PRES. This was supported by characteristic findings on MRI. With antihypertensice therapy child had complete recovery. Cerebral edema commonly occurs during the first few hours of management of DKA and is the leading cause of morbidity and mortality in children presenting with DKA [1,8]. Encephalopathy occurring during DKA therapy could be due to shock, cerebral edema, severe acidosis, central venous thrombosis, Thrombocy-

topenia associated multi organ failure (TAMOF), Thrombotic thrombocytopenic purpura (TTP), mucormycosis, hypoglycemia and PRES. Encephalopathy due to cerebral edema is predominantly osmotic while in PRES it is likely to be vasogenic edema and the later occurs after recovery in DKA and has a favourable outcome. Since this child had recovered from cerebral edema and other metabolic parameters were stable, vision loss with severe hypertension was attributed to PRES. Sudden visual loss can occur in children with diabetes following PRES, mucormycosis, transient ischemic attacks, co-existing migraine and occipital seizures. Literature search revealed few case reports of PRES in children with DKA. Rapid resolution can be seen on correcting the underlying cause precipitating PRES.

Endothelial injury secondary to hypertension and dysfunction caused by excessive circulating inflammatory cytokines are postulated to produce vasogenic edema leading to PRES in DKA [1,9]. The metabolic crisis of DKA and its treatment, can lead on to increased proinflammatory cytokines and there is upregulation of vascular endothelial growth factor, both of which can lead to increased vascular permeability seen in PRES [10,11]. Since this child had AKI, underlying electrolyte imbalance could also be a contributary factor. Though, PRES indicates posterior segment involvement, brain edema can involve more anterior and entire region as noticed with this child [1]. Children with PRES may need to be evaluated for autoimmune disorders like hypothyroidism and systemic lupus erythematosus.

Multiple factors could have led to the development of PRES in this child, enhanced by the metabolic derangements in DKA and postulated indirect effects of electrolyte imbalance on vascular permeability. As witnessed in this child, one can anticipate complete neurological recovery within a few days to week in children with PRES.

Conclusion

It is essential to monitor for development of clinically apparent brain injury in children undergoing treatment for DKA. Cerebral edema usually develops within 24 hours of initiating treatment while late development of encephalopathy requires scrutinizing and PRES should be considered in differentials. Children swiftly recover on correcting the underlying precipitating cause of PRES.

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Competing Interest

None stated.

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