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Case Report

Severe diabetic ketoacidosis complicated with severe dyslipidemia, cerebral edema and acute kidney injury in a pediatric girl with type 1 diabetes mellitus: a case study

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ABSTRACT

Diabetic ketoacidosis (DKA) is a life-threatening acute metabolic complication occurring in patients with type 1 diabetes, due to an insulin deficiency. Moderate hypertriglyceridemia is commonly observed in DKA but severe hypertriglyceridemia with a triglyceride level exceeding 10 g/l is very rarely reported. Acute kidney injury (AKI) is a serious condition which still carries a mortality of around 50%. Cerebral edema is a devastating complication of DKA which is leading cause of diabetes-related death in the pediatric population. Newly diagnosed diabetes, younger age, first episode of DKA, severity of DKA at presentation, and administration of bicarbonate are predictive of cerebral edema in DKA. We present a case of 8-year-old girl who presented with severe DKA, whose clinical course was complicated by renal failure, severe dyslipidemia and cerebral edema.

Keywords: Diabetic ketoacidosis, Renal failure, Severe dyslipidemia

INTRODUCTION

Diabetic ketoacidosis (DKA) is a common and life threatening complication of uncontrolled setting of depleted insulin availability, which creates an acidic environment from the production of β-hydroxybutyric acid and acetoacetic acid.[1] DKA has been linked to several devastating metabolic derangements including osmotic diuresis, depletion of intracellular potassium, accumulation of toxic ketoacids, and dysregulation of sodium hydrogen exchange rmechanisms.[2,3] A destructive consequence secondary to these abnormalities is cerebral edema that is more common in pediatric patients than adult population. Cerebral edema results in poor outcomes with mortality occurring in 21-25% of patients and neurological morbidity occurring in 15-26% of patients.[4] Acute kidney injury (AKI) is another rare but potentially lethal disorder in children with DKA with an estimated mortality of about 50%. The poor outcome of acute kidney injury associated with DKA underlines the importance of early recognition of acute kidney injury and early initiation of renal replacement therapy. Severe hypertriglyceridemia (TG>1,000 mg/dl) is another rare complication found in pediatric DKA patients. Mild to moderate elevations of triglycerides are often seen during states of insulin deficiency such as diabetic ketoacidosis (DKA) but severe hypertriglyceridemia is rare manifestation. Insulin is required for lipoprotein lipase (LPL) activity that hydrolyzes and degrades triglycerides carried by chylomicrons and very low- density lipoproteins. Severe hypertriglyceridemia presents with “milky” plasma in the pediatric population.[5] We are reporting this case to discuss

the DKA as a cause of severe dyslipidemia which don't require medical treatment other that glycemic control.

CASE REPORT

8 years old girl child presented to pediatric emergency department with complaint of polydipsia and polyuria for last 15 days and altered consciousness for last 2 days. No family history of dyslipidemia was reported. For these complaints she took symptomatic treatment from local pediatrician and referred to us for further management as the condition was worsening. On admission she had gasping respiration and altered sensoruim with GCS score 6/15. Vital signs revealed body temperature of 38°C, pulse rate 122/min, respiratory rate 34/min with Kussmaul pattern, and blood pressure 116/94 mmHg. She was intubated and shifted on mechanical ventilation with neuroprotective measures. Blood gas analysis show Blood sugar level 699 mg%, blood pH 6.6, pCO_2 14.4 mmHg, HCO_3- 3.4, and BE- 20.5 meq/l, along with 3+ ketonuria; so management was started on the line of Severe diabetic ketoacidosis with cerebral edema. Cerebral edema was diagnosed according to 1 major criterion (alteration and fluctuation of consciousness) and 2 minor criteria (lethargy and diastolic blood pressure >90 mmHg). CT of the brain was not performed due to the unstable clinical condition of our patient. Blood sample turned milky within seconds, so lipid profile was done which show severe dyslipidemia with total cholesterol of 782 mg% and triglyceride level of 10680 mg%.

Patient had no abdominal pain and serum amylase was 52 IU/l. Therefore, acute pancreatitis was excluded. We have to analyze blood gas samples within seconds and we were unable to get other blood reports as the serum turned milky every time for next few days. Baby start to improve gradually in terms of DKA but on day 2 of admission urine output started to decrease and by day 3 of admission complete renal shutdown occurred. In view of acute renal failure Peritoneal dialysis was started which was continued for next 6 days; after which urine output start to improve. On day 4 of admission baby was extubated on HHHFNC and weaned to room air by day 6. By day 7 of admission lipemic serum start to improve and we were able to get actual blood reports. Triglyceride level was reduced to 298 mg/dl within 8 days of admission Lipid profile improved without any specific treatment and renal function tests became normal. Hb A1c level was 16 with normal thyroid profile. She was discharged on day 15 of admission on subcutaneous insulin and dietary modifications. Why this case was unique: first, child had severe diabetic ketoacidosis with cerebral edema and respiratory failure; for which fluid titration is very difficult. In this case baby also had renal failure simultaneously which further made decision making difficult. Second, even in severe diabetic ketoacidosis; low blood pH of 6.6 is seen rarely. Third, diabetic ketoacidosis and acute renal failure make electrolyte imbalance in opposite directions. As we have to supplement potassium despite renal failure due to hypokalemia in this patient. Last, for about 1 week all decision making was clinical as serum was lipemic and we were able to get only blood gas analysis; which further made decision making difficult.

Figure 1: Lipemic serum.

DISCUSSION

Diabetic ketoacidosis is an end result of abnormal metabolism of carbohydrate, protein, fat, and derangement of fluid and electrolyte homeostasis. There manifestations are caused by absolute decrease in the net effective action of circulating insulin. As counter-regulatory response to insulin deficiency; stress hormones such as glucagon (causing increased glycogenolysis), epinephrine, cortisol, and stress hormone are elevated. This combination leads to the increased production of non-esterified fatty acids (NEFA) and glycerol from breakdown of triglycerides in DKA. Glycerol is used as a substrate for gluconeogenesis and the great amount of NEFA results in the production of ketone bodies.

The clearance of ketone bodies is impaired due to low insulin concentrations, increased glucocorticoids, and decreased peripheral glucose utilization. The buffer capacity of bicarbonate is limited and when this capacity is exhausted, metabolic acidosis occurs.[6] Hypertriglyceridemia is one of the rare complication at the time of initial presentation of DKA and has been reported rarely in the pediatric population.[7,8] Severe hypertriglyceridemia, defined as triglyceride level greater than 1,000 mg/dl (11.3 mmol/l), has been found in about 8% of the adult population presented with DKA, but data on the pediatric population is limited.[7] Severe hyperlipidemia can increase the risk of pancreatitis, which has been seen in pediatric patients in DKA. The pathophysiology of hypertriglyceridemia in DKA is poorly understood. It may be related to secretion of free fatty acids from adipocytes in the setting of severe insulin deficiency.[7,8] Lack of insulin action, activates lipolysis in adipose tissue stores in body. This results in free fatty acid

(FFA) formation and increases in VLDL formation by the liver.[9]

In addition to this, insulin normally inhibits ApoC-III expression, which plays a major role in inhibiting lipoprotein lipase (LPL) and hepatic lipase (HL). Insulin deficiency results in decreased hydrolysis and delayed VLDL-TG clearances from plasma. As a result, ApoC-III increases with a subsequent increase in plasma TG level. It has been suggested by many authors that patients presented with lipemic serum and severe elevations in triglycerides (>1,495 mg/dl, >16.9 mmol/l) should be considered for further screening for lipid metabolism and structural abnormalities.[9] Mild to moderate hypertriglyceridemia is common during episodes of DKA. However, severe hypertriglyceridemia which is defined as a TG level >2,000 mg/dl, is rare. Although morbidity is <1%, clinicians should be aware about devastating consequences such as acute pancreatitis or lipidemia retinalis are possible during treatment of DKA in these patients.

Severe hypertriglyceridemia causes pseudohyponatremia or pseudonormoglycemia due to laboratory interference, which may lead to delay of proper management. Frier et al suggested that if serum triglyceride concentration exceeds 2,500 mg/dl, measured electrolyte can decrease by over 5% because of the intracellular movement of serum lipid components. Treatment of hypertriglyceridemia include management of episode of diabetic ketoacidosis with several days of intravenous insulin infusion with other supportive treatment. In severe cases with comorbidities or refractory cases, plasmapheresis is an option for management of hypertriglyceridemia.[7] Our patient also had cerebral edema at the time of admission. The association between severe hypertriglyceridemia and cerebral edema is unclear. The hypothesized mechanism is that hyperviscosity due to extremely high TG level likely causes decreased cerebral blood flow, which may correlate with cerebral edema.[10] Yuen et al found that severe dehydration and hypertriglyceridemia aggravated cerebral hypoperfusion, which had the effect of worsening cerebral edema.

CONCLUSION

There is limited data on the effects and therapy of severe hypertriglyceridemia in pediatric DKA patients and continued research is needed. Appropriate management of DKA with hypertriglyceridemia includes intravenous fluid and insulin administration according to DKA guideline, because the major mechanism of hypertriglyceridemia is insulin deficiency.

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