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Severe hypertriglyceridemia: A rare complication of diabetic ketoacidosis in a 3-year-old with SARS-CoV-2 infection

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ABSTRACT

Introduction: Children commonly present in diabetic ketoacidosis (DKA) secondary to Type 1 diabetes mellitus. Electrolyte imbalances and cerebral edema are common complications in the pediatric age group; however, patients may also have additional metabolic disturbances such as hyperlipidemia. We report a case of a pediatric patient with new-onset type 1 Diabetes Mellitus (DM) and DKA complicated by severe hypertriglyceridemia with recent exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Case presentation: A three-year-old male noted to be SARS-CoV-2 positive, presented with hyperglycemia, metabolic acidosis, and ketosis consistent with DKA. Patient was later found to have severe hypertriglyceridemia (greater than 5680 mg/dL). He was managed with intravenous (IV) fluids and IV insulin replacement with improvement of triglycerides.

Conclusion: Severe hypertriglyceridemia in DKA, though rare in the pediatric population, responds very well to IV insulin therapy. This case also highlights possible need for early lipid screening in DKA patients with SARS-CoV-2 positive status.

1. Introduction

Diabetic Ketoacidosis (DKA) is a complication that is seen in insulin-dependent diabetes mellitus patients. The cause of DKA is due to insulin deficiency, which leads to hyperglycemia, ketosis and acidosis. This insulin deficiency leads to an activation of counter-regulatory hormones, namely cortisol, growth hormone, glucagon as well as catecholamines. These counter-regulatory hormones stimulate lipolysis and proteolysis, hepatic glucose production as well as oxidation of fatty acids to ketone bodies [1]. Diagnostic criteria for DKA include hyperglycemia with blood glucose >200 mg/dL (11 mmol/L), metabolic acidosis with venous pH < 7.3 or serum bicarbonate <15 mEq/L (15 mmol/L), and the presence of ketones in the blood or urine. Complications of DKA include cerebral edema, peripheral venous thrombosis, rhabdomyolysis, and pulmonary edema [2].

Lipid derangements, specifically severe hypertriglyceridemia (TG > 1000 mg/dL), is another potential but rare complication in patients with DKA due to insulin deficiency. This severe hypertriglyceridemia puts these patients at increased risk of acute pancreatitis that increases patient morbidity and mortality [3]. However, this is rarely seen in the

pediatric population.

Here, we report a case of a 3-year-old male with new onset type 1 diabetes mellitus in DKA, who was subsequently found to have severe hypertriglyceridemia.

2. Case description

A 3-year-old male was sent to the emergency department (ED) from his pediatrician's office with a one week of increased fatigue, polyuria, and polydipsia, necessitating evaluation for new onset diabetes mellitus. His past medical history was significant for bilateral tympanostomy tube placement for recurrent otitis media with effusion, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection 11 days prior to presentation. In the ED, his vital signs were significant for temperature of 98° F, heart rate of 171 beats per minute, respiratory rate of 33 breath/min, and arterial oxygen saturation of 100% in room air. On physical exam, he was irritable and crying with normal mental status. He did not have any rash or show any signs of respiratory distress. His point of care test (POCT) glucose was 541 mg/dL, and POCT beta ketones were 5.2 mmol/L. A venous blood gas was consistent with

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metabolic acidosis (pH 7.19, HCO₃ 11.9) and urine was positive for glucose and ketones. Clinical picture was consistent with acute DKA. Initial management with intravenous (IV) fluids was started in the ED.

Other laboratory results were significant for hyponatremia with a sodium level of 126 mmol/L, but chloride level and anion gap could not be reported as absorbance was too high. The test for SARS-CoV-2 infection by polymerase chain reaction (PCR) resulted positive.

After initial management in the ED, the patient was admitted to the pediatric intensive care unit (PICU) for further management with IV insulin drip at 0.1u/kg/hr and IV fluids.

Repeat laboratory tests obtained 4 hours after starting insulin drip were significant for sodium level of 119 mmol/L, chloride level of 99 mmol/L, bicarbonate level of 13 mmol/L and an anion gap of 7 mmol/L. Patient's metabolic acidosis slowly improved with decreasing ketone levels. Given the concerns of decreasing sodium levels, despite hydration with normal saline and improving glucose levels (Glucose: 173 mg/dL), repeat lab work was sent on day 2 of admission. After labs were sent, the PICU team was contacted by the lab stating that the patient's blood sample for the basic metabolic panel was noted to be "thick and milky" and due to this, they could not process the sample. Though serum osmolality could not be done, the milky color of sample with low sodium levels prompted PICU to do a lipid panel, which revealed a triglyceride level >5680 mg/dL, total cholesterol 513 mg/dL, High-density lipoprotein (HDL) 18 mg/dL, Low-density lipoprotein (LDL) 33 mg/dL. Given the very high triglyceride level, there was concern for pancreatitis and levels of serum amylase and lipase were checked which were noted to be normal (Amylase: 35 U/L; lipase: 89 U/L).

Although the anion gap and metabolic acidosis normalized in about 24 hours on IV insulin infusion, hypertriglyceridemia was still persistent. Given the patient's young age, a decision was made to continue the IV insulin drip with close monitoring for hypoglycemia. Serum triglycerides levels slowly improved and came down to 312 mg/dL over 52 hours. After approximately 60 hours of IV insulin, the patient was eventually transitioned to subcutaneous (SQ) insulin therapy. Triglyceride levels continued to improve after the transition to SQ insulin with the lowest triglyceride level being 238 mg/dL. Patient was subsequently transferred to the general pediatric floor, where the family underwent diabetic education, and the patient was ultimately discharged home on a regimen with short- and long-acting insulin. Patient had antibody testing indicating that the patient had Type 1 DM with an elevated glutamic acid decarboxylase 65 antibody level of greater than 250 IU/mL and elevated insulin autoantibody level of greater than 50.0 U/mL. Patient has continued to do well in his outpatient follow-up and has maintained good glycemic control.

3. Discussion

Hypertriglyceridemia is a common lipid abnormality that can be primary in nature or secondary to other causes such as obesity, metabolic syndrome, alcohol, renal disease, pregnancy, and diabetes [4]. According to the Endocrine Society's guidelines, severe hypertriglyceridemia is classified as a triglyceride level of >1000 mg/dL, and very severe hypertriglyceridemia >2000 mg/dL. Severe hypertriglyceridemia has only been found in 8% of the adult population with DKA, with limited documented pediatric cases [5]. This case demonstrated an unusual case of a pediatric patient with new onset type 1 DM in DKA presenting with severe hypertriglyceridemia. In our patient, it was the unexplained hyponatremia and high turbidity with the milky color of the sample that led to measurement of the lipid profile. A normal serum osmolality (though not measured in our patient) with low sodium levels, unexplained by the level of blood glucose, should raise suspicion for hypertriglyceridemia, due to the inaccuracy of indirect potentiometry [6].

The postulated mechanism of hypertriglyceridemia in DKA involves activation of lipolysis of adipose tissue in the setting of insulin deficiency, causing the release of free fatty acids with subsequent

acceleration of the formation of very low-density lipoprotein (VLDL) by the liver. In addition, insulin deficiency is associated with reduced activity of lipoprotein lipase in peripheral tissues, the enzyme responsible for triglyceride metabolism, causing reduced clearance of VLDL and chylomicrons from the plasma thus resulting in hypertriglyceridemia. Conventional treatment includes IV fluids and insulin replacement, as insulin deficiency is the primary mechanism of hypertriglyceridemia. In one literature review, plasma triglyceride levels were found to be reduced to less than 500 mg/dL within 3–17 days in most cases [3,5,7]. In our patient, triglyceride level of >5680 mg/dL was effectively lowered by administering IV insulin to 312 mg/dL within 2–3 days.

Patients with severe hypertriglyceridemia are at risk of additional comorbidities including lipemia retinalis and pancreatitis. Lipemia retinalis is a complication that can be found in up to 23% of patients with severe hypertriglyceridemia (>2000 mg/dL). These patients have fundoscopic changes due to changes in retinal blood vessels [8]. The treatment of lipemia retinalis involves decreasing triglyceride levels down to <500 mg/dL [9]. Therefore, patients with severe hypertriglyceridemia warrants a fundoscopic exam to screen for this. Pancreatitis occurs in about 14% of patients with hypertriglyceridemia. The cause of the pancreatitis is due to the breakdown of triglycerides by pancreatic lipase to free fatty acids that become toxic to the pancreas [10]. Diabetic ketoacidosis can also increase the risk of pancreatitis due to hypertriglyceridemia [11]. In addition, there have been some reports showing an association between COVID-19 and pancreatitis [12]. Therefore, patients with these risk factors should be screened for pancreatitis with amylase and lipase levels.

The cause of the severe hypertriglyceridemia seen in our patient could not be ascertained. The patient did not have a family history of hyperlipidemia. There have been documented accounts of severe hypertriglyceridemia seen in adult COVID-19 patients [13]. Children with current or recent COVID-19 infection are predominantly asymptomatic, but hypertriglyceridemia is observed in up to 70% patients with MIS-C [14]. Our patient was still positive with SARS-CoV-2, 11 days after his initial positive test prior to admission, and he therefore did not fulfill diagnostic criteria for MIS-C. Whether SARS-CoV-2 exacerbated the hypertriglyceridemia that is associated with DKA is difficult to ascertain and requires further investigation. However, given the possibility that this could be a cause of this patient's severe hypertriglyceridemia, this is another reason for COVID-19 vaccinations of parents and caretakers and continuing other preventive measures for COVID-19. At the time of writing this case report, there has not been any documented cases that could link high triglyceride levels to exposure of SARS-CoV-2 virus in the pediatric age group with type-1 DM.

Although the American Diabetes Association recommends that a lipid screening be done after glycemic control is achieved, this case illustrates that lipid profile should be considered in patients with new onset DM [15]. This is especially important in a patient with unexplained hyponatremia that is not improving with treatment with normal osmolality. The potential role of SARS-CoV-2 infection as a cause of severe hypertriglyceridemia in Type 1 DM needs to be further studied.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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