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Case Report

Diabetic Ketoacidosis Induced 'Terrible Triad' Associated with Seizures and Acute Renal Failure: A Rare Case Report

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Abstract

We report a case of diabetic ketoacidosis with a severely elevated triglyceride level (25,585 mg/dL) complicated by acute pancreatitis, renal involvement, and generalized seizures. The proposed mechanism is triglyceride excess due to increased lipolysis, resulting in the formation of excess free fatty acids. A 17-year-old male patient came to the emergency department with abdominal pain, headaches for 2 days, lethargy, and Kussmaul breathing. Diabetic ketoacidosis with several complications was diagnosed. The objective of this case report is to present and describe the clinical features, laboratory investigations, case management, and natural course of hypertriglyceridemia in DKA.

Key words: diabetes mellitus; hypertriglyceridemia; diabetic ketoacidosis; acute pancreatitis

Introduction

An acute metabolic complication known as diabetic ketoacidosis (DKA) primarily affects people with type 1 diabetes mellitus [1]. Type 1 diabetes mellitus results from the destruction of insulin-producing β-cells in the pancreatic islets of Langerhans [2].

DKA is the result of absolute or relative insulin deficiency combined with counter-regulatory hormone excess (glucagon, catecholamines, cortisol, and growth hormone). The decreased ratio of insulin to glucagon promotes gluconeogenesis, glycogenolysis, and ketone body formation in the liver [3]. In DKA, insulin deficiency activates lipolysis in adipose tissue, releasing increased free fatty acids, which accelerates the formation of VLDL in the liver. Additionally, decreased removal of VLDL from the plasma by peripheral tissue lipoprotein lipase results in hypertriglyceridemia [4]. DKA-induced hypertriglyceridemia is a rare cause of acute pancreatitis, which accounts for around 4% of cases [5]. This case involves DKA-induced severe hypertriglyceridemia complicated by acute pancreatitis, acute renal involvement, and generalized seizures.

Case Report

A 17-year-old boy presented to the hospital with abdominal pain, headache for two days, lethargy, and Kussmaul breathing for the last few hours. The patient was admitted to the ICU for lethargy and severe respiratory distress. The patient was put on ventilator support. Finger stick blood glucose level was more than 500 mg/dL; hence a probable diagnosis of diabetic ketoacidosis (DKA) was made. Glasgow Coma Scale score was 4 (E1M2V1), so he was immediately intubated, commenced on ventilator support, and management of shock was started. Aggressive intravenous (IV) fluids and injection insulin were started after collecting blood samples, as per BSPED guidelines for DKA 2020. Initial laboratory findings were ABGA (pH 6.9, $PaCO_2$ 21 mmHg, PaO_2 93 mmHg, HCO_3^- 4 mM/L) which was suggestive of severe metabolic acidosis. Normal saline (NS)bolus of 10 ml/kg was given along with bicarbonate correction. IV antibiotics were started for suspected sepsis. After the initial bolus of 20 mL/kg, the patient was started on noradrenaline for low diastolic blood pressure. Blood investigation reported leukocytosis with a triglyceride (TG) level of 25,585 mg/dL, serum glutamic pyruvic transferase (SGPT) 70.4 U/L, creatinine 1.8 mg/dl with CRP of 42.9 mg/dL. Serum amylase was 394 U/L which implied that the patient had acute pancreatitis.

The patient developed generalized seizures, hence fosphenytoin was administered (20 mg/kg/dose). However, he had persistent seizures, so needed levetiracetam (40 mg/kg/dose) loading dose was dispensed. A neurologist was consulted for the same, who advised an MRI brain which revealed a small acute non-hemorrhagic infarct in the right half of the midbrain without mass effect or midline shift. Electroencephalogram (EEG) report showed abnormal diffuse slow background activity suggestive ofencephalopathy. The patient was continued on fosphenytoin (6 mg/kg/day) and levetiracetam (40 mg/kg/day) maintenance doses. The laboratory

parameters were monitored throughout admission (Table 1). On the third day of hospitalization, a nephrologist was consulted due to bilateral mild renal involvement seen on abdominal ultrasonography and for rising serum creatinine and urea levels. A hemodialysis catheter was inserted, and hemodialysis was initiated and continued for four cycles over a week. The TG was 9500 mg/dL, total leukocyte count was 6270 /$mm^{3.}$ On the fifth day of hospitalization, the ABGA revealed a normal pH and normal PaO_2 and $PaCO_2$. On the seventh day of hospitalization, the patient was weaned from the ventilator and kept on low-flow oxygen for the next 4 days. The TG level had returned to a normal level of 135 mg/dL.

Parameters	Reference values	Initial	After 7	After 12	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 14	Day 21
Serum Triglycerides (mg/dL)	<150	25585	-	-	16600	9500	7500	-	-	135	-	-
Total Cholesterol (mg/dL)	<200	1277	-	-	1250	-	844	-	-	-	-	-
Serum Urea (mg/dL)	5.0-20	28.3	-	-	-	149	119	159	215	195	73.5	-
Serum Creatinine (mg/dL)	0.6-1.2	1.8	-	-	-	4	4.3	5.1	5.8	6.22	1.25	-
Serum Amylase (U/L)	40-120	394	-	-	-	-	93	-	-	-	-	-
pH	7.35-7.45	6.9	7.06	7.1	7.2	7.27	7.28	7.44	7.47	-	-	-
$PaCO_2$ (mmHg)	38-42	21	21	17	21	16	14	17	28	-	-	-
PaO_2 (mmHg)	75-100	93	128	128	138	127	112	138	113	-	-	-
HCO_3^- (mEq/L)	22-28	4	6.5	5.4	8.6	7.6	6.6	15.5	19.9	-	-	-
Total Leukocyte Count (/mm^3)	4000-11,000	19120	-	-	-	6270	4230	-	-	9210	10430	7960
Hemoglobin (g/dL)	13.3-16.6	10.7	-	-	-	9	9.2	-	-	9.2	7.3	8.2
Na^+ (mEq/dL)	135-145	126	-	-	139	146	155	151	152	152	147	-
K^+ (mEq/dL)	3.6-5.2	7.5	-	-	3.6	3	4.3	4.2	4.5	4.6	2.9	-
Serum Acetone (mmol/L)	<0.6	72	-	-	-	5	-	-	-	-	-	-

Table 1: Sequential Laboratory Parameters

Physiotherapy was started during the hospital stay. After [3] days, feeding via Ryles tube was started and was gradually upgraded. The blood culture remained sterile after [5] days of incubation.

An endocrinologist was consulted and the child was shifted to subcutaneous regular insulin injection. Repeat blood investigations showed improvement in serum creatinine levels. The patient developed melena episodes, so Packed Cell Volume was transfused.

The patient was tolerating the management well, so physiotherapy was stopped and he was discharged after 21 days of admission. The patient and his parents were taught how to administer insulin using an insulin pen injection.

Discussion

This case report describes a patient presenting with symptoms consistent with diabetic ketoacidosis and acute pancreatitis. Blood reports confirmed hypertriglyceridemia and severe metabolic acidosis. Milky blood (Fig.1) as described by Chaurasiya et al.[6], shows a clear supernatant layer of triglycerides above the cellular components of blood. The patient's clinical course was complicated by generalized seizures, an MRI suggestive of a small acute non-hemorrhagic infarct in the right half of the midbrain without mass effect or midline shift, and a USG suggestive of bilateral mild renal involvement. In this patient, hypertriglyceridemia was well controlled with insulin without lipid-lowering agents. However, in severe hypertriglyceridemia, Furuya T et al. [7] recommended plasmapheresis to avoid severe adverse effects.

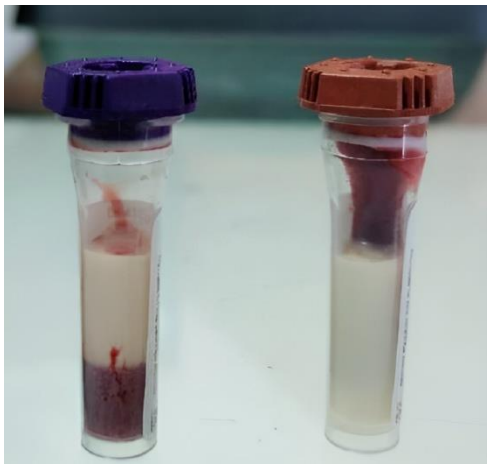

Figure 2: Hyperlipidemic blood sample on the day of admission

Diabetic Ketoacidosis is an acute severe complication of Type 1 diabetes mellitus. DKA can be accompanied or complicated by the presence of hypertriglyceridemia and pancreatitis. This is known as the 'Terrible Triad' or 'Enigmatic Triad' which can be an unusual presentation of Type 1 and Type 2 diabetes mellitus [8]. The actual trigger is not known, but after onset, it creates a 'domino effect' [9]. The triad can lead to a continuous loop of events (Figure.2).

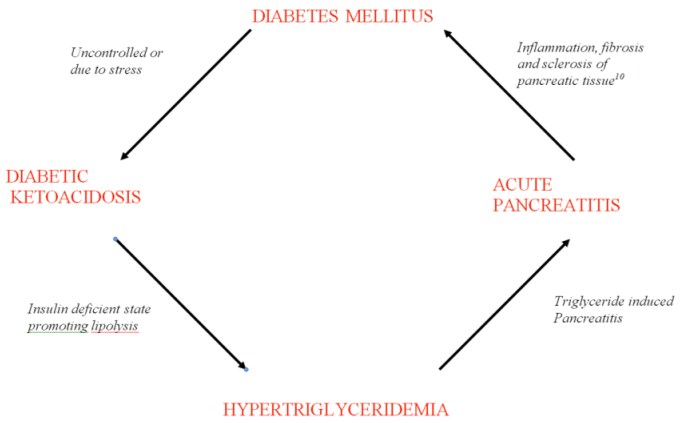

Figure 2: Complex interrelationship between the Terrible Triad

While one case reports Hypertriglyceridemia to be the trigger of Acute Pancreatitis which then causes DKA1 [1], in another case DKA is suggested to be the cause of hypertriglyceridemia and acute pancreatitis [12].

Several neurologic deficiencies have been associated with DKA, including cerebral edema with increased intracranial pressure resulting in a coma; partial and generalized seizures; and cerebrovascular occlusive disease resulting in motor and/or sensory dysfunction [13]. Neurological deterioration during an episode of DKA is usually assumed to be caused by cerebral edema, but hemorrhagic infarction is an infrequent cause. During an episode of DKA, increased inflammation increases the risk of vascular disruption and also due to hyperglycemia and acidosis-induced oxidative injury [14]. Acute renal involvement in DKA is probably affected by multiple factors, but it is most likely due to hypotension and hypovolemia [15]. Myers et al [16] found an association between renal involvement and signs of cerebral injury with DKA.

To our knowledge, this is a very rare case involving the Terrible Triad and required immediate medical management for the control of DKA as well as hypertriglyceridemia.

Conclusion

We report a rare case of DKA with extremely high triglycerides complicated with acute pancreatitis, renal involvement, and a hemorrhagic infarct which was managed with fluids and insulin. Early diagnosis of the Terrible Triad helps in identifying the complications and proper management helps in preventing its long-lasting adverse effects. Further research into this triad is required to completely understand its pathophysiology and the effects it has on the human body.

References

1. Kitabchi AE, Nyenwe EA. (2006). Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinology and Metabolism Clinics. 35(4):725-751.
2. Culina S, Brezar V, Mallone R. (2013). Insulin and type 1 diabetes: immune connections. Eur J Endocrinol. 168(2):19-31.
3. Harrison's Principles of Internal Medicine, 21e Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. Loscalzo J, & Fauci A, & Kasper D, & Hauser S, & Longo D, & Jameson J(Eds.), Eds. Joseph Loscalzo, et al.
4. Hahn SJ, Park JH, Lee JH, Lee JK, Kim KA. (2010). Severe hypertriglyceridemia in diabetic ketoacidosis accompanied by acute pancreatitis: case report. Journal of Korean medical science. 25(9):1375-1378.
5. Fortson MR, Freedman SN, Webster PD. 3rd Clinical assessment of hyperlipidemic pancreatitis. (1995). *Am J Gastroenterol*. 90:2134-2139.
6. Chaurasiya OS, Kumar L, Sethi RS. (2013). An infant with milky blood: an unusual but treatable case of familial hyperlipidemia. Indian Journal of Clinical Biochemistry. 28(2) :206-209.
7. Furuya T, Komatsu M, Takahashi K, Hashimoto N, Hashizume T, Wajima N, Kubota M, Itoh S, Soeno T, Suzuki K, Enzan K. (2002). Plasma exchange for hypertriglyceridemic acute necrotizing pancreatitis: report of two cases. Therapeutic Apheresis. 6(6):454-458.
8. Denecker N, Decochez K. (2013). Poorly controlled type 2 diabetes complicated by an episode of severe hypertriglyceridaemia-induced pancreatitis. Case Reports.
9. Shaikh BH, Sohaib M, Alshantti R, Barerra F, Faridi FS, Murvelashvili N. (2018). Diabetic ketoacidosis and the domino effect. The American Journal of Case Reports.
10. Wynne K, Devereaux B, Dornhorst A. (2019). Diabetes of the exocrine pancreas. Journal of Gastroenterology and Hepatology. 34(2):346-354.
11. Donelli D, Morini L, Trenti C, Santi R, Arioli D, Negri EA. (2018). Plasma exchange for the treatment of transient extreme hypertriglyceridemia associated with diabetic ketoacidosis and acute pancreatitis. European Journal of Case Reports in Internal Medicine. 5(5).
12. Shaikh BH, Sohaib M, Alshantti R, Barerra F, Faridi FS, Murvelashvili N. (2018). Diabetic ketoacidosis and the domino effect. The American Journal of Case Reports.
13. Atluru VL. (1986). Spontaneous intracerebral hematomas in juvenile diabetic ketoacidosis. Pediatr Neurol 2:167-169.
14. Foster JR, Morrison G, Fraser DD. (2011). Diabetic ketoacidosis-associated stroke in children and youth. Stroke research and treatment.
15. Murdoch IA, Pryor D, Haycock GB, Cameron SJ. (1993). Acute renal failure complicating diabetic ketoacidosis. Acta Paediatr. 82(5):498-500
16. Myers SR, Glaser NS, Trainor JL, Nigrovic LE, Garro A, Tzimenatos L, Quayle KS, Kwok MY, Rewers A, Stoner MJ, Schunk JE. (2020). Frequency and risk factors of acute kidney injury during diabetic ketoacidosis in children and association with neurocognitive outcomes. JAMA network open. 3(12).

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