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CASE REPORT

Diabetic ketoacidosis associated with hypertriglyceridemia in the pediatric age group: a case report

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Diabetic ketoacidosis, Hypertriglyceridemia, Diabetes *mellitus*, type 1.

Abstract

Objective: Report a case of diabetic ketoacidosis (DKA) in the pediatric age group associated with hypertriglyceridemia. **Case Report:** Female patient, 13 years old, previously healthy, with abdominal pain, nausea, vomiting, lowered level of consciousness and hyperglycemia. Diagnosis of primary decompensation of type one diabetes *mellitus* with DKA was made. After collecting laboratory tests, a lipemic sample was identified and hypertriglyceridemia was confirmed. In addition to the DKA treatment, the patient required statin treatment with an improvement in lipid profile. During hospitalization, the patient did not present elevated levels of serum amylase or lipase or change in imaging tests that could suggest pancreatitis. **Comments:** The differential diagnosis between DKA associated or not with acute pancreatitis is challenging due to the overlapping symptoms and laboratory tests. DKA is a severe complication mainly related to type 1 diabetes *mellitus* and its association with other disorders can worsen the prognosis. There is a lack of data in the literature regarding the treatment of acute hypertriglyceridemia. As far as the authors are aware, this is the first Brazilian case report in the pediatric age group of DKA associated with severe hypertriglyceridemia.

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INTRODUCTION

Diabetic ketoacidosis (DKA) is considered a hyperglycemic emergency, and it can be potentially fatal when associated, mainly, with type 1 diabetes *mellitus* (T1D)[1]. The main signs and symptoms are dehydration, tachycardia, tachypnea, nausea, vomiting, ketone breath, abdominal pain, and decreased level of consciousness. Biochemical criteria for the diagnosis of DKA include hyperglycemia (serum glucose >200 mg/dL), serum pH <7.3 or serum bicarbonate <18 mmol/L, ketonuria, or ketonemia[2].

DKA is classified as mild (pH <7.3 or bicarbonate <18 mmol/L), moderate (pH <7.2 or bicarbonate <10 mmol/L), or severe (pH <7.1 or bicarbonate <5 mmol/L)[2]. In Brazil, about 20% of patients present DKA as the primary decompensation of T1D[3], with the most frequent complications being hypoglycemia, hypokalemia and hyperglycemia, followed by cerebral edema and hyperchloremic acidosis[1,2].

The association between DKA and acute pancreatitis has already been previously discussed in case reports and epidemiological studies, with an estimated prevalence of 2% in children and 11% in adults[3]. Epidemiological data in the pediatric age are scarce and not well established.

Several studies correlate DKA with hypertriglyceridemia, however, these episodes are also commonly associated with acute pancreatitis. It came to be called the "cryptic triangle", as its etiology is still not fully known, referring to the association between DKA, hypertriglyceridemia and pancreatitis, which is a rare and serious condition[4-7].

This report is about a case of DKA associated with severe hypertriglyceridemia (>7000 mg/dL), without association with acute pancreatitis. No other reports were found in the literature with such triglyceride values in the same age group.

CASE REPORT

A 13-year-old female patient, brown, from São Paulo, Brazil, was referred due to severe DKA and hypertriglyceridemia. Initially, she was evaluated in an emergency room at her hometown due to abdominal pain, for the past two days, associated with nausea and vomiting. She received the diagnostic hypothesis of acute viral gastroenterocolitis and was discharged with symptomatic treatment. She evolved with worsening vomiting, excessive sleepiness and dyspnea in the next day with the need to call the pre-hospital care service due to lowered level of consciousness (AVDI scale-responded to verbal stimulation), tachycardia, tachypnea and capillary blood glucose of 484 mg/dL, is referred to a secondary hospital. A severe DKA hypothesis was made (glucose serum of 354mg/dL, arterial blood gas pH 7.14, bicarbonate 2.1mmol/L and urine with ketones).

During exam collection, an intense lipemia was found in the serum, with a confirmed triglyceride dosage of 7110mg/dL. Serum amylase was in the normal range and PCR SARS-COV2 was not detected.

The patient received volume expansion, sodium bicarbonate and regular insulin at hometown. She was transferred for admission to a pediatric intensive care unit (PICU). On the admission, the patient was in regular general condition, dehydrated, sleepy, but reactive to calls and oriented, with a capillary blood glucose of 178mg/dL. Arterial blood gases showed metabolic acidosis with hypokalemia, hyperchloremia and hyperglycemia (Table 1). Figure 1 demonstrates high turbidity in the blood sample.

After 24 hours in the PICU, the DKA was solved, oral diet and subcutaneous insulin were initiated. Simvastatin was introduced after 48 hours with significant improvement in hypertriglyceridemia (652mg/dL) on the fifth day of hospitalization (Table 1).

The hypothesis of associated pancreatitis was ruled out through imaging exams.

The patient was discharged from the hospital after 16 days of hospitalization, with outpatient follow-up guidance, using simvastatin (20mg/day), NPH insulin (20IU/day) and regular insulin (17IU/day) in a basal-bolus regimen (0.8IU/kg/day).

During the outpatient follow-up, simvastatin was suspended after 3 months of use due to decreased triglyceride levels. Patient returned to medical evaluation after 1 year, due to pandemics, with a triglyceride dosage of 102mg/dL. During follow-up, evolved with normalization of triglyceride levels after 2 years of diagnosis (64mg/dL). Unfortunately, this patient is institutionalizes, therefore we do not have family history data.

Table 1. Evolution of lipidogram.

Laboratory tests (Reference Value)	Origin (External exams)	Day 1 (Admission)	Day 2	Day 11	Day 42	1 year later	2 years later
Triglycerides (RV: 0-90 mg/dL)	7.110	5.396	1.334	302	144	102	64
Total Cholesterol (RV: 0-170 mg/dL)		258	588	241	107		
High-density Lipoprotein (RV: > 45mg/dL) /			17	27	38		
Low-density Lipoprotein (RV: < 110 mg/dL)			151	154	40		

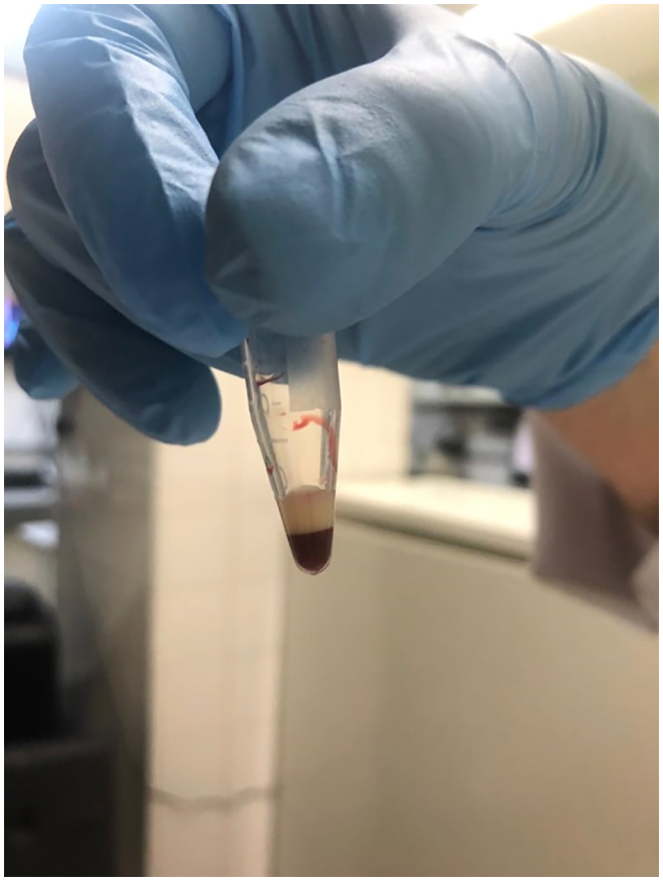


Figure 1. Lipemic serum sample.

DISCUSSION

Hypertriglyceridemia can induce acute pancreatitis and, therefore, to DKA by destroying pancreatic beta cells. However, it can also be a consequence of DKA, as the lack of insulin leads to an increase in triglycerides, which in turn could lead to acute pancreatitis[4,5,8]. It is known that the higher the serum triglyceride value, the higher correlation with the severity of pancreatic involvement[4,5]. The triad hypertriglyceridemia, DKA and pancreatitis are related to the increase in mortality and complications[6].

A study carried out at the State University of Campinas (UNICAMP) identified that 41% of the cases analyzed presented DKA as the first manifestation of T1D in the pediatric age group[7]. However, there are few reports in the literature about severe hypertriglyceridemia associated with DKA[9,10].

The association between DKA and hypertriglyceridemia occurs due to lack of insulin, leading to enlarged lipolysis, increased production of very-low-density lipoprotein (VLDL) by the liver due to increased hepatic fatty acid flow, which, in addition to ketogenesis, can be secreted as VLDL. In addition, VLDL clearance is decreased by inhibiting lipoprotein lipase activity, responsible for hydrolyzing triglycerides into fatty acids, in peripheral tissues[4,6].

Two main mechanisms for pancreatitis due to changes in lipid metabolism resulting from DKA are suggested: (a) fatty acids when carried by albumin are not toxic, but if they are in large quantities, endothelial lipase degrades the fatty acids and increases the pancreatic lysolecithin activity[11]; (b) chylomicrons would damage the distal pancreatic circulation, inducing ischemia and altering the acinar function, in addition to exposing the tissue to triglycerides and activating pancreatic lipase[12].

During the admission tests collection, the lipemic aspect of the blood alerted to the possibility of metabolic decompensation, and the results confirmed the diagnostic suspicion (Figure 1).

The reasons why some patients have such high levels of triglycerides are not fully understood. Some genetic mutations in the LPL, APOC2 and APOA5 genes have been identified as probable causes of some cases in adults[13], but there are still no data in the literature for the pediatric age group.

The differential diagnosis between DKA associated or not with acute pancreatitis is challenging, because of the overlapping of symptoms (nausea, abdominal pain, vomiting, poor general health) and the laboratory tests. It is known that DKA can lead to an increased pancreatic enzyme. In contrast, acute pancreatitis secondary to hypertriglyceridemia can present normal pancreatic enzyme values, requiring an imaging test for the diagnosis[4-6].

During the entire hospital stay, the patient did not present elevated levels of serum amylase or lipase that could suggest pancreatitis, with an important reduction in the level of triglycerides during evolution. Furthermore, the imaging exams showed no changes, ruling out the diagnosis of acute pancreatitis.

There is a paucity of data in the literature about treatment recommendations for acute hypertriglyceridemia, with most case reports using fibrates for handling it[9,11,14]. Carlesso et al, 2023, cites in the review article statins as the first choice of treatment[15]. There is a single Brazilian case report about an adult patient with comorbidities (type 2 diabetes *mellitus* and obesity) mild DKA and severe hypertriglyceridemia (11758 mg/dl)[9]. As far as the authors' knowledge, this is the first Brazilian case report in the pediatric age group of DKA associated with severe hypertriglyceridemia.

REFERÊNCIAS

1. Souza LCVF, Kraemer GC, Koliski A, Carreiro JE, Cat MNL, Lacerda L, et al. Diabetic ketoacidosis as the initial presentation of type 1 diabetes in children and adolescents: Epidemiological study in southern Brazil. Rev Paul Pediatr. 2020 [cited 2022 Sep 2]; 38:e2018204. DOI: https://doi.org/10.1590/1984-0462/2020/38/2018204. Available from: https://www.scielo.br/j/rpp/a/3TVhtphZTZzZGfCCdCHKpMs/?lang=en.

2. Glaser N, Fritsch M, Priyambada L, Reawers A, Cherubini V, Estrada S, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes. 2022;23(7):835-6. DOI: https://doi.org/10.1111/pedi.134063.

3. Lopes CLS, Pinheiro PP, Barberena LS, Eckert GU. Diabetic ketoacidosis in a pediatric intensive care unit. J Pediatr (Rio J). 2017; [cited 2022 Sep 2]; 93(2):179-84.: DOI: https://doi.org/10.1016/j.jped.2016.05.008. Available from: https://pubmed.ncbi.nlm.nih.gov/27770618/.

4. Bialo SR, Agrawal S, Boney CM, Quintos JB. Rare complications of pediatric diabetic ketoacidosis. World J Diabetes. 2015 Feb 15;6(1):167-74. DOI: https://doi.org.10.4239/wjd.v6.i1.167.

5. Timilsina S, Mandal A, Paudel R, Gayam V. Triad of Diabetic Ketoacidosis, Hypertriglyceridemia, and Acute Pancreatitis: Severity of Acute Pancreatitis May Correlate with the Level of Hypertriglyceridemia. Cureus. 2019; [cited 2022 Sep 8]; 11(6):e4930. DOI: https://doi.org/10.7759/cureus.4930. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6695235/.

6. Yagnik PJ, Desai PH, Modem VM. Hypertriglyceridemia with Acute Pancreatitis in Pediatric Diabetic Ketoacidosis: A Case Report. Cureus. 2019; [cited 2022 Sep 8]; 11(1):e3844. DOI: https://doi.org/10.7759/cureus.3844. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6411334/.

7. Simons-Linares CR, Jang S, Sanaka M, Bhatt A, Lopez R, Vargo J, et al. The triad of diabetes ketoacidosis, hypertriglyceridemia and acute pancreatitis. How does it affect mortality and morbidity? A 10-year analysis of the National Inpatient Sample. Medicine (Baltimore). 2019; [cited 2022 Sep 8]; 98(7):e14378. DOI: https://doi.org/ 10.1097/MD.0000000000014378. Available from: https://pubmed.ncbi.nlm.nih.gov/30762737/.

8. Castro L, Morcillo AM, Guerra-Júnior G. Cetoacidose diabética em crianças: perfil de tratamento em hospital universitário. Rev Assoc Med Bras. 2008; [cited 2022 Set 8]; 54(6):548-53. DOI: https://doi.org/10.1590/S0104-42302008000600021. Disponível em: https://www.scielo.br/j/ramb/a/zJS3C4cq5HD9r4SnMXLjqKb/.

9. Joustra ML, Raidt JJ, Droog F, Veneman TF. Diabetic Ketoacidosis, Hypertriglyceridemia and Abdominal Pain due to Acute Pancreatitis Complicated by Non-immune Haemolytic Anaemia. Eur J Case Rep Intern Med. 2020; [cited 2022 Sep 12]; 7(12):002085. DOI: https://doi.org/10.12890/2020_002085. eCollection 2020. Available from: https://pubmed.ncbi.nlm.nih.gov/33585328/.

10. Lucchetti G, Granero AL, Almeida LGC, Battistella VM. Hipertrigliceridemia grave na cetoacidose diabética: relato de caso. Arq Bras Endocrinol Metab. 2009; [citado 2022 Set 12]; 53(7):880-3. DOI: https://doi.org/10.1590/S0004-27302009000700013. Disponível em: https://www.scielo.br/j/abem/a/hw4PQZKzTX8kkHxhKrjDLcN/.

11. Stefansson H, Sigvaldason K, Kjartansson H, Sigurjonsdottir HA. Severely increased serum lipid levels in diabetic ketoacidosis - case report. Laeknabladid. 2017;103(7-8):331-333. DOI: https://doi.org/10.17992/lbl.2017.0708.146.

12. Fleiszig ZB, Quera R, Teller JP, Reisberg DO, Peralta JG. Heparina e insulina en el tratamiento de la pancreatitis aguda por hipertrigliceridemia. Experiencia en 5 casos. Rev Méd Chile. 2001; [cited 2022 Sep 12]; 129(12):1373-8. DOI: https://doi.org/10.1590/S0004-27302009000700013. Available from: https://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0034-98872001001200002.

13. Gan SI, Edwards AL, Symonds CJ, Beck PL. Hypertriglyceridemia induced pancreatitis: A case-based review. World J Gastroenterol. 2006; [cited 2022 Sep 17]; 12(44):7197-202. DOI: https://doi.org/10.3748/wjg.v12.

14. Oliva CP, Pisciotta L, Volti GL, Sambataro MP, Cantafora A, Bellocchio A, et al. Inherited apolipoprotein A-V deficiency in severe hypertriglyceridemia. Arterioscler Thromb Vasc Biol. 2005; [cited 2022 Sep 17]; 25(2):411-417. DOI: https://doi.org/10.1161/01.ATV.0000153087.36428.dd. Available from: https://pubmed.ncbi.nlm.nih.gov/15591215/.

15. Wang Y, Attar BM, Bedrose S, Trick W, Rivas-Chicas O, Simons-Linares CR, et al. Diabetic Ketoacidosis with Hypertriglyceridemia-Induced Acute Pancreatitis as First Presentation Of Diabetes Mellitus: Report Of Three Cases. AACE Clin Case Rep. 2017; [cited 2022 Sep 17]; 3(3):e195-9. DOI: https://doi.org/10.4158/EP161389.CR. Available from: https://www.sciencedirect.com/science/article/pii/S2376060520301760.

16. Carlesso GL, Azevedo GZ, Ton BS, Vieira TGE, de-Oliveira MCR, Pinasco GC. Dyslipidemia in childhood: A literature review. Resid Pediatr. 2023;3(1):819.