CASE REPORTS

PANCREATITIS AND DIABETIC KETOACIDOSIS IN AN ADOLESCENT TREATED WITH SERTRALINE

PANCREATE E CETOACIDOSE DIABÉTICA NUMA ADOLESCENTE TRATADA COM SERTRALINA

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ABSTRACT

Acute pancreatitis (AP) is a rare entity in pediatric age. Reports of AP in the context of diabetic ketoacidosis (DKA) have established the role of transient hyperlipemia as a consequent factor. Pharmacological etiology is responsible for 0.3−1.4% of AP cases, with no case reports of an association with the use of sertraline in the pediatric population to date. Herein is described the case of a 15-year-old girl with poorly controlled type 1 diabetes, taking sertraline for a depressive disorder, who developed AP associated with DKA. With this report, the authors intend to emphasize the importance of diagnosing AP in DKA setting. In addition, since the patient had normal serum triglyceride levels and no other risk factors for AP, it is hypothesized that sertraline may have been a triggering event in this context.

Keywords: acute pancreatitis; adolescent; diabetic ketoacidosis; sertraline; thyroiditis

RESUMO

A pancreatite aguda (PA) é uma entidade rara em idade pediátrica. Estão descritos casos clínicos que evidenciam uma associação entre PA e cetoacidozide diabética (CAD), postulando o papel da hiperlipidemia transitória como um fator consequente. A etiologia farmacológica é responsável por 0.3−1.4% dos casos de PA, não existindo até o momento casos descritos na literatura que associem a condição ao uso de sertralina na população pediátrica. Os autores descrevem o caso de uma adolescente de 15 anos de idade com diabetes mellitus tipo 1 mal controlada, medicada com sertralina devido a um transtorno depressivo, que desenvolveu PA associada a CAD. Com este caso, os autores pretendem enfatizar a importância do diagnóstico de PA no contexto de CAD. Adicionalmente, dado que a adolescente apresentava níveis séricos de triglicerídeos normais e nenhum outro fator de risco para o desenvolvimento de PA, especula-se que o uso de sertralina pode ter atuado como um evento desencadeante neste contexto.

Palavras-chave: adolescente; cetoacidozide diabética; pancreatite aguda; sertraline; tiroidite

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INTRODUCTION

Acute pancreatitis (AP) is a reversible pancreas inflammation. Despite increasing incidence over the last two decades, it remains an uncommon disease in pediatric age. AP has variable etiologies and can be secondary to several clinical conditions, namely biliary lithiasis, infection, pharmacotherapy, vascular pathology, and trauma, among others.\(^1\)\(^-\)\(^4\)

AP occurs in approximately 2% of children with diabetic ketoacidosis (DKA) and this association seems to be more frequent in cases of severe DKA.\(^5\)\(^-\)\(^7\) However, the association is controversial, with some authors referring to AP as a causative agent and others as a rare complication of DKA.\(^5\)\(^-\)\(^6\)

The pathogenesis of this association is still unknown. Transient hyperlipidemia (usually triglyceride levels greater than 1000 mg/dL) caused by excessive lipolysis from lack of insulin effect during DKA has been referred as a triggering factor for AP development.\(^5\)\(^-\)\(^7\) In absence of hypertriglyceridemia, co-occurrence of AP with DKA is uncommon.\(^5\)\(^-\)\(^6\)

Diagnosing AP in the context of DKA is challenging, since abdominal pain may be a concomitant symptom of both conditions. Additionally, in about 20–40% of DKA cases, non-specific amylase and lipase elevation is reported, which appears to be due to direct pancreas damage with enzymatic release, extra-pancreatic secretion, or decreased renal clearance.\(^5\)\(^-\)\(^7\)

It is acknowledged that AP can coexist with DKA. However, this association is rare in pediatric age and may be difficult to diagnose given symptom similarity between both pathologies, including abdominal pain, nausea, and vomiting. Nevertheless, its early detection is crucial for optimizing therapy and improving prognosis of both conditions.\(^5\)\(^-\)\(^7\)

The relationship between AP and DKA as a cause or consequence remains the subject of considerable controversy.\(^6\)

Isolated and non-specific elevation of serum pancreatic enzyme levels is relatively common in DKA patients, especially in the context of poor metabolic control with frequent hyperglycemia, but after DKA treatment initiation most patients do not have abdominal pain or delayed recovery.\(^5\)\(^-\)\(^7\)

In a prospective cohort study of 50 children with DKA, Haddad et al reported an elevation of amylase and/or lipase in 22 cases.\(^7\) The magnitude of lipase elevation seemed to be related to acidosis severity and advanced age.

In another prospective study of 100 consecutive episodes of adult DKA, Nair et al described an association between DKA and AP in at least 10–15% of cases.\(^6\) Moreover, hypertriglyceridemia was suggested as a possible factor associated with AP development in the context of DKA. Although drug-induced AP is uncommon, several drugs have been implicated as possible triggers of this acute inflammation, mainly in the adult population.\(^1\)\(^-\)\(^2\) Only two adult AP cases have been reported in the literature as associated with sertraline treatment.\(^3\) Antipsychotic-associated AP has been described in adults in association with several drugs, such as olanzapine, clozapine, quetiapine, and valproic acid.\(^11\) Moreover, the association between selective serotonin reuptake inhibitors (SSRIs), as sertraline, and AP in adults has been acknowledged by WHO.\(^2\)\(^-\)\(^10\) However, no cases have been reported of an association between sertraline intake and AP in children or adolescents. In Portugal, sertraline is not indicated in pediatric age, except in cases of adolescents with obsessive-compulsive disorder. Nonetheless, studies have shown that sertraline and other SSRIs have some efficacy and are generally safe in the treatment of adolescent depressive disease.\(^12\)

CASE REPORT

A 15-year-old girl with unmedicated lymphocytic thyroiditis and type 1 diabetes mellitus diagnosed at 3 years of age, taking multiple daily insulin injection regimens with a total daily insulin dose of 0.9 U/kg (50% corresponding to long-acting analogue) but with poor metabolic control due to non-compliance, was admitted due to DKA. Noteworthy, the patient had a severe DKA episode at the age of 9 requiring admission in a Pediatric Intensive Care Unit and two other hospitalizations since, due to moderate DKA. She had anti-nuclear antibodies persistently high for several years, but remained clinically asymptomatic. Her mother had systemic lupus erythematosus and had little family support due to conflicting parental relationship.

The girl started taking 50 mg of sertraline once a day for depressive disorder and four months later was admitted to the Emergency Department due to acute epigastric pain with dorsal irradiation, vomiting, prostration, and polydipsia. She referred nonadherence to insulin therapy and subsequent hyperglycemia in the previous two days. On physical examination, the girl was hemodynamically stable but dehydrated, with ketonic breath, and anicteric. She weighed 54.4 kilograms, was 156.7 cm high, and had a body mass index of 22.2 kg/m\(^2\). Laboratory study showed moderate metabolic acidosis (pH 7.1) with ketonemia 4.8 mmol/L, hyperglycemia (306 mg/dL), hemoglobin A1c 11.4%, C-peptide 0.01 ng/mL (normal range 1.1–4.4 ng/ml), leucocytes 14,800/ul with neutrophilia, C-reactive protein 0.84 mg/dL, AST 14,800/ul with neutrophilia, C-reactive protein 0.84 mg/dL, AST 98 U/L (normal range 4–27 U/L), ALT 528 U/L (normal range 4–23 U/L), total bilirubin 0.41 mg/dL (normal range 0.1–1.1 mg/dL), alkaline phosphatase 255 U/L (normal range 54–187 U/L), gamma-glutamyl transferase 86 U/L (normal range 5–61 U/L), total calcium 9.2 mg/dL (normal range 9.2–11 mg/dL), and normal renal function (creatinine 0.87 mg/dL, urea 34 mg/dL).

Treatment was initiated according to hospital protocol. However, due to the onset of fever and persistent abdominal pain, analytical study was repeated, revealing amylase 466 U/L (normal range 13–53 U/L), lipase 1230 U/L (normal range 13–60 U/L), and normal triglycerides (178 mg/dL). Abdominal ultrasonography was suggestive of acute pancreatitis, without individualized collections, and abdominal computed tomography confirmed absence of organized fluid collections.
The patient was admitted for moderate DKA associated with AP, stopped sertraline, and began a low-fat diet after fluid replacement for two days. During hospital stay, she gradually improved, both clinically and analytically (glycemia, ketonemia, metabolic acidosis, and amylase and lipase serum levels [85 U/L and 786 U/L, respectively]).

In AP etiological study, serologies (CMV, HVS I/II, EBV, Mycoplasma, Chlamydia, and legionella) were not suggestive of acute infection. Immunological study showed anti-nuclear antibodies 1/640 with large speckled pattern, negative anti-liver antigens, and negative extractable nuclear antigen antibodies.

Regarding lymphocytic thyroiditis, thyroid function deteriorated with positive anti-thyroid antibodies (TSH 12.78 uUI/ml; free T4 1.16 ng/dl; anti-tiroglobulin antibody 458 UI/ml, and anti-thyroid peroxidase 368.7 UI/ml). Previous thyroid ultrasonography showed a heterogeneous echostructure of the thyroid tissue and the patient was started on oral levothyroxine 0.025 mg/day during hospitalization. The girl had been taking sertraline four months before the AP episode and a clinical and analytical reversal was noticed after drug discontinuation. In addition, no risk factors for AP were identified, such as trauma, alcoholism, or lithiasis history.

Two months after discharge, the patient continues without sertraline and has normal serum amylase, lipase, and transaminases. However, she maintains poor metabolic control and hypothyroidism due to poor compliance, with hyperglycemia, HbA1c 11%, and TSH 11.25 uUI/ml.

DISCUSSION

AP is a rare but increasingly acknowledged entity in pediatric age. Despite the etiological study required for diagnosis, approximately 25% of cases are idiopathic, with no identified triggering factor. In the case described, no acute infectious agent or pancreatic malformation were identified and autoimmune and lipid profile were normal. Therefore, the authors hypothesize metabolic acidosis and daily 50 mg sertraline intake as possible risk factors for AP. Moderate DKA (pH 7.1) was observed in this teenager with a history of poorly controlled diabetes and frequent hyperglycemia. Diagnosis was established during investigation of the persistent abdominal pain and fever. Although triglyceride elevation is the main factor described in the literature for development of AP in DKA setting, in this case serum values remained normal.

Regarding the association of AP with pharmacotherapy, most data available in the literature comes from clinical cases reports, and hence most robust evidence is required to confirm this causal relationship. Few reports in the literature correlate AP with SSRIs. Regarding sertraline, only two cases establish its association with AP in the adult population, with no cases reported to date in pediatric age.

REFERENCES


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Received for publication: 14.06.2019
Accepted in revised form: 11.03.2020