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CASE REPORT

Two cases of decompensated diabetes with ketoacidosis in pediatric patients with COVID-19

Victoria Hernandez Girnys[1], Cesar Augusto Becci Silvério[1], Samanta Vieira Ferreira[1], Monique Maria Steffen[1], Andrea Sayuri Murata[1], Bianca de Oliveira Lima[1]

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Abstract

The pandemic caused by the new coronavirus (SARS-CoV-2) has caused diseases that manifests itself from flu-like symptoms of mild to severe intensity, to varied spectra of clinical presentations, involving different organs and systems. It is known that the association between diabetes and infections is very common, with diabetic ketoacidosis being its main acute complication. The authors report in this article two cases that suggest diabetic ketoacidosis (DKA) as the initial manifestation of COVID-19: two previously healthy patients, one 11 and the other 9 years old, admitted in a health unit with symptoms compatible with DKA, subsequently tested positive for coronavirus. This article discusses the importance of considering COVID-19 among the possible infectious causes of diabetes decompensation.

[1] Augusto de Oliveira Camargo Hospital/Leonor de Barros Camargo Foundation, Pediatrics Department - Indaiatuba - SP - Brazil.

Correspondence to:
Victoria Hernandez Girnys.
Hospital Augusto de Oliveira Camargo. Av. Francisco de Paula Leite, 399 1 - Jardim Santa Cruz, Indaiatuba - SP, Brasil.
CEP: 13344-700. E-mail: victoriagirnys@gmail.com

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INTRODUCTION

The novel coronavirus (SARS-CoV-2) outbreak started in the city of Wuhan, China, in December 2019, and propagated quickly around the world[1]. In March 2020, the World Health Organization (WHO) described the disease as a pandemic. The first death by the disease was recorded in Brazil on March 17, 2020.

The first systematic study to feature clearer answers about the disease was published on The Lancet on February 15 by authors from Yin-Tan Hospital in Wuhan, China. Forty-one patients diagnosed with COVID-19 in January 2020 were analyzed. Most were males (73%) and almost a third (32%) of the patients had chronic diseases, including diabetes (20%), hypertension (15%), and cardiovascular disease (15%)[2]. Subsequent studies have reported greater impact of the disease on individuals with chronic comorbidities such as diabetes mellitus[1,3,4].

The spectrum of clinical manifestations derived from coronavirus infection has been broadly discussed, and may range from mild flu-like symptoms to severe pneumonia, followed by respiratory failure and death[5]. In pediatric patients, the disease caused by SARS-CoV-2 has produced milder symptoms when compared to adults with the condition[5]. Atypical manifestations have also been described, including abdominal pain and/or diarrhea[6], acrocyanosis, lower-extremity ulcers, and skin alterations[7]. In April 2020, journal *Hospital Pediatrics* of the *American Academy of Pediatrics* published article "COVID-19 and Kawasaki Disease: Novel Virus and Novel Case," in which the authors described the case of a six-month-old patient diagnosed with and treated for Kawasaki Disease (KD) while with novel coronavirus disease[8].

In addition to the growing number of cases of disease by SARS-CoV-2 and studies developed to describe populations at risk, it is relevant to cite the increase in the number of children and adolescents with diabetes, obesity, and metabolic disorders in recent years[4]. The association between diabetes mellitus (DM) and infection has been often described to interfere with glucose management[3]. Pediatric patients with diabetes present with immune disorders, which heighten the risk of infection and severity of involvement when associated with increased glucose levels; and infection further increases glucose levels and the risk of complications such as DK[9]. Thus, on account of the pandemic, considering COVID-19 as a cause of decompensated diabetes in children and adolescents becomes relevant.

OBJECTIVE AND METHOD

This paper presents two cases of decompensated diabetes associated with infection by SARS-CoV-2 involving two previously healthy patients aged 11 and nine years. Patient chart data were used in the case reports.

CASE #1

Interview

An 11-year-old female patient reportedly weighing 40 kg was taken to a health clinic for weakness, repeated episodes of nausea and vomiting, bilateral upper quadrant pain, and lack of appetite lasting for four days that became worse the day before she was taken to the clinic. She was described as suffering from polydipsia and polyuria for seven days. No respiratory complaints were recorded during the interview, although flu-like symptoms were mentioned to have occurred one or two weeks earlier. Her capillary glucose level was 574 mg/dl, and she was administered 1320 ml of saline solution. Workup tests were not performed at the health clinic.

Previous comorbidities and allergies were not mentioned. The patient had eaten five hours before admission. She had a deceased grandfather who had insulin-dependent type 2 diabetes mellitus.

Physical Examination

Her overall condition was fair; she was dehydrated (+++/4+), pale (++/4+), with 97% oxygen saturation in ambient air, and afebrile; RR 48 bpm; HR 126 bpm; weight 36.2 kg (9.5% weight loss); regular cardiac rhythm; audible vesicular breath sounds; abdomen without alterations. She had an indwelling urinary catheter (placed at the health clinic), a capillary refill time of three seconds, and cold pale extremities. The patient was confused, awake (responding to requests), tending to upper limb hypertonicity and with a Glasgow Coma Scale score of 15 in neurological examination.

Conduct

Workup tests were ordered immediately and the patient was diagnosed with metabolic acidosis based on arterial blood gas (pH 7.019; HCO3 1.6; BE -27), ketonuria (+++) and glucosuria (478 mg/dl) on urinalysis, and hyperglycemia (blood glucose: 613 mg/dl). The patient was diagnosed with diabetic ketoacidosis. Her complete blood count revealed leukocytosis without deviation and increased reactive lymphocytes. Other tests, including chest x-ray images, did not show significant alterations.

The patient was treated initially with 0.9% intravenous saline solution. She was referred to a pediatric intensive care unit (PICU) for severe dehydration associated with severe metabolic acidosis and acute confusional state indicative of cerebral edema. The patient was kept on intravenous saline solution at the PICU and was started on intravenous regular insulin infusion via pump 0.1U/kg/hour and mannitol 1g/kg/dose on account of her neurological state. She responded well to mannitol.

The patient progressed and improved her pH and HCO3- levels. She was moved to subcutaneous insulin injections and placed on an oral diet. As she started on the oral diet, the

patient complained that she was unable to smell or taste the food she ate, which prompted suspicions around infection by the novel coronavirus. A quick IgG-IgM test came back positive. Although she had no sign of airway involvement, the patient was placed on isolation with airborne and contact precautions. An RT-PCR test for SARS-CoV-2 infection was ordered and she was placed on a diabetes stabilization protocol.

The patient was discharged after her general condition improved, her workup normalized, and ketonuria resolved. She was referred for pediatric endocrinology outpatient care.

CASE #2

Interview

A female patient aged nine years and four months reportedly weighing 30 kg was taken to a pediatric clinic with diffuse abdominal pain lasting for a day after vomiting one hour prior to admission. The patient had been dispirited and quiet since the day before. Respiratory symptoms and fever were not mentioned during the interview. Her mother reported the patient had lost 4 kg within the last three months, in addition to presenting with polyuria and more pronounced nocturia in the last seven days. Respiratory complaints were not recorded in the interview.

Previous comorbidities, allergies, and use of prescribed medication were not mentioned. Her mother reported the child had taken all vaccines listed for individuals of her age in the immunization schedule. The patient had a maternal grandfather on metformin for type 2 diabetes mellitus and a maternal uncle with insulin-dependent (unclear if type 1 or 2) diabetes.

Physical Examination

Her overall condition was fair; she was dehydrated (+++/4+), pale (++/4+), eupneic, and afebrile; BP 100x80mmhg; weight 26.5 kg (11.6% weight loss); RR 22 bpm; HR 159 bpm; enanthem and cracked lips; regular cardiac rhythm; audible vesicular breath sounds; abdomen without alterations; capillary refill time of three seconds. Neurological examination found the patient was sleepy, responsive, without signs of meningeal involvement, with a Glasgow Coma Scale score of 14, and experiencing leg weakness.

Conduct

Workup tests were ordered immediately and the patient was diagnosed with metabolic acidosis based on arterial blood gas (pH 7, 016; HCO3 2.5; BE -24.4), ketonuria (+++) and glucosuria (>500mg/dl) on urinalysis, and hyperglycemia (blood glucose: 480 mg/dl). The patient was started on a protocol for diabetic ketoacidosis. Other tests, including chest x-ray images, did not show significant alterations.

She was promptly referred to a pediatric intensive care unit (PICU) for severe ketoacidosis and started on 0.9% intravenous saline solution, intravenous regular insulin infusion via pump 0.1U/kg/hour, and bicarbonate correction to 10mEq/L.

The patient improved her pH and HCO3- levels and was subsequently started on subcutaneous insulin injections and oral diet after the resolution of ketoacidosis. Since another patient with diabetic ketoacidosis had tested positive for COVID-19 on the same week and on account of the protocols in effect at the hospital for the pandemic, quick IgG-IgM and RT-PCR tests for SARS-CoV-2 infection were performed. All were positive. The patient was discharged after her general condition improved and her glucose levels normalized. She was referred for pediatric endocrinology outpatient care.

DISCUSSION

The pathophysiology of SARS from novel coronavirus infection has been extensively studied. SARS-CoV-2 may involve tissues beyond the respiratory tract and affect the bowel mucosa, the renal tubular epithelium, and blood vessels, to name a few. The virus binds to target cells through angiotensin-converting enzyme 2 (ACE2), an enzyme expressed in different organs of the body. Genetic predisposition has been linked to increased risk for SARS-CoV-2 infection, possibly due to ACE2 polymorphisms associated with diabetes mellitus, stroke, and hypertension, particularly in Asian populations. As discussed previously, severe cases of COVID-19 have been reported in individuals with chronic comorbidities such as diabetes mellitus[1].

Pediatric patients with diabetes present with immune disorders that, when combined with high blood glucose, increase the risk of severe infection, while infection increases blood glucose levels and the risk of complications such as diabetic ketoacidosis[9]. Ketoacidosis is the principal acute complication of diabetes mellitus (DM) and potentially the first manifestation tied to type 1 DM[4]. The most common precipitating factors are infection and inadequate use of insulin (particularly in adolescents), which interferes directly with glucose management[11].

Although individuals with diabetes appear to present the same risk of contracting infection by SARS-CoV-2 when compared with subjects without diabetes, they appear to be more predisposed to developing severe complications. Recent studies indicated that patients with DM often develop ketoacidosis, a complication associated with higher death rates that requires specific care in an intensive care unit setting.

There is no evidence in literature that infection by coronavirus increases the incidence of ketosis or ketoacidosis in patients with or without DM to levels higher than the ones observed in other infections[12]. However, it remains a plausible possibility, since severe hyperglycemia has been reported in individuals with severe forms of COVID-19[12].

In the setting of the current pandemic, infection by the novel coronavirus should be considered as a potential causal factor in cases of diabetic ketoacidosis. Physicians must be able to promptly identify and manage diabetic ketoacidosis in patients with COVID-19[4]. Such effort involves identifying treatment options, which may include administration of insulin via a pump instead of

subcutaneous injections, in order to protect health care providers by decreasing contact with patients with the disease. In addition to the general care measures required in cases of infectious disease, treatment is designed to restore normal osmolarity, manage glucose levels, and prevent potential complications.

CONCLUSION

In times of novel coronavirus pandemic and in light of the wide array of symptoms and clinical manifestations produced by the disease, COVID-19 must be considered in the roster of infections linked to decompensated diabetes. Protocols must be followed to allow early diagnosis and proper treatment with intravenous saline solution, insulin therapy, and rigorous workup control to prevent complications, in addition to isolation and proper measures to address cases of decompensation triggered by infectious diseases.

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