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Case Report

New Onset Type-1 Diabetes Mellitus in a Toddler with Sars-Cov-2 Infection Presenting In Diabetic Ketoacidosis: A Case Report

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Abstract

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), though mostly sparing the lungs in children, has been found to affect other organs including the endocrine pancreas. Type 1 diabetes mellitus (T1DM) may occur through direct negative effects of the virus on beta cell function leading to diminished insulin production. Diabetic ketoacidosis (DKA) is a known and life-threatening complication of T1DM.

Case presentation: This is a case of a 3-year-old previously healthy male who presented with 4 days history of fever, with malaise and hyperpnea for one day. Review of systems was notable for increased thirst and urination, nausea, vomiting, fatigue, and visible weight loss for 4 days. Initial investigations done showed elevated blood glucose, ketonuria, increased anion gap metabolic acidosis, and positive SARS-CoV-2 polymerase chain reaction (PCR). He was immediately commenced on intravenous fluids and insulin with progressive improvement and was discharged on hospital day 6.

Conclusion: Coronavirus disease-2019 (COVID-19) has impacted children most profoundly with the new post-infectious multi-inflammatory syndrome, however it is important to remember that primary coronavirus infection is still a threat to pediatric patients, for example, its cytotoxic effects on the pancreatic beta cells that may lead to T1DM. We therefore recommend that caregivers, parents, and medical professionals should have a high index of suspicion when children present with symptoms consistent with a diagnosis of T1DM during the COVID-19 pandemic so that diagnosis can be made promptly and DKA prevented.

Keywords: type 1 diabetes mellitus; diabetic ketoacidosis; SARS-CoV-2; COVID-19

Introduction

Multiple reports on the current coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have described asymptomatic infection and mild self-resolving infection in children without progression to lower pulmonary disease requiring hospitalization as seen in adults [1]. However, SARS-CoV-2 infection, though mostly sparing the lungs in children, is now seen to be affecting other organs including the endocrine system [2,3]. The most common reported endocrine comorbidity associated with COVID-19 is diabetes mellitus which occurs when SARS-CoV-2 enters the islet cells via angiotensin-converting enzyme 2 (ACE2) receptors and damages the beta cells causing decreased or absent insulin production which leads to hyperglycemia [4,5]. Type 1 diabetes mellitus (T1DM; previously called insulin-dependent diabetes) is predominantly seen in children and adolescents [6]. Recent studies have shown a global trend of increasing prevalence of T1DM which may be multifactorial including the rising prevalence of obesity and increased awareness [6], and more recently, the COVID-19 pandemic [7]. In a multi-centered study in United Kingdom, 30 children aged 23 months to 16.8 years presented with new-onset T1DM during the peak of the pandemic, 5 of whom had evidence of acute or recent SARS-CoV-2 infection; an 80% increase in cases of T1DM was estimated to be associated with the pandemic [7]. Diabetic ketoacidosis (DKA) is the most common complication of T1DM and can be potentially fatal [8]. We present a case of new-onset T1DM presenting as DKA in a 3-year-old child with SARS-CoV-2 infection.

Case Presentation

The patient is a 3-year-old previously healthy male who presented with 4 days history of fever and generalized body weakness, and "deep breathing" for 1 day. On review of systems, the mother reported increased thirst and urination, vomiting, fatigue, and visible weight loss for 4 days.

There is no family history of type 1 diabetes mellitus or autoimmune disease, however maternal grandfather had a history of type 2 diabetes. Patient was afebrile on presentation, and physical examination was significant for Kussmaul breathing and an ill-appearing toddler. Results of investigations done showed – blood glucose 582, pH 6.9, anion gap 23, lactate 2.7 mmol/L, urine ketones 2+ (80 mg/dl), urine glucose 3+ (>= 500mg/dl), which made the diagnosis of DKA. SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) is done routinely on patients who require inpatient hospitalization and was positive. In the pediatric intensive care unit, patient was given titratable intravenous fluids and a continuous infusion of insulin, while blood glucose, venous blood gas, basic metabolic panel, and urine ketones were closely monitored (Table 1). Subsequent laboratory findings include elevated HbA1c (10.0%), low insulin (<15 mIU/L), and low C-peptide (<0.1 ng/ml) which confirmed an underlying diagnosis of T1DM. Antibodies to insulin and glutamic acid decarboxylase 65 (GAD 65) were within normal range (<0.4 U/mL and <5 IU/mL respectively). Screening for celiac disease and thyroid disorders were also within normal limits (Table 1).

VBG	First: pH 6.95, pCO2 19, pO2 35, HCO3 4.2, BE -26.6
	Final: pH 7.37, pCO2 32, pO2 75, HCO3 18.5, BE -5.8
BMP	First: Na 134, K 4.8, HCO3 <6, Cl 111, BUN 16, Cr 1.24, Gluc 582
	Final: Na 140, K 3.5, HCO3 13, Cl 120, BUN 11, Cr 0.65, Gluc 138
Urinalysis	First: pH 6, SG 1.028, glucose 3+ (>=500 mg/dl), ketones 2+ (80 mg/dl), protein 2+ (100 mg/dl), nitrite negative, LE negative
	Final: pH 9, SG 1.011, glucose 3+ (>=500 mg/dl), ketones negative, protein negative, nitrite negative, LE negative
Respiratory multiplex panel	SARS-CoV-2 RT-PCR: Positive Influenza A: Negative Influenza B: Negative RSV: Negative
CBC	WBC 26.5, Hb 12.9, Hct 41.2, N 70.3, L 18.1, M 8.3, B 0.3, E 0, Plt 406
CRP	<0.1 mg/dl
Serum osmolality	322 mOsm/kg
Hemoglobin A1c	10.0 %
C-peptide	<0.1 ng/ml
Insulin autoantibody	<0.4 U/ml
Insulin	<15.7 mIU/L
Gliadin deaminated IgA antibody	<10.0 U
Gliadin deaminated IgG antibody	<10.0 U
TTG IgG antibody	9 U/ml
GAD65 antibody	<5 IU/mL
BNP	24 pg/ml
Troponin I	<0.02 ng/ml
Thyroid peroxidase antibody	<1
Thyroglobulin antibody	<1.8
Thyroglobulin tumor marker	30 ng/ml

B: Basophils, **BE:** Base excess, **BMP:** Basic metabolic panel, **BNP:** Brain natriuretic peptide, **BUN:** Blood urea nitrogen, **CBC:** Complete blood count, **Cl:** Chloride, Cr Creatinine, **CRP:** C-reactive protein, **E:** Eosinophils, **GAD65:** Glutamic acid decarboxylase 65, **Gluc:** Glucose, **Hb:** Hemoglobin, **HCO3:** bicarbonate, **Hct:** Hematocrit, **L:** Lymphocytes, **LE:** Leukocyte esterase, **M:** Monocytes, **N:** Neutrophils, **Na:** Sodium, **pCO2:** Partial pressure of carbon dioxide, **pO2:** Partial pressure of oxygen, **SG:** Specific gravity, **RSV:** Respiratory syncytial virus, **TTG:** Tissue transglutaminase, **VBG:** Venous blood gas, **WBC:** white blood cell.

Table 1: *Laboratory results.*

Glucose rates progressively declined at a rate less than 100 mg/dl per hour. Acidosis resolved and anion gap closed on day 1 of admission. On day 2 of admission, he was transitioned to subcutaneous insulin and started on diabetic diet regimen and received subsequent care and education by the pediatric endocrinologist on the general pediatrics floor. He was discharged on hospital day 6. He had no further complications and had no respiratory symptoms throughout his hospital stay.

Discussion

The association between COVID-19 and new-onset type 1 diabetes mellitus (T1DM) is becoming increasingly frequent. This case highlights the possibility of SARS-CoV-2 acting as an infectious precipitant for T1DM. Although the presence of multiple autoantibodies greatly increases the probability for T1DM with about 96% of affected individuals being positive for at least one of the autoantibodies [9], this patient did not have autoantibodies, which may suggest a different mechanism of pancreatic beta cell insufficiency. Children have been mostly spared the life-threatening sequelae of coronavirus infection in the lungs, and the current understanding is that pediatric nasal and lung epithelial cells have less ACE2 receptors that permit viral entry; also, these receptors have lower affinity for SARS-CoV-2 and a different distribution in the body, making SARS-CoV-2 entry into the cells more difficult [10]. However, ACE2 receptors are known to be present in pancreatic beta cells causing direct viral cytotoxicity and decreased

insulin production leading to diabetes [4,5]. There are concerns that the reported increase in presentations of children with T1DM already in a state of DKA during the COVID-19 pandemic may be attributed to delayed presentation to primary care physicians and hospitals to reduce risk of exposure to the virus [11], however, similar to the UK report, [7] the index patient had a relatively short duration of symptoms and the acuity of presentation may be as a result of the SARS-CoV-2 infection. It is important for individual patient care as well as for the pediatric community to be aware that children are still at risk from primary coronavirus infection even if they do not get frequent pneumonias.

Conclusion

In conclusion, it is possible that we are seeing a rapid onset of severe acute disease due to COVID-19 in children which may be attributable to pancreatic viral destruction based on the science that we have in adults. We therefore recommend that caregivers, parents, and medical professionals should have a high index of suspicion so that diagnosis can be early and DKA potentially prevented. We hope that future studies including the ongoing CoviDIAB Project [3] will address questions on predisposing factors, treatment, and prognosis of COVID-19-related diabetes.

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