Case Report

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Severe Diabetic Ketoacidosis and Coronavirus 2019 (COVID-19) Infection led to Diagnosis of Autoimmune Polyglandular Syndrome

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ABSTRACT

To this day, millions of people in the world have been diagnosed with corona virus 2019 (COVID-19). This disease cannot only lead to higher mortality rates among those with underlying Diabetes Mellitus (DM), but also may trigger DM in susceptible patients. Therefore, incidence of new-onset DM increased during the pandemic as a result; treatment of patients with diabetes and COVID-19 is important and needs further investigations. Here, we report a 27-year- old woman with past medical history of premature ovarian failure (POF) since14 years ago, who initially presented with severe diabetic ketoacidosis (DKA) which was triggered by COVID-19 and later through her lab results hypoparathyroidism was also detected. She was treated for DKA and COVID-19 Infection concomitantly, and she was also diagnosed with autoimmune polyglandular syndrome due to her multiple autoimmune endocrine organ involvements.

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Introduction

On January 30, 2020, the world health organization (WHO) announced the coronavirus disease 2019 (covid-19) outbreak as a public health emergency of international concern and later called it a pandemic on 11th of March 2020 (1). At the present time, more than 117 million patients and more than 3 million deaths have been attributed to COVID-19 around the world. Old age and co-morbidities such as diabetes, chronic respiratory disease, hypertension, cardiovascular disease, and cancer have been regarded as significant predictors of morbidity and mortality. Also, it has been suggested that COVID-19 may induce a new diagnosis of DM or acute metabolic complications of DM such as diabetic ketoacidosis (DKA)(2, 3).COVID-19 can damage pancreatic islet cells and reduce insulin release through binding to its angiotensin converting enzyme 2 receptors expressed on beta cells (4, 5). Consequently, it can predispose diabetic patients to acute complications such as DKA. There are few reports about DKA due to COVID-19.

Here we report a 27-year-old woman with history of premature ovarian failure (POF): who was admitted with severe DKA as the first manifestation of her DM following a COVID-19 infection. Hypoparathyroidism diagnosis was made later based on recent laboratory tests in this admission. Since multiple endocrine organ involvements were detected in the patient, the new diagnosis of autoimmune polyglandular syndrome (APS) was considered.

Case Presentation

A 27-year-old woman presented to the emergency department with a 5-day history of drowsiness, nausea, vomiting, polyuria, and polydipsia. She did not have any headache, fever, abdominal pain, or diarrhea, or any history of drug allergies or past medical history of Diabetes Mellitus. Her past medical history was remarkable for primary amenorrhea and she was receiving estrogen and progesterone hormone replacement therapy (HRT) from 14 years ago. Previously, she had been evaluated for primary amenorrhea. Her karyotype was 46XX and pelvic ultrasonography was normal. She also had family history of POF in her sister and a history of DM in her aunt.

On Physical examination, she was lethargic, her resting heart rate was120 pulses per minute, her blood pressure was 100/80mmHg, her temperature was 37.2°c, respiratory rate was 20 breaths per minute, and oxygen saturation was 97% on room air. Her height was 168cm, weight was 67kg (body mass index [BMI] = 23.7kg/m.) and her mucous membranes were dry. Head and neck exams were normal. Her thyroid was normal on palpation. Breath sounds were normal and her abdomen was soft without any tenderness or guarding. There was no pigmentation or any other skin or mucosal lesions. Neurologic and other examinations were also normal.

The lab results on admission indicated severe DKA: Blood glucose of 370 mg/dL, 3+ urine ketone, 3+ glucose in the Urine, venous blood gas: pH = 7.00, and bicarbonate= 5.6meq/L.

Also, in the other lab tests that were carried out, an iPTH<3 and calcium=6 indicated an underlying hypoparathyroidism, as well as an LH = 68 and FSH = 102 due to patient's medical history of POF. All lab tests have been stated in Table 1 below.

The patient was admitted to the intensive care unit (ICU) with severe DKA and was initially treated with isotonic saline IV fluids. After correction of potassium, the continuous infusion of insulin with a dose of 7 units per hour was started. In addition, the diagnosis of hypoparathyroidism was made with regard to calcium and parathyroid hormone (PTH) values, and treatment with calcium gluconate was started. Her phosphorus level was also low in her initial investigations owing to her Vitamin D deficiency and DKA state. Her potassium and calcium were both closely monitored and lab tests were verified.

During admission, she had osmotic polyuria (urine output: 10 lit/day) that was replaced with IV fluids. The vital signs and laboratory tests were closely monitored. The polyuria resolved after 48 hours. When her acidosis also resolved (PH=7.38, HCO3=24meq/l) and she was able to tolerate oral intake, then IV insulin infusion was switched to a subcutaneous insulin regimen. In order to find the predisposing factor of DKA, blood culture (B/C), urine culture (U/C), chest x-ray (CXR), and electrocardiography (ECG) were done. CXR was normal but because of COVID19 prevalence, the COVID-19 PCR test was also done which was reported positive, while she had no recent symptoms of fever, cough, or dyspnea. Hence, hydroxychloroquine was started according to the protocol of our hospital at the time. Although COVID19 infection predisposed
predisposed

her to DKA, the combination of a new-onset DM and hypoparathyroidism alongside past medical history of POF suggested diagnosis of autoimmune polyglandular syndrome (APS) in this patient. She was discharged in good condition after 7 days of admission on a basal-bolus insulin regimen; calcium carbonate 2 gr/daily, Calcitriol 0.25ug/twice per day, estrogen and progesterone replacement, and follow-up was advised. In her follow-up, her calcium level had reached the lower normal limit and her phosphorus level had risen up to the higher normal limit

Table 1: Results of laboratory findings

Parameter	Admission	Reference values
Blood glucose	370	70-100mg/dL
Blood pH	7	7.35-7.45
Bicarbonate	5.6	22-26meq/L
Urine ketone **Urine SG**	+3 1020	
Urea	14	15-50 mg/dL
Creatinine	1	0.7-1.4 mg/dL
Potassium	3	3.5-5 mg/dL
Sodium	140	135-145meq/L
Magnesium	1.8	1.6-2.6mg/dL
Albumin	3.6	3.5-5 g/dl
Calcium	6	8.6-10.2mg/dL
Phosphorus	1	2.5-5mg/dL
25Vit D	17.6	<20 ng/ml (deficiency)
iPTH	<3	10-60pg/ml
LH	68	Follicular phase 1.2-12 mIU/ml
FSH	102	Follicular phase 3.2-15 mIU/ml
CRP	12	< 10 mg/L
ESR	7	0-15 mm/h
Hb A1c	16	4-5.7%
WBC/mm **Hb** **Neutrophil (%)** **Lymphocyte (%)** **Platelet /mm**	13500 15.9 81% 18% 268	4,000-10,000/mm 12-15 g/dl (55-70%) 2,500-8,000/mm (20-40%) 1,000-4,000/mm 145,000-450,000/mm
AST	35	20-48u/l
ALT	30	10-40u/l
ALP	190	50-120u/l
Cortisol	15.8	5-25 µg/dl
T4	9.35	5-12.5µg/dl
T3	117	70-200ng/dl
TSH	3.5	0.5-5mIU/l
TPO Antibody	46	<2IU/ml

CRP, C reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell count; Hb, hemoglobin; Alt, Alanine aminotransferase; AST, Aspartate aminotransferase; Alp, Alkaline phosphatase

Discussion:

Here we reported a 27-year-old woman with history of premature ovarian failure (POF) from 14 years ago who was admitted with severe DKA as the first manifestation of her diabetes as well as detection of COVID-19 infection as a potential triggering factor for her DM. However, this patient had not been screened for diabetes previously. Additionally, she presented with a very significant HbA1c (16%); this can be indicative of a long-term underlying diabetes mellitus. Having said that, the only precipitating factor detected for her DKA was her ongoing COVID-19 infection. Also, she was diagnosed with hypoparathyroidism following the detection of hypocalcemia and low PTH levels in her laboratory test results. She was managed for both her DKA and COVID-19 infection and received treatment for COVID-19 and was then discharged in good condition after 7 days of hospital admission.

Association of DKA and COVID-19 in a patient, as in our case, is of great clinical importance as it can potentially lead to a worse prognosis for the patient (6). DKA is an acute and serious complication of diabetes that is the result of a relative or absolute deficiency of insulin or absolute insulin deficiency and is a common presentation in a new-onset DM. Patients with diabetes also have increased risk of infections compared to the general population due to hyperglycemia induced by immune dysfunction (7, 8). Viral infections such as COVID-19 also may trigger autoimmune insulitis and pancreatic B cell destruction COVID-19 infection, via binding to ACE2 receptors expressed in beta cells, can damage islets and reduce insulin release (4), therefore, predisposing susceptible patients to DKA. On the other hand, in our case, the diagnosis of APS was considered because of multiple endocrine disorder involvement, including premature ovarian failure (POF), DM, and hypoparathyroidism. The diagnosis of APS is usually made when two or more autoimmune endocrine organ disorders are present. Autoimmune polyglandular syndromes are characterized by circulatory autoantibodies and lymphocytic infiltration of multiple organs, eventually leading to organ failure.

T cells play a key role in the pathogenesis of many autoimmune diseases, and therapies targeting these cells will likely be developed. This syndrome could occur from infancy to old age and its new components may appear throughout life. There is marked variation in the frequencies and patterns of autoimmunity in affected patients and their families. Although there has been rapid development in the immune checkpoint blockade to regulate the immune system and suppress autoimmune reactions, generally, management of APS is based on hormonal replacement and treatment of complications (8, 9).

There are generally 4 different types of APS according to the organs effected by the syndrome. In this case, since the patient developed diabetes mellitus, premature ovarian failure and hypoparathyroidism, she had some of the characteristics of two different types of APS. Hence, her APS type can be considered as an overlapping of type 1 and type 4. (10) Since different components of APS develop over years to decades, its surveillance is mandatory for associated autoimmune disorder. Siblings of patients should be screened for autoimmune diseases. In this case, the patient was also evaluated for other autoimmune diseases and cortisol level and thyroid function test were also carried out as well as long term follow-up recommendation.

Conclusion:

Our case was admitted with severe DKA as the first manifestation of her diabetes as well as detection of COVID-19 infection as a potential triggering factor for her DM. Our knowledge about COVID-19 effects on patients with DM is limited. COVID-19 can either trigger a new-onset DM or complicate a pre-existing one. The relationship between COVID-19 infection and other autoimmune diseases is not well known. Whether COVID-19 can trigger other autoimmune diseases like DM needs to be further studied.

Ethical Considerations

Compliance with ethical guidelines

Informed consent was obtained from the patient included in this case report

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Conflict of interest

The authors declared no conflict of interest.

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