Presentation of Severe Diabetic Ketoacidosis in New-Onset Type One Diabetes Mellitus: The Importance of a Broad Differential in an Otherwise Healthy Population in the Operational Environment

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ABSTRACT  Diabetic ketoacidosis (DKA) is a serious disease entity that must be diagnosed quickly for urgent management in the intensive care unit. Keeping DKA in the differential diagnosis is important, especially in a forward-deployed, resource-poor setting. The symptoms and signs of DKA are non-specific, including fatigue, polydipsia, polyuria, weakness, weight loss, nausea, vomiting, and abdominal pain with tachycardia and tachypnea on exam. The testing capability to evaluate for DKA includes a glucometer, urine dipstick, and basal metabolic panel, all of which can be done in most forward deployed settings. The need for a high index of suspicion for DKA in patients with these symptoms is required due to the lack of life-saving insulin and intensive lab monitoring required. The downstream effects of DKA include diabetic coma and death. We present a case report of a 21-year-old otherwise healthy, active duty, male Marine who presents to the clinic with a chief complaint of 4 days of headache and 1 day of nausea with four episodes of non-bloody, non-bilious emesis along with epigastric abdominal pain. He returned to the clinic 2 days later with evidence of tachycardia and increased work of breathing, at which time there was a concern for a pulmonary embolus. By the time he was transferred to the emergency room, he was in severe DKA. The patient was treated in the intensive care unit and made a full recovery. He was processed for limited duty and medical board upon hospital discharge.

INTRODUCTION AND LITERATURE REVIEW

Epidemiology and Clinical Presentation
Several articles point to the increasing rates of type 1 diabetes (T1D) among adolescents and young adults. It is estimated that 1.6 million adults aged 20 years or older have T1D. Data from the 2018-2019 National Health Interview Survey and the 2019 U.S. Census Bureau observed an overall incidence of T1D of 3.2 (2.3-4.4) per 1,000 people with a 95% confidence interval among people aged 18-44 years. Complaints of new-onset T1D include polydipsia, polyuria, weakness, weight loss, nausea, vomiting, and abdominal pain with evidence of tachycardia and tachypnea on exam. Often, new-onset T1D presents itself with diabetic ketoacidosis (DKA), and other times, T1D is discovered incidentally. Diabetic ketoacidosis (DKA) is one of the most common complications of T1D and remains the most frequent cause of death in children and young adults with T1D.

Pathophysiology of DKA
The pathophysiology of T1D and DKA is complex. It can be summarized as follows: The body causes the autoimmune destruction of the insulin-producing beta cells of the islets of Langerhans in the pancreas. This destruction causes an insulin deficiency which normally functions to (1) inhibit lipolysis, (2) stimulate glucose uptake into cells, and (3) inhibit glycogenolysis and stimulate glycogen synthesis. The counter-regulatory hormones (cortisol, catecholamines, or glucagon) increase during times of stress, which together led to a further reduction in insulin-mediated cellular glucose uptake. As an alternative energy source, lipase is upregulated, causing an increase in triglyceride breakdown with the release of free fatty acids forming acetyl coenzyme A (acetyl CoA) and entering the tricarboxylic acid cycle. When this system is overwhelmed, acetyl CoA is converted into ketones in the liver, which clinically results in the high anion gap metabolic acidosis seen in DKA. It is important to note that other causes of an anion gap metabolic acidosis include ethylene glycol or methanol ingestion, lactate or 5-oxoproline accumulation, aspirin overdose, rhabdomyolysis, renal failure, and ketoacidosis from other causes, e.g., liver disease.

CLINICAL COURSE

Day 1 Clinic
A 21-year-old otherwise healthy, active duty, male Marine presents to his base clinic with a chief complaint of 4 days of headache and 1 day of nausea with four episodes of non-bloody, non-bilious emesis along with epigastric abdominal pain. The patient denied sick contacts and recent travel. On review of symptoms, the patient denied dizziness, shortness of breath, palpitations, loss of taste/smell, cough, and diarrhea. At the time, the patient could not tolerate food but could tolerate small sips of water. On physical exam, blood pressure was 138/90 mm Hg, pulse rate was 111 beats per minute, respiratory rate was 16 respirations per minute, and temperature was 310 Kelvin. On exam, the patient was generally well-appearing, well-developed, in no acute distress, and...
neurologically intact. The assessment and plan was COVID testing in accordance with clinic protocol and symptomatic treatment with ondansetron and acetaminophen.

**Past Medical History**

On an occupational health exam 13 months prior, the patient had evidence of glycosuria (500 mg/dL) on urinalysis, which resolved on repeat urinalysis the following day. The medical chart noted that the patient denied experiencing any weight loss, polyphagia, polyuria, or polydipsia at the time. There was a remote family history of diabetes mellitus. The patient’s fasting glucose was normal at 91 mg/dL.

**Day 3 Clinic**

The patient returned to his base clinic 2 days later, complaining of 5 days of shortness of breath and an intermittent headache. He denied fever, chest pain, pleuritic pain, cough, abdominal pain, leg swelling, neck stiffness, and focal deficits. On exam, vitals were blood pressure of 135/82 mm Hg, pulse rate of 130 beats per minute, respiratory rate of 20 respirations per minute, temperature of 97.7 Fahrenheit, and pulse oximetry of 95% on room air. On exam, the patient was in acute distress, with increased work of breathing and speaking in half sentences. His lungs were clear to auscultation without wheezing, rhonchi, or rales/crackles heard. The assessment and plan was emergency room transfer due to tachycardia and increased work of breathing for consideration of pulmonary embolus versus pneumonia, less likely asthma with no prior history and no wheezing on exam.

**Day 3 Emergency Room**

The patient reported to the emergency room on day 7 of symptom onset and was found to have severe DKA after ruling out pulmonary embolus. Pertinent labs included an anion gap metabolic acidosis of 31, glucose of 391 mg/dL, and venous blood pH of 6.98. In addition, the patient tested negative for three autoantibodies associated with T1D (glutamate decarboxylase 65 Ab, insulin autoantibody, and pancreatic islet cell antibody). The patient was also found to have a concomitant respiratory acidosis due to being unable to compensate for the degree of acidosis. Due to the severity of his DKA, telehealth critical care medicine was consulted. The patient stayed in the hospital for 5 days and was subsequently discharged on glargine and insulin aspart. The patient was placed on limited duty after discharge and processed for medical separation.

**DISCUSSION**

The importance of recognizing rising cases of T1D and DKA in the young adult population is important for military medicine, especially for general medical officers. Recent studies have shown that more than half of new-onset T1D occurs in adults. Approximately 92.1% of the active duty population are between the ages of 18 and 40 years. Using the incidence rate of 3.2/1,000 for adults aged 18-44 and given an active duty population of 1.185 million, we can grossly estimate that 3,792 active duty members will develop T1D in a given year. A certain portion of these individuals will present with DKA as the first sign of T1D. One study shows that of 805 children (0-18 years of age), DKA at the onset of T1D occurred in approximately one-third of the subjects and one-sixth with severe DKA. A study published in The Journal of Pediatrics analyzed data in separate age groups showing an increase in the rate of DKA at the new onset of T1D over time from 2002 to 2010. In the bracket of ages 15-19, the rate of DKA per 100 new-onset T1D increased from 22.9 (16.8-29.1, n = 46) in 2002 to 23.5 (19.4-27.7, n = 95) in 2010. Given these data, the importance of keeping T1D in the differential cannot be underestimated, considering that nearly a quarter of late adolescents with T1D will initially present with DKA. According to the Centers for Disease Control and Prevention’s United States Diabetes Surveillance System, the rate of DKA hospitalizations for those patients under age 45 was approximately 27 times the rate of those over 65 years old in 2014. The rate of DKA hospitalization for those under 45 years old also increased over time, from 31.7 per 1,000 to 44.3 per 1,000 from 2000 to 2014. In addition, the in-hospital case-fatality rate for all age groups is estimated to be about 0.4%. These statistics again emphasize the importance of keeping T1D and DKA in the differential diagnosis, given the corresponding age group with those serving on active duty.

Most active duty members seen in clinic with DKA will have complaints of a combination of symptoms including fatigue, polydipsia, polyuria, weakness, weight loss, nausea, vomiting, and abdominal pain with evidence of tachycardia and tachypnea on exam. This case report shows the importance of early recognition of T1D in a young healthy population with broad nonspecific symptoms. Our patient had nonspecific symptoms ranging from headache, nausea, vomiting, and epigastric pain, with tachycardia on exam. It is

**TABLE I. Laboratory Values**

<table>
<thead>
<tr>
<th>Lab value</th>
<th>Value</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>138</td>
<td>137-145 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>102</td>
<td>87-107 mmol/L</td>
</tr>
<tr>
<td>Bicarb</td>
<td>&lt;5</td>
<td>22-30 mmol/L</td>
</tr>
<tr>
<td>Anion gap [Na–Cl + bicarb]</td>
<td>31</td>
<td>3-10 mEq/L</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>391</td>
<td>74-106 mg/dL</td>
</tr>
<tr>
<td>Venous blood pH</td>
<td>6.98</td>
<td>7.31-7.41</td>
</tr>
<tr>
<td>CO₂</td>
<td>25 mm Hg</td>
<td>41-51 mm Hg</td>
</tr>
<tr>
<td>Urine glucose (mg/dL)</td>
<td>&gt;1,000 mg/dL</td>
<td>NEG</td>
</tr>
<tr>
<td>Urine protein (mg/dL)</td>
<td>100 mg/dL</td>
<td>NEG-TRACE</td>
</tr>
<tr>
<td>HgbA1C</td>
<td>10.1%</td>
<td>4.8-5.6</td>
</tr>
<tr>
<td>Glutamate decarboxylase 65 Ab</td>
<td>NEG</td>
<td>NEG</td>
</tr>
<tr>
<td>Insulin autoantibody</td>
<td>NEG</td>
<td>NEG</td>
</tr>
<tr>
<td>Pancreatic islet cell antibody</td>
<td>NEG</td>
<td>NEG</td>
</tr>
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important to note that abdominal pain is correlated with a later and more severe manifestation of DKA. One study shows that abdominal pain was present in 86% of patients with a serum bicarbonate of <5 mmol/L versus only 13% of patients with serum bicarbonate between 15 and 18 mmol/L. Comparing the patient’s serum bicarbonate level and anion gap values in Table I with the American Diabetes Association definition of DKA as mild, moderate, and severe, our patient meets diagnostic criteria for severe DKA

In addition, it must be emphasized that the required testing capability is minimal to evaluate for DKA in a new-onset T1D patient. Most clinics and ships have a glucometer and urine dipsticks. The only other necessary lab is the basal metabolic panel to assess the presence of an anion gap, which can also be done at most clinics and aboard most ships. Being operational oftentimes forces general medical officers to use supplies judiciously. When a patient presents with headache, fatigue, polydipsia, nausea, and/or vomiting, new-onset T1D presenting with DKA must be in the differential diagnosis. This patient had symptoms for 7 days before being referred to the emergency room for further evaluation. Fortunately, this patient was not forward deployed at the time and had access to a hospital. However, the importance of diagnosing a new T1D with DKA expeditiously in a forward deployed setting cannot be underestimated, as resources such as insulin and constant lab monitoring for electrolyte disturbances are minimal if not near impossible at a battalion aid station or aboard a ship. It can require an immediate medical evacuation spelled out accepted (MEDEVAC), which can be delayed due to being out of range or due to operational necessity. Therefore, timely diagnosis is the key. The downstream effects of DKA include diabetic coma and death.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES