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Case Report

Unexpected Origin of Infection in a Patient with Diabetic Ketoacidosis: Candida Esophagitis - @

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KEYWORDS

Diabetic Ketoacidosis; *Candida Albicans*; Esophagitis

INTRODUCTION

Diabetic Ketoacidosis (DKA) is an acute complication of Diabetes Mellitus (DM) that can be life-threatening. The basic underlying mechanism for DKA is insulin deficiency coupled with elevated levels of counter-regulatory hormones, such as glucagon, cortisol, catecholamine's, and growth hormone. The most common precipitating factor in the development of DKA is infection [1]. Other precipitating factors include discontinuation of insulin therapy or inadequate insulin therapy, myocardial infarction, cerebrovascular accident, pancreatitis and drugs [2,3]. The management of DKA includes: correction of dehydration, hyperglycemia and electrolyte imbalances, identification of comorbid precipitating events, and frequent patient monitoring [2].

Esophagitis is predominantly caused by noninfectious conditions, mainly gastroesophageal reflux disease [4]. Generally, infectious esophagitis is strongly associated with immunodeficiency including human immunodeficiency virus infection, malignancies, chemotherapy and malnutrition. The mostly seen pathogen is *Candida* among infectious esophagitis. *Candida* esophagitis is being increasingly recognized in the practice of clinical gastroenterology with the frequent use of endoscopy for the evaluation of esophageal symptoms. The main clinical features of *Candida* esophagitis are odynophagia and dysphagia. However, gastrointestinal bleeding may rarely be the only presenting symptom [5,6].

The high frequency of *Candida* infections in patients with diabetes mellitus has been well identified for many years. Especially, patients with poorly controlled diabetes are susceptible to the colonization of *Candida* species [7]. Since both neutrophil chemotaxis and phagocytosis decreased in patients with DM, uncontrolled DM may be considered to be immunocompromised hosts [8,9].

Herein, we present a poorly controlled diabetic patient presenting with diabetic ketoacidosis and resistance to insulin therapy with nausea, vomiting and dysphagia due to *Candida* esophagitis without any other infections.

CASE REPORT

A 54-year-old man from a rural area was admitted to the emergency department of our state hospital with nausea, vomiting, dysphasia, abdominal pain, weakness and drowsiness. He had a history of diabetes mellitus for ten years and he had been under insulin therapy for the last two years. He reported that he was not in compliance with adequate insulin therapy. He was fully oriented but tended to fall asleep. Clinical examination revealed that a dehydrated and cachectic male with a heart rate of 114 beats/ min, temperature of 37°C and a blood pressure of 90/50 mmHg. He was tachypneic and dyspneic with a respiratory rate of 28 breaths/ minute. The patient's skin was hot and dry, pupils were isochoric and he had no focal neurological deficit. Lung auscultation was normal and the abdomen was soft and non-tender; bowel sounds were present in 2 of the 4 quadrants. His body mass index was 17.6 kg/ m². Laboratory investigation revealed a metabolic acidosis with arterial blood pH of 7.29 and bicarbonate of 16.6 mmol/ L. Arterial pO₂ and pCO₂ levels were 92 mm Hg and 30 mm Hg, respectively. Plasma glucose was 1140 mg/ dL. 2+ ketones and 4+ glucose were present in the dipstick urine test. There were no erythrocyte and leukocyte casts in the microscopic

evaluation of the urine. Blood urea level was 178 mg/ dL and serum creatinine level was 2.37 mg/ dL. Serum sodium level was 133 mmol/ L and potassium was 4.2 mmol/ L, cardiac enzymes, serum amylase and lipase level was normal. Liver function tests were within normal range. Complete blood count showed an elevated white blood cell count of 16.400 mm³/ μL with a 90% rate of neutrophil. High-sensitive C-reactive protein (hs-CRP) was 7.11 mg/ dL. Both urinary and blood cultures were taken. Abdomen ultrasonography was reported to be normal findings. There were no any sign of pneumonia and urinary infection. Serum hemoglobin A1c level was 12.1%. The patient was diagnosed as diabetic ketoacidosis with acute kidney failure. Intravenous fluid and insulin treatment were started promptly. On the third day, metabolic acidosis was resolved, urinary ketone was negative and the renal function was normal with the creatinine level of 0.9 mg/ dL. However, nausea, vomiting and dysphagia have been continued and insulin requirement was still at high levels with 120 unit/ day to control the blood glucose level. Serum hs-CRP level was still high with a level of 6.99 mg/ dL. Both urinary and blood cultures were found as negative. Hepatitis and HIV tests were all negative. Upper gastrointestinal endoscopy performed to evaluate the resistant nausea, vomiting and dysphagia. The endoscopy was showed the thrush lesions in the distal esophagus (Figure 1). The biopsy was taken for the diagnosis. The gram staining showed yeasts. Treatment with fluconazole (200mg/12hours) was started intravenously. The culture reported the *Candida albicans* and the pathologic examination of the biopsy specimen demonstrated the *Candida* esophagitis in the light microscopy with hematoxylin and eosin staining (Figure 2). On the 3rd day of fluconazole treatment, nausea, vomiting and dysphasia were ceased. His glucose level was normalized between 100-140 mg/ dL with total 36 unit/ day (3*8 pre-meal, 1*12 basal) insulin dosages. On the 7th day of the fluconazole treatment the patient was discharged from hospital with oral fluconazole (200 mg / 12hours) for seven days. 14th day of the fluconazole treatment hs-CRP level was 0.3 mg/ dL and there was no complaint, thus fluconazole treatment was stopped. Three months later his hemoglobinA1c level was 7.5%.

DISCUSSION

Diabetic ketoacidosis is an acute and potentially mortal complication of diabetes mellitus, sometimes it could be the first manifestation of the disease [1]. Although it has been repeatedly shown that infection is a common precipitating event in DKA [1,2], the omission of insulin or inadequate treatment with insulin may be the most important precipitating factor [9,10]. Moreover, acute medical illnesses involving the cardiovascular system (myocardial infarction, stroke) and gastrointestinal tract (bleeding, pancreatitis), diseases of the endocrine axis (acromegaly, Cushing's syndrome), and stress of recent surgical procedures may contribute to the development of DKA by an increase in insulin counter-regulatory hormones, causing dehydration, and worsening of peripheral insulin resistance. Other factors that can contribute to DKA include psychological problems, eating disorders and illegal substance use [11,12]. The initial management of DKA consists of fluid and electrolyte therapy, insulin therapy, treatment of precipitating causes, the monitoring of therapy and complications.

Urinary tract infection and pneumonia are the most common infections in patients with DKA [1]. Otherwise, fungal infection is commonly seen in patients with DM. These infections involve skin, respiratory system and also genitourinary system [13]. Additionally, some specific types of fungal agents such as zygomycosis have been reported in many diabetic cases [14]. Piziak, et al. [15] reported



Figure 1: Upper gastrointestinal endoscopy images illustrate the white colored plaques in distal Esophagus of the patient.

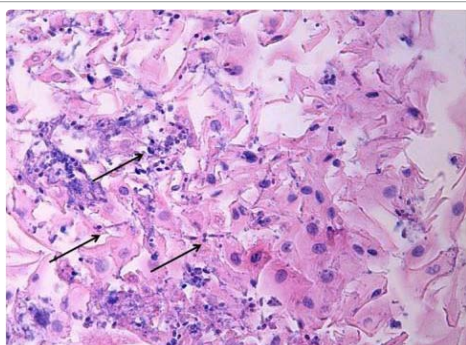


Figure 2: Biopsy specimen of the distal esophagus indicates the Candida hyphae and spores in the light microscopy (Hematoxylin and Eosin stain *400).

a case with *Candida* sepsis due to urinary colonization manifested by DKA. Dooley, et al. [16] have reported a diabetic patient with *Candida albicans* sinusitis as a potential reason for DKA. Cox, et al. [17] reported oral candidiasis in a patient with DKA. Additionally, there are few case reports in the literature with *Candida* esophagitis and diabetic ketoacidosis [18-20].

Infectious esophagitis is associated with in patients with impaired immunity such as AIDS, malignancy and chronic steroid therapy. The mostly seen pathogen is *Candida* among infectious esophagitis [4,5]. Uncontrolled DM may be considered to be immunocompromised hosts [9,15]. Granulocyte chemotaxis and phagocytosis are decreased, and granulocytes reportedly have a decreased ability to kill *Candida* [8]. It has been shown that *Candida* colonization is increased in patients with DM [9]. Our patient had uncontrolled DM and he was from rural area which made him vulnerable to fungal infection. The development of DKA in this patient can be explained by his non-compliance in insulin therapy. *Candida* esophagitis may simply occur because of his poorly controlled diabetes mellitus.

The salient clinical features of *Candida* esophagitis include odynophagia and dysphagia, although gastrointestinal bleeding may occasionally be the sole presenting symptom [5]. The diagnosis of *Candida* esophagitis is usually made when white mucosal plaque-like lesions are seen on endoscopy. Confirmatory biopsy shows the presence of yeast and pseudohyphae with invasion of mucosal cells. This kind of esophagitis requires systemic antifungal therapy [21]. Intravenous therapy may be required initially in patients with severe disease if the patients could not take oral therapy. In our patient, dysphasia was resolved, and serum glucose level was normalized on the 3rd day of the systemic fluconazole therapy.

In conclusion, continuation of the high serum glucose level with nausea, vomiting and dysphagia despite the resolution of metabolic acidosis could be a clue for the esophagitis in patients with DKA. Physicians should be alert to fungal infections in patients with DKA because a delay in diagnosis may be fatal.

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