Severe Esophageal Candidiasis In An Immunocompetent Patient
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INTRODUCTION
Infection by Candida species is the most common cause of infectious esophagitis. Major predisposing factors include antibiotic use, radiation therapy or chemotherapy, hematologic malignancies and Acquired Immunodeficiency syndrome (AIDS). Other conditions associated with an increased incidence of Candida esophagitis include esophageal stasis, alcoholism, malnutrition, and advanced age (1, 2).

In the future, because of the progress of the modern medicine, still more immunocompromised patients will live and thus candida species will have more potential victims. In this report the most up to date knowledge about epidemiology, pathophysiology and clinical presentation of candida esophagitis is presented.

CASE REPORT
We report a case of 70-year-old lady with history of hypertension was admitted to the hospital because of progressively worsening odynophagia to liquids and solid food for the last 2 weeks. She denied nausea, vomiting, melena, hematochezia, diarrhea, constipation, weight loss, fever, cough and chills. She denied any use of antibiotics in last 2 years and her medication history included norvasc 5mg daily at home. She had a colonoscopy 2 years ago that showed hemorrhoids. She never smoked cigarettes, denied use of alcohol or any other illicit drugs. She denied allergies to any medication.

Physical examination on admission revealed a well developed, chronically ill appearing woman. She was afebrile, had a heart rate of 82 beats per minute, and a blood pressure of 130/78 mm Hg. She was breathing at a rate of 16 breaths per minute. Oropharynx did not show any sign of infection or thrush. She had a moderate epigastric discomfort, no rebound tenderness or guarding and dark brown heme negative stools. Rest of physical examination was unremarkable. Her admission labs including complete blood counts, metabolic profile, coagulation profile, liver function tests, iron studies, thyroid function test, glycosylated hemoglobin and urinalysis were normal.

The patient's admission chest radiograph was non contributory. Computed tomography scan of abdomen and pelvis showed no evidence of paraaortic or pelvic retroperitoneal lymphadenopathy. Liver, gallbladder, adrenal glands, pancreas, spleen and kidneys were unremarkable. There were no pelvic masses noted and urinary bladder was also unremarkable. Echocardiogram showed Ejection fraction of 55%, with normal wall motions and mild tricuspid insufficiency. The focus of the patient's evaluation then turned to the possibility of esophageal malignancy. Upper GI endoscopy with biopsy of esophageal mucosa demonstrated multiple plaques throughout the esophagus consistent with severe Candida esophagitis. Histopathologic findings were also consistent with esophageal candidiasis.

Additional workup to find out the cause of candida esophagitis including hepatitis profile, T-lymphocytes
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counts, HIV test, syphilis screen, antinuclear antibodies, and assessment of T-lymphocytes function by Mitogen stimulation test came back normal.

She was started on intravenous fluconazole and hydration that was gradually discontinued over 5 days at that time she was discharged home. At the time of discharge, she was tolerating oral intake well. She was scheduled to complete 14 days of fluconazole at home. Seven months later, the patient continued to be symptom-free without any evidence of recurrence or any major medical illnesses or infections.

DISCUSSION

We report an apparently immunocompetent patient with infectious esophagitis. In our case, her previous unremarkable history, rapid recovery, normal laboratory evaluations, normal immunologic testing and absence of recurrence make the possibility of an underlying immunodeficiency, such as human immunodeficiency virus infection, extremely unlikely. Our patient's endoscopic appearance and histologic evidence confirmed a candidal infection.

EPIDEMIOLOGY

Infection by Candida species is the most common cause of infectious esophagitis in adults. Infections of the esophagus are rare and most commonly seen in immunocompromised individuals. Common infectious agents include Candida species, HSV and cytomegalovirus (3, 4). Immunosuppression is one of the main predisposing factors for candidal esophagitis. Patients with cancer or defects of cellular immunity such as acquired immunodeficiency syndrome and those receiving chemotherapy, radiotherapy or corticosteroid treatments are at particular risk. Other predisposing factors include broad spectrum antibiotic therapy, diabetes and blood dyscrasias (4, 3). Use of proton pump inhibitors has been implicated as a contributor to the development of candidal esophagitis (4).

PATHOPHYSIOLOGY

Candida esophagitis results from fungal overgrowth of the esophagus, impaired cell-mediated immunity, or both. Fungal overgrowth typically occurs in the setting of esophageal stasis resulting from abnormal esophageal motility (eg, achalasia or scleroderma) or mechanical causes (eg, strictures). Impaired cell-mediated immunity can result from immunosuppressive therapy (with, eg, steroids or cytotoxic agents), malignancies or AIDS. Chronic mucocutaneous candidiasis is a congenital immunodeficiency state that is also associated with Candida esophagitis (4).

The usual causative agent is Candida albicans, but other species, including C. glabrata, C. krusei, and C. tropicalis, have been isolated from cases of esophagitis (4, 3). These other species are usually present along with C. albicans, which is the probable cause of the symptoms in most patients. However, in highly immunosuppressed AIDS patients, non-albicans species appear to cause disease (4).

The pathologic appearance of Candida esophagitis ranges from a few superficial white plaques on the mucosal surface to a dense, thick pseudomembrane composed of desquamated squamous epithelial cells, fungus, and fibrin (4). Histologically, in the presence of invasive candidal esophagitis, Candida species are seen along with squamous cells and invading hyphae on smears (4, 9).

Complications of esophageal candidiasis include ulceration and hemorrhage; esophageal obstruction secondary to sticture or mycetoma formation; and, rarely, fistula formation into the bronchial tree (10).

CLINICAL FINDINGS

As in our patient, candida esophagitis usually presents with an acute onset of symptoms as opposed to the more gradual course in patients with reflux or eosinophilic esophagitis (4, 5). Odynophagia, dysphagia, retrosternal chest pain; vomiting and fever are the usual manifestations of candida esophagitis. Symptoms are variable in severity, ranging from mild difficulty in swallowing to such intense odynophagia that the patient is unable to eat or swallow saliva. Other patients may present with chest pain or gastrointestinal tract bleeding, and occasionally, they may be asymptomatic (5).

Oropharyngeal candidiasis is commonly associated with esophageal candidiasis; therefore, the presence of oral thrush may be helpful in suggesting the diagnosis of Candida esophagitis in the appropriate clinical setting (4). Nevertheless, only 50-75% of patients with Candida esophagitis have oropharyngeal disease, and some patients with oropharyngeal candidiasis and dysphagia are found to have other types of esophagitis; therefore, the correct diagnosis cannot always be suggested on the basis of clinical presentation (12, 13).

DIAGNOSIS

The diagnosis of Candida esophagitis is usually made at
endoscopy when white mucosal plaque-like lesions are noted. Confirmatory biopsy shows the presence of yeasts and pseudohyphae invading mucosal cells, and culture reveals Candida (\(C\)).

**TREATMENT**

Antifungal agents used in esophageal candidiasis treatment include nystatin, fluconazole, flucytosine, itraconazole and amphotericin B (\(A\), \(B\)). The choice of agent depends on the immune status of the patient and the extent of the disease. Nystatin has little efficacy in immunosuppressed patients. Fluconazole therapy for 14 days is usually well tolerated and effective for candidal esophagitis (\(A\)).

Concomitant infection of the esophagus with herpes and candida is rare and is most commonly seen in the immunosuppressed or the elderly. Rarely, it may occur in healthy young immunocompetent individuals. Endoscopy to obtain biopsies for histology and culture is the best way to determine the cause of infection and choose the appropriate antimicrobial therapy. In severe cases of esophagitis with two organisms, therapy against both pathogens is recommended (\(A\)).

**CONCLUSIONS**

At present, the progress of medicine allows to successfully treat an increasing number of immunocompromised patients. However, development of candidiasis in immunocompetent patients is quite rare though challenging. Therefore, prevention and therapy of candidal infection will deserve special attention. Despite of increasing knowledge about the pathogenesis of candidal infection, we are still not able to fight successfully against the organism. Nowadays, with the use of less sensitive methods, a lot of infected patients are not properly diagnosed and treated. The development of new antifungal drugs seems very promising.

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