Candidiasis in Malignancy

Diany N Taher, Ari F Syam**, Murdani Abdullah**, Jumhana A***, Khie Chen*****

* Department of Internal Medicine, Faculty of Medicine,
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
** Division of Gastroenterology, Department of Internal Medicine,
Faculty of Medicine, University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
*** Division of Hematology and Medical Oncology, Department of Internal Medicine,
Faculty of Medicine, University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
**** Division of Infectious Disease & Tropical Medicine, Department of Internal Medicine,
Faculty of Medicine, University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital

ABSTRACT

Esophageal candidiasis presents with a range of clinical findings and is rarely found among immunocompetent patient without predisposing factors. Between 20-50% of patient may be asymptomatic. One of predisposing factor of candidiasis is immunocompromised condition due to malignancy. Dysphagia is the most frequently presented feature of esophageal carcinoma. We demonstrated a case of esophageal candidiasis as one of early clinical presentation in patient with esophageal carcinoma.

***Keywords**: esophageal candidiasis, esophageal carcinoma*

INTRODUCTION

Candida is part of the normal flora in many areas of the body and without alteration in host defense, does not cause disease. Factors particularly important to preventing infection are normal bacterial flora, intact skin and mucous membranes within the GI tract and normal cell-mediated immunity.[1-3]

In the United State, *Candida* species are ubiquitous and colonize also in healthy people. Up to 14% of patients with immunocompromising disease develop systemic candidiasis. *Candida albicans* is the most common cause of esophagitis. Most Candida infections are superficial and are associated with death in as many as 77%.[2]

Oropharyngeal candidiasis (OPC) is most prevalent in infants, elderly, compromised hosts and occurs in association with serious underlying condition including diabetes, leukemia, neoplasia, steroid use, antimicrobial therapy, radiation therapy and HIV infection. Esophageal Candidiasis presents with a range of clinical findings. Between 20-50% of patient may be asymptomatic, others will note dysphagia odynophagia epigastric pain, nausea and vomiting or hematemesis. Constitutional findings, including fever, only occasionally occur. Although Candida esophagitis may arise as an extension of oropharyngeal candidiasis, in more than 66% of cases, the esophagus was the only site involved and more often in the distal 2/3 than in the proximal 1/3 of the esophagus.[1,3]

Oral mucosal candidiasis, also called oral thrush; indicates T-cell immunodeficiency. In patients with cancer, condition that predispose to oral candidiasis include cytotoxic chemotheraphy causing mucosal disruption, high dose corticosteroids and use of broad-spectrum antibiotic.[4,5]

Candidiasis most often presents in one of two ways: the Mucocutaneous Syndrome (MS) or the invasive (deep tissue) syndrome. The MS include oropharyngeal (thrush), esophageal and gastrointestinal (stomach to colon) GI candisiasis, intertrigo, vulvovaginitis (the most common form of MS), balanitis and Chronic Mucocutaneous Candidiasis. While invasive candidiasis of the oropharynx and esophagus occurring in the absence of bowel or colon should prompt an investigation for a GI malignancy.[4]

A reliable diagnosis of Esophageal Candidiasis can only be made by histological evidence of tissue invasion in biopsy material. Esophagography with contrast is indicated for diagnosis of esophagitis caused by Candida species. Peristaltic abnormalities caused by small plaques appear as superficial filling defect nodular or cobblestone pattern may be seen, findings

may be similar to those seen with esophagitis caused by cytomegalovirus and herpes simplex virus (HSV). Strictures may be seen with severe esophageal candidiasis. Endoscopy provides direct visualization of small, white, mucosal plaques which esophageal candidiasis, biopsies, may be obtained for a more definitive diagnosis.[1,2,4]

Esophageal candidiasis is classified on the basic of endoscopic appearance: type I, a few white or beige plaques, up to 2 mm in diameter, type II, plaques are more numerous, larger than 2 mm in diameter, type III, confluent, linear and nodular elevated plaques with hyperemia and frank ulceration and type IV, similar to type III but with increased mucosal friability and occasional narrowing of the lumen.[3]

Esophageal cancer is one of the least studied and deadliest cancers worldwide. Cancers arising from the esophagus, including the gastroesophageal junction, are relatively uncommon in the United States, with 13,900 new cases and 13,000 deaths anticipated in 2003. Esophageal cancer is the seventh leading caused of death from cancer among American men, particularly black men, who have a higher incidence of this disease (13 cases per 100,000 people) than do men in other racial or ethnic groups. Worldwide, esophageal cancer is the sixth leading cause of death from cancer.[5,6,7]

More than 90% of esophageal cancers are either squamous-cell carcinomas or adenocarcinomas, the pathogenesis of esophageal cancer remains unclear, smoking is associated with and increased risk of both squamous-cell carcinoma and adenocarcinoma of the esophagus.[5,6,7]

Dysphagia is the most frequently presented feature of esophageal carcinoma, the patient may recount a short of progressive dysphagia, initially affecting only but gradually affecting the swallowing of fluids. The interruption of the passage of food may cause the individual to slowly alter from solid to liquid nutrition, success with this approach may be at the expensive medical self referral, and a short history of dysphagia in an elderly male is almost certainly carcinoma of esophagus or the cardia of the stomach.[6]

ILLUSTRATION

Mr. T, 54 years old, admitted to Cipto Mangunkusumo hospital with the chief complaint swallowing difficulties since 4 months before admission.

Since 4 months before being admitted to the hospital, the patient has had swallowing problem, sometimes with pain. He felt a constriction somewhere in his chest. His swallowing problem has been worsened; he could only swallow half a glass of water in an hour recently. If forced, he vomited. The patient had also complained of hearth burns, no fever, and mild cough without sputum when he has forced himself swallowing food or water. The amount of food he has consumed was decreasing. His body weight had been reduced by 27 kg in 4 months. He had muscle weakness. There was no history of fever and no complain of micturition problem. His pattern of defecation was unremarkable.

Before being admitted to Cipto Mangunkusumo hospital, the patient was hospitalized in other hospital. He was given intravenous fluid therapy and he was diagnosed with achalasia.

The patient has never been hospitalized and never experienced these symptoms before. There were no history of diabetes mellitus, hypertension or malignancy and nor did in his family. He had denial for the history of using drugs like steroid or antibiotic in long period of time, drug abuse, or free sex and smoke cigarette a pack per day since he was 20 years old.

On the physical examination, the patient looked moderately ill, fully conscious, blood pressure of 120/100 mm Hg, heart rate 80 times per minute, temperature 37^{o}C, respiratory rate 16 breaths per minute. Heart and lung were within normal limits, abdominal tenderness on the right quadrant, liver and spleen were not palpable, and bowel sound was normal.

From the laboratory examination: Hemoglobin 15.2 g/dL, leukocyte 6,700/uL, thrombocyte 350,000/uL, ureum 26 g/dL, creatinin 0.9 mg/dL, electroytes: natrium 135 meq/L, potassium 3.93 meq/L, urinalysis was normal, ALT 28 U/L, AST 12 U/L, total protein 6.1, albumin 3.30, globulin 2.80, total bilirubin 0.60 and blood uric acid 8.4 mg/dL.

The faces analysis showed blood. Oesophaghogram showed cicatrical stenosis from esophagus suggested appearance of achalasia esophagus. Chest X-ray indicated bronchitis.

The working diagnosis of this patient was achalasia, which was based on the complaint of difficult to swollen since 4 months before admitted, vomiting, lost of body weight 27 kg on 4 months and difficulties to drink water or liquid food, with differential diagnosis obstruction by tumor, inflammation caused by nfection.

Our planned to confirm diagnosis was upper gastrointestinal endoscopy. The treatment plans were intravenous fluid therapy and enteral liquid diet by nasogastric tube (NGT).

On the 2nd day of hospitalization, endoscopy was done with result are appearance like Candidiasis esophagus from the distal esophagus, no biopsy was performed. From that result we considered that the problem of this patient was odynophagia due to esophageal candidiasis. He was given mycostatin. Then the symptom was relieved but no completely cured.

On the 8th day of hospitalization, patient could eat little of porridge, and he also complaint diarrhea 3 times that day. There was no blood in the feces. He had nausea, vomiting, cough and felt discomfort on his abdomen. From the physical examination patient looked moderately ill, hemodynamic was stable, heart and lung were within normal range, the liver and the spleen were not palpable and decreased bowel sound.

The result from esophageal Swab there was colonization of Candida. Our assessment dysphagia caused by oesophagitis due to mucosal candidiasis with differential diagnosis was obstruction by tumor. The plans for diagnosis were endoscopy for biopsy, abdominal USG paracentesis ascites with guided USG. We also check for CD4 count and cholinesterase level. Treatment given was antifungal fluconazole 150 mg once daily.

The result of upper gastrointestinal endoscopy was described: Oesophagoscopy: from the distal of oesophagus 35 from incicivus there were mass at 6 with granuler mucosa, fragile and the tumor mass was covered almost all lumen, the scope could not pass through, NGT was inserted by endoscopy. Conclusion of endoscopy result was mass in distal of esophagus with differential diagnosis esophagus carcinoma and mass in Cardia. The abdominal USG showed right and left lobes of hepar were contracted, irregular, presence of diffuse SOL. The conclusion was liver cirrhosis.

The biopsy result indicated esophagus mucosa with a typical cell, difficult to confirmed malignancy from this specimen. The result from laboratory examination: non-reactive HIV, T- lymphocyte 454, T-helper limfosit 290; CEA: 1.5 mg/mL, HbsAg was negative, and anti HCV was negative. The ascitic fluid analysis showed yellow, reddish fluid, positive Rivalta test, cell count of 800/uL, PMN 24/ul, MN 776/uL, LDH 159 U/L, serum LDH level of 181 U/L and total protein concentration of 2.8 g/dL. Pathological anatomy examination of ascitic fluid showed epithelial cell like mesotel andalteration to malignancy. The 3rd endocopy showed normal upper third esophagus, normal middle third, stenosis in the lower third, tumor mass in cardia, corpus and fundus of gaster were hyperplasic, fragile, hyperemia in pylorus. The conclusion of endoscopic result was gastric tumor mass, gastroesophageal junction tumor. The problems of this patient were dysphagia due to distal oesophagus tumor and gastrooesophageal junction; esophageal candidosis; hepatic cirrhosis; ascites suspected due to metastases. The patient was discharge from the hospital after 30 days of treatment. His family was disapproved when the Digestive Surgery Department would implant stent on his esophagus.

DISCUSSION

The problem in this patient is difficulty in swallowing that might be caused by several things such as achalasia, tumor, and inflammation (including bacterial, fungal). Dysphalgia results from propulsive or structural abnormalities of either the oropharynx or the esophagus. The structural abnormalities may result from neoplasm, surgery, trauma, etc.[8] The possible cause in this patient was tumor or inflammation caused by Candida. Dysphagia is the most frequently presented feature of esophageal carcinoma, the patient may recount a short of progressive dysphagia, thus, gradually affecting the swallowing of fluids.[6]

The patient also had esophageal candidiasis which was established due to the complaint of dysphagia and the result from endoscopy at the distal of esophagus there were redness and edema with focal white patches areas, and also the result from brushing esophagus, there were many colonization of Candida.[1,2,4] Common location of esophageal candidiasis is in the distal 2/3 of the esophagus.[2] The finding of Candida within an esophageal lesion by smear or culture or in esophageal brushing does not allow distinction between Candida as a commensal or invasive pathogen. Positive esophageal brushing is highly sensitive but very non specific in the diagnosis.[2]

The predisposing factors that lead esophageal Candidiasis are diabetes mellitus, HIV, malignancy. The predisposing factor in this patient was immunocompromissed caused by malignancy. Malignancy could decrease the T-lymphocytes and T-helper cell. The development of mucosal candidiasis is influenced by lymphocytes and neutrophile or cellular immunity.

In this case Candidiasis was recognized before diagnosis of malignancy established. Esophageal Candidiasis is rarely found among imunocompetent patient without predisposing factors. Thus, we have to be alert of underlying disease that can lead to imunocompromissed status. HIV infection and other predisposing factors were not found in this patient, but based on several examinations; it suggested that malignancy was the underlying disease of this patient.

Absolute neutrophil count from this patient was greater than 2,500/mm while the normal range for neutrophils is between 2,500 and 6,000 per cubic millimeter of blood. An ANC below 1,000/mm is called neutropenia, a condition that increase the risk of infection. The level of neutropenia, less than 500 severe risk for infection, 500 – 1,000/mm moderate risk 1,000- 1,500 minimal risk, 1,500 – 2,000 no significant risk.13 So based on that level there were no risk for infection to this patient, but as a fact

candida was infected him, the literature said on this condition some level of risk of infection may still exist. The malignancy itself may be associated with an immune defect due to quality of neutrophil.[10]

Infections that commonly affect people with cancer tend to have one feature in common – they are often caused by germs that are normally present in the environment and people bodies. These germs usually do not cause infections in people with normal protective barriers and strong immune system.[9,11]

Based on the terms of underlying malignancy and the level of immunosuppression we knew that Candida most susceptible in cancer patient with the abnormality of qualitative defect of phagocytic function or neutropenia and defective cell-mediated immunity.[9,10,11]

Nutritional intake for this patient was liquid diet by NGT. There are several reasons why people with cancer often are malnourished. The cancer itself may make eating or digestion difficult. This is common in people with cancer in mouth, throat, or gastrointestinal (digestive) system.[9,11]

Mucosal malignancy candidacies also contribute to this condition, although esophageal candidiasis rarely fatal but it can decrease food and fluid intake and worsen general condition. Thus, the adequate treatment is needed to improve symptoms of the disease not only directly to treat the esophageal candidiasis itself but also to improve the intake of the patient.

Based on the diagnosis, the patient was given the antifungal therapy Fluconazole. From the literature we found that treatment to oropharyngeal and esophageal candidiasis was fluconazole.Fluconazole has markedly improved safety profiles and become the standard of care, especially for patients with moderate to severe oropharyngeal candidiasis (Hay 1990; Darouiche 1998; Vasquez 2000). The goal of antimycotic therapy in OPC is rapid relief symptoms, prevention of complication and prevention of early relapse following cessation of therapy.[1,2,12]

There were several options of antifungal drugs are amfoterisin A, azol, and amfoterisin B. Mycostatin is used only for imunocompetent patient. Amfoterisin B has severe side effect and only for critically ill or candidemia. Azol is treatment of choice for Oropharyngeal Candidiasis.

Esophageal cancer is classified according to the 2002 American Joint Committee on Cancer tumor node metastasis (TNM), more than 50% of patients have unrespectable or metastasis disease at the time presentation.[6]

From the recent problem of the patient, we conclude that it was esophageal carcinoma stage IV. Esophageal carcinoma that is treated with palliative chemotheraphy has median survival of less than one year. Surgery offers the most immediate and best long-term palliation for dysphagia in patients with localized esophageal cancer. Patient with dysphagia may have prompt palliation of symptoms after balloon dilatation, placement of coated, expandable metal stent, laser ablation, or photodynamic therapy. The stenting offers similar degrees of relief from dysphagia and at lower cost, but that the stent may cause severe acid reflux if extended beyond the gastroesophageal junction.[6]

This is a demonstrative case about gastrointestinal malignancy with esophageal candidiasis as early clinical presentation.

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