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Fatal Esophageal Perforation Caused by Invasive Candidiasis

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Instrumental lesions, spontaneous rupture, and trauma cause most esophageal perforations. Transmural fungal infection is extremely rare, although *Candida* may be detected in as many as 25% of normal esophagus. In this report we present a case of fatal esophageal perforation due to transmural *Candida* infection in a 76-year-old woman. The patient died from septic shock and multiorgan failure, despite esophageal resection and systemic antifungal therapy. Pathogenetic aspects and treatment strategies are discussed.

(Ann Thorac Surg 2005;80:1120–2)

Esophageal perforation is an uncommon clinical entity, which is associated with increased morbidity and mortality rates [1]. Among different reasons that may lead to esophageal perforation, transmural *Candida* infection of the esophageus is extremely rare. We could only identify four cases in current English literature.

Particularly characterized by its ability to survive in distinct anatomical sites, *Candida albicans* mucositis of the gastrointestinal and urogenital tract is further facilitated by changes of a host immunity (eg, depletion of CD4+ leukocytes in patients with AIDS) [2]. Immunosuppression regimen after organ transplantation and prolonged stay in intensive care units due to major surgery particularly promote *Candida* infection of the esophagointestinal mucosa [3].

We report a case of fatal esophageal perforation as a sequel of transmural esophageal *Candida* infection in a woman with a symptomatic paraesophageal hernia.

A 76-year-old woman had been treated as in-hospital patient for actinic skin lesions that occurred after radiation therapy for vaginal carcinoma, when she had acute left-sided chest pain and shortness of breath develop. Coronary heart disease, mild impairment of renal function, and ileocecal resection for small bowel carcinoma were preexisting comorbidities.

Chest roentgenogram revealed left pleural effusion and pulmonary infiltration, as well as an enlarged mediastinum. Cardiac ischemia was suspected because of electrocardiographic changes, whereas laboratory findings were all within normal ranges, particularly troponin and D-dimer. Empirical antibiotic treatment was started without further investigations, and the patient slightly improved during the following 2 days. Then the patient became rapidly septic with cardiopulmonary disturbances, increasing pain, and C-reactive protein (CRP) levels. Computed tomographic scan of the thorax demonstrated a seropneumothorax and extensive left-sided pulmonary atelectasis formation. In addition, multiple mediastinal air bubbles and a large paraesophageal hernia were detected (Fig 1).

The patient underwent emergency surgical exploration by a median upper laparotomy. Intraoperatively, a 4-cm longitudinal opening of the distal esophagus was detected that had induced extensive necrosis formation in the posterior mediastinum. Due to the advanced inflammatory changes, esophageal resection and mediastinal drainage were performed through an additional right anterior thoracotomy. A right-sided descending aorta further complicated the operation. Restoration of gastrointestinal continuity was achieved by creating a gastric tube vascularized by the right gastroepiploic artery that was connected with the proximal esophagus in the upper mediastinum. The postoperative course was severely protracted by the ongoing sepsis and development of a multiorgan failure. The patient never recovered and died on postoperative day 17.

Histologic examination of the specimen revealed transmural ulceration at the esophagogastric junction with concomitant severe mediastinitis. Within that ulceration, large masses of fungal hyphal elements were found (Fig 2). Additional microbiological analysis identified *C. albicans* and *Candida norvegensis*. These *Candida* species were also detected in the sputum, vagina, and pleural cavities.

Comment

Candida represents a commensal fungus of different mucous membranes in healthy individuals. The esophagus is colonized in as much as 25% of normal individuals [4]. However, invasive infections causing extensive tissue necrosis and ulceration predominantly occur in immunocompromised patients after major surgical procedures or prolonged intensive care unit stays, and also in patients with organ transplantations [3]. It has only been partially elucidated which factors may contribute to promote progression from simple colonization to invasive disease [5]. Competent T-cell immune response is a crucial protecting mechanism against cutaneous, vaginal, and oral Candidiasis in patients with AIDS who are known to develop oral Candidiasis in as much as 70% [6]. Resistance to systemic fungal infection is closely associated with normal mononuclear phagocytes and neutrophil response [5]. Moreover, it has been hypothesized that depending on specific preexisting host deficiencies, different forms of Candidiasis may occur. The invasive-

Accepted for publication Feb 20, 2004.

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Published by Elsevier Inc
0003-4975/05/$30.00
doi:10.1016/j.athoracsur.2004.02.147

ness of different *Candida* strains induces various types of diseases and host responses accordingly [2, 5].

Transmural invasive *Candida* infection remains an extremely rare cause of esophagointestinal perforation. By thoroughly reviewing the current English literature, we could only find 4 patients with esophageal perforation that were histologically confirmed to be caused by transmural *Candida* infection [7, 8]. Jones and colleagues [8] reported severe necrotizing *Candida* esophagitis in 2 insulin-dependent diabetic patients after renal transplantation. The first patient was a 34-year-old woman who died 6 months after transplantation. She had ulcerative *Candida* esophagitis develop 2 weeks postoperatively. Despite amphotericin B treatment she had an esophagomediastinal fistula develop, and she died after sudden massive hematemesis. Autopsy disclosed a ruptured mycotic aneurysmal of a peripheral pulmonary artery. The second patient was a 40-year-old human who had characteristic *Candida* esophagitis develop 35 days after transplantation. An esophagram taken 66 days after the operation showed a fistula between the esophagus and the main stem of the left bronchus. Despite treatment with amphotericin B, decompressive gastrostomy, esophagostomy above the fistula, and dissection below the fistula, the patient became septic and died 3 months after transplantation. An autopsy showed a septal myocardial infarction as the cause of death [8]. Both patients developed invasive *Candida* esophagitis in the early posttransplant course. Despite prophylactic oral nystatin treatment, esophageal perforation could not be prevented.

Another two cases of nonfatal esophageal perforation related to invasive Candidiasis were reported by Gaissert and colleagues [7]. The first patient (a 10-year-old boy with Down syndrome) underwent chemotherapy for acute B-cell lymphocytic leukemia when he had esophageal necrosis develop. The second patient (a 27-year-old autistic human) underwent diagnostic esophagogastroscopy for esophageal Candidiasis. Delayed perforation of the esophageal wall occurred 3 months later at the biopsy location. Emergency esophagectomy and cervical esophagostomy were performed. Moreover, systemic antifungal therapy was started. Both patients survived and revealed a good long-term outcome after restoration of gastrointestinal continuity by using a gastric conduit.

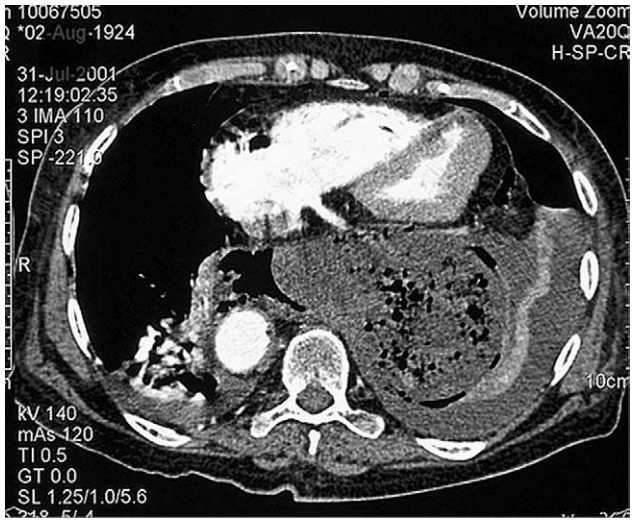

Fig 1. Computed tomographic scan of the thorax shows a seropneumothorax with extensive pulmonary atelectasis formation on the left side, multiple mediastinal air bubbles, a large paraesophageal hernia, and a right-sided descending aorta.

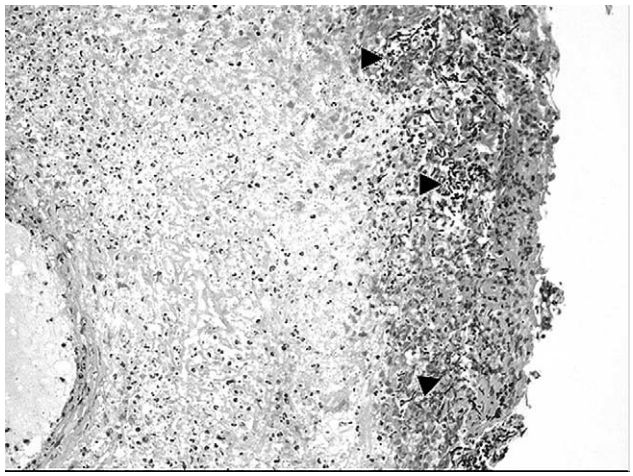

Fig 2. Histologic specimen of the esophageal wall. Arrowheads *show large masses of fungal hyphal elements.*

In our patient, a preexisting esophageal colonization with *Candida* can be assumed. Temporary incarceration of the paraesophageal hernia probably caused a mucosal damage at the gastroesophageal junction. Transmural ulceration by invasive Candidiasis was therefore facilitated by the impaired mucosal defense. At the time of delayed diagnosis, esophageal perforation was advanced and extensive mediastinitis was already established.

Successful treatment of invasive *Candida* infection complicated by esophageal perforation requires both long-term systemic antifungal therapy and emergency surgical intervention. Surgery must include esophageal resection, extensive necrosectomy, and drainage of the pleural cavities and mediastinum. Correction of the patient's immunosuppressive drugs should be attempted. Because there are only a very few cases that have been reported so far, no established treatment regimen has been validated and long-term outcome probably remains poor.

In conclusion, esophageal perforation due to invasive Candidiasis is an extremely rare complication, although its true incidence may be underestimated. Despite aggressive medical and surgical treatment, the patient's prognosis remains poor.

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FEATURE ARTICLES

Esophageal Replacement by Lexer's Esophagoplasty: Adenocarcinoma as Late Complication

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The most successful method for esophageal reconstruction in the early 20th century was the jejunodermatoesophagoplasty after Lexer, involving the presternal formation of a skin tube for passage reconstruction. A 59-year-old patient presented to our hospital with adenocarcinoma at the dermatojejunostomy 47 years after undergoing a Lexer procedure. The neoesophagus was removed, and the passage was reconstructed by a retrosternal colonic interposition. Although squamous cell carcinoma is known as a late complication of dermatoesophagoplasties, this is a reported case of adenocarcinoma formation.

(Ann Thorac Surg 2005;80:1122–4)

Esophageal surgery in the early 1900s was associated with a very high mortality as a result of insufficient experience in thoracic surgery, infection problems, and the lack of methods that allowed for adequate ventilation of the patient while performing surgery on the open chest. At that time benign esophageal strictures caused by acid or lye ingestion were quite frequent [1, 2].

In those days the most successful method of passage reconstruction was the antethoracic jejunodermatoesophagoplasty developed by Lexer [1, 3], involving the creation of an antethoracic skin tube as an esophageal bypass.

Several cases have been reported in the literature in which squamous cell carcinoma developed in the skin tube decades after esophagoplasty [4–7]. We report herein a case of adenocarcinoma formation in a skin-tube esophagus.

A 59-year-old female patient was admitted to our hospital with biopsy-proven diagnosis of esophageal adenocarcinoma. The history received from the referring hospital indicated that in 1956 the patient had undergone a presternal reconstruction of the food passage for esophageal stricture as a result of an accidental acid burn she had suffered at the age of 13 years (1955).

During routine endoscopy a biopsy sample had been taken at the aboral anastomosis of the neoesophagus that contained malignant tissue.

After a barium study it became clear that a presternal bypass of the occluded esophageal segment had been achieved by the operation (Fig 1). The barium study, as well as an additional endoscopy, showed no signs of intraluminal tumor growth. Nevertheless extensive biopsy samples were taken at the site of the anastomosis, which however failed to show tumor on histologic examination. The computed tomography and positron-emission tomography scans likewise could not detect any signs of tumor or distant metastases. Tumor markers carcinogenic embryonic antigen, CA 19-9, and CA 72-4 were within the normal range. The biopsy specimen in question was reevaluated independently by two experienced gastrointestinal pathologists and found to definitely show adenocarcinoma.

The decision was made to remove the tumor-bearing neoesophagus and reconstruct the food passage by retrosternal colonic interposition. During the course of the operation and macroscopic examination of the specimen it became clear that the occluded esophagus had been bypassed by a presternal skin tube that was cranially connected to the prestenotic cervical esophagus and to the gastric antrum by means of retrocolic interposition of a jejunal segment (Fig 2).

After removal of the neoesophagus, the food passage was reconstructed by retrosternal interposition of a transverse colon segment between the cervical esophagus and the stomach. The colon was connected with the anterior wall of the stomach by means of an end-to-side anastomosis. The postoperative course was uncomplicated, and swallowing function was good. The patient could be discharged 20 days after the operation and is doing well up to the time of this report.

Close histologic examination of the specimen showed a small remnant of adenocarcinoma right in the area of the anastomosis between the skin tube and the jejunal segment invading the submucosa. Most of the tumor had been removed by the biopsy that led to the diagnosis (Fig 3). Cytokeratin 7 negativity and positive staining for cytokeratin 20 in the immunohistochemical analysis confirmed the origin of the carcinoma from the jejunal epithelium.

Accepted for publication Feb 17, 2004.

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Published by Elsevier Inc
0003-4975/05/$30.00
doi:10.1016/j.athoracsur.2004.02.081