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Early Postoperative Anastomotic Leakage due to Necrotizing Candidiasis after Abdomino-Thoracic Resection for T1 Esophageal Cancer

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Abstract

We present a case of early postoperative anastomotic leakage after abdomino-thoracic esophageal resection for cancer in a female, due to a necrotizing, transmural infection with *Candida* species (spp). The infection was treated successfully with redo surgery and systemic antimycotic therapy with caspofungin. The patient was disease-free at 49 month follow-up, but her long-term quality of life, as assessed by the EORTC questionnaire (QLQ C-30) was reduced. Aggressive surgical and medical therapy led to successful treatment of this rare complication.

Key words: *Candidiasis; anastomotic leak. esophageal resection; esophageal cancer*

Introduction

Candida species (spp) constitute a commensal fungus of the various mucous membranes. The esophagus is colonized in about 25% of normal individuals [1], but normal esophageal mucosa is resistant to infection. Invasive, necrotizing transmural esophageal infection leading to perforation is very rare, occurring mainly in patients with reduced immune status due to hematological malignancy or acquired immunodeficiency syndrome (AIDS), or after solid organ transplantation [2,3].

The case is reported here of early postoperative anastomotic leakage after abdomino-thoracic esophageal resection in a 77-year-old female, which was caused by transmural esophageal *Candida* infection, and was treated successfully with combined surgical and medical therapy.

Case Report

A 77-year-old female was referred for surgery after incomplete endoscopic submucosal resection of a T1 esophageal adenocarcinoma of the gastroesophageal junction. As no lymph node involvement or distant organ metastases were detected in the preoperative tumor staging (CT- scan, endoscopic endosonography), esophageal resection without neoadjuvant therapy was indicated. Preoperative pulmonary function testing and cardiological assessment were performed, as the patient had a history of chronic obstructive pulmonary disease (COPD) GOLD II stage (FEV1 70.4%), treated with long-term glucocorticoids (budesonid), coronary heart disease (CHD), and stent implantation in the left internal carotid artery. Additionally, the patient had suffered from deep vein thrombosis (1984), and had undergone median laparotomy for an incisional hernia after surgical treatment of an umbilical hernia.

The patient underwent abdomino-thoracic esophageal resection, cholecystectomy, pyloroplasty, and D2 lymphadenectomy, including reconstruction with conventional gastric conduit formation according to the Kirschner-Akiyama procedure. The intrathoracic esophagogastric anastomosis was performed end-to-side, using a 25mm circular stapler. Intraoperative testing using methylene blue revealed an intact anastomosis. No intraoperative blood transfusion was required and the patient was referred to the intensive care unit (ICU) postoperatively.

On the first postoperative day, the patient experienced tachyarrhythmia absoluta with hemodynamic instability, for which electric cardioversion and amiodaron application were required. The inflammatory indices, white blood cell count (WBC), procalcitonin, C-reactive protein (CRP) were not elevated initially and the secretion from the intraoperatively inserted chest tubes was normal. On the second postoperative day, a brown- green secretion from the intrathoracic drains was observed, with clinical

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deterioration of the patient, and emergency re- thoracotomy was performed.

An anastomotic leakage 1.5 cm in diameter and macroscopically necrotic, inflamed tissue in the anastomotic region, suspicious of "anastomositis", were observed. The inflamed, necrotic tissue was resected and a new end-to-end, double-layer, hand-sewn esophagogastric anastomosis was performed (with PDS 4-0 sutures). The further postoperative course was prolonged due to concomitant sepsis. Following the identification of *Candida albicans* in the blood culture samples and subsequent administration of antimicrobial therapy with meropenem and caspofungin the patient gradually recovered and was discharged 43 days after the initial surgery.

Histological examination of the excised anastomosis revealed areas of augmented vascularization exhibiting markedly elevated cellularity with an abundance of lymphocytes, plasma cells, and polymorphonuclear neutrophils. Other areas disclosed an increased collagen fiber content. The distribution of fibrinoleukocytic material was consistent with a transmural ulceration. Yeast-like elements, some of which displayed features of budding and filamentous pseudohyphal and hyphal forms, were considered to be *Candida spp* [4,5] (Figure 1). The postoperative tumor stage was pT1N0. The patient was tumor-free at 49 month follow-up, but reported reduced quality of life, as assessed by the EORTC questionnaire (QLQ C-30).

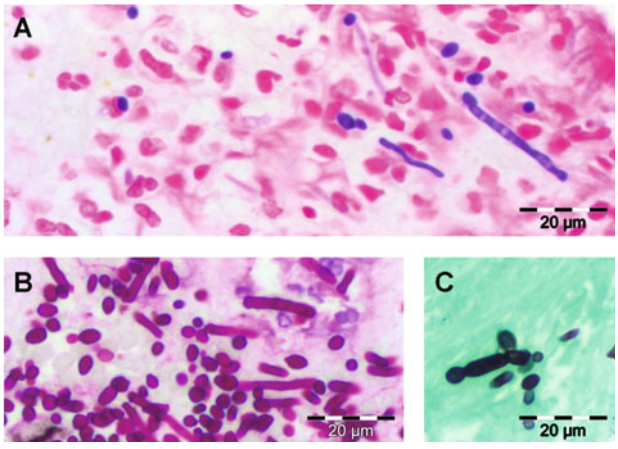

Figure 1. Gastro-esophageal anastomotic leak: Microscopic appearance of tissue surrounding the anastomotic leak, showing suppurative "anastomositis". A: Gram stain, B: Periodic Acid Schiff's (PAS) reaction, C: Grocott's (syn.: Grocott methenamine silver, GM) stain on buffered formalin fixed sections of the region of interest highlightened the presence of a gram-positive yeast-like organism with a budding and filamentous (pseudohyphal and hyphal) morphology, compatible with *Candida spp*. [Sangoi AR *et al* 2009] (NCBI Taxonomy ID: 1535326 [Wheeler DL *et al* 2000]).

Discussion

Anastomotic leakage is a major cause of postoperative morbidity after abdomino-thoracic esophagectomy [6]. Various factors promote anastomotic leakage, including tension on the anastomosis, technical failures and inadequacy of blood supply of both organs at the connection site. Early postoperative anastomotic leakage after esophageal resection due to invasive candidiasis has rarely been reported in a non-immunodeficient patient. In the reported case the complication was treated successfully with redo surgery and concomitant, systemic antifungal therapy, and the patient remained disease-free 49 months after surgery.

Invasive esophageal infection causing perforation has been described in immunocompromised patients, during prolonged ICU stays, for example, or after transplantation of solid organs [7]. These predisposing factors were not present in this patient, buta pre-existing colonization with *Candida* can be assumed, as colonization of esophagus occurs in 25% of normal individuals [1] and her long-term glucocorticoid medication for COPD may have been a predisposing factor. In addition, she had undergone, preoperatively a partial endoscopic submucosal resection. Post-endoscopic mucosal damage and glucocorticoids may have facilitated the esophageal infection with *Candida spp*, causing ulceration and anastomotic leakage at the esophagogastrostomy site.

Two reports have reviewed cases of necrotizing esophagitis, either spontaneous, or after endoscopic intervention. In the first case series Gaissert and colleagues described the outcome of 25 patients with infective necrotizing esophagitis since 1976, four of which were treated by them [2]. Fungi were detected as the pathogenic organisms in 15, viruses in 7 and bacteria in 7 cases. Of these patients, 21 (84%) were immunodeficient, while only one patient was receiving corticosteroid therapy, as the patient presented here, but none had undergone esophageal surgery. Surgery was required in 12/25 patients (48%). The overall mortality was 48% (12/25), while in the group of patients with conservative treatment the mortality was 90% (9/10). The authors concluded that surgical intervention should be favored in order to control the sepsis. Redo surgery was chosen to treat the early appearance of leakage on day 2 in the case presented here, although in many cases of anastomotic leakage of with non-infective etiology after esophageal resection endoscopic treatment with stent insertion is frequently applied. The data documented by Gaissert and colleagues. [2] and the good long-term outcome in this case (survival of at least 49 months) justify the surgical approach.

Hoffmann and colleagues reviewed a case series of 80 patients with esophageal perforation [8], most occuring after endoscopic intervention (55 patients, 44%). Invasive candidiasis was detected in 24/68 patients (35%), with

Candida albicans being the most common species (76%). Because of the growing prevalence of non-albicans species and the concomitant growing resistance to fluconazole, these authors recommended echinocandin application as first line treatment in cases of invasive candidiasis [8], and an echinocandin (caspofungin) was administered as antimycotic therapy in the present patient.

The patient´s long-term quality of life was evaluated, using the QLC-30 questionnaire. In contrast to previous reports [1,2], the patient was disease free at 49 month follow- up, and the impact of the surgical therapy on her quality of life was reported here. As was to be expected from the prolonged clinical course and the presence of comorbidities (COPD, CHD), the quality of life was impaired in the domain of physical activity, and she had respiratory discomfort and regurgitation symptoms. Taking into account the very high mortality rate after esophageal perforation, the outcome in this case is considered to be satisfactory.

In conclusion, anastomotic leakage due to invasive candidiasis is a rare complication after esophageal surgery. With combined surgical and systemic antimycotic therapy the long-term outcome can be good.

Ethical Approval – Informed Consent: *The authors declare that the study has been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Also all patients gave their written informed consent prior to their inclusion to the study.*

Conflict of Interest: *The authors declare that there is no conflict of interest.*

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