

East African Medical Journal Vol. 89 No. 7 July 2012

OESOPHAGEAL CANDIDIASIS IN AN IMMUNOCOMPETENT ADULT, AN ADVERSE EFFECT OF ANTIBIOTIC THERAPY FOLLOWING CARDIAC SURGERY: CASE REPORT AND REVIEW OF LITERATURE

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OESOPHAGEAL CANDIDIASIS IN AN IMMUNOCOMPETENT ADULT, AN ADVERSE EFFECT OF ANTIBIOTIC THERAPY FOLLOWING CARDIAC SURGERY, CASE REPORT AND REVIEW OF LITERATURE

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SUMMARY

Dysphagia following cardiac surgery is a frequently encountered problem, being most commonly due to the sternotomy incision and/or prolonged intubation. Oesophageal candidiasis is an increasing problem that is usually associated with immunosuppression or immunodeficiency. We report a 59 years age, immunocompetent lady whom had developed dysphagia and odynophagia following open cardiac surgery and long term course of antibiotics. Diagnosis of Candida oesophagitis was established after radiological, endoscopic and microbiological evidence, and successful treatment with combined topical and systemic antifungal therapy was achieved. Possibility of immunodeficiency was excluded. We believe that this lady developed oesophageal candidiasis due to a long term course of broad spectrum antibiotics. We discuss the various diagnostic modalities and treatment options.

INTRODUCTION

Dysphagia is well known to complicate cardiac operations. It is most commonly related to median sternotomy and intra-operative or post-operative interventions, such as transesophageal echocardiography and/or endotracheal intubation (1). Candida oesophagitis is an increasingly recognised problem which presents with dysphagia and odynophagia, but it is usually associated with immunodeficiency or immunosuppression, and it is not usually suspected following cardiac surgery in an immunocompetent adult (3, 4).

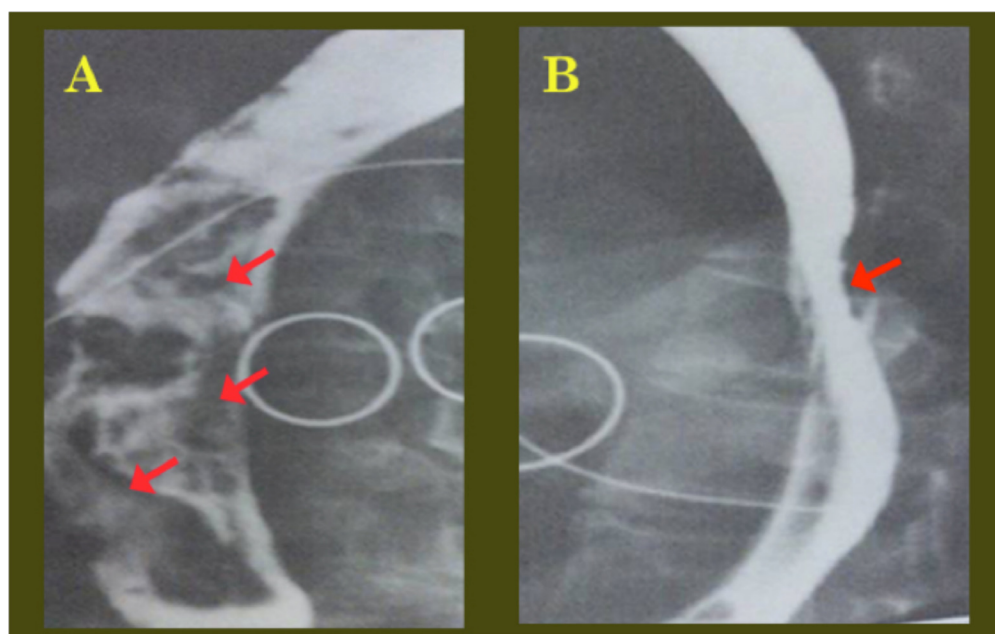
In this article, we report an immunocompetent lady who developed Candida oesophagitis following open cardiac surgery and a course of antibiotics.

CASE REPORT

Our patient, a 59 year old female, with severe mitral stenosis and huge left atrial thrombus. She is not known to have diabetes or HIV or any other immunodeficiency conditions, and she was not on any immunosuppressant medications. She underwent open mitral valvotomy and removal of the thrombus through a median sternotomy

incision. She was covered with prophylactic pre and post-operative antibiotics. On the fifth post-operative day, she developed severe chest infection, for which, a potent cephalosporin was prescribed and continued for two weeks, and then discharged in a good condition. Three weeks after discharge, she came with dysphagia and odynophagia. Barium swallow showed multiple large plaque like lesions, cobblestone appearance of oesophageal mucosa and a pseudo-membrane mimicking a double lumen oesophagus, features suggestive of Candida infection. Endoscopy showed severe hyperemic mucosa, patchy ulcerations, whitish streaks and stricture of the middle third of the oesophagus. Oesophageal brush was taken for culture and sensitivity and the results proved Candida albicans infection. Possibility of immunodeficiency was excluded by normal Full blood count (FBC), Renal Function Test, Liver function test (LFT), Blood Sugar, CD4 and negative HIV tests. She was successfully treated with oral nystatin and intravenous Amphotericin B, with repeated endoscopic oesophageal dilatations. She was discharged after one month. Her follow-up showed complete resolution of the stricture and she was asymptomatic.

Barium study of the oesophagus in a patient with Candida Oesophagitis. (A) Before treatment showing plaque like lesions in a linear pattern (arrows), separated by normal mucosa. (B) After treatment showing residual stricture (arrow).



DISCUSSION

Swallowing difficulties, and subsequent pulmonary aspiration, is a common problem, being observed in as many as 15% of patients in acute care facilities (5). Patients undergoing cardiac surgery, due to their complex risk profile, are especially more vulnerable to sustain post-operative morbidities, including dysphagia (6-9). In one study, swallowing dysfunction was found in 4% of patients undergoing cardiac surgery, with significant association to the post-operative outcome and morbidity including post-operative pneumonia, need for tracheostomy, and increased length of hospital and ICU admission (1). The main risk factors for dysphagia following cardiac surgery are prolonged endotracheal intubation, the use of transoesophageal echocardiography (TOE) and the need for tracheostomy tube (1, 2, 10, 11). In our patient, intra-operative transoesophageal echocardiography was not performed, and she did not need prolonged intubation or tracheostomy tube, so we thought of other potential causes of dysphagia and odynophagia. Candida oesophagitis is an increasingly recognised condition in the past two decades (13). This systemic mycosis is mainly associated with conditions of immunodeficiency or immunosuppression, such as AIDS, cancer, and prolonged steroid therapy (14, 15). Other possible predisposing factor is local oesophageal stasis caused by severe oesophageal motility disorders such as achalasia and scleroderma (18). All these predisposing factors were excluded in our patient and the immunological workup was normal. The only possible predisposing factor in our case was the use of potent antibiotics for her severe

chest infection.

Oesophageal candidiasis in immunocompetent adults is an area of extensive research. There is an evidence of some alterations in cellular immunity in some patients. These alterations include low CD4 and CD8 lymphocyte count and abnormal Yeast phagocytosis and neutrophil chemotaxis (43). Another, and contradicting, study about the immunological profile of seven patients with oesophageal candidiasis had shown no cellular immunity changes including immunoglobulins, complement and lymphocytes population in most of the patients examined, with severe IgG hypogammaglobulinemia in only one patient (44). Candida oesophagitis due to antibiotic therapy has been reported only in few articles (4, 12, 15, 32). Bacterial commensals in the gut inhibits fungal growth and colonisation, thus protect against candidal infection, and this inhibitory effect is eliminated by administration of potent antibiotics (3, 33).

Diagnosis of oesophageal candidiasis remains challenging and involves clinical, radiologic and endoscopic visualisation, but the gold standard is the microbiological identification of the organism from an oesophageal brushings or biopsy, with determination of the causative species and it is drug susceptibility (16, 17). Although *Candida albicans* is still the most common species, there is a recently observed shift towards other non-*albicans* species such as *C. glabrata* and *C. krusei* (31). Double contrast barium study is useful and the main finding is the discrete, linear plaque-like lesions separated by normal mucosa, but this needs to be carefully differentiated from the resembling rounded plaque like lesions of Glycogenic acanthosis, a condition that usually affect elderly

people (19-21). These plaques may coalesce in severe disease to form the classical cobblestone appearance (24). The ability of double contrast barium study to identify these plaque like lesions gives it a sensitivity of 90% (19, 22). Endoscopy plays an important role in the diagnosis and it allows direct visualisation of the characteristic candidal lesions, as well as taking a biopsy or brushings for mycological identification (23). In our patient, the double contrast barium study findings were consistent with the above mentioned literature, with typical and large filling defects arranged in a longitudinal pattern and separated by normal mucosa. Moreover, a pseudomembrane appearance giving the picture of double lumen is observed, a finding not commonly reported with oesophageal candidiasis.

Early treatment with the appropriate antifungal therapy is essential to reduce morbidity and mortality (16, 30). The aim of treatment is the elimination of symptoms and signs of the disease, as well as prevention of future recurrences (25). Generally, topical therapy is ineffective for oesophageal candidiasis, whereas Azoles (fluconazole or itraconazole) or intravenous amphotericin B are effective (25). Resistance to fluconazole is an emerging problem (26). New antifungal agents like echinocandin are proved effective for azole resistant cases, better tolerated and with less adverse effects than amphotericin B (27-29). The choice of the initial therapy depends on the condition of the patient. In non-leucopenic patients' initial therapy with fluconazole or one of the three approved echinocandin compound is appropriate, liposomal amphotericin B and voriconazole are second line options because of their adverse effect profile (17). On the other hand, echinocandins or liposomal amphotericin B are recommended as first line in those with leucopenia (17). Due to the high risk profile of our patient and the no availability and cost of echinocandin, we preferred to give intravenous amphotericin B as a practical option, and the response was excellent.

One aspect of controlling *Candida* infections is the identification of high risk patients for consideration of prophylactic or empirical therapy, through validated risk assessment scoring tools (34-39). However, this issue of prophylactic antifungal therapy is still controversial and the data are contradicting. In one study, the use of prophylactic antifungal therapy was associated with reduced proportion of candidaemia and other fungal infections, reduced need for amphotericin B for systemic infections, a trend towards reduction in hospital morbidity, with no significant contribution to the fluconazole resistance (40). On the other hand, there are significant data on the a clear correlation between fluconazole use control and decreasing incidence of non-albicans candidaemia (41). Recently, there are some promising results on the use of monoclonal

antibodies, like Mycograb (a human recombinant monoclonal antibody that inhibits heat shock protein 90), combined to antifungal medications for the immunoprophylaxis of candidal infections in high risk groups, but these are still in the stage of *in vitro* and animal experiments (42).

In conclusion, candida oesophagitis should be suspected as a cause of dysphagia following cardiac surgery and antibiotics use, even in immunocompetent patients. Diagnosis needs clinical, radiological, endoscopic and microbiological tests, and treatment with combined topical and systemic antifungal is effective. More research and clear consensus is needed to guide the use of prophylactic antifungal medications for high risk patients.

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