Case Report

Fungal Pyopneumothorax: A Rare Entity

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Abstract

Fungal empyema is rare but severe infection with high mortality. *Candida* spp are the most common isolates among all fungal empyema patients. *Candida glabrata* (older name: *Torulopsis glabrata*) is often the second or third most common cause of candidiasis after *Candida albicans*. *Candida glabrata* infections can be mucosal or systemic and are common in immunocompromised patients, especially in patients with diabetes mellitus. We report a case of fungal pyopneumothorax in a patient having underlying diabetes mellitus and cirrhosis of the liver. *Candida glabrata*, being an uncommon pathogen for fungal pyopneumothorax was the causative agent in the present case. **[Indian J Chest Dis Allied Sci 2019;61:211-213]**

Key words: Fungal empyema, Pyopneumothorax, *Candida glabrata.*

Introduction

Empyema thoracis is a serious condition characterised by the accumulation of purulent fluid in the pleural cavity, typically following pneumonia, sub diaphragmatic abscess or oesophageal rupture. Fungal empyema thoracis is a rare form of this condition with high mortality, in which the most frequently isolated fungus is *Candida* species.[1] *Candida glabrata* has been considered a relatively non-pathogenic saprophyte of the normal flora of healthy individuals, rarely causing serious infections in humans. However, following the widespread and increased use of immunosuppressive agents and broad-spectrum antibiotics, the frequency of mucosal and systemic infections caused by *C. glabrata* has increased significantly.[2]

Case Report

A 42-year-old male, a chronic alcoholic and reformed smoker doing a desk job was referred to our institute for the management of left-sided effusion with diabetes mellitus (DM) and cirrhosis of liver with extra-hepatic portal venous obstruction with oesophageal varices (post banding). He had fever, chest pain and shortness of breath for the last one month and on anti-tuberculosis treatment after repeated pleural aspiration at another hospital before reporting to us. His diabetes was well controlled with oral medications. Family history was unremarkable.

At the time of presentation to us, his general condition was poor with a oxygen saturation of 94% on 4 L/min via nasal prongs, pulse rate was 120 per minute, blood pressure of 110/60 mmHg, respiratory rate was 34 breaths per min with use of accessory muscles of respiration. There was no icterus, pallor, cyanosis, clubbing or lymphadenopathy. The breath sounds were absent on the left side. There was no other significant abnormality in any other systemic examination.

The patient was admitted in the intensive care unit and started on injectable antibiotics (piperacillin-tazobactam, amikacin and clindamycin), oxygen and other supportive measures. Arterial blood gas analysis at fraction of inspired oxygen (FiO_2) of 36% revealed pH-7.459, partial pressure of arterial carbon dioxide ($PaCO_2$)-30.3mmHg, partial pressure of oxygen (PaO_2)- 65.9mmHg, arterial oxygen saturation (SpO2)-94% and bicarbonate (HCO_3)- 26.6mEq/L, with a PO_2/FiO_2 ratio of 183mmHg. Haematological investigations revealed haemoglobin-10.9 gm/dL, total leucocyte count of 9200/mm^3 with normal differential cell percentage and platelet counts of 1.03 lakh/mm^3. Kidney and liver function examination revealed urea 30mg/dL, creatinine 1.2mg/dL, bilirubin (total) 0.7mg/dL, serum glutamic-oxaloacetic transaminase (SGOT) 20IU/L, serum glutamic-pyruvic transaminase (SGPT)-38IU/L, total protein 6.6g/dL, albumin 3.2g/dL with an elevated alkaline phosphatase of 450IU/L. Glycosylated haemoglobin was 6.5%. Enzyme linked immunosorbant assay for human immunodeficiency virus was negative. Chest radiograph showed left-sided hydro-pneumothorax (Figure 1). Ultrasound of the chest revealed posterior loculated collection on the left pleural space. Pleural fluid showed frank pus. Consequently intercostal drainage tube (ICD) was inserted. Analysis of pleural fluid showed protein of 5.0g/dL, sugar of 58mg/dL, adenosine deaminase (ADA) - 105U/mL, lactate dehydrogenase (LDH) 4230 units/L, cell counts of 22000cells/μL with predominant lymphocytes. Examination of pleural fluid for acid-fast bacilli, Gram staining and GeneXpert was negative. Contrast enhanced computed tomography of the chest revealed left-sided loculated collection with collapse consolidation (Figure 2). Pleural pus, blood culture and urine culture were sterile

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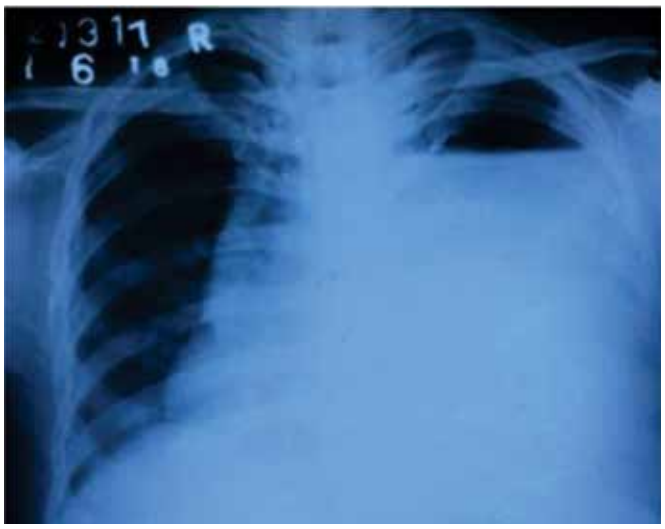

Figure 1. Chest radiograph (postero-anterior view) showing left-sided hydro-pneumothorax with a mediastinal shift.

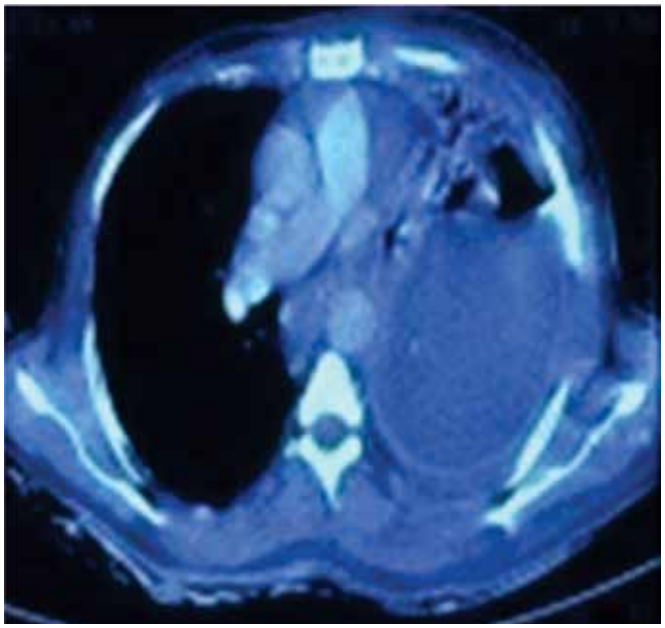

Figure 2. CECT chest showing left-sided loculated collection with air-fluid level and collapse consolidation.

after 48-72 hours. Despite seven days of antibiotics and ICD, there was persistent daily drainage of 100-120 mL of pus, with intermittent fever. Microbiological investigations on Gram stain revealed the presence of fungal element resembling *Candida* spp. Therefore, patient was started on caspofungin; which did not show much response. Finally, the fungal culture report revealed growth of *Candida glabrata* (Figure 3), intermediate sensitive to caspofungin but sensitive to voriconazole, micafungin, amphotericin B and flucytosine. The patient was administered voriconazole 200mg injection initially for 10 days, then orally for two months. The ICD was removed after three weeks. His symptoms improved and chest radiograph showed marked

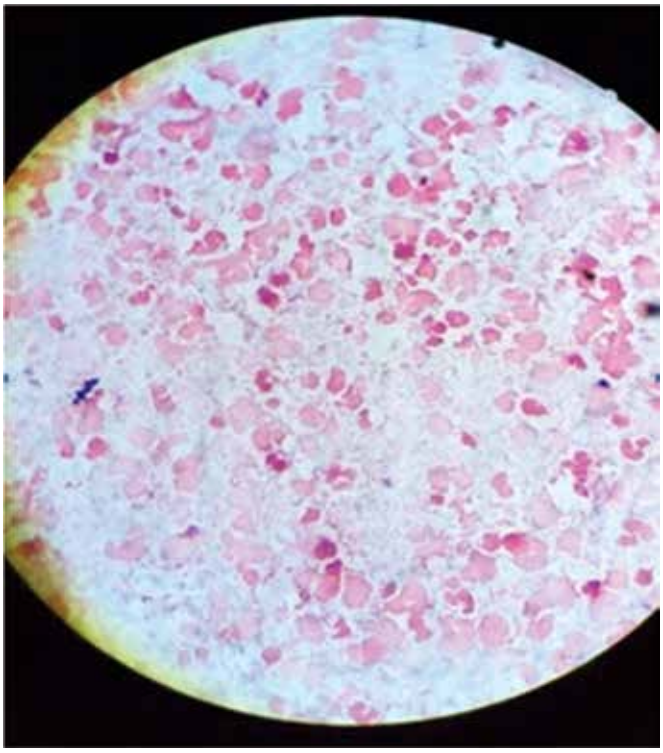

Figure 3. Photomicrograph showing *Candida glabrata* on chromoagar with its characteristic pink to purple appearance (Magnification)

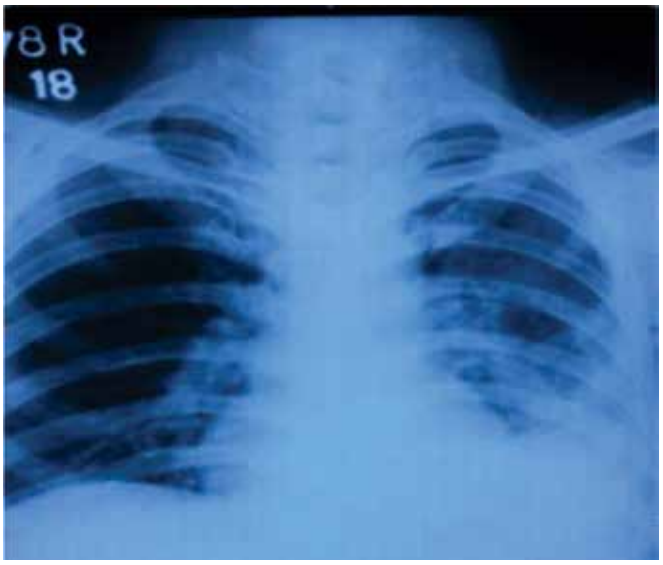

Figure 4. Chest radiograph (postero-anterior view) done after one month of treatment showing significant improvement.

improvement (Figure 4) and the patient was discharged after three weeks. On follow-up after two-month course of voriconazole, patient became asymptomatic.

Discussion

Fungal infections have increased in the last few decades as a result of the widespread use of broad-spectrum antibiotics and the growing number of immunocompromised

patients. In 2008, the European Organization for Research and Treatment of Cancer/Invasive Fungal Infection Cooperative Group and Infectious Diseases Mycosis Society Group (EORTC/MSG) revised the diagnostic definition for invasive fungal infection to improve its consistency and reproducibility. However, the diagnostic accuracy of these criteria for unusual sites of infection, such as the pleura remains to be established.[3]

Although fungal empyema was described over 60 years ago, there has been little progress on the diagnosis and management of this condition, partly due to its low prevalence. Historically, *Candida albicans* accounted for 70% to 80% of the isolates recovered from the infected patients. *C. glabrata* and *C. tropicalis* each accounted for approximately 5% to 8% of isolates, while other non-albicans *Candida* species occur rarely. However, more recent epidemiological data revealed a mycological shift from *C. albicans* to the non-albicans *Candida,* species such as *C. glabrata, C. tropicalis, C. parapsilosis,* and *C. krusei*.[2]

In a study of 67 patients with fungal empyema thoracis, the most common fungi encountered were *Candida* species in 47 (64%) isolates, *Torulopsis glabrata* in 13 (18%) isolates and *Aspergillus* species in 9 (12%) isolates. In another study from Taiwan[5] among 63 patients, 35 (55.6 %) had contiguous infection. The crude mortality was 61.9% and *Candida albicans* was the most common isolate.

The pathogenic mechanisms of *Candida* empyema thoracis were divided into two categories: contiguous infection for empyema in patients who had adjacent infection, such as oesophageal rupture, pneumonia, mediastinitis, paraspinal abscess, or sub-diaphragmatic liver abscess; and non-contiguous infection for empyema in patients who had a distant infection focus, such as intra-abdominal abscess, ischaemic bowel, bowel perforation or fungemia, or an unidentified infection source.[5] The most common route for the fungus to reach pleural cavity are via direct lung infection, complication of pre-existing chronic empyema, oesophageal bronchial fistulas, or repeated thoracentesis.[2] In our case, it was possibly due to the previous pleural aspiration. Our patient was suffering from co-morbid diseases, like diabetes mellitus and chronic liver disease making him further prone for the fungal infection.

Many factors have been reported to be associated with mortality of the patients with *Candidemia* including advanced age, septic shock, non albicans *Candidemia* and a greater severity of the disease.[5] Among antifungal agents, voriconazole and micafungin have better pleural penetration,[6] in contrast to liposomal amphotericin B and anidulafungin.[7] It has been reported by Kuo *et al*[8] that the patients who received drainage (surgical or ICD) had lower mortality rate than those who did not (66% *versus* 87% with and without drainage).

In a recent study by Vazquez and colleagues[8], multivariate prospective case-control analysis along with molecular analysis of *C. glabrata* demonstrated that patients with new acquisition of *C. glabrata* need a longer duration of hospitalisation. Nosocomial acquisition of *C. glabrata* is not uncommon and may be due to exogenous acquisition. In addition, two major risk factors associated with *C. glabrata* colonisation are prolonged duration of hospitalisation and prior antimicrobial use.[2]

In conclusion, the crude mortality of fungal empyema is very high. Patients without systemic antifungal therapy or pleural drainage had poor outcomes. Pyopneumothorax with fungal infection per se is rare. Early diagnosis and proper choice of antifungal agents improves the survival, as in our case. The recommended duration of the treatment is six to eight weeks or two weeks after the culture becomes sterile.

References

1. Nigo M, Vial MR, Munita JM, Jiang Y, Tarrand J, Jimenez CA, *et al.* Fungal empyema thoracis in cancer patients. *J Infect* 2016;72:615–21.
2. Fidel PL Jr, Vazquez JA, Sobel JD. *Candida glabrata:* review of epidemiology, pathogenesis, and clinical disease with comparison to *C. albicans. Clin Microbiol Rev* 1999;12:80–96.
3. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, *et al.* Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. *Clin Infect Dis* 2008;46:1813–21.
4. Ko SC, Chen KY, Hsueh PR, Luh KT, Yang PC. Fungal empyema thoracis: an emerging clinical entity. *Chest* 2000:117;1672–8.
5. Lin KH, Liu YM, Lin PC, Ho CM, Chou CH, Wang JH, *et al.* Report of a 63-case series of Candida empyema thoracis: 9-year experience of two medical centers in central Taiwan. *J Microbiol Immunol Infect* 2014;47:36–41.
6. Matsuda T, Koreeda Y, Mataki H, Taira T, Noma S, Higashimoto I, *et al.* A case of *Aspergillus* empyema successfully treated combination therapy of voriconazole and micafungin: excellent penetration of voriconazole and micafungin into pleural fluid. *Intern Med* 2010;49:1163–9.
7. Weiler S, Bellmann-weiler R, Joannidis M, Bellmann R. Penetration of amphotericin B lipid formulation into pleural effusion. *Antimicrob Agents Chemother* 2007;51:4211–3.
8. Vazquez JA, Dembry LM, Sanchez V, Vazquez MA, Sobel JD, Dmuchowski C, *et al.* Nosocomial Candida glabrata colonization: an epidemiologic study. *J Clin Microbiol* 1998;36:421–6.