

Diagnosis of Pulmonary Candida Non-albican in Immunocompetent Patient

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ABSTRACT

Back ground: Pulmonary candidiasis is a fungal airway infection caused by the genus candida species, often in immunocompromised patients, and it spreads through hematogenous or other diseases. This case report aims to inform that the disease is rare in immunocompetent patients and difficult to diagnose.

Methods: Through a medical record search, a 40-year-old Indo-Chinese man complained of chest pain, cough, shortness of breath, and a lump in the neck. A history of pulmonary tuberculosis was completed after six months of treatment with no diabetes mellitus. Then, wheezing and rhonchi were heard during the physical examination of the lungs. When a contrast HRCT (high resolution computed tomography) examination was performed, fibrocalcification with a tree in a bud was found in the bilateral superior lobes of the lung, solid mass in the distal bronchus with atelectasis and enlarged paratracheal nodules. Then, a fungal culture of the right BAL (bronchoalveolar lavage) sample was found candida-non albican.

Conclusion: Pulmonary candidiasis is not only common in immunocompromised patients but also in immunocompetent conditions; diagnosis using HRCT with contrast and fungal culture from BAL.

KEYWORDS: Candida pulmonary, Candida non-albican, Candida immunocompetent, Diagnosis of candida non-albicans. Pulmonary candida non-albicans.

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INTRODUCTION

Based on data from WHO in 2019 lower respiratory tract infections, which rank fourth in the world, are among the leading causes of death worldwide¹, where one of these respiratory tract infections is caused by candida fungal infections, predominantly albican candida^{2, 12}. However, in this decade, non-albican candida infections have also been found to infect humans³ and in indonesia alone, patients with fungal infections have a high burden of fungal infections, especially in patients who experience candidemia, totaling 26,710⁴. In addition, candidiasis is very difficult to diagnose and manage because candida colonizes the upper airway and produces positive cultures without significant disease⁵, candida can also infect organs in the thorax cavity, including tracheobronchial, mediastinal, and pneumonia, so that

people with weak immune systems, most often experience candidaemia until candida pneumonia occurs⁶.

This case describes an immunocompetent patient experiencing pulmonary candida non-albican with a history of pulmonary tuberculosis (TB) complete treatment for six months, without diabetes, negative tumor marker test results, and negative HIV status. To confirm the diagnosis, contrast HRCT and fungal culture of BAL can be used, and the patient is given per-oral itraconazole and replaced by per oral voriconazole. Therefore, the presentation of this case can add insight into science for other clinicians.

METHODS

In the form of a case presentation, a 40-year-old Indo-Chinese man came to the pulmonary clinic with complaints of chest pain, cough, shortness of breath, and a lump in the

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neck. The patient had a history of pulmonary TB, completed six months of treatment, did not have diabetes mellitus, and examination of vital signs was found to be within normal limits; a physical examination of the lungs revealed wheezing and rhonchi sound, and blood tests only found thrombocytosis. From the results of these examinations, the patient was given symptomatic therapy at the outpatient clinic and scheduled for a lung contrast HRCT examination one week later.

At the time of the scheduled imaging examination, the patient was admitted for lung contrast HRCT examination and found fibrocalcification with tree in bud in the bilateral superior lobes of the lung, solid mass in the distal bronchus with atelectasis, and enlarged paratracheal nodules as shown in Figures 1 and 2. After that, the patient was examined for tumor markers CYFRA-21, NSE (Neuron Specific Enolase), and fiber optic bronchoscopy to take fungi and bacteria culture samples from the suitable BAL material, forceps biopsy, and cytology. The results of bronchoscopy found that in the trachea, there is a lump, hypersecretion of thick yellow mucus, the right main bronchus has a circular narrowing lumen until the scope cannot enter the lumen, the mucosa bleeds easily, hypersecretion of mucus, there is an intraluminal mass of the superior lobe that cannot be evaluated because the scope cannot enter the lumen of the medius and inferior lobes seen in Figures 3, 4, and 5.

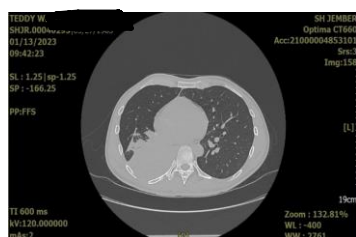


Figure 1. Axial HRCT non-contrast section of the lung showing total obliteration of the right intermediate bronchus solid mass distally and the impression of filling the entire airway branching.



Figure 2. Coronal medial HRCT contrast lung sections showing node enlargement in the right upper paratracheal, left and right lower tracheal, prevascular, and subcarina.

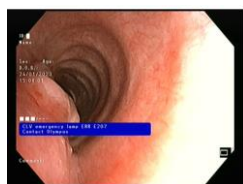


Figure 3. There is a lump and hypersecretion of thick yellow mucus in trachea

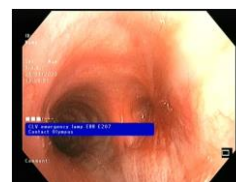


Figure 4. The right main bronchus has a circular narrowing lumen, the mucosa bleeds easily and hypersecretion



Figure 5. The right main bronchus has a circular narrowing lumen until the scope cannot enter the lumen, the mucosa bleeds easily, hypersecretion of mucus, and there is an intraluminal mass

After a few weeks, the result of fungal culture was obtained candida-non albican, aerobic culture of direct preparation pus was found gram-negative and positive rod germs, yeast formation, PMN (polymorphonuclear) cells, and aerobic culture was found pseudomonas aeruginosa and Klebsiella pneumoniae ESBL (Extended-spectrum beta-lactamase). In the examination of tumor markers, CYFRA-21 and NSE obtained negative results, negative HIV status, β -D-Glucan did not detect fungi, and negative galactomannan results. Meanwhile, histopathological examination of bronchial wash tissue and cytology found atypical epithelial hyperplasia with non-specific chronic inflammation, and the patient was given oral therapy of itraconazole 2x200 mg.

DISCUSSION

In the genitourinary tract, respiratory tract, gastrointestinal tract, and skin, Candida species are typical commensals, but can also be ubiquitous and most pathogenic fungi in humans. For a person with cutaneous, mucosal, and even systemic candidiasis, there is an increased risk of invading tissues that are not normally susceptible to fungal invasion. Candida also has a yeast-like form that forms true hyphae and pseudohyphae, so humans and animals can be its reservoir and sometimes the fungus can be acquired from hospitals, food, tables, air-conditioning vents, floors, breathing apparatus, as well as the hands and nails of healthcare workers⁷.

In general, candida albicans are the most commonly isolated Candida species, including those that cause rare and emerging pathogens in humans⁸. In addition, there are non-albican candida species, which are candida other than albican candida have many variations containing candida tropicalis, candida glabrata, candida parapsilosis, and

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Candida krusei, which can cause an increase in the ratio of infection. *Candida auris* causes drug resistance and presents a poor clinical picture. It was clinically identified in 2009 for the first time, and it appeared to pose a global threat and a significant outbreak in healthcare facilities⁶.

The groups of people who can be infected with candidiasis are Intensive care inpatients, patients who use central venous catheters, have a weak immune system (cancer patients, organ transplants, and people with low white blood cell count), surgical patients, multiple antibiotic users, parenteral nutrition recipients, patients who have a history of renal failure, hemodialysis, diabetes, and premature babies^{2, 3, 7, 9, 10, 14}. Pulmonary candidiasis is a rare condition and the most often found in patients with cancer, as evidenced by research from Mirosław et al. in 2023 that lung cancer patients have an increase in infection up to five times with the discovery of candida colonization in the nasopharynx¹⁰, from a study by Mehdi et al. in 2019 that there can be co-infection with albicans and non-albicans in TB patients associated with a poor response for anti-tuberculosis drugs and other risk factors such as smoking, old age, diabetes, and poor body mass index^{11, 12}, finally in another report from Ali et al in Jordan in 2023 it was found that immunocompetent people can also be infected with *Candida pneumonia*¹³.

Pulmonary candidiasis can be formed by hematogenous to the lung parenchyma, where the infection originates from below or through direct invasion of inhaled microorganisms^{5, 24}, the characteristics of hematogenous pulmonary lesions are diffuse, bilateral, hemorrhagic margins, necrosis in the centre, and miliary nodules⁸. Endobronchial infections do not have a distinctive interstitial component seen in hematogenous forms, but radiologically, endobronchial lesions show small, patchy, asymmetrical lung lesions, often in the lower lobes⁵. During early colonization, candida must adhere to the host surface in order to allow for host persistence, and plays a role in the progression to colonization that turns into infection. This is illustrated if there are subsequent changes in ligand and receptor expression adherence that begin during the initial adhesion between candida in the form of yeast and epithelial cells. This adhesion is expressed exclusively on important hypha cells during subsequent attachment^{17, 18}.

Candida also has virulence that is regulated by various stimuli ranging from the environment to quorum-sensing molecules due to its ability to change the shape of budding yeast and filamentous hyphae forms^{10, 19, 20}. When candida forms hyphae, it can signify increased virulence, invasiveness, and greater pathogenicity. These fungi release hydrolytic enzymes that break down molecules in search of nourishment and injure the surface tissue of their hosts, which can lead to increased adhesion and deeper

invasiveness^{14, 15, 16, 17, 18, 19, 20}. When the body's defence mechanisms decline or epithelial integrity is lost, candida colonization and infection will occur due to risk factors such as critical illness, weak immunity, antibiotic exposure, mechanical ventilation use, and a history of intensive hospitalization, transmission to the respiratory tract can occur^{20, 21}.

The diagnosis of pulmonary candidiasis can be made in the presence of symptoms such as cough, shortness of breath, purulent sputum, weight loss, chest pain, and high fever^{2, 28}. A physical examination revealed wheezing and a histopathological biopsy examination of lung tissue was mandatory to establish the presence of candida in the respiratory tract^{2, 6, 22, 23}. Histopathologically, lesions can be found to have areas of central necrosis with pseudohyphae, budding yeast and invisible cavities, pulmonary haemorrhage, central small abscesses, and pulmonary infarction^{24, 28}.

Candida diagnosis is also difficult to establish from antibody examination, which will be detected in normal colonization in the blood, for that blood culture itself has a sensitivity of up to 70% but takes a long time^{18, 25}, and β -D-glucan in serum can help distinguish colonization from invasive candida infection which has a sensitivity of up to 100% and specificity of 75%^{7, 26}, culture from LAB has a sensitivity and specificity can reach 89%²⁷. When secondary pulmonary candidiasis occurs, the radiography image will display many nodules that range in size from 3 to 30 mm, bilateral consolidation that spreads unevenly, pulmonary oedema, haemorrhage, or alveolar damage, which is found in advanced disease^{24, 28}. Particularly in contrast, HRCT of the thorax, nodules, ground glass opacity, consolidation, halo sign, and cavities were found²⁹.

The recommended candida management is echinocandin, micafungin, and anidulafungin. Administration of fluconazole as an alternative either intravenously or orally with an initial dose of 800 mg, then continued 400 mg daily and administration for non-albican candida infections such as *Candida glabrata* can be given high doses of fluconazole or voriconazole 200-300 mg twice daily^{28, 30}.

CONCLUSIONS

Pulmonary candidiasis is not only common in immunocompromised patients but also in immunocompetent conditions. Diagnosis can use HRCT with contrast and fungal culture taken from BAL, and management can be given fluconazole or voriconazole.

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