Case Report

Candida Glabrata Pneumonia in Post COVID-19 Patient: A Rare Case Report

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Abstract

Background: One of the issues in post COVID-19 is secondary infection and fungal infection is one of the complications that must be detected at early stage to prevent. Early detection to prevent underdiagnosed and undertreatment. *Candida glabrata*, one of the pathogens in fungal infection is rare and can acts as infectious agent with immunocompromised patients.

Case: A 69-year-old man came to hospital with major complaints of cough and shortness of breath for five days. He was diagnosed COVID-19, After completed treatment the nasopharyngeal PCR swab show negative result for COVID-19. After being discharged, he did several chest X-ray examinations with progressively worsening cough. Chest CT-Scan revealed consolidations and cavity. Sputum culture was positive for *Candida glabrata* and negative for BTA. He received echinocandins as anti-fungal treatment, which inhibits enzymes that is necessary for fungi's cell wall synthesis, shows clinical and radiological improvement.

Discussion: COVID-19 affect immune system which resulting higher risk for secondary infection. The use of broad-spectrum antibiotics, immune-suppression of the host, and use of medical devices are major risk factors for *Candida* infections. Meanwhile *C. Albicans* is still the most common cause of fungal pneumonia by *Candida*, we should consider *C. glabrata* as one of its pathogens.

Conclusion: COVID-19 affects many aspects in our life, even after we treat the main problem, some patients manifest symptoms later. Diagnosing fungal infection especially invasive candidiasis is quite challenging with higher mortality rate. Not only *C. glabrata* more uncommon than *C. albicans*, but also it was one of difficult to treat pathogens.

Keywords: *candida*, glabrata, pneumonia, post COVID-19

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INTRODUCTION

Since March 2020, World health organization (WHO) has been declared severe acute respiratory syndrome (SARS-CoV2) as global pandemic and it affects many aspects in civilization.[1] It can develop into long COVID-19 syndrome, which means people suffering from symptoms after SARS-CoV2 infection, and it had been an issue we all have to face.[2]

Secondary infection in post COVID-19 is a problem with high mortality (56.7%) and often underdiagnosed especially fungal infection.[3] COVID-19 carries a risk of developing secondary infection and health practitioner should recognise and treat it properly. *Candida* species rarely cause pneumonia with the most common pathogen among the *Candida* species is *C. albicans*. C. *glabrat*a is known as non-pathogen *Candida* species and rarely acts as infectious agent but it can present in immunocompromised patients.[4] In this study, we present a case study regarding post COVID-19 patient with *Candida glabrata* pneumonia.

CASE

A 69 years old male came to our hospital with main complaints progressively worsened purulent cough in the last 4 days. He also Suffered with shortness of breath, fever, and myalgia.

A month before, he had prior infection of COVID-19 (confirmed by PCR swab) 1 month before admission and hospitalized for 9 days. Figure 1 showed first chest X-ray when diagnosed with COVID-19. One day after being discharged, he suffered with another episode of cough, fever, and desaturation (90–91%) with worsening lung infiltrates

and hospitalized for 8 days. Later on, he was confirmed negative for COVID-19. Figure 2 is serial chest x-ray upon admission in our hospital showed worsening infiltrate followed by cavitary lesion. Past medical history is diabetes mellitus without prior infection of tuberculosis. From physical examination showed fever (37.8^{o}C) with slightly increased respiratory rate 26/minute, and decreased peripheral saturation (92%).

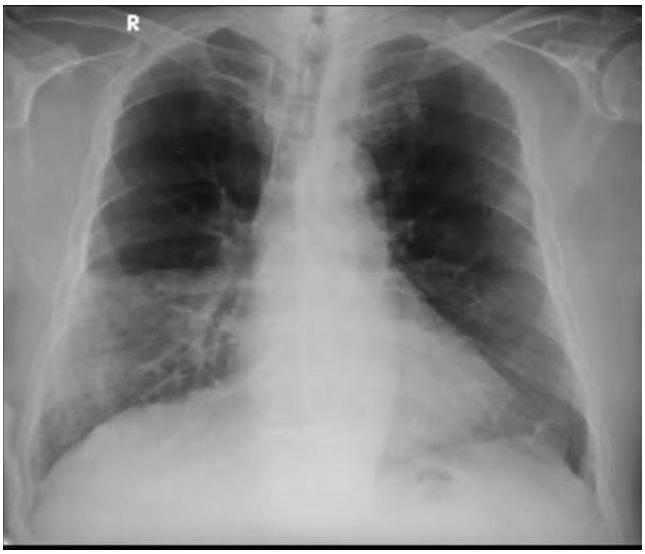

Figure 1. Chest X-Ray when he first admitted for being positive for COVID-19

Figure 2. Chest X-Ray on current state, showed areas of consolidation with cavitation in right mid and lower lobes

Rales were present on auscultation on mid and lower zones of right lung. He showed no oral candida and showed no respond on antibiotics (based on his previous prescription). Laboratory investigation showed leucocytosis with WBC count of 11.8/mm^3 and negative swab PCR test for COVID-19. On third day of admission, he had chest CT-scan (Figure 3a) showed consolidations, nodule with irregular wall thickening and cavitation (doughnut sign) on upper and mid right lung with suggestive fungi infection with differential diagnosis lung tuberculosis. He was confirmed negative infection of tuberculosis from rapid molecular sputum testing and Ziehl-Nielseen sputum smear. Microbiology finding showed *Candida Sp*. (Figure 3b) and sputum culture was positive for *Candida galbrata* (*C. galbrata*). He started anidulafungin, an anti-fungal agent which belong to echinocandins group. Echinocandins inhibit beta-(1,3)-D-glucan synthase, an enzyme that is necessary for the synthesis of fungi's cell wall. There is gradual improvement within clinical and radiological findings, while patients being discharged.

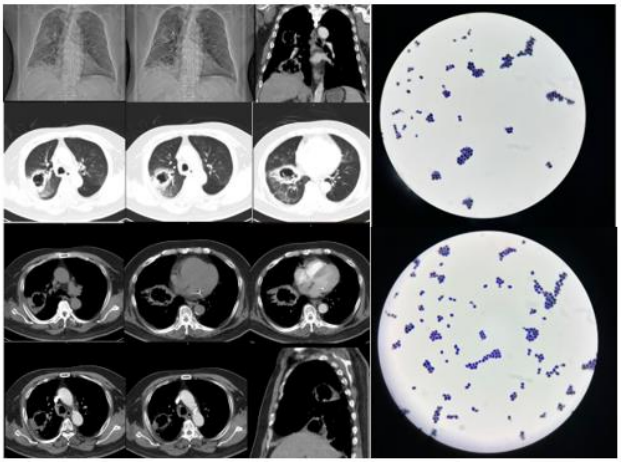

Figure 3. (a) CT-scan showed consolidation with nodule with irregular wall thickening and cavitation; (b) microbiology findings showed *Candida Sp.* and continued with sputum culture showed *Candida galbrata*.

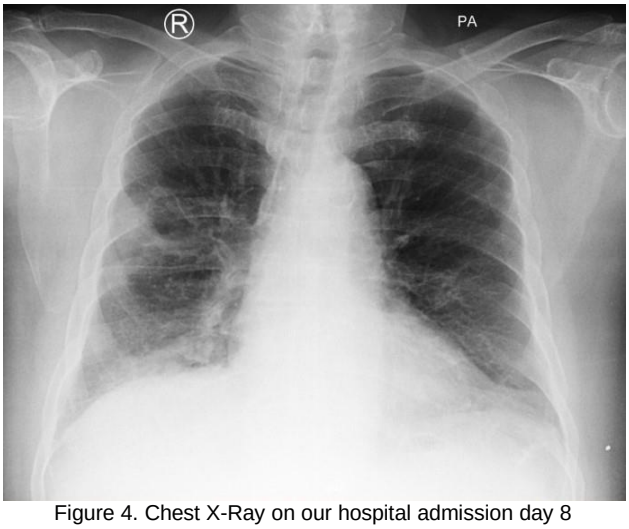

Figure 4. Chest X-Ray on our hospital admission day 8

Figure 4 showed a decreased of infiltrates within the cavitary lesion 4 days after starting antifungal treatment. Figure 5 showed faded cavitary lesion within 1 week after discharged. He was allowed to discharge from hospital and did some follow up treatments.

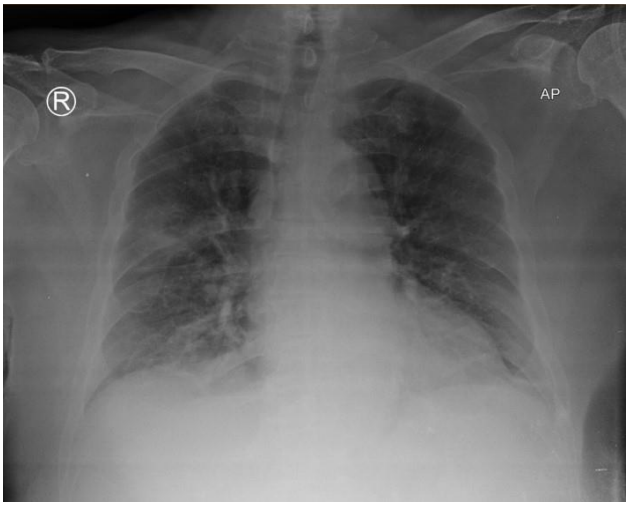

Figure 5. Chest X-Ray Followed up on clinic, one week after discharged

DISCUSSION

Severe Acute Respiratory Syndrome (SARS-CoV-2) affects many aspects in life. Even after being treated, it still affected part of human population. Researchers and several studies have reported the long-term complications of COVID-19 has variety of symptoms and organ-related injuries, which referred as “long COVID” or “post-acute COVID-19 syndrome”.[5]

Post COVID-19 is condition to describe health issues that persists more than four months after first being infected with the virus. Most people with COVID-19 infection recovered within weeks to months of illness, but some do not.[6] Even after the infection being properly treated, the massive number of people who have been infected with SARS-CoV-2 suggests that this will represent a public health issue leading to a major consumption of healthcare resources. Long COVID has been identified as a clear priority of the utmost importance for the World Health Organization.[7]

Secondary infection and fungal infection are major issue in post COVID-19 patients. COVID-19 patients especially with comorbid like diabetes mellitus, are severely immunocompromised thus could be easily infected with fungal infection. It is often underdiagnosed and undertreatment which can leads to mortality.

Fungi Is a normal colonization in body without harming the host. The true pathogens will generating variety of syndromes. Fungal pneumonia is an infectious process in the lungs caused by one or more endemic or opportunistic fungi. From studies, the main fungal pathogens for fungal coinfections in severe COVID-19 are *Aspergillus* and *Candida*. Other infrequent opportunistic pathogenic fungus caused lung infections also need to be considered, such as *Mucormycosis* and *Cryptococcus*. Opportunistic fungal organisms like we mentioned before, tend to cause pneumonia in patients with congenital or acquired defects in the host immune defences such as COVID-19 patients.[8,9]

The recent global pandemic of COVID-19 has predisposed a relatively high number of patients to acute respiratory distress syndrome (ARDS). This carry risk to develop super-infections and dysregulation in immune system. *Candida* species are major constituents of the human mycobiome and non-pathogen if the host immune is normal and it is inhabiting various mucosal surfaces. Although being commensal within the human host, *Candida* species are equipped with virulence attributes, enabling them to invade when opportunities arise and cause various infections in humans, especially when the immune system is impaired.

The most prevalent *Candida* species as per the recent studies COVID-19 patients, is *Candida albicans* (44.1%); followed by *C. auris* (23.2%); *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, and *S. cerevisiae* (4.6% each); and *C. krusei* and *Rhodotorula spp*. (2.3% each). *Candida* infection is rare, meanwhile the estimated mortality attributed to invasive candidiasis is 19–40%.[10,11]

The use of broad-spectrum antibiotics, Immunosuppresants agents, and the use of medical devices are major risk factors for *Candida* infections. Meanwhile *C. Albicans* is still the most common cause of fungal pneumonia by *Candida*, non-*C. albicans* species has increased over the years and

need more attention. *C. glabrata* is the second or third most frequently isolated *Candida* species. This high incidence can be partially explained by the inherent low susceptibility of *C. glabrata* to the most used class of antifungal drugs, the azoles, and consequently *C. glabrata* are associated with high mortality rates.

Invasion of the pulmonary parenchyma by *Candida* is rare, due to its presence in respiratory specimens is usually regarded as contamination. However, with the increased use of immunosuppressive agents, mucosal and systemic infections caused by *C. glabrata* have increased significantly, especially in the HIV-infected population.[12,13]

The wide usage of antibiotics, steroids, along with insult by SARS CoV-2 infection, causes commensal *Candida* to invade internal organs. When *Candida* enters the blood and spreads to other body sites, there occurs invasive candidiasis. The various predisposing factors include immunosuppression, surgical procedures, renal failure, prolonged placement of central venous catheter, malignancy, prolonged antibiotic usage, late sepsis. Fear of missed secondary infection and lack of specific therapy for COVID-19 leads to over-prescription of antibiotics.

Sending appropriate cultures, use of biomarkers like procalcitonin and galactomannan and antibiotic time-out at 48 hours of prescription can help in reducing unnecessary antibiotic prescriptions.[1,3] Awareness of the possibility of fungal co-infection is essential to reduce delays in diagnosis and treatment in order to help prevent severe illness and death from these infections.[14]

In this patient, COVID-19 carries its own risk as major risk factor for Candida infection along with his diabetes mellitus as his comorbid. It made host immune system became impermeable. One of risk factor for fungal infection is prior used of AB. This is due to bacterial infection is the most common secondary infection in COVID-19. Cavitary pneumonia presentation of pulmonary candidiasis is rare but was seen in the present case and chest X-Ray.

This patient was diagnosed as invasive candidiasis by clinical features, positive sputum cultures, Chest X-Ray and chest CT-Scan. Although differential diagnosis arise such as tuberculosis infection that has similar manifestation but the acid fast bacilli (AFB) stain and rapid molecular testing (RMT) was negative MTB.

After given anidulafungin, an anti-fungal treatment which belongs to echinocandins group, The patient's condition was getting better and showed less infiltrates and cavitation in his follow-up chest X-Ray. The echinocandins have a unique mechanism of action, inhibiting beta-(1,3)-D-glucan synthase, an enzyme that is necessary for the synthesis of an essential component of the cell wall of several fungi. Echinocandins show as effective treatment against most *Candida spp.*, including strains that are fluconazole-resistant.[15]

Health practitioner should be aware that COVID-19 can develop secondary infection even after we treat the main COVID-19. When it is developing into secondary infection, it is hard to diagnose the etiologic and relies on a combination of clinical, radiologic, and microbiological factors.[9] COVID-19 itself is a risk factor, furthermore there are other risk factors besides immunosuppression condition made by COVID-19 like the use of broad-spectrum antibiotics and host immune status and patients comorbid. Antibiotics should be given wisely and think about the benefits and the risks. Diagnosis and prompt treatment should be delivered quickly, especially when the patient gets candidiasis as secondary infection because it has high mortality.

LIMITATION

Specific tests or biomarkers to diagnose candidiasis in this case like the Galactomannan test were not performed due to lack of facility.

CONCLUSION

COVID-19 affects many aspects in our life, even after we treat the main problem, some patients can occur symptoms after it. Fungal infection especially invasive candidiasis is difficult to diagnose

and have high mortality rate. Health practitioner should consider host immune status, comorbid such diabetes mellitus, to diagnosed it thoroughly and treated it properly. Although *C. glabrata* is rarer than *C. albicans,* it has its own problem and hard to treat too.

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CONFLICT OF INTEREST

None.

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