A 47-year-old Liver and Kidney Transplant Patient with *Candida* Pneumonia

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Candida species inhabit the gastrointestinal tract. Isolation of *Candida* from the respiratory tract has been found and reflects colonization, particularly among mechanically ventilated patients [1]. However, the existence of *Candida* as a respiratory pathogen was previously doubted. *Candida* pneumonia is a rare and challenging-to-diagnose entity. We present a histopathologically confirmed case of necrotizing *Candida* pneumonia and lung abscess in a solid organ transplant recipient.

PATIENT DESCRIPTION

A 47-year-old male was admitted because of fever of unknown origin. His medical history included Caroli's syndrome and a liver and kidney transplantation 20 and 4 years prior to presentation, respectively, with residual chronic kidney disease, cigarette smoking, and diabetes mellitus. His regular immunosuppressive regimen included rapamycin 1.5 mg and prednisone 5 mg.

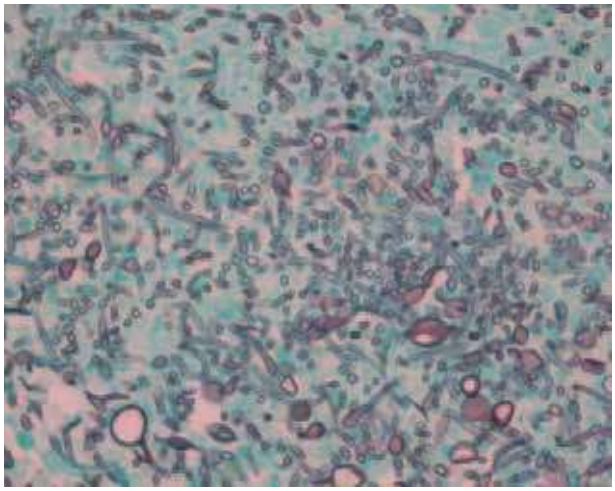
Approximately 4 months prior to the current hospitalization, the patient was admitted with continuous high-grade fever and chronic cough. Total body computed tomography (CT) revealed multiple hepatic hypodense lesions, pulmonary opacities in the left lung, and randomly distributed pulmonary nodules, while multiple blood cultures grew extended spectrum beta-lactamase (ESBL) Escherichia coli and Klebsiella oxytoca. Liver biopsy revealed portal and lobular inflammation without evidence of malignancy. Bacterial, fungal, and mycobacterial cultures were negative while on antibiotic therapy. A diagnosis of hepatic microabscesses secondary to cholangitis was made, and a peripherally inserted central catheter (PICC) was placed to allow prolonged meropenem therapy. One month later, the patient's chronic cough worsened. 18F-fluorodeoxyglucose positron-emission tomography/computed tomography (18F-FDG PET/CT) revealed resolution of the pulmonary nodules and hepatic lesions and improvement of the lung opacities with no sign of malignancy.

One month later the patient was readmitted with breakthrough fever while still on meropenem. Inflammatory markers were elevated, and a CT scan showed resolution of the hepatic findings with reappearing pulmonary opacities. Cultures revealed persistent fungemia with *Candida albicans* (10 of 10 culture sets) and bacteremia of ampicillin resistant Enterococcus faecium. The PICC was removed. The tip also tested positive for *C. albicans*. The isolate was tested sensitive to all echinocandins, including micafungin for which the minimum inhibitory concentration was ≤ 0.06. Susceptibility testing was performed in accordance to CLSI guidelines [2]. Consequently, vancomycin and micafungin (100 mg per day) treatment was initiated. Clearance of bacteremia and fungemia was documented shortly after as repeated blood cultures were negative. Clinical improvement was noted. Transesophageal echocardiography revealed normally appearing valves with no signs of endocarditis. Ocular examination was negative for chorioretinal involvement. Repeated 18F-FDG PET/CT revealed new lung opacities, predominantly on the left lower lobe (LLL), bilateral cavitary lymphadenopathy, and bilateral pleural effusion.

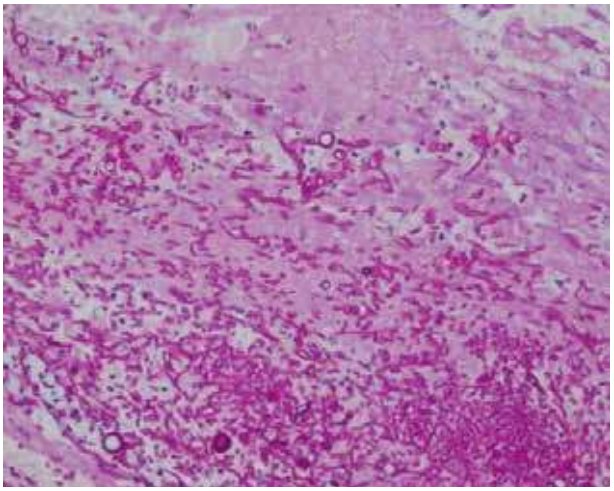
Subsequently, the patient's condition deteriorated. A diagnostic thoracentesis was negative for any pathogen with no indices of empyema. Microbiological assessment on bronchoalveolar lavage (BAL) specimen included bacterial, fungal, and mycobacterial cultures incubated for prolonged period grew no pathogen/ Polymerase chain reaction (PCR) for Pneumocystis jirovecii, Cytomegalovirus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were all negative. BAL and serum galactomannan and cryptococcal antigen were also negative. BAL cytology was unremarkable. Transbronchial biopsy revealed acute necrotizing pneumonia with marked neutrophilic infiltration.

Despite the addition of meropenem to the antimicrobial therapy, the patient's respiratory symptoms continued to worsen, and fever rebounded. Repeated blood cultures were negative. A repeated chest CT revealed a large LLL abscess and loculated left pleural effusion. Shortly

Figure 1. Histopathological findings of lung segment



[A] Silver methenamine stain



[B] Periodic acid Schiff stain revealing hyphae within necrotic lung tissue, consistent with pulmonary candidiasis

after, the patient developed hemoptysis and was promptly taken to the operating room for an anatomical basal segmentectomy of the necrotic LLL and decortication. Despite intensive care, the patient continued to deteriorate, and he died.

Histopathologic report revealed severe acute necrotizing pneumonia with massive necrosis and foci of intravascular yellow pigment associated with fibrin and neutrophils, without granulomas. Hyphae were visualized on methenamine silver stain and periodic acid Schiff (PAS) stain [Figure 1]. Fungal culture of lung tissue was positive for *C. albicans*. These findings provided a definitive diagnosis of pulmonary candidiasis.

COMMENT

Our case shows a unique presentation of *Candida* pneumonia. In the clinical setting, *Candida* spp. isolated from respiratory secretions, including BAL, usually reflects colonization [1]. Only two cases of definitive *Candida* pneumonia have been reported in solid organ transplant recipients in the literature [3,4]. *Candida* usually reaches the lungs by either aspiration of oropharyngeal material or through hematogenous speared. Histologic demonstration of *Candida* remains the gold standard for diagnosis.

Our patient was appropriately treated for invasive candidiasis, including early withdrawal of the PICC. Clearance of fungemia was confirmed by recurrent negative cultures. It is most likely that micafungin's delivery to the infection site was disturbed by the necrotic lung segment. This finding is despite its adequate pulmonary penetration, reaching effective intrapulmonary concentrations above the MIC for invasive fungal infections [5]. Furthermore, micafungin modestly elevates rapamycin blood levels and further suppressing the immune system; however, in this case, serum concentration was within the normal range.

Conclusions

Clinicians should be aware of *Candida* pneumonia, a rare entity, and have high index of suspicion while caring for susceptible populations.

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