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Case report of invasive, disseminated candidiasis with peripheral nodular cavitary lesions in the lung

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ABSTRACT

We report a case of invasive candidiasis presenting as multiple lung nodules and cavitary lesions with minimal pleural effusion. *Candida* infections of the lung are rare but can occur after hematologic dissemination of the yeast from other body sites, such as the skin and the gastrointestinal and genito-urinary tracts. Here, we describe the case of a 56-year-old female with a history of end-stage renal disease (ESRD) who presented with fever, productive cough, and pulmonary nodules and cavitary lesions seen on a chest computed tomography (CT). The patient's blood cultures were positive for *Candida* zeylanoides.

1. Introduction

Candida lung infections are extremely rare but occur due to hematogenous spread of the yeast, rather than aspiration of oropharyngeal secretions. Candidiasis usually presents as colonization, not infection [1], and its risk factors include immunosuppression, neutropenia, hematologic malignancy, long-term antibiotic use, late sepsis, and total parenteral nutrition [2].

Radiologic presentation of *Candida* infections in the lung varies from pneumonia, ground-glass opacity, miliary patterns, nodules, micro-abscesses, thickening of the bronchial wall, and pleural effusion with a rare finding of cavitary lesions [3,4].

The fourth most common cause of hospital-acquired bloodstream infections in the United States is candidemia [5]. Invasive candidiasis is associated with high mortality in adults, approximately 15%–25% of infected patients [6].

2. Case report

A 56-year-old woman with ESRD presented to the ER with fever, painful rash on the hands, and an abnormal blood culture report indicating growth of yeast identified 2 days prior to her visit. The patient reported shortness of breath, a progressively worsening cough that produced a small amount of non-bloody white sputum for 2 weeks, and subjective fever and chills.

The patient had been receiving hemodialysis through a left-arm arteriovenous graft, and her other co-morbidities included hypertension and diabetes mellitus. She was referred to the hospital from her dialysis center after yeast were identified in her blood cultures, later identified as candida zeylanoides.

Physical examination revealed an obese female who appeared alert and comfortable. She was febrile at 102 °F, her blood pressure was 156/86 mmHg, and her oxygen saturation was 98% on room air. The left-arm arteriovenous graft had good thrill, although a further skin exam revealed 1-mm violaceous macular lesions on the palm and ventral aspects of 4th and 5th fingers of her left hand (Fig. 1).

Basilar crackles were noted upon auscultation with normal heart sounds and no murmurs. Fundoscopic examination of the eye revealed hypertensive retinopathy, and the patient had a White, hypo-pigmented inferotemporal lesion suggestive of fungal chorioretinitis (Fig. 2).

Other results from the initial physical examination were unremarkable.

Laboratory values were significant for leukocytosis with a WBC count of $1.34 \times 10^4/\mu L$ that increased to $1.82 \times 10^4/\mu L$ on day 3. The patient's blood cultures were positive for yeast.

Ultrasound image showed fluid collection around the patent

Abbreviations: CT, Computed Tomography; ESRD, End Stage Renal Disease.

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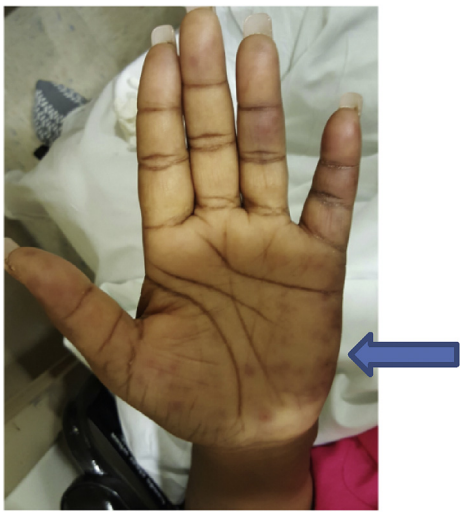

Fig. 1. 1-mm violaceous nodules on the palm.

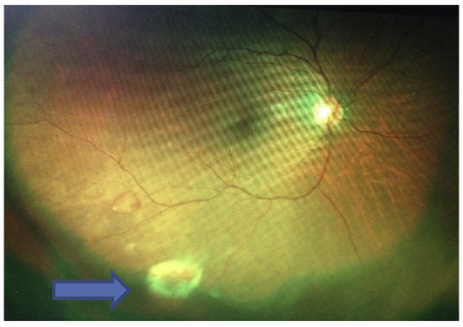

Fig. 2. White, hypo-pigmented inferotemporal lesion suggestive of fungal chorioretinitis.

arteriovenous graft (Fig. 3).

Fine needle aspiration was done under ultrasound guidance and culture grew candida zeylanoides. Vascular surgeon did excision of infected arteriovenous graft and placed temporary Shiley catheter for hemodialysis. Later when blood cultures were negative, patient had permanent permacath.

A transesophageal echocardiogram was negative for vegetation, but a chest CT showed peripheral nodular lesions suggestive of infective emboli (Fig. 4).

A subsequent bronchoscopy with bronchoalveolar lavage revealed white exudate (Fig. 5), and tissue cultures collected during a transbronchial biopsy yielded *Candida zeylanoides* (Fig. 6).

The mycology laboratory affiliated with our hospital uses VITEK 2 system for identification of Candida species which was zeylanoides in our case. VITEK 2 system is a rapid method for the identification of medically important yeasts and yeast-like organisms. VITEK ID-YST card along with VITEK 2 system identify the yeast in 15 hours. The card consist of 47 biochemical reactions to identify yeast and the system uses fluorescence–based technology.

Her negative test for serum precipitins to *Aspergillus fumigatus* and *Aspergillus niger* excluded concomitant aspergillosis.

The patient was started on caspofungin, which was later replaced with fluconazole per recommendations by the Infectious disease team. Repeat blood cultures were negative for fungal growth. The patient was discharged from the hospital with orders to complete 6 weeks of parenteral fluconazole during hemodialysis 3 times a week. Patient completed antifungal therapy as outpatient and being followed with us in dialysis center.

3. Discussion

Invasive candidiasis occurs when *Candida* species enter the bloodstream and spread to other body sites. Risk factors for invasive candidiasis include renal failure, surgical procedures, prolonged central venous catheter placement, immunosuppression neutropenia, hematologic malignancy, long-term use of antibiotics, late sepsis, and total parenteral nutrition [2,7]. For example, a study by Ostrosky-Zeichner showed 10% of patients in Intensive care units have increased risk for candidemia secondary to central venous catheter placement, prolonged antibiotic and systemic steroid use, and major surgeries [8]. *Candida* species account for 9% of all infections in intensive care unit patients, although the frequency of opportunistic *Candida* infections in AIDS patients has decreased with improved antiretroviral therapy [9].

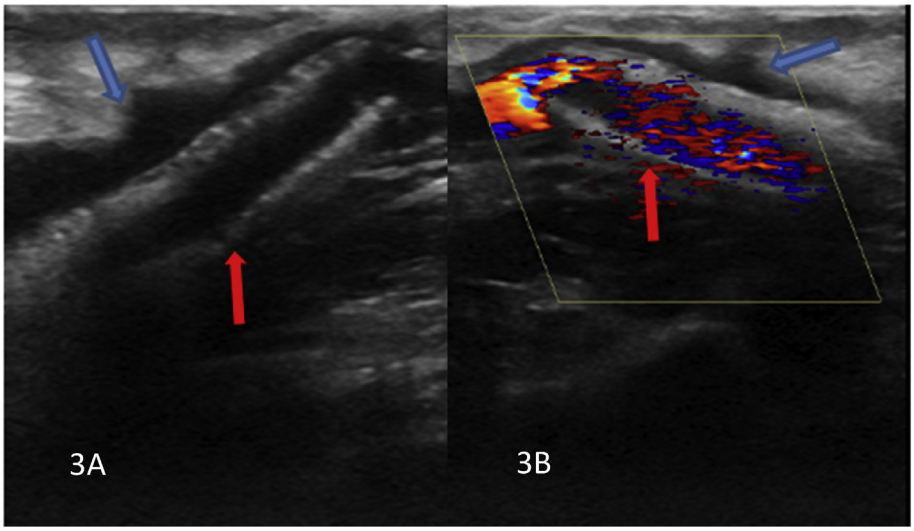

Fig. 3. Ultrasound image [3A] showing anechoic fluid collection (blue arrow) around the arteriovenous graft and [3B] doppler ultrasound showing patent arteriovenous graft (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

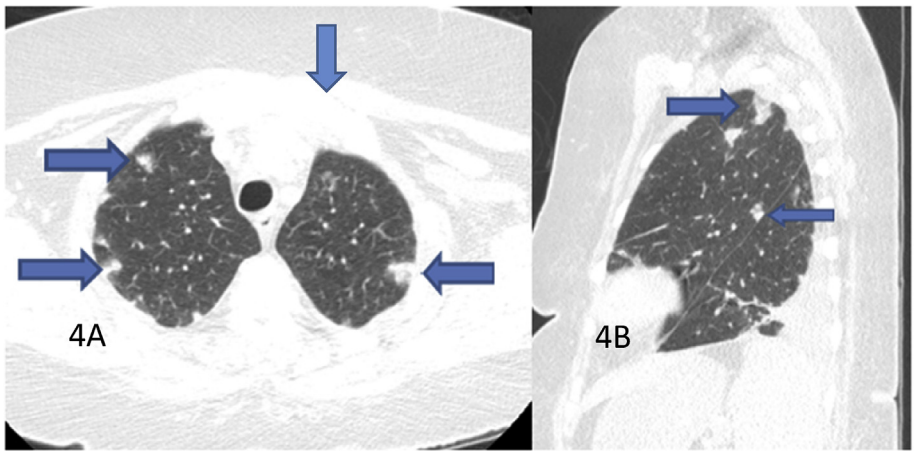

Fig. 4. Chest CT axial [4A] and sagittal [4B] views showing multiple peripheral pulmonary cavitary nodules.

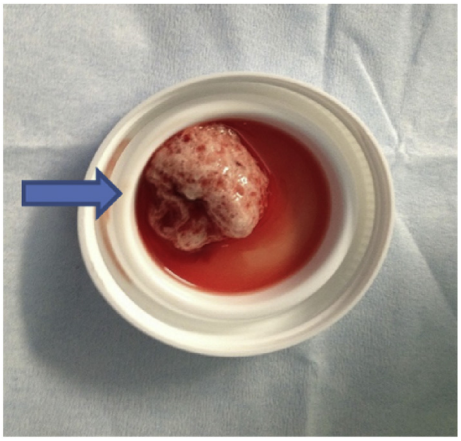

Fig. 5. Bronchoalveolar lavage yielding white exudate.

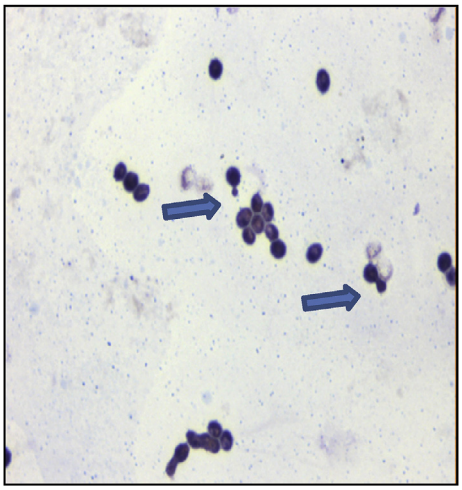

Fig. 6. Gram stain of bronchoalveolar lavage showing budding yeast cells.

Candida invasion to the lung parenchyma is rare, and its presence in respiratory samples is often regarded as contamination. According to Kassner et al., three histologic forms of pulmonary candidiasis occur: embolic, disseminated, and bronchopulmonary [10]. A study by el-Ebiary determined that the incidence of *Candida*-associated pneumonia is 8%, and its colonization pattern is usually uniform throughout the lung [11]. Bronchoalveolar lavage, cytologic and morphologic analyses with accompanying cultures [12], and histopathology showing *Candida* invasion of the lung (the gold standard of pulmonary *Candida* diagnosis) [13] should be performed to reliably bronchopulmonary and disseminated *Candida* infection.

Azoulay et al. found that intensive care unit patients on mechanical ventilation for more than two days often exhibited *Candida* colonization in the respiratory tract, and other studies showed that *Candida* colonization increased risk of ventilator-associated, multidrug-resistant bacterial pneumonia [1,14]. Moreover, Delisle et al., observed that respiratory tract colonization with *Candida* was also associated with increased hospital stay length and mortality rates [15]. One potential explanation is that *Candida*-related immune dysfunction enhances susceptibility to other respiratory pathogens.

Lung transplant recipients have a high incidence of *Candida* colonization in the trachea and bronchial secretions. In a study performed by Brooks et al., one autopsy-diagnosed case of invasive *Candida* pneumonia involving both lungs in a transplant patient had repeatedly produced *Candida* from pre-mortem sputum and bronchoalveolar lavage samples. *Candida* colonizes 86% of lung transplant recipients, while other fungal species, such as *Aspergillus* spp., are only found in 25% of recipients [16]. As the yeast colonize the upper airway, sputum cultures become unreliable for *Candida* diagnosis, and cultures of blood, body cavities, and/or sterile organ sites are then required for its definitive identification [17].

Franquet et al. found that 70% of patients with pulmonary candidiasis presented with nodules sometimes surrounded by discrete areas of ground-glass opacities [3]. Fine nodular patterns seen after radiography could be due to superimposed pulmonary pathology or may represent disseminated candidiasis [18]. Pulmonary candidiasis may also present as an isolated parenchymal pulmonary nodule without recurrent infections in patients with low immunoglobulin G levels [19]. Candidiasis may also present as dermatitis, esophagitis, thrush, peritonitis, mediastinitis, endocarditis, septic arthritis, vulvovaginal candidiasis, and osteomyelitis [20]. Nodular cavitary pneumonia presentation is rare but was seen in our clinical case. Vision-threatening findings of disseminated candidiasis, such as endophthalmitis and chorioretinitis, are seen in 10% of patients [21].

One other case report by Yasuda et al. describes invasive candidiasis that presented as multiple pulmonary cavitary lesions [22]. Our patient had features of disseminated candidiasis,

including chorioretinitis, macular lesions on the hands, and nodular cavitary lesions of the lung. However, the source of infection in our case was an infected arteriovenous fistula, rather than an infected central venous catheter as described in their case.

Treatment of *Candida* in sputum and bronchoalveolar lavage exudate alone is not recommended, although patients with disseminated candidiasis should be treated. If *Candida* is found in respiratory samples, treatment is mandated only if other risk factors and sepsis are present [23]. Leon et al. showed that a *Candida* score greater than 2.5 accurately identified patients who would benefit from early antifungal treatment (sensitivity 81%, specificity 74%). Candida score calculator is used to determine the likelihood of invasive candidiasis versus colonization in non neutropenic critically ill patient. Candida score comprise of severe sepsis (2 points), total parenteral nutrition (1 point), initial surgery (1 point), multifocal candida colonization (1 point) in patients. These are the predictors of proven candida infection. Our patient had severe sepsis (2 point) and multifocal candida colonization (1 point) which lead to score of 3. Candida score of 3 has 8.5% risk of invasive candidiasis without treatment [24].

The most common antifungal agents used for treatment of candidemia are the echinocandins (casponfungin, micafungin, anidulafungin) and azoles (fluconazole, itraconazole and voriconazole). Polyenes (amphotericin B dexoycholate and lipid formulations of amphotericin B) are used less often secondary to risk of toxicity [25].

We diagnosed our case as invasive, disseminated candidiasis by the patient's positive blood cultures, eye and skin lesions, and chest CT findings. Aspergillus precipitin detects the type and quantity of specific aspergillus antibodies in blood. Antibodies are immunoglobulin proteins made by the immune system in response to antigens which is aspergillus. The aspergillus precipitin test looks for IgG, IgM, IgE antibodies in blood. Our case serum precipitin was negative. So aspergillus which is common fungal infection of lung was excluded [26].

4. Conclusion

Respiratory tract *Candida* colonization often leads to poor clinical outcomes and is independently associated with increased hospital stay length and development of complications. Delayed initiation of therapy for invasive candidiasis results in considerably increased mortality. Our case report emphasizes the need for early, comprehensive diagnosis of disseminated candidiasis and initiation of appropriate antifungal treatment for clearance of the infection.

Author disclosure

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the manuscript. No financial support was used for this case series.

Authors contributions

M Khaja and H Arshad searched the literature and wrote the manuscript. M Khaja conceived and edited the manuscript. M Khaja supervised the patient treatment, critically revised and edited the manuscript. S Garcia was involved in patient care along with M Khaja. All authors have made significant contributions to the manuscript and have reviewed it before submission. All authors have confirmed that the manuscript is not under consideration for review at any other Journal. All authors have read and approved the final manuscript.

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