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A rare case of *Candida parapsilosis* pneumonia in an immunocompetent patient

Raiya Habib, Zeeshan Ismail, Anthony Nanajian, Matthew Calestino, Christopher Bray

ABSTRACT

Introduction: The presence of fungus in an immunocompetent host is usually disregarded as a mere contaminant, as it can be a commensal organism of the skin, gastrointestinal, urogenital, and respiratory tract. Hence, its growth in cultures has to be interpreted within a clinical context. This case illustrates the challenges experienced when diagnosing *Candida parapsilosis* necrotizing pneumonia, and the importance for considering *Candida* pneumonia as a differential diagnosis for an immunocompetent patient. After a thorough literature review, we would like to present the first case report of *C. parapsilosis* causing necrotizing pneumonia in an immunocompetent patient.

Case Report: We present a case involving a middle-aged smoking male who presented with respiratory and metabolic abnormalities and was found to have necrotizing pneumonia. He was managed for severe sepsis with lactic acidosis, respiratory failure, and severe acute kidney injury (AKI), which improved with broad spectrum antibiotics and fluids.

These conditions improved; however, his respiratory distress did not despite a prolonged course of antibiotics. This led to a workup for other causes of necrotizing pneumonia, after which cultures revealed the growth of *C. parapsilosis*. He was then started on antifungals and subsequently improved.

Conclusion: *Candida* necrotizing pneumonia is a rare disease for an immune-competent individual; however, chronic lung damage in the setting of a smoking history may make individuals more susceptible. This case illustrates the challenges associated when dealing with such a case, and it is the team's hope that publishing this case will add to awareness. Additionally, this can contribute to improved antibiotic stewardship and earlier diagnosis which will hopefully lead to a shorter hospital stay and improved morbidity and mortality.

Keywords: *Candida* pneumonia, Immunocompetent, Necrotizing pneumonia

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INTRODUCTION

Bacterial pneumonia is a frequently diagnosed condition in hospitalized patients. Candida, as a primary cause of pneumonia, is extremely rare.

The microorganism is a common component of the gastroesophageal tract, upper respiratory tract, and skin flora [1], and it is often disregarded as a cause of infection among immunocompetent patients. Hence, *Candida* encountered in the lower respiratory tract is thought to be associated with recurrent microaspirations [2]. Risk factors such as neutropenia, immunosuppression, injection drug use, prolonged admission to the Intensive Care Unit (ICU), and prolonged antibiotic use increase susceptibility to *Candida* pneumonia [3]. Diagnosing *Candida* pneumonia is extremely difficult due to its unpredictable clinical manifestations and radiological appearances [4]. The only definitive way of diagnosing *Candida* pneumonia is by a histopathology specimen obtained after exhausting all other common possibilities of pneumonia [4].

Its rarity can be demonstrated by a study in multiple cancer centers, which discovered the frequency of autopsy confirmed *Candida* pneumonia to be approximately 1% [5]. Among the types of *Candida* that can cause pneumonia, the frequency of *C. parapsilosis* infection is very rare. In addition to pneumonia, this species can contribute to a variety of systemic infections including meningitis, arthritis, and peritonitis [6]. *Candida parapsilosis* pneumonia has been postulated to occur in patients with chronic parenchymal lung damage from agents such as nicotine, or after a viral infection [6]. Hence, as highlighted above, isolation of *Candida* within cultures needs to be interpreted within a clinical context, and there is no definitive framework for management currently [3].

CASE REPORT

We report the case of a 61-year-old with an unknown past medical history who presented complaining of a cough and progressive dyspnea for over a week. He reported a history of tuberculosis (TB) over 30 years ago, with an unclear treatment course. Further history was unremarkable except for a 40 pack-year smoking history.

On presentation, his heart rate was 120 beats per minute, oxygen saturation was 85% on room air which improved to 98% with 3 L of oxygen, respiratory rate was 32 breaths per minute, and blood pressure was 117/81 mmHg. Physical exam was normal except for mild respiratory distress, rales were audible in the left upper lobe. He was also mildly confused, and his answers were noted to be slowed. His admission workup can be found in Table 1. Imaging was consistent with a dense left upper lobe consolidation with cystic features concerning for cystic pneumonia (Figure 1). He was given a one-time dose of Vancomycin, Piperacillin/Tazobactam, and Doxycycline. Blood, sputum, and acid-fast bacilli (AFB) cultures were ordered, and respiratory droplet precautions were instituted.

He was admitted to the ICU for severe sepsis secondary to cystic pneumonia, mixed metabolic and respiratory acidosis, acute hypoxic and hypercapnic respiratory failure, stage 3 acute kidney injury (AKI), and metabolic encephalopathy.

Piperacillin/Tazobactam and Doxycycline were continued for cystic pneumonia, and intravenous fluids were administered for pre-renal AKI. Over the ensuing few days all acute conditions resolved, except for ongoing respiratory insufficiency, requiring 3 L of oxygen. Left upper lobe infiltrate remained persistent on follow up imaging (Figure 2), blood cultures were aseptic, and AFB cultures were not obtained.

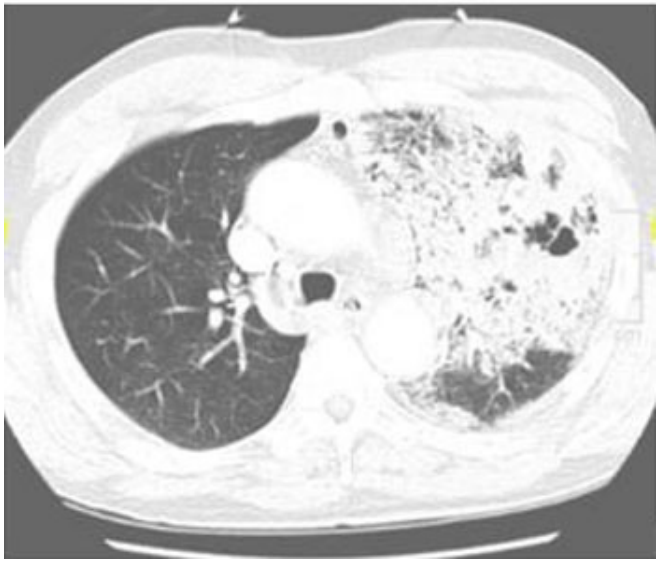

Figure 1: Large left upper lobe infiltrate with cystic changes of left lung apex, reactive mediastinal hilar adenopathy. No filling defect to suggest pulmonary embolism. No pneumothorax or pleural effusion.

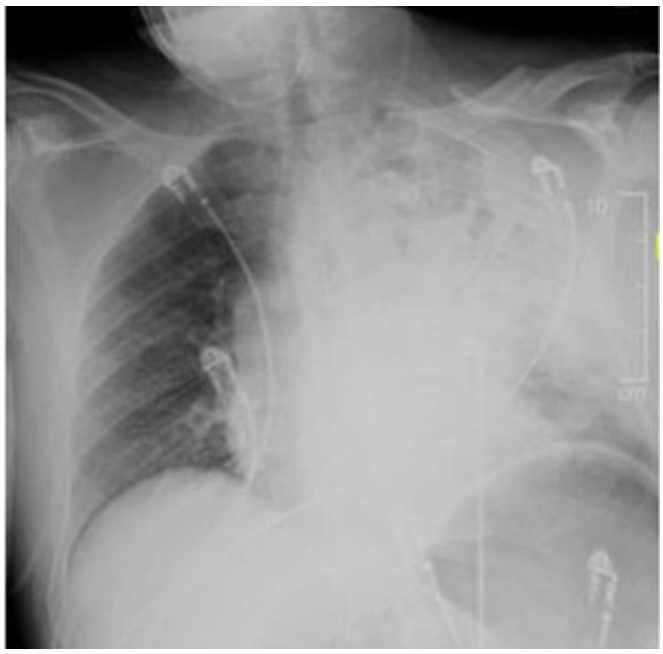

Figure 2: Extensive infiltrate of the entire left lung, possibly suggestive of bacterial pneumonia. The right lung is normally aerated. No cardiac enlargement. Severe gastric distention is noted.

Upon improvement, the patient was transferred to the medical floor. Since sputum cultures were difficult to be obtained through induction or expectoration, an interferon gamma release assay (IGRA) and bronchoscopic bronchoalveolar lavage (BAL) was incorporated. On day 6 of isolation, the bronchoscopy revealed thick, copious mucopurulent secretions upon entry of the left mainstem. Tuberculosis testing was negative, and cultures grew *C. parapsilosis*.

He did not show improvement after completing ten days of antibiotics; hence, further workup for autoimmune and other possible infectious etiologies were pursued (Table 1). Beta-D-glucan was noted to be elevated, and a repeat computed tomography (CT) showed progression of cystic pneumonia with an increase in size and frequency of cystic lesions (Figure 3).

A repeat bronchoscopy was performed on day 12, noting mild oropharyngeal thrush, left upper lobe irritation, thick, and copious secretions. Again, the BAL testing for TB was negative, while biopsies and cultures continued to show *C. parapsilosis*. Histopathology did not show fungal growth. Hence for majority of the management for this patient *C. parapsilosis* was thought to be a contaminant and disregarded. However his condition improved on antifungals in the end. On day 17, fluconazole was started, and the patient's fatigue and functionality improved, along with a decrease in oxygen support requirements. Upon improvement, the patient was discharged with follow-up imaging recommended after one week of anti-fungal therapy.

Table 1: Objective data on presentation

Parameters	Level on admission	Normal range
White blood cell count	4.5	(4.5–11.0 thousand/mm^3)
Absolute neutrophil count	3015	<1000 cells/µL
Hemoglobin	12.8	(12.0–15.0 g/dL)
Hematocrit	39.3	(35.0–49.0%)
Mean corpuscular volume (MCV)	101	80–100 fL
Platelet count	140	150–450 thousand/mm^3
Sodium	134	136–145 mmol/L
Potassium	3.7	3.5–5.1 mmol/L
Chloride	96	98–107 mmol/L
Carbon dioxide	20	21–31 mEq/L
Blood urea nitrogen	63	7–18 mg/dL
Creatinine	4.26	0.6–1.30 mg/dL
Thyroid-stimulating hormone	1.8	0.5–5.0 mIU/L
Troponin	<0.03	0.00–0.045 ng/mL
Lactate dehydrogenase (LDH)	152	87–241 U/L
Lactic acid	7	<2
Hemoglobin A1C	4.8	<5.4%
Atrial blood gas (ABG)	7.18/60/69.8/22.5	7.4/40/60–80/24
Methicillin-resistant Staphylococcus aureus (MRSA)	Negative	
HIV 1+2 Ag/Ab	Negative	
SARS-CoV-2	Negative	
Urine histoplasmosis, Legionella, Aspergillus, Strep pneumonia antigen	Negative	
Acid fast bacilli culture	Indeterminate	
Antinuclear antibody (ANA)	Negative	
Immunoglobin G (IgG), Immunoglobin A (IgA), Immunoglobin M (IgM), Perinuclear antineutrophil cytoplasmic antibodies (p-ANCA), Cytoplasmic-antineutrophil cytoplasmic autoantibody (c-ANCA), Complement factor 3+4	WNL	
Beta-(1,3)-D-glucan	106	<80 µg/L
Tuberculosis (TB) AFB, Nucleic acid amplification (NAA), mycobacterial culture	Negative	

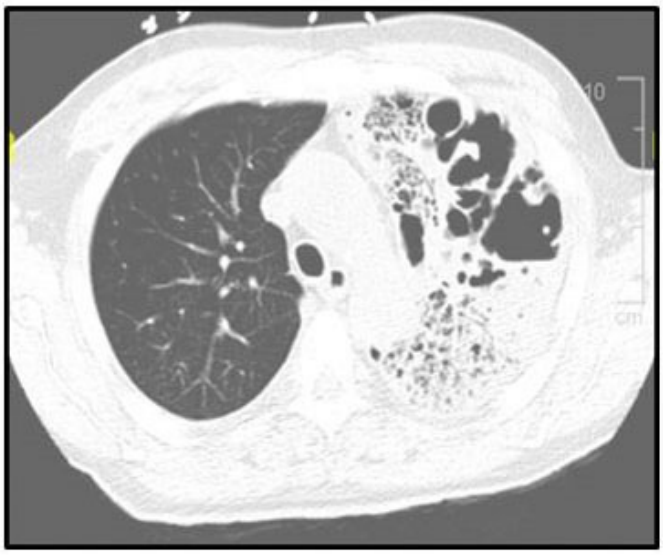

Figure 3: Extensive progression of left upper lobe infiltrate with interval increase in size and number of previously seen cysts. Reactive mediastinal and hilar adenopathy. No pneumothorax. Not shown, worsening consolidation of left lower lobe, and bilateral small pleural effusions greater than right.

DISCUSSION

Candida species is a commonly known commensal organism of the mouth and upper respiratory tract [7], and its growth in the sputum cultures of immunocompetent patients is usually dismissed as a contaminant [1]. Its invasive tendency to cause pneumonia tends to mainly occur in immunocompromised patients, with some studies suggesting an incidence of 0.7% [2, 7]. Our workup for an immunocompromised state, which included testing for human immunodeficiency virus (HIV), diabetes, enzyme deficiencies, autoimmunity, and malignancy, was unremarkable. We suspect that chronic parenchymal lung damage from smoking, caused architectural and immunological impairments, likely making this patient susceptible to an infection.

The prevalence of *Candida* has become an increasingly common cause of invasive fungal disease in the past few decades [2]. The diagnosis is difficult to make due to its unpredictable clinical manifestation and radiological appearance [3]. Currently, molecular-based diagnosis for invasive candidiasis is in the process of development [8]. A definitive diagnosis requires a biopsy for histopathological evaluation, which is done only after exhausting all other common possibilities of pneumonia. The organism forms biofilms and adheres to prosthetics, making patients with risk factors such as immunosuppression, indwelling catheters, prolonged admission to the ICU, or prolonged antibiotic use vulnerable to invasive infection [1, 5].

Candida parapsilosis infections are rare and include, but are not limited to, meningitis, arthritis, and peritonitis [2]. Pneumonia is not a typical manifestation of this *Candida* species. Here we present the first reported case of *C. parapsilosis* necrotizing pneumonia in a non-neutropenic immunocompetent patient. The infection may be triggered by trivial viral infections [6]. In a case such as this one, involving worsening antibiotic resistant cystic pneumonia in an immunocompetent patient, it is important to keep in consideration unusual nonbacterial pathogens.

CONCLUSION

In light of the above case, we can concede that although a meticulous diagnostic approach is the most appropriate way to diagnose pneumonia and customize antibiotics accordingly, the presence of *Candida* should not be overlooked as a probable pathogen. Here we report a rare case of isolated primary *C. parapsilosis* as a cause of necrotizing pneumonia in a non-neutropenic immunocompetent patient diagnosed by histopathology from BAL specimens.

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Author Contributions
Raiya Habib – Conception of the work, Design of the work, Acquisition of data, Interpretation of data, Drafting the work, Revising the work critically for important

intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Zeeshan Ismail – Conception of the work, Design of the work, Acquisition of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.