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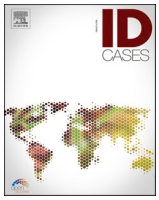

Case report

Candida pneumonia in young and immunocompetent lady: A case report and literature review

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ABSTRACT

Background: Candida is a frequent respiratory tract colonizer. True candida pneumonia is rare and seen with predominance in immunosuppressed patients. Our aim is to document a previously unreported case of Candida pneumonia in a young and immunocompetent patient, highlighting, an unusual pathological manifestation of this infection in immunocompetent individuals.

Case summary: We report a previously healthy young lady who remained symptomatic with fever, cough and shortness of breath for three weeks duration despite treatment with extensive antibiotics regimen for community acquired pneumonia. She was eventually treated as a probable, rare case of candida pneumonia. The patient demonstrated a dramatic response to single antifungal treatment both clinically and biochemically within the first 24hrs of treatment. Candida albican was isolated on repetitive cultures form the sputum and bronchoalevolar lavage samples. The patient had negative blood cultures. Her HRCT scan revealed bilateral basal air space opacities with peri bronchovascular distribution and centrilobular nodules with branching pattern suggestive of tree in bud predominantly in lower lobes. Her endobronchial biopsies was mostly unremarkable apart from rare non-necrotizing granuloma.

Conclusion: Candida can rarely cause clinically significant pneumonia in immunocompetent patients and should be considered in the differential diagnosis of granulomatous lung disease.

Introduction

Candida is part of the normal microflora of the skin, oral cavity, respiratory tract, gastrointestinal mucosa and genitourinary tract [1]. Candida pneumonia is uncommon in immunocompetent individuals; it is considered as a potential cause of pulmonary illness in patients who are taking immunosuppressive therapy or those with repeated and long-term antibiotic use [2].

It is frequently isolated from respiratory tract samples (sputum and broncho-alveolar lavage [BAL]) and typically indicates airway colonization [3]. It is believed that hematogenous spread [3] and micro-aspiration of colonized oropharyngeal and stomach contents are the sole cause of Candida lung disease [4]. Clinical manifestations of primary Candida pneumonia include fever and tachypnea. [5] Radiologically, nonspecific progressive multifocal airspace nodular opacities, pulmonary abscess and cavitory lesions are described [4,5].

We describe a case of Candida pneumonia in an immunocompetent patient in this report. The patient was treated as probable candida pneumonia with good clinical response after failing to respond to multiple antibiotics regimen, having showed persistent candida albicans cultures with negative other pathological cultures. This is the first case report of its kind up to our knowledge.

Case presentation

A 38-year-old Jordanian lady, with no known chronic illness, presented the 3rd time to emergency department with worsening symptoms of high grade fever, productive cough, exertional shortness of breath and dizziness for 10 days. Patient had positive sick contact with her kids whom suffered from upper respiratory tract infection symptoms. On her previous two visits to the emergency departments, she was vitally stable and treated as a case of community acquired pneumonia with oral

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Table 1
Laboratory test results.

Details	Value w/Units	Normal Range
On Admission		
WBC	11.8 × 10^3/uL	4.0–10.0
Hemoglobin	11.7 gm/dL	12.0–15.0
Urea	30 mmol/L	2.5–7.8
Creatinine	56 umol/L	44–80
Sodium	130 mmol/L	133–146
Potassium	4.6 mmol/L	3.5–5.3
Chloride	99 mmol/L	95 – 108
Bicarbonate	24 mmol/L	22 – 29
Adjusted calcium	2.38 mmol/L	2.20 – 2.60
Total protein	72 gm/L	60 – 80
Albumin	28 gm/L	35 – 50
ALP	285 U/L	35 – 104
ALT	22 U/L	0 – 33
AST	25 U/L	0 – 32
C-reactive protein	295.1 mg/L	0–5
Procalicitonin	0.47 ng/ml	
TSH	1.27 m IU/L	0.3 – 4.20
HbA1c	5.8%	

Autoimmune tests

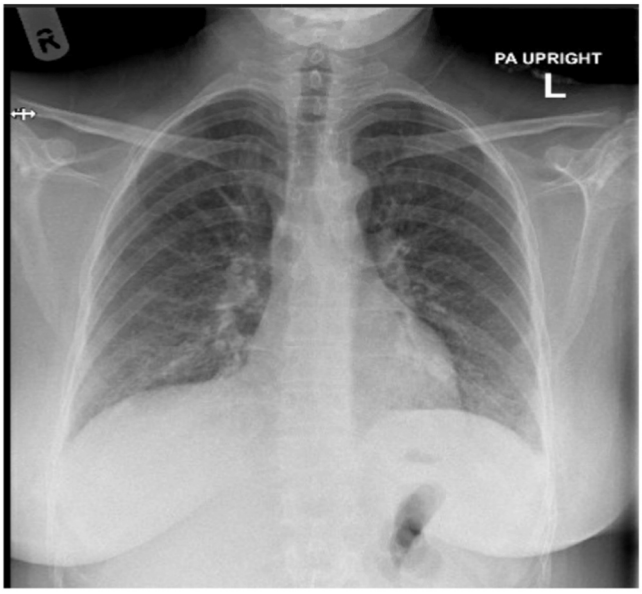
Details	Result	Interpretation/normal range
Rheumatoid factor	< 10 IU/ml	0–14
Anti CCP Ab	< 8 IU/ml	0–17
ANCA	Negative	
ANA CTD int	Negative	
Jo-1	< 0.3 U/ml	negative
LA	< 0.3 U/ml	negative
RNP 70	0.3 U/ml	negative
RO	< 0.3 U/ml	negative
Scl-70	< 0.6 U/ml	negative

General Immunology

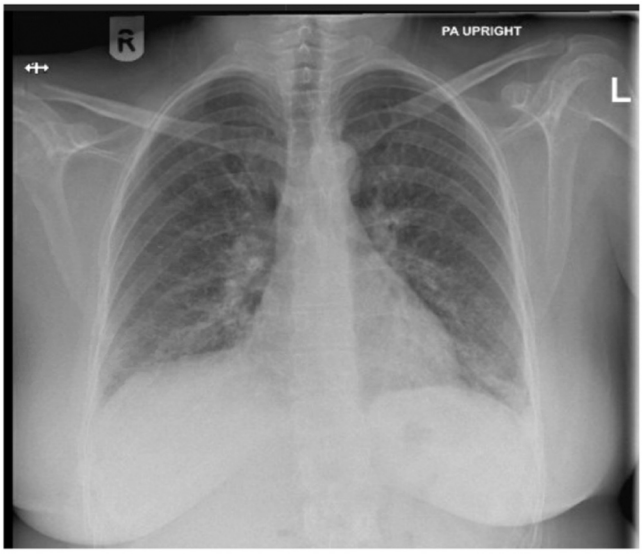
Detail	Value w/Units	Normal Range
IgG Sub 1	7.007 mg/L	3824–9286
IgG Sub 2	3.356 mg/L	2418–7003
IgG Sub 3	2,2092 mg/L	218–1761
IgG Sub 4	413 mg/L	39–864
C3	1.53 gm/L	0.90–1.80
C4	0.75	0.1–0.4

Microbiology Tests

Detail	Result
2 sets of blood cultures on admission	No growth at 5 days
Repeated 2 sets of blood cultures with persistent fever	No growth at 5 days
Sputum culture on admission	Normal upper respiratory flora including moderate candida albicans
Repeated sputum culture	Normal upper respiratory flora including moderate candida albicans
2 sets AFB smear (sputum)	Negative
AFB PCR (sputum)	MTB NA not detected
TB culture (sputum)	No growth at 42 days
2 sets AFB smear (BAL)	Negative
AFB PCR (BAL)	MTB DNA not detected
TB culture (BAL)	No growth at 42 days
Respiratory lower culture	No growth at 48 h
Pneumocystis Jiroveci detection (BAL)	Negative
BAL fungus culture	Candida albicans isolated
Blankflour stain (BAL)	No fungal elements seen
Aspergollus gallactomannan antigen (serum)	Negative
M3 Aspergillus fumigatus	0.00
M3 Aspergillus fumigatus Cl	Class 0, negative
Beta-D-Glucan	Not checked
Influenza A and B PCR	Negative
Covid-19 PCR	Negative
CMV Ab	IgG: reactive IgM: Non-reactive
EBV capsid Antigen	IgG: positive IgM: negative
HIV Ag/Ab combo	Non-reactive
Cytology (BAL)	Negative for malignancy Microscopic description of differential count: Eosinophils 0% Lymphocytes 0% Macrophages 64% Neutrophils 36%
Endo-bronchial biopsy	Rare non-necrotizing granuloma Grocott's & Ziehl-Neelsen stains: negative



(A)



(B)

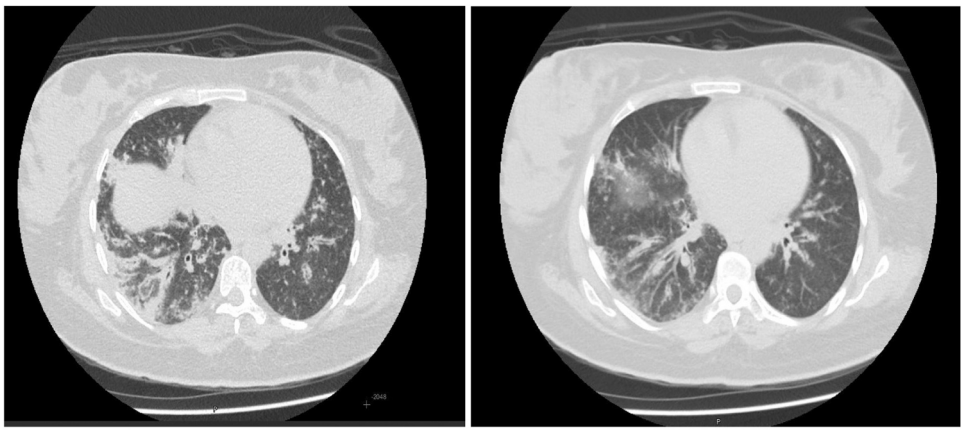
Fig. 1. (A) PA view of X-ray of the chest on 1st ED visit as compared to (B) 3rd ED visit, shows worsening bilateral lower zones infiltrates more pronounced on the right lower zones.

antibiotics – Amoxicillin / clavulanic acid on the first visit and azithromycin on the 2nd visit, however, she was unable to complete the treatment due to multiple vomiting episodes, thus, she presented for the 3rd time in 10 days to the emergency department with worsening symptoms. She looked septic with oral temperature of 38.5 degree celsius, blood pressure of 86/51 mmhg, heart rate of 108 beats/minute, tachypenic with respiratory rate of 26 breaths / minutes, peripheral oxygen saturation of 93% on room air. Chest auscultation was remarkable for bilateral diffuse crackles on middle and lower lobes with scattered wheezes, other systematic examination was unremarkable. Lab test results showed markedly elevated C-reactive protein of 295 mg/L with negative procalcitonin of 0.47 ng/ml (Table 1). X-ray of the chest – PA view (Fig. 1) showed worsening bilateral lower zones infiltrates more pronounced on the right lower zones as compared to her 1st ED visit. Patient was treated as a case of sepsis secondary to community acquired pneumonia with intolerance to oral therapy. Her blood pressure improved with fluid resuscitation and she was commenced initially on IV ampicillin/ sulbactum plus azithomycn with symptomatic treatment. Patient continued to spike high grade fever with no clinical improvement for which antibiotics escalated to IV piperacillin/tazobactam on day 4 of admission and further work up was requested. High resolution CT scan was done and revealed bilateral basal air space opacities with peri bronchovascular distribution and centrilobular nodules with branching pattern suggestive of tree in bud predominantly in lower lobes (Fig. 2). Tests for tuberculosis from the sputum and autoimmune disorders did not yield any positive results. Bronchoscopy (Fig. 3) was done on day 9 of admission and showed inflamed looking airways, especially right upper lobe secondary carina with inflamed submucosal and mucosal changes. Broncho-alveolar lavage (BAL) was positive for candida albicans but negative for TB work up. Her BAL cell count differential revealed 36% Neutrophils and 64% Macrophages with no eosinophil or Lymphocytes present. The endobronchial biopsies revealed a rare non-necrotizing granuloma. She had negative sputum and blood cultures apart from persistently positive candida albicans isolated from the sputum. She had no clinical response to 6 days of IV piperacillin/tazobactam on day 10 of admission, she was therefore started on anidulafungin to treat a probable case of candida pneumonia infection after a thorough discussion with the infectious disease team in the hospital. She fortunately improved dramatically, this was reflected in both her clinical and biochemical status within the first 24hrs of starting anidulafungin (Fig. 4) which she continued intravenously for 4 days then discharged on oral fluconazole for another 20 days based on the susceptibility results. She showed complete recovery upon her post discharge follow up both clinically and radiologically (Fig. 5). Notably, our patient has been previously healthy with no preceded history of acute infection or visits to healthcare facilities prior to her acute illness, she has 5 kids and all delivered via normal vaginal delivery and her last child is 10 months old. She has naïve surgical history and had not been on any acute or chronic medications besides no prior history of candida infections.

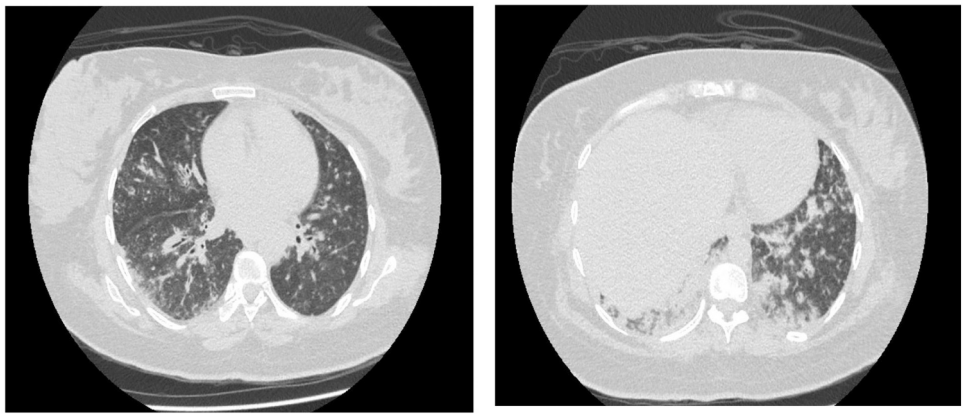
Discussion

Candida acts as a benign saprophyte where it can persist for an extended period of time without producing any symptoms of disease in various parts of human body [6]. Candida pneumonia cases are mostly caused by the organism's dissemination from distant sites, such as the gastrointestinal tract and the skin [7]. It has mainly been observed in patients with severe immune system deficiencies, infants with very low birth weights, and individuals with cancerous tumours [8]. What is interesting about our patient is that she has no history of immunodeficiency, systemic disease, or any risk factor for candida infection that we are aware of.

Our patient was treated as a probable case of candida pneumonia while demonstrating a persistent positive candida albicans isolates from the sputum and BAL cultures with very good clinical response. While candida isolates are frequently considered colonisations in respiratory tracts specimens, samples from sterile sites such as BAL, pericardial fluid and biopsied lung tissue should be treated with cautions as it may signify the present of true candida infection [9]. Besides the importance of bronchoalveolar lavage as an adjuvant in the diagnosis of fungal pneumonia [6], the diagnosis of Candida pneumonia requires a biopsy to confirm the presence of the fungus infection [10]. Treatment is not recommended to be started for Candida solely based on the presence of the fungus in a bronchoalveolar lavage sample in immunocompetent patients because the results of this test and those of a biopsy have a weak correlation [11]. Referring to a study by Wood et al. mortality rates were observed to be similar in patients who received antifungal treatment based on positive culture of candida in BAL and those who did not. The positive and negative predictive values of BAL cultures were, 29% and 89% respectively in the same study [12].



(A &B)



(C &D)

Fig. 2. (A, B, C & D) HRCT scan cuts show plaque like consolidative changes with lower lobe volume loss, multiple randomly distributed micro-nodules with tree-in bud-appearance with thickening of the peri-broncho-vascualr intersitium.

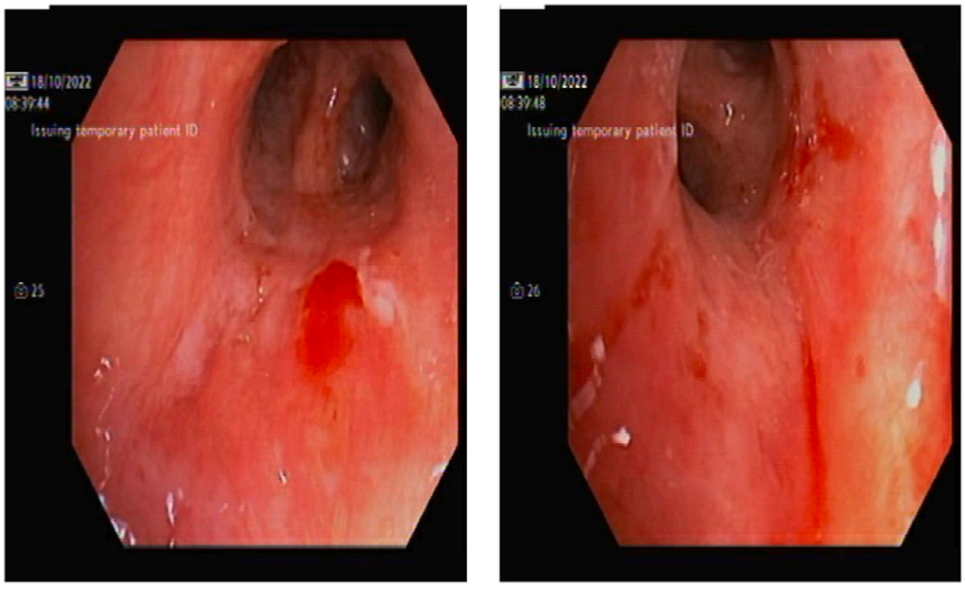


Fig. 3. Bronchoscopy shows inflamed looking airways, especially right upper lobe secondary carina with inflamed submucosal and mucosal changes.

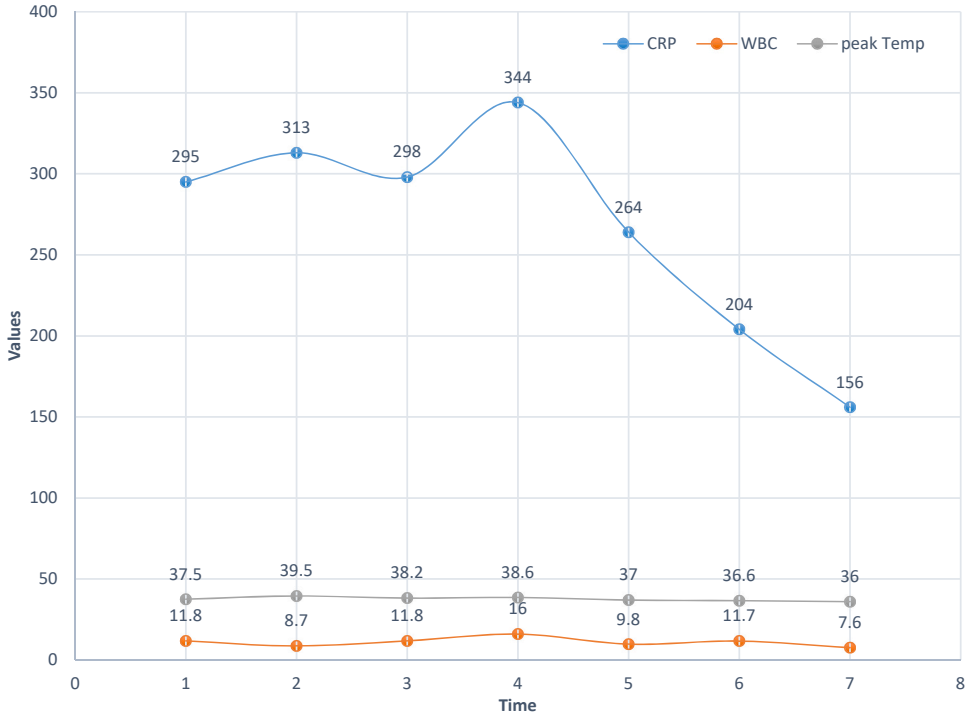
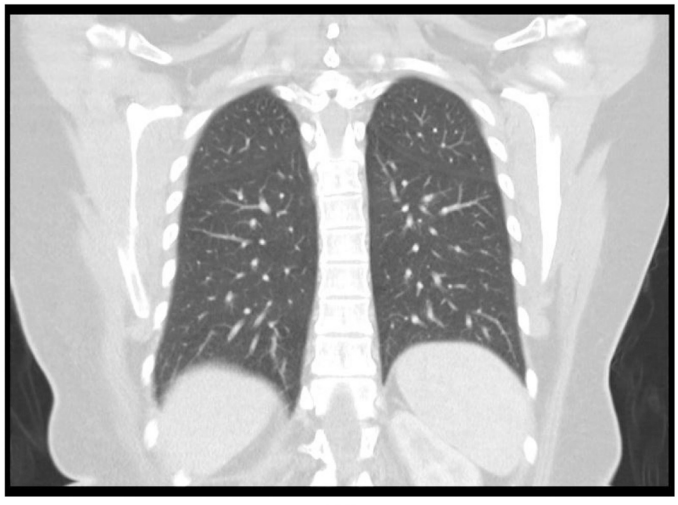
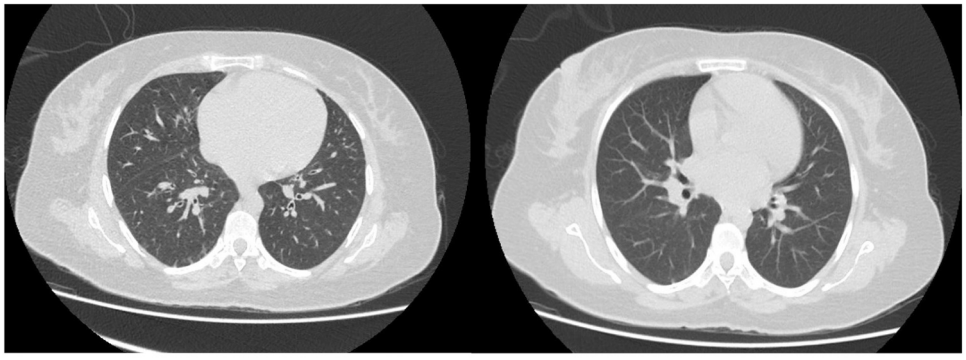


Fig. 4. Plot chart illustrates progressive decline in crp, wbc and temperature post anti-fungal treatment.



(A)



(B &C)

Fig. 5. (A, B & C) post treatment follow up HRCT scan cuts show near complete resolution of the consolidative changes and micronodules as compared to images in Fig. 2.

In reference to the endo-bronchial biopsy results of non-necrotizing granuloma in our patient, pathological findings of granulomas are commonly seen in lung biopsies. The most common causes of non-necrotizing granuloma still remain infectious in aetiology, such as, mycobacteria, fungi and parasites, frequently, admixed with necrotizing granulomas which can be easily missed in small biopsies. Other causes like vasculitis - which will point towards granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis – and sarcoidosis are seen less frequently. The latter diagnosis of sarcoidosis is considered – a diagnosis of exclusion - after extensive workup, ruling out all other apparent causes of non-necrotizing granuloma [13].

The fact that our patient did not respond to antibiotics but showed rapid improvement with antifungal treatment leads us to believe that she had Candida pneumonia. Although Candida pneumonia is uncommon in people with normal immune systems, and it can be difficult to diagnose, healthcare providers should keep this possibility in mind when treating patients who have Candida in their bronchoalveolar lavage sample and do not respond to standard treatments.

Conclusions

Physicians should consider candida pneumonia as one of the differential diagnoses of non-necrotizing granuloma in the lung, even though it is extremely rare in immunocompetent patients. Especially when all other, more typical differentials were excluded, following numerous unsuccessful trials of broad-spectrum antibiotics.

Ethics statement

This study is approved by the Medical Research Center (MRC) of Hamad Medical Corporation (HMC).

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Author contribution

Writing manuscript: Ali Y, Mousa A, Mohamed H, Ibrahim M, Reviewing, editing and performing procedure: Naveed M, Alsamawi M.

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Author statement

We describe a case of Candida pneumonia in an immunocompetent patient in this report. The patient was treated as probable candida pneumonia with good clinical response after failing to respond to multiple antibiotics regimen for total of 20 days including both outpatient and inpatient treatments, having showed persistent candida albicans cultures with negative other pathological cultures, she was treated with antifungals and showed dramatic clinical and biochemical improvement in 24hrs post treatment intiitaion. This is the first case report of its kind up to our knowledge. And our aim is to document a previously unreported case of Candida pneumonia in a young and immunocompetent patient, highlighting, an unusual pathological manifestation of this infection in immunocompetent individuals.

Declaration of Competing Interest

The authors report no conflict of interest.

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