Case Report

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Microbiology Section

Mixed Fungal Lung Infection with *Aspergillus Fumigatus* and *Candida Albicans* in an Immunocompromised Patient: Case Report

JAYA S.[1], HARITHA VIPPARTI[2]

ABSTRACT

The frequency of invasive, opportunistic mycoses has increased significantly over the past 2 decades. In the immune-compromised host, many fungi, including species of fungi typically considered non-pathogenic, have the potential to cause serious morbidity and mortality. Here we report a rare case of mixed fungal infection of the lung with *Candida albicans* and *Aspergillus fumigatus* in a patient on prolonged steroid therapy.

Keywords: *Aspergillus fumigatus, Candida albicans*, Fungal pneumonia, Opportunistic mycoses

CASE REPORT

A 53-year-old female, from Ananthapur (Andhra Pradesh), was admitted to Narayana Hrudayalaya Hospital, Bangalore, India in the month of February 2013, with history of loose stools, vomiting since 3-4 days and loss of consciousness since that day morning. Patient was intubated immediately due to low Glasgow Coma Scale (GCS). She was treated for the same in another hospital and was referred to our hospital for further management. She was a known case of type 2 diabetes mellitus, coronary artery disease with anterior wall MI, LV dysfunction, hypothyroidism and adrenocortical insufficiency and was on medications for all these conditions since one year.

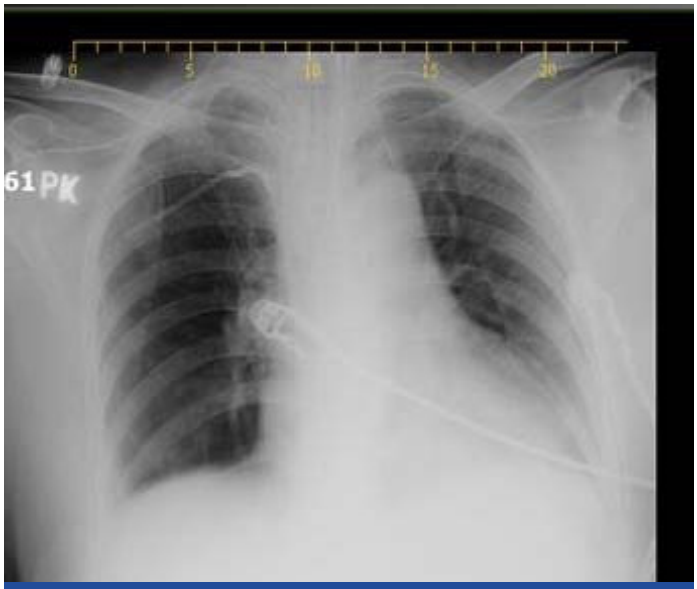
Investigations – Chest X-ray of patient showed features of pulmonary edema. Total count was 3,500, Neutrophils- 94%, Liver Function Test and Renal Function Test were normal, Procalcitonin 8.4, Stool routine showed occult blood, no ova and cyst. Stool was also sent for culture. Serology for HIV was non-reactive. She was managed medically for pulmonary oedema and started on meropenem and vancomycin in view of infection.

Her endotracheal aspiration was sent next day for culture and sensitivity which grew multi-drug resistant *Klebsiella pneumonia*. Blood cultures were sent which did not yield any growth. Stool did not show any growth of pathogens. Antibiotics were changed based on sensitivity pattern.

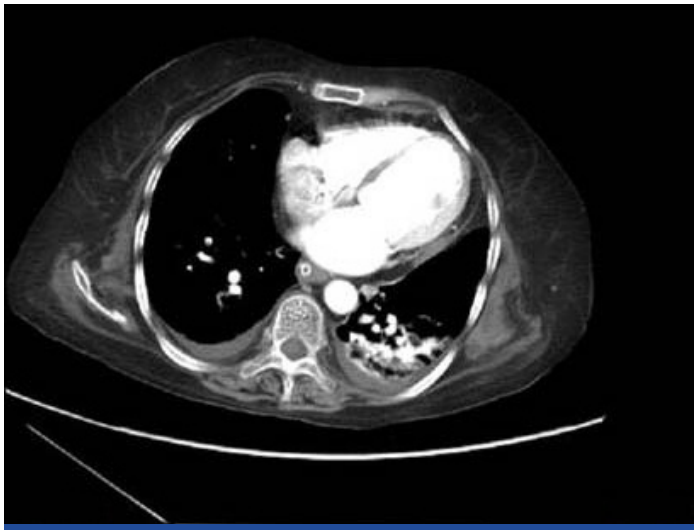
After 4 days, a repeat chest X-ray was taken in view of desaturation showed patch in the left lung [Table/Fig-1]. A CT scan showed thin walled cavity in the left lower lobe of the lung [Table/Fig-2] with pulmonary edema and in the abdomen there was diffuse large bowel thickening. Due to these radiological findings, bronchoscopy was planned. On bronchoscopy necrotic mucosa was seen at the lower end of the trachea extending to the left lower lobe. It was filled with necrotic material and biopsy was taken which was sent for histopathological examination. Bronchioalveolar lavage was sent for culture and sensitivity test, Potassium hydroxide (KOH) preparation and Cytomegalovirus (CMV) qualitative Polymerase chain reaction (PCR).

The sample was streaked on Blood agar, Chocolate agar and incubated at 37ºC for 48 hours and Sabouraud Dextrose Agar (SDA) which was incubated at both 37ºC and 25ºC for a week.

On KOH mount, there were septate hyphae with acute angle branching and oval budding yeast cells seen [Table/Fig-3]. On Gram



[Table/Fig-1]: Chest X-ray showing a patch in left lung



[Table/Fig-2]: CT scan of chest showing pathology on left lung

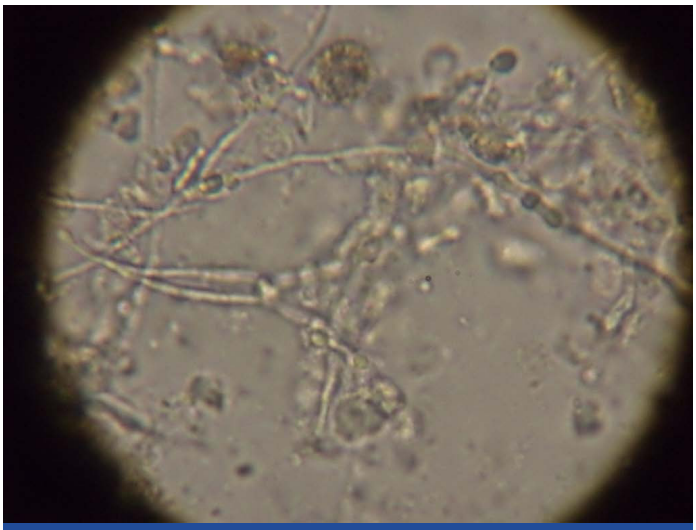
stain there were few inflammatory cells with oval budding yeast cells with pseudohyphae and septate hyphae seen [Table/Fig-4]. The patient was started on voriconazole and micafungin.

Histopathological examination of the biopsy sent, showed necro-inflammatory slough with fungal structures consisting of yeast cells with pseudohyphae and acute angle branching hyphal structures, suggestive of mixed *Candidal and Aspergillus* invasive fungal disease. After 48 hours there were creamish colonies on SDA resembling yeast, on Gram stain it showed oval budding yeast cells. The yeast like colonies were processed in Vitek 2 for further identification and sensitivity. It was identified as *Candida albicans* sensitive to amphotericin B(MIC- 0.5), flucytosine, fluconazole (MIC <1) and voriconazole(MIC <0.12), caspofungin (MIC <0.25)

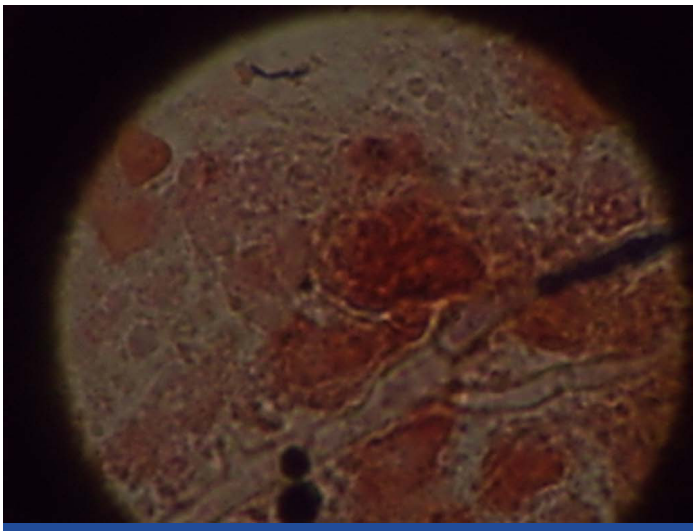
Patient remained on ventilator support with antibiotics and antifungal agents. The clinical condition remained the same.

After 4 days, there were white velvety colonies resembling a mould in the tube incubated at 37^{0}C. The whitish colonies turned green with pale yellow reverse on further incubation and later a Lactophenol cotton blue (LPCB) mount was performed which revealed septate hyphae, terminal vesicles which support a single row of phialides on the upper two-thirds of the vesicle [Table/Fig-5].

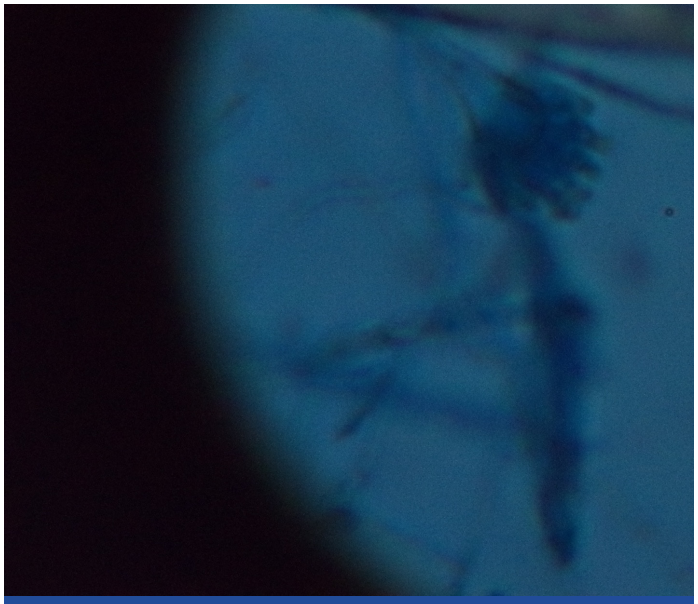
Three days later her repeat chest X-ray showed patch on both right and left side [Table/Fig-6]. A repeat bronchoscopy was performed which revealed necrotic material similar to the previous study. The sample was sent for microbiological and histopathological examination, the results of which were similar to the previous sample.



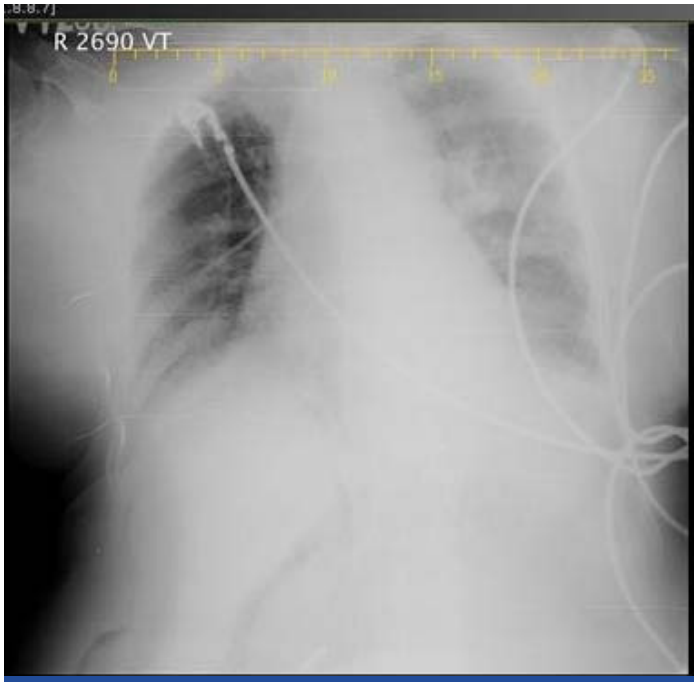
[Table/Fig-3]: KOH preparation of broncho alveolar lavage showing septate hyphae



[Table/Fig-4]: Gram stain of bronchoalveolar lavage showing septate hyphae and oval budding yeast cell



[Table/Fig-5]: LPCB mount showing *Apergillus fumigates*



[Table/Fig-6]: Chest X-ray showing deterioration in the picture

A colonoscopy was performed and biopsy taken which was sent for histopathological examination. Histopathological examination of biopsy showed no evidence of fungal infection.

But next day she developed metabolic acidosis and decreased cardiac output. She had persistant hypotension later and succumbed due to cardiac arrest.

DISCUSSION

The frequency of invasive, opportunistic mycoses has increased significantly over the past two decades. Patients who are at risk for the development of serious fungal infections, including patients undergoing blood and marrow transplantation (BMT), solid-organ transplantation, patients with Acquired immunodeficiency syndrome (AIDS) neoplastic disease, advanced age, patients receiving immunosuppressive therapy and premature Infants [1].

The human airway is continuously open to the non-sterile environment where fungal spores have the potential to reach lung tissue and produce disease. In the immune-compromised host, many fungi have the potential to cause serious morbidity and mortality [2]. The widespread implementation of antimicrobial prophylactic regimens

for a variety of immune-suppressed patient groups has rendered the host at greater risk for colonization with more resistant fungal species, enhancing the increase of invasive fungal infection in these already immune-suppressed patients [3]. In our case the patient was a known case of adrenocortical insufficiency and was on steroids for the last 1 year, which could be the cause of immunodeficiency.

The opportunistic yeasts of the *Candida* species are endogenous flora that can gain access to the bloodstream, usually through the bowel [4]. Two forms of *Candida* pneumonia have been reported: primary pneumonia, which follows aspiration of *Candida* laden oropharyngeal secretions, and pneumonia secondary to hematogenously disseminated *Candidiasis*, especially in immunocompromised hosts [5]. The debate about the diagnosis of pulmonary *Candidiasis*, the definite diagnosis of pulmonary *Candidiasis* still rests on histologic demonstration of the yeast in lung tissue with associated inflammation [6]. To rule out dissemination of *Candida* from the large intestine, a colonoscopy was performed and biopsy taken. But there was no histopathological evidence of fungal infection.

The spores of *Aspergillus* species enter the body commonly through the sinuses or the respiratory tract. In the early stages of the disease the chest radiograph may be normal. As the disease progresses, a nodular appearance or patchy consolidation may be evident [4]. Similarly in our case in the chest X-ray taken on admission did not show any patch or infiltrate. A patch was seen on the left lung only four days after admission.

The definition for proven *Aspergillosis* requires histopathological documentation of infection and a positive result of culture of a specimen from a normally sterile site. *Aspergillus fumigatus* is the most common species recovered from cases of invasive *Aspergillosis* [7]. Similarly in our case we have isolated *Aspergillus fumigates* from the culture along with *Candida albicans*. This is a definite proven case of mixed infection with *Candida* and *Aspergillus* due to both histopathological and culture evidence.

Aspergillus fumigatus is inhibited by *Candida spp.* in culture and the inhibitory effect is fungistatic and not fungicidal [8]. In our culture there was a delay in growth of *Apergillus* most probably due to the inhibition of growth by *Candida spp*.

Other than *Aspergillus*, angioinvasive molds, such as *Fusarium* and *Zygomycetes* species, are increasingly encountered in severely immunocompromised hosts [9]. Many of these emerging fungi are resistant to antifungal agents, and despite advances in antifungal therapy, Invasive fungal infections caused by them have high mortality [10].

Simultaneous infections with multiple fungi may be misinterpreted as monomicrobial infections by current diagnostics with ramifications for the choice of antimicrobial agents that may impact patient outcomes. The application of molecular methods on tissue samples may be useful to decipher the aetiology of mixed fungal infections. The combination of broad-range PCR with sequence analysis and FISH applied on tissue samples is a powerful approach to identify the aetiology of invasive fungal infections, including mixed infections [11].

As per the Infectious diseases society of America (IDSA) guidelines for treatment of invasive pulmonary *aspergillosis,* voriconazole is the recommended drug for primary therapy and alternative drugs are amphotericin B, caspofungin, micafungin and itraconazole [7]. *Candida* should be treated with antifungal agents, selecting one of the following agents: fluconazole, an amphotericin B formulation, an echinocandin, voriconazole, or the combination regimen of fluconazole and amphotericin B [5].

Inspite of all the appropriate antibiotic and antifungal agents the patient succumbed probably due to the underlying comorbid conditions, resistance of the fungi to the antifungal agents and due to mixed fungal infections which have a higher mortality rate.

CONCLUSION

Immunocompromised individuals are highly susceptible to the fungal infections. High rate of mortality and morbidity is noticed in patients with mixed fungal infection. Hence high clinical suspicion and appropriate antimicrobial therapy needs to be initiated in immunocompromised patients.

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PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Microbiology, Shridevi Institute of Medical Sciences and Research Centre, Rajiv Gandhi University, Tumkur, Karnataka, India.
2. Assistant Professor, Department of Microbiology, Malla Reddy Institute of Medical Science, Dr. NTR University, Hyderabad, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Jaya S.,
No. 7, Harishree, Near Venkateshwara College, Brindavannagar, D.R. College, Bangalore-560029, India.
Email: drsjaya@gmail.com

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