Case Report

Invasive pulmonary aspergillosis in an immunocompetent adult A Case Report

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Abstract

Invasive pulmonary aspergillosis is a severe potentially life-threatening infection, usually affecting immunocompromised patients and caused by many species of *Aspergillus.* It is usually diagnosed based on a combination of clinical, microbiological and radiological findings. Since it is rarely reported in immunocompetent people, diagnosis can be delayed. We report a case of invasive pulmonary aspergillosis in a male patient who presented with features of community acquired pneumonia. The importance of radiological features and serological tests and timely institution of appropriate treatment, monitoring and assessing clinical response has been emphasised.

Keywords: *Aspergillosis, Invasive Pulmonary, Lung Diseases, Fungal, Immunocompetent*

Introduction

Aspergillus is a ubiquitous genus of filamentous fungi that can cause a variety of infections or allergic diseases according to the host's immune status. Among the various Aspergillus species that cause the disease in humans, *Aspergillus fumigatus* is the most common cause of aspergillosis. Invasive pulmonary aspergillosis (IPA) is a potentially life-threatening infection which primarily affects immunocompromised patients with prolonged neutropaenia or on immune suppressive therapy.[1] IPA is now an emerging infection in patients with chronic obstructive pulmonary disease (COPD) or on corticosteroid therapy.[2]

IPA is acquired through the inhalation of infectious spores. In the absence of effective defense mechanisms, spores germinate and invade the lung with haematogenous spread to other organs.[2] Fever, cough and dyspnea are the major symptoms of IPA, resembling bronchopneumonia, which is usually unresponsive to antibiotics.[2] Diagnosis of IPA is based on the combination of clinical, microbiological and radiological findings, but histological examination and culture remain the

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gold standard.[3] Typical radiological findings on high resolution computed tomography (HRCT) are single or multiple pulmonary nodules with surrounding ground glass appearance (Halo sign) or air crescent sign which strongly support the diagnosis.[3,4] Additionally, laboratory tests such as serum galactomannan and 1-3-beta-D-glucan assays play a critical role in supporting the diagnosis of IPA.[4] The recommended first-line treatment for invasive aspergillosis is voriconazole which should be administered for a minimum of 6-12 weeks depending on the clinical improvement, degree and duration of immunosuppression.[5]

We report a possible case of IPA in the absence of classical risk factors. While invasive aspergillosis is typically observed in immunocompromised individuals, there have been only a limited number of case reports in immunocompetent patients and there are no documented cases of IPA in immunocompetent patients reported in Sri Lanka.

Case presentation

A 53-year-old male with a bipolar affective disorder, treated with Benzhexol and sodium valproate, and with no other comorbidities, presented with a productive cough of two weeks and fever, shortness of breath and reduced level of consciousness for one day. On admission to hospital, his Glasgow coma scale (GCS) was low, he was tachycardic, tachypneic, with low right sided lower zone air entry, and his on-air saturation was 93%.

Initial investigations showed a total white blood cell count of 7,290 cells/μL, with 85.5% neutrophils, C-reactive protein (CRP) of 226mg/dl, and chest X-ray revealed right sided lower lobe consolidation without effusions. He was managed as having a probable community-acquired pneumonia with supplemental oxygen therapy, intravenous (IV) fluids, IV ceftriaxone and oral clarithromycin. However, within the next two days he deteriorated significantly and required intubation and treatment in the intensive care unit (ICU).

The patient's antibiotics were switched to IV meropenem and levofloxacin in the ICU. On the second day of ICU admission, a bronchoscopy and bronchoalveolar lavage (BAL) were performed, revealing complete blockage of the right lower lobe. Samples were collected for bacterial, fungal and mycobacterial studies. Despite receiving antibiotic therapy, the patient's condition did not improve. He required higher respiratory support and experienced failed extubation. Despite prolonged antibiotic therapy, he continued to have intermittent fever spikes.

Bacterial and mycobacterial studies of the bronchoalveolar lavage did not provide any significant results. Although the fungal direct smear and culture performed from BAL samples were negative, BAL galactomannan received on day 22 was 5.1 (normal value <0.5). The patient was started on oral voriconazole 200mg 12 hourly after an initial loading dose (400mg 12 hourly). The first HRCT scan, performed on day 35 showed patchy consolidation around the bronchus and a ground glass appearance with a halo sign, indicative of invasive pulmonary aspergillosis (Figure 1A). Oral antifungal treatment was continued, and antibiotics gradually de-escalated and discontinued.

The patient showed gradual clinical improvement, achieving extubation after 12 days of antifungal therapy and becoming afebrile by the 8th day of treatment. His response was monitored through successive measurements of serum galactomannan levels and HRCT scans (Figures 1B, 1C).

Serum galactomannan levels performed on day 18 and day 36 of voriconazole were 0.74 and 0.41 respectively. Once the serum galactomannan levels normalised and the HRCT indicated complete resolution of the invasive aspergillosis features, oral antifungals were omitted after a complete treatment duration of 62 days. The patient tolerated the prolonged course of voriconazole therapy well, without any signs of adverse effects.

During this long stay in the ICU, the patient developed critical illness myopathy (CIM) and several hospital-acquired infections such as catheter-associated urinary tract infection, hospital-acquired pneumonia and percutaneous endoscopic gastrostomy (PEG) site infection. All these infections were successfully managed without further complications. Following discharge from the ICU, the patient received ward care for 6 days, before being transferred to a rehabilitation facility.

Figure 1- HRCT chest imaging across the clinical course

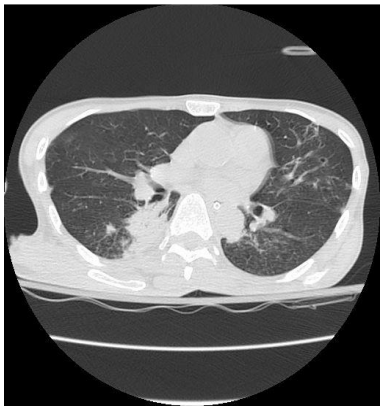

Figure 1A - 1st HRCT on day 35

Consolidation of the R/S lower lobe and bronchial dilatation. Patchy consolidation & ground glass appearance with halo sign around the bronchus and Interstitial thickening. Suggestive of invasive aspergillosis

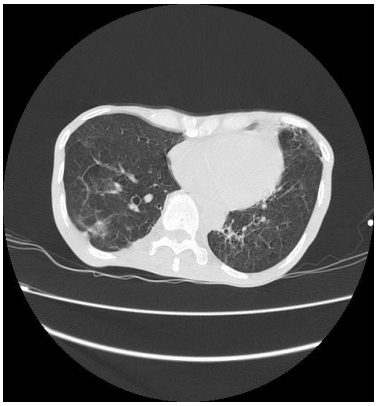

Figure 1B – 2nd HRCT on day 63

Reduction of the bronchial dilation, consolidation and ground glass appearance. Compared to the previous CT scan, inflammatory areas have reduced in size, with very small right-side pneumothorax

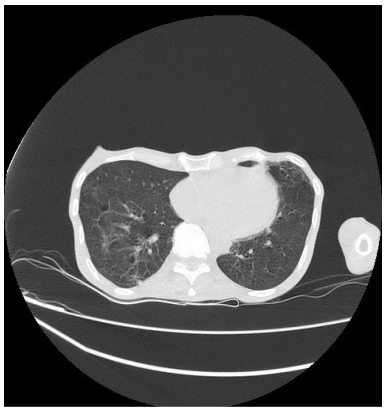

Figure 1C – 3rd HRCT on day 76

Compared with previous CTs the invasive aspergillosis changes have completely resolved.

New appearance of tree in bud changes is in favor of new super added infections

A timeline of the patient's progress is shown in Figure 2

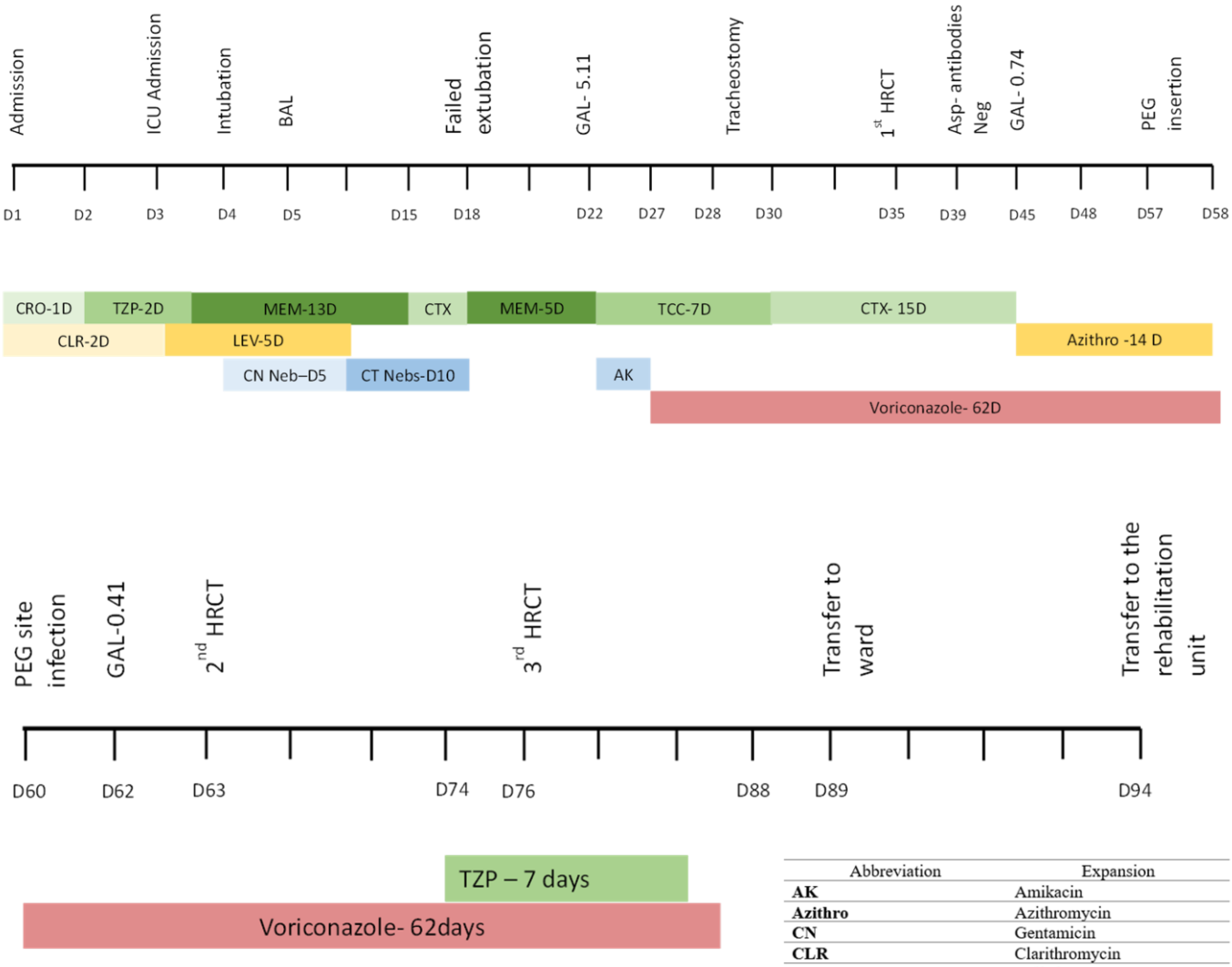

Figure 2: Timeline of the patient's progress

Abbreviation	Expansion
AK	Amikacin
Azithro	Azithromycin
CN	Gentamicin
CLR	Clarithromycin
CT	Colistin
CTX	Cefotaxime
CRO	Ceftriaxone
Gal	Galactomannan
LEV	Levofloxacin
MEM	Meropenem
Neb	Nebulization
PEG	Percutaneous Endoscopic Gastrostomy
TCC	Ticarcillin-clavulanic Acid
TZP	Piperacillin- Tazobactam

Discussion

Aspergillosis presents with a broad range of clinical manifestations, from non-invasive forms such as allergic bronchopulmonary aspergillosis and aspergilloma to invasive aspergillosis. While invasive aspergillosis is predominantly observed in immunocompromised patients, a few cases have been reported in immunocompetent individuals without identifiable risk factors.[6,7,8] These cases were successfully treated with voriconazole, despite significant challenges in diagnosis.

The present case involves a patient who was diagnosed with bipolar affective disorder and had no other concurrent medical conditions affecting his immune system. The patient had no history of pre-existing structural lung damage, tuberculosis or viral pneumonia, including influenza or SARS-CoV-2 infection, and potential predisposing factors were not observed during clinical assessment.

On presentation, the patient showed features suggestive of community-acquired pneumonia of probable bacterial origin, but despite the administration of appropriate antibiotic therapy he continued to deteriorate.

Although the definitive diagnosis of IPA using direct smear and fungal culture was negative, the BAL galactomannan levels and typical features in the HRCT were useful in making the initial diagnosis. To detect IPA, the sensitivity and specificity of galactomannan assay is 82% and 81% respectively in neutropenic patients, but in non-neutropenic patients the diagnostic value of this test is limited because galactomannan antigens are cleared by neutrophils.[9] However, in this case, the galactomannan test was useful for initial diagnosis as well as in monitoring. The delay in the first galactomannan test was due to the unavailability of the test in the country which led to a delay in diagnosis and management. However, in spite of this delay, the patient recovered fully with antifungal treatment.

The main challenge in managing this case revolved around monitoring the patient's clinical response and determining the appropriate duration of the treatment. This was effectively addressed by serial monitoring of serum galactomannan and HRCT.

Take home message:
The unavailability of some essential tests often leads to prolonged antibiotic use, particularly in patients in intensive care units. This case highlights the importance of diagnostic stewardship, which is inseparable from antimicrobial stewardship. Managing a ventilated patient to prevent hospital-acquired infections is a significant challenge, highlighting the critical need for a multidisciplinary approach in diagnosis and tailoring the treatment.

Declaration

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Author contributions:
All authors have contributed: involved in the process of patient management and diagnosis.
MPKG: wrote the manuscript.
SC and PIJ: supervised the manuscript writing
The patient management was by JNK, SC, WS, SM, AS, PIJ

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