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Case Report

Invasive pulmonary *Aspergillus* infection in an immunocompetent host following severe dengue

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Abstract

Aspergillus species are widespread in the environment with *Aspergillus fumigatus* being the most common pulmonary pathogen. In a person with normal immunity, Aspergillosis in the lung can mainfest as hypersensitivity reaction. It can also present as an invasive infection in immunocompromised patients. In its severe form, invasive pulmonary aspergillosis (IPA) is commonly seen in severe immunodeficient individuals and is often fatal. We report a case of IPA in an immunocompetent patient following severe dengue fever who was successfully treated with voriconazole.

Keywords: Aspergillosis, dengue fever, immunocompetent host, severe dengue

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INTRODUCTION

Aspergillosis in the lung can mainfest as hypersensitivity reaction. It can also present as an invasive infection in immunocompromised patients. Invasive aspergillosis is a disease of immunocompromised host and is often rapidly fatal infection. This is characterised by invasion of blood vessels and lymphatics with multifocal infiltrates.[1] Immunosuppression which predisposes to invasive disease is in the form of profound neutropenia, transplant recipient patients and patients of AIDS or chronic granulomatous disease. Here, we report a case of invasive pulmonary aspergillosis (IPA) in a host following severe dengue fever, without any apparent immunodeficient state.

CASE REPORT

A 34-year-old female, resident of a village in Davanagere near a poultry farm, housewife, presented with high-grade fever, icterus and vomiting for the past 4 days. At presentation, she was conscious, oriented and afebrile. Icterus was present. Petechial rash was present on both lower limbs. There were no cyanosis, no clubbing and no lymphadenopathy. Pulse rate was 88 bpm, regular, blood pressure was 120/80 mmHg and B/L breath sounds was normal. Adventitious sounds-Rhonchi present. Examination of the abdomen and nervous, the cardiovascular system were normal. Investigations revealed: haemoglobin 11.9 g/dL, total leucocyte count 12,900/mm^3, band forms 8%, lymphocytes 18% (reactive forms) and platelets 34,000/mm^3. Erythrocyte sedimentation rate 21 mm/ at the end of the first hour. Quantitative buffy coat test for material parasite was negative. Random blood glucose was 231 mg/dL; glucosylated haemoglobin was 6%, total Bilirubin 8.1 mg/dL, aspartate aminotransferase 5432 IU/L, alanine aminotransferase 1809 IU/L, alkaline phosphatase 219 IU/L and serum albumin 3.1 g/dL. Chest radiograph

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was normal [Figure 1a]. She tested positive for NS1Ag and dengue immunoglobulin M by enzyme linked immunosorbent assay (ELISA). Testing for malaria, leptospira, scrub typhus, acute viral hepatitis A, B and E were negative. Working diagnosis of dengue fever with hepatic dysfunction was made and her blood counts and liver profile were monitored.

With symptomatic treatment, her thrombocytopenia recovered and liver function tests normalized. During the hospital stay, she developed new-onset fever and cough with breathlessness. She was diagnosed with hospital-acquired pneumonia with sepsis, septic shock requiring inotropes and non-invasive ventilation. She was treated with injectable meropenem for *Escherichia coli* pneumonia and bacteremia as per sensitivity for 14 days. Despite the improvement in haemodynamic status and hypoxia, she continued to be febrile with no resolution of consolidation [Figure 1]. Computed tomography of the thorax showed consolidation and cavitatory lesion in the left upper lobe and consolidation with ground glassing in the right upper lobe, few enlarged subcarinal lymph nodes [Figure 2]. Bronchoscopy showed fleshy mass in the right upper bronchus which on biopsy showed *Aspergillus fumigatus* [Figure 3].

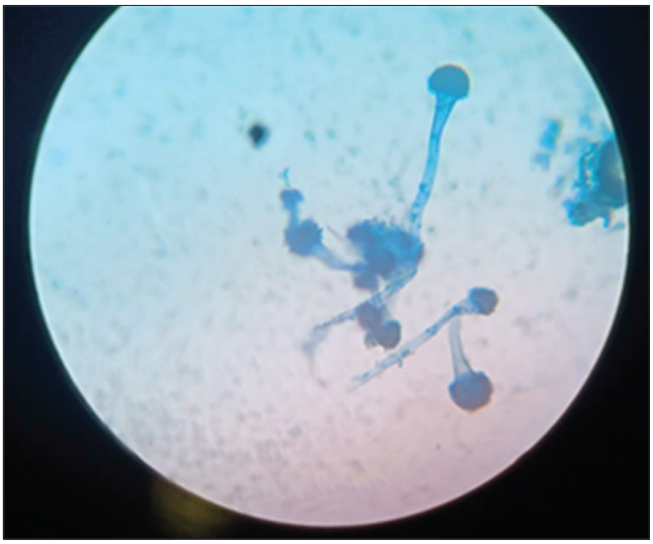

Figure 3: Photomicrography showing *Aspergillus fumigatus* KOH mount ×40 magnification

Serum galactomannan was positive. Bronchoalveolar lavage (BAL/fluid) tested positive for galctomannan

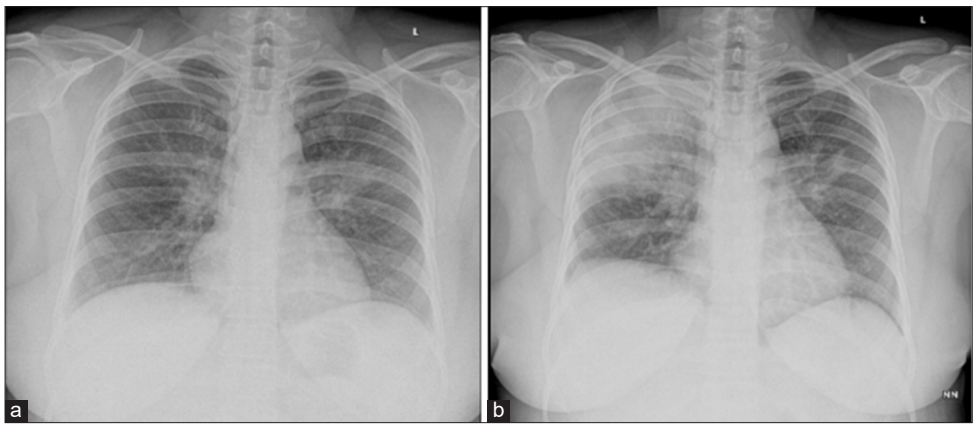

Figure 1: Normal chest radiograph (postero-anterior view) (a). Chest radiograph (postero-anterior view) of the same patient showing right Upper zone consolidation

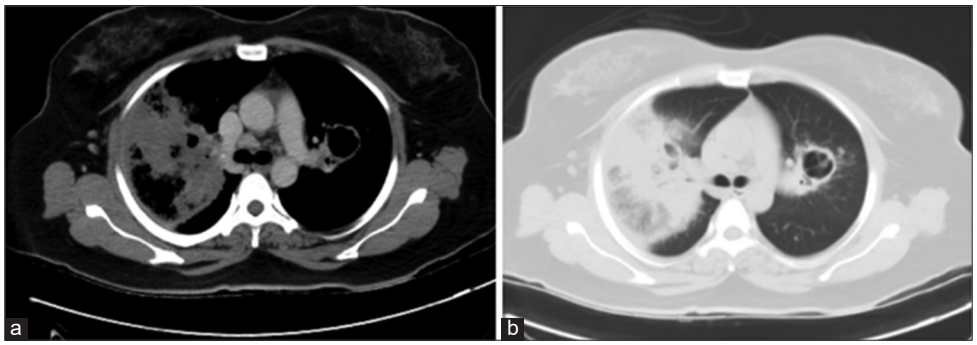

Figure 2: Contrast-enhanced computed tomography thorax [mediastinal window (a) lung window (b)] showing the right upper lobe necrotising pneumonia with cavity in the left upper lobe

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antigen and showed growth of *Aspergillus* mould [Figure 4]. The patient, thus, had both histopathological and serological diagnosis of invasive aspergillosis. She was treated with intravenous (IV) Voriconazole after which she became afebrile and improved symptomatically and hence, later was changed to oral maintenance dose.

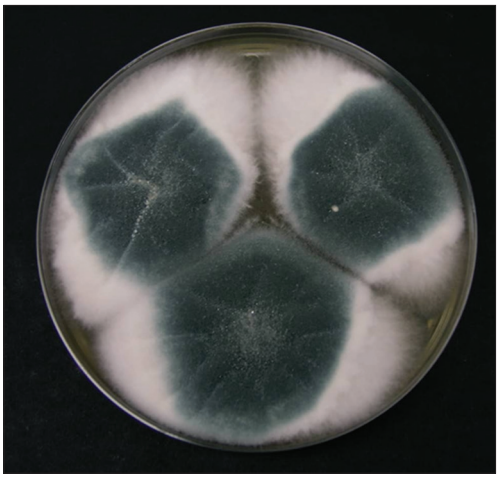

Figure 4: *Aspergillus fumigatus* growth on Sabouraud Dextrose Agar plate

DISCUSSION

Pulmonary aspergillosis is a collective term used to refer to a number of conditions caused by infection with a fungus of the *Aspergillus* species, usually *A. fumigatus*. Invasive aspergillosis is a disease of immunocompromised host and is often rapidly fatal infection. This is characterised by invasion of blood vessels and lymphatics with multifocal infiltrates. Histopathological examination with microbiological confirmation remains the gold standard in diagnosis. The isolation of *Aspergillus* spp. from BAL fluid from immunosuppressed patients is highly indicative of invasive aspergillosis (97% specificity), but is only positive in 50%–58% of patients.[2]

Immunosuppression which predisposes to invasive disease is in the form of profound neutropenia, transplant recipient patients and patients of AIDS or chronic granulomatous disease. Invasive aspergillosis in immunocompetent hosts has been documented in the literature, and few case reports[3-5] have been published. Natural immunity plays a major role in defence against aspergillosis. Risk factors for IPA in nonneutropenic patient are prolonged treatment with corticosteroids, chronic obstructive pulmonary disease, liver cirrhosis with prolonged intensive care units stay (>7 days) and broad-spectrum antibiotic use and liver failure. Immunoparalysis is sepsis with multiple organ dysfunction syndrome may also contribute to IPA.[6]

In our patient, residence near poultry farm is a risk factor for exposure to *Aspergillus* mould.[7] Sudden severe stress, associated hyperglycaemia and dengue fever induced severe hepatitis may have compromised immune barriers and led to the invasion of the vasculature and spread to lymph nodes. Further, prolonged hospital stay and broad-spectrum antibiotic use might also have contributed. Multitude of factors might have contributed to IPA in our patient. The patient responded to IV voriconazole, was afebrile and was continued on maintenance dose. High index of suspicion in critically ill patients will result in early diagnosis and treatment of IPA. Fungal infections following dengue fever are reported as isolated case reports.[8,9]

Treatment with IV voriconazole arrests the growth of *Aspergillus*. It is administered at a dose of 6 mg/kg q12 h for 2 doses, then 4 mg/kg q12 h IV for 5–7 days. Later, oral maintenance dose of 400 mg BD 2 doses, followed by 200 mg BD. Mean duration of treatment is 76 days.[10,11]

Informed consent was obtained from all the participants included in the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted.

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Conflicts of interest
There are no conflicts of interest.

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