

Invasive pulmonary aspergillosis in an immunocompetent patient with severe dengue fever

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Abstract

We report a case of a 65-year-old female diagnosed with severe dengue fever. She started showing recovery from dengue fever with medical management. On day 6 of admission, she had leukocytosis, altered mental sensorium, and hemoptysis. Chest tomography showed air space consolidation with multiple nodules in the left upper and middle lobe sputum and bronchoalveolar lavage cultures were positive for *Aspergillus flavus*. The patient showed improvement with voriconazole and therapy was continued for 6 weeks.

Keywords: Dengue fever, fungal pneumonia, invasive pulmonary aspergillosis

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.132505

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Introduction

Invasive pulmonary aspergillosis (IPA) is a serious disease and has been found mainly in immune-compromised patients. We report a case of a 65-year-old female patient who was admitted with severe dengue fever and developed IPA during recovery from dengue fever.

Case Report

The case we present here is about a 65-year-old female patient who was admitted in intensive care unit (ICU) with a history of fever since 5 days, pain abdomen and decreased urine output. She had no previous history of any comorbidity.

On admission, her blood pressure was 110/70 mmHg, heart rate 98 beats/min, and respiratory rate 28 breaths/min. Physical examination revealed dry skin and oral mucosa, and tender right hypochondrium. On laboratory analysis, her serum glucose was 124 mg/dL, creatinine

1.3 mg/dL, hematocrit 39%, platelets 50,000/mm³, and leukocytes 11,000/mm³ (70% neutrophils), serum amylase 677 U/L and serum lipase 580 U/L, and dengue serology (IgM and IgG) was positive. The electrocardiogram showed sinus tachycardia, chest radiography was normal.

The provisional diagnosis of severe dengue fever with acute pancreatitis and acute kidney injury (AKI) was made and she was resuscitated as per World Health Organization guidelines.^[1] She was not started on any antibiotics in the absence of any associated bacterial infection and her chest X-ray was within normal limits. On day 2, her renal functions deteriorated with decrease urine output, arterial blood gas showed metabolic acidosis and hyperkalemia, for which she was hemodialyzed. In view of persistent anuria, she required alternate day hemodialysis. On day 6, she developed cough with mucoid expectoration, tachypnea and hemoptysis. Her chest X-ray showed new left lingular lobe and upper lobe nonhomogenous infiltrates [Figure 1]. Tomography of the chest showed air space consolidation with multiple nodules in the left upper and middle lobe [Figure 2]. Sputum examination revealed branched septate hyphae on gram's stain and sputum cultures grew *Aspergillus flavus* (*A. flavus*). Fiber-optic bronchoscopy and bronchoalveolar lavage (BAL) done on day 8, also was

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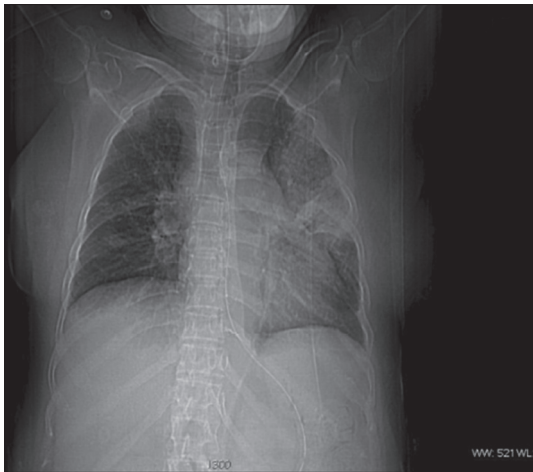


Figure 1: Chest X-ray showing left lingular lobe and upper lobe nonhomogenous infiltrates

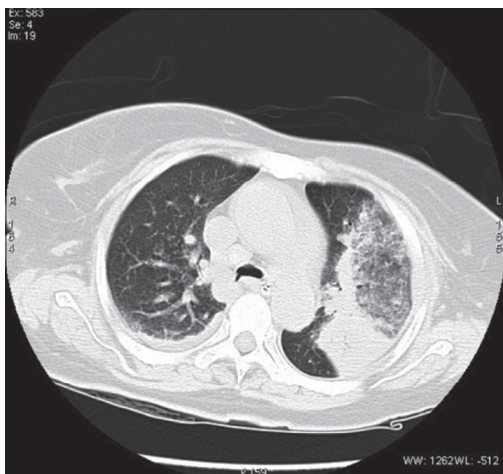


Figure 2: Tomography of the chest showing air space consolidation with multiple nodules in the left upper and middle lobe

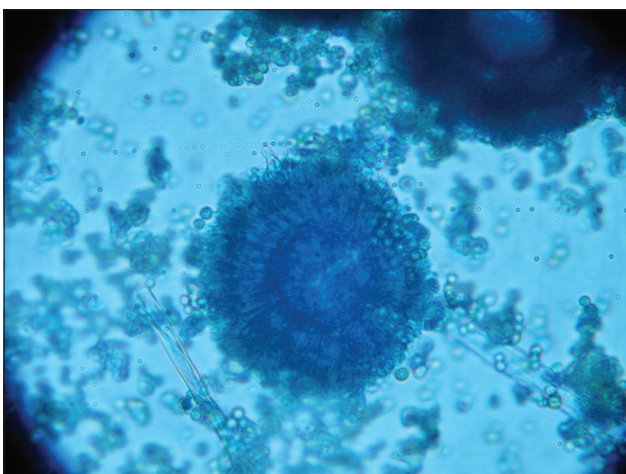


Figure 3: Lactophenol cotton blue tease mount showing conidiophores of *Aspergillus flavus* (x40)

positive for *A. flavus* [Figure 3]. She was started on intravenous voriconazole 800 mg/1st day, 400 mg/day

for 2 days more and then switched to oral voriconazole 400 mg/day in two divided doses with suspicion of IPA. She started showing clinical improvement with resolution of AKI and was discharged from ICU on day 9 and from hospital on day 11. She was continued on oral voriconazole for 6 weeks and her chest X-ray showed clearance of consolidation.

Discussion

Invasive pulmonary aspergillosis is a serious disease and has been found mainly in immunocompromised patients.^[2] In an immunocompetent host IPA is infrequent and has been found in especially two risk-groups: patients with severe chronic obstructive pulmonary disease (COPD) and critically ill patients.^[2]

Invasive pulmonary aspergillosis in critically ill patients without the classical risk factors described for IPA such as neutropenia, leukemia, hematopoietic stem cell transplantation, corticosteroids and broad spectrum antibiotics has been reported and the mortality is high.^[3,4] Meersseman *et al.*, in a retrospective study, found an incidence of 5.8% of invasive aspergillosis in a medical ICU and pulmonary involvement was present in most these cases. About 70% of the cases were patients without leukemia or cancer and the disease had a high mortality rate exceeding 90%.^[3] In another study of critically ill patients, 172 had positive sputum samples for *Aspergillus*, of which 83 had IPA, and 60% of the patients had no known risk factors for IPA.^[4] The risk factors described for IPA such as COPD, systemic corticosteroid therapy, nonhematological malignancy, chronic renal or liver disease, diabetes mellitus, HIV infection, autoimmune diseases, extensive burns, and malnutrition are commonly present in critically ill patients. Another proposed mechanism is disturbance in immunoregulation in critically ill patients which predisposes them invasive aspergillosis.^[2,4]

In our case, patient had no above-mentioned risk factors; however the patient had severe dengue fever. IPA has been reported in isolated case reports of patients with immunosuppression with viral infections like influenza virus.^[5,6] This is first case to our knowledge where IPA is found in a patient with severe dengue fever. The viral induced cell mediated immunity suppression has been proposed as the increased risk of IPA in these patients.^[6]

The gold standard for diagnosis of IPA requires a histological demonstration of tissue obtained by thorascopic or open-lung biopsy invasion by the fungus and the growth of *Aspergillus* species on culture.^[7]

However, in view of high mortality with IPA in critically ill patients, clinical diagnostic criteria can be used and early antifungal therapy should be started once IPA is suspected in these patients.^[2,8] Bronchoscopy with BAL is generally helpful in the diagnosis of IPA, especially in patients with clinical and radiographically lung involvement.^[2] The tissue confirmation in our case could not be done in view of coexistent thrombocytopenia with high bleeding risk for invasive open or trans-bronchial biopsy.

In our patient with respiratory distress and hemoptysis with new onset parenchymal infiltrates along with two consecutive samples from respiratory secretions including BAL and positive for *A. flavus* and therapeutic response to voriconazole confirmation requires tissue diagnosis or BAL fluid galactomannan levels. The evidence in the present case points to probable IPA. In the absence of classical risk factors of IPA, we propose the risk factor for IPA in this case is infection with dengue virus. However, such causal relationship warrants further research.

Conclusion

Invasive pulmonary aspergillosis is rare in patients with severe dengue fever. However, in view of high mortality with IPA, especially in critically ill patients, a high index of suspicion is required to ensure timely diagnosis and treatment of this potentially lethal condition.

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How to cite this article: Nasa P, Yadav R, Nagrani SK, Raina S, Gupta A, Jain S. Invasive pulmonary aspergillosis in an immunocompetent patient with severe dengue fever. *Indian J Crit Care Med* 2014;18:323-5.

Source of Support: Nil, **Conflict of Interest:** None declared.

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