Case Report

Invasive aspergillosis in near drowning nonneutropenic patient

Kartik Munta, Palepu B. N. Gopal[1], Ajit Vigg[2]

Abstract

Invasive aspergillosis in immunosuppressed people has been well documented, but to diagnose and treat in an immunocompetent individual after near drowning, it requires early suspicion and proper empirical treatment. We report a case diagnosed to have invasive aspergillosis with systemic dissemination of the infection to the brain, gluteal muscles, and kidneys after a fall in a chemical tank of a paper manufacturing company. He was ventilated for acute respiratory distress syndrome and managed with antibiotics and vasopressors. Due to nonresolving pneumonia and positive serum galactomannan, trans-tracheal biopsy was performed which confirmed invasive aspergillosis and was treated with antifungals. With the availability of galactomannan assay and better radiological investigative modalities, occurrence of such invasive fungal infections in cases of drowning patients should be considered early in such patients and treated with appropriate antifungals.

Keywords: Acute respiratory distress syndrome, invasive aspergillosis, near drowning, voriconazole

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Introduction

Invasive infections by fungi have been described in immunocompetent hosts after submersion and near drowning.[1] Fungi known to cause invasive diseases in cases of near drowning patient are *Pseudallescheria boydii* and, to a much lesser degree, *Aspergillus* species.

Case Report

A 28-year-old male presented to casualty posttreatment at a local hospital from near drowning in a paper factory. He was ventilated there in view of acute respiratory distress syndrome for 5 days. He received ceftriaxone as empiric antibiotic along with other therapies.

The patient presented with high-grade fever, tachypnea, and oxygen saturation of 87% on 15 L oxygen through a tracheal tube *in situ*. Lab investigations revealed leukocytosis (17,200/cumm), hemoglobin 11.1 g%, normal electrolytes, and creatinine of 1.8 mg/dl. Endotracheal secretions, blood and urine samples were sent for gram, fungal, acid-fast stain, and cultures. Antibiotic coverage was changed to cefoperazone + sulbactam.

Chest X-ray revealed bilateral alveolar shadows and a cystic lesion in the lung parenchyma [Figure 1]. Computed tomography (CT) brain showed multiple ill-defined, round hypodense lesions in bilateral cerebral hemispheres with surrounding edema [Figure 2]. CT chest with contrast [Figure 3] showed multiple, well-defined, round, variable sized nodular lesions scattered in both lungs, with few of them showing central cavitation. CT scan abdomen revealed patchy hypodensities in both kidneys and patchy hypodensities

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in the gluteal muscles bilaterally. Echocardiography was normal. Bronchoalveolar lavage (BAL) and transbronchial biopsy were performed, and antibiotic for bacterial coverage was escalated to meropenem in view of patient's unstable condition.

On the 2nd day of Intensive Care Unit (ICU) admission, all the microbiological laboratory reports were negative, but for serum galactomannan (1.5) they were raised and endotracheal aspirate for fungal stain showed *Aspergillus* species. Voriconazole and caspofungin combination were started with suspicion of invasive aspergillosis with hemodynamic unstability. The patient meanwhile developed hemoptysis, tachycardia, and desaturation, which were controlled with fresh frozen plasma and tranexamic acid.

The patient developed septic shock requiring vasopressors and worsening respiratory acidosis with leukopenia (2200/cumm). Transbronchial biopsy report revealed neutrophilic exudates and foci of fungal broad hyphae, broad angle branching [Figure 4]. These features were suggestive of fungal infection due to *Aspergillus*. BAL specimen on culture revealed *Aspergillus fumigatus* growth. The patient expired on day 5 of ICU admission due to severe multiorgan organ dysfunction.

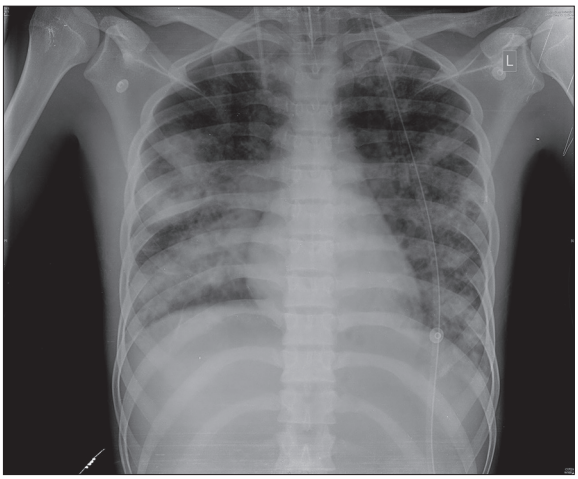

Figure 1: Chest X-ray showing alveolar shadows

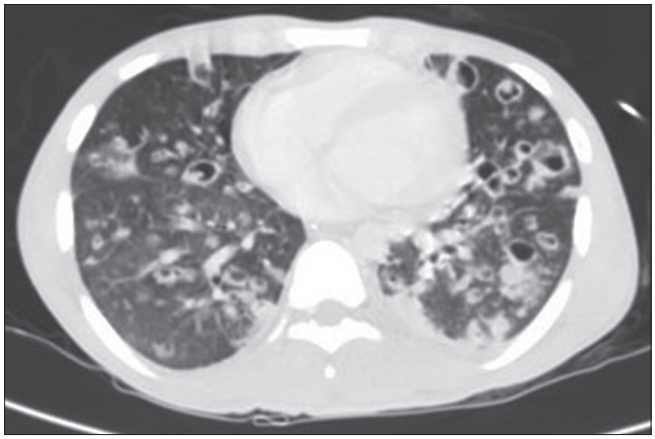

Figure 3: Computed tomography scan chest with contrast showing cavitary lesions

Discussion

Unfortunate incidents such as drowning and near drowning can lead to catastrophic outcomes in young and healthy individuals. *Aspergillus* species have been shown to be present in soil, sewage, and polluted waters.

Signs and symptoms of invasive pulmonary aspergillosis (IPA) are often missed due to low index of suspicion causing delayed additional diagnostic examination. However, if the patient is slow to respond to broad-spectrum antibiotic therapy, develops pneumonia few days to several weeks after the submersion event or develops brain abscess and/or meningitis, a diagnosis of invasive fungal disease should be aggressively pursued. These should include chest CT, direct microscopy, and culture of sputum or BAL sample.

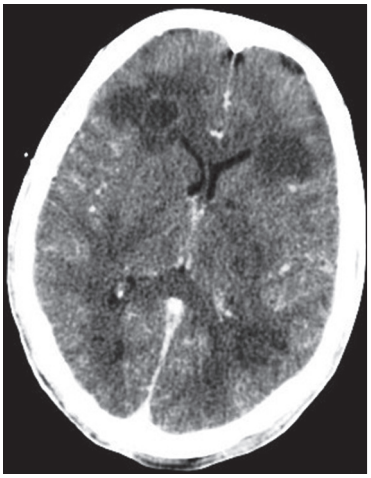

Figure 2: Computed tomography scan brain with contrast showing lesions

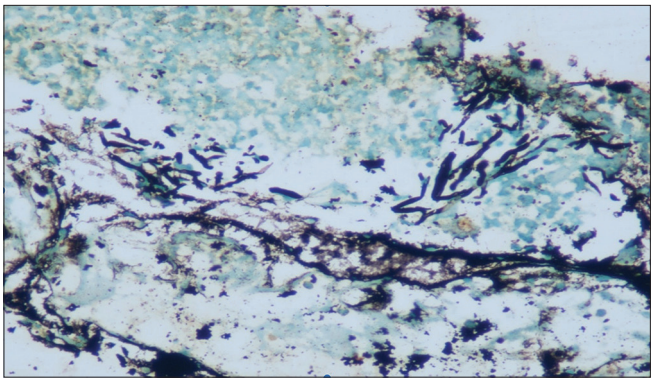

Figure 4: Transbronchial biopsy showing branching *Aspergillus* hyphae

Specific fluorescent stain of sputum or BAL with chitin is easy, rapid to read, and improves the sensitivity of microbiological examination.[2,3] Visualization of septate (e.g., *Aspergillus*, *Fusarium*, and *Scedosporium*) and nonseptate (e.g., *Mucorales*) molds can be made easily on direct microscopic examination.

Chest radiological signs include "halo sign," which is relatively frequent in the early stages and air crescent sign.[4-10] Together these two signs, increase the sensitivity to more than 80% and specificity to 60–98%.[7] Galactomannan is a major *Aspergillus* cell-wall component released during the growth phase of the fungus.[11] Its specificity in diagnosing IPA is at least 85%, but the sensitivity varied considerably between 29% and 100%. A recent meta-analysis on serum galactomannan showed median sensitivity in proven cases of 71% and specificity of 89%. In probable cases, it was 61% and 93%, respectively.[12] A prospective study in adult allogeneic stem cell transplant recipients demonstrated that positive galactomannan titers preceded fever by 3.5 days, positive chest high-resolution CT by 6 days, positive chest radiograph by 8 days, positive cultures by 9 days, and a definitive diagnosis by 14 days (all values are medians).[13]

CT scan and magnetic resonance imaging brain should be high on priority for near drowning patients with neurological abnormalities with proven/probable cases of aspergillosis due to preferential central nervous system (CNS) localization of this disease, secondary to high vascular tropism. The determination of serum galactomannan, with two positive results, coupled with typical radiological findings, is highly sensitive and specific to support the diagnosis.[14] Extension of invasive aspergillosis to the CNS is associated with an exceedingly high mortality which approaches 100%.[15]

Prophylactics antifungals should not be administered in all individuals of near drowning.[1] Amphotericin B deoxycholate had been the standard therapy for IPA. Due to an increasing antifungal resistance and nephrotoxicity of this compound, in particular nephrotoxicity, various studies have tried to find an alternative.[16] In a large multi-center trial, voriconazole provided better survival and lesser drug-related adverse events than amphotericin B in the treatment of "probable or proven" IPA among patients with hematological diseases.[17] Consequently, voriconazole is increasingly recommended as initial therapy for IPA.[18] At present, out of three approved echinocandins, caspofungin has demonstrated efficacy for the treatment of IPA. In general, there is no conclusive evidence that extended-spectrum triazoles are superior to echinocandins or polyenes or vice versa for monotherapy of IPA in ICU patients.

Factors responsible for the fatal course in this particular case could have a higher concentration of *Aspergillus* inoculum in the pulp extract, lack of early suspicion of invasive aspergillosis along with the injury sustained by the lungs, and hypoxic damage to the blood-brain barrier, which caused proliferation and invasion of *Aspergillus* in these organs.

Conclusion

Nonspecific signs and symptoms, low clinical suspicion, and time delay due to high risks involved in invasive procedures to obtain histopathological evidence for diagnosing IPA are some of the reasons for the lack of timely diagnosis. Persistent pulmonary infection despite broad-spectrum antibiotics should trigger further diagnostic exploration. If galactomannan is not available, endotracheal cultures, CT scan, and lung biopsy must be considered early in the management of non-neutropenia patients with pulmonary involvement due to near drowning.

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Conflicts of interest

There are no conflicts of interest.

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