Unexpected outcome (positive or negative) including adverse drug reactions

Acute community acquired *Aspergillus* pneumonia in a presumed immunocompetent hostVarun Sridhar,¹ Natarajan Rajagopalan,² Shivaprasad C,³ Mahantesh Patil,³ Jaicob Varghese³¹Internal Medicine Department, Narayana Hrudayalaya Hospital, Bangalore, Karnataka, India;²Pulmonology and Critical Care Department, Narayana Hrudayalaya Hospital, Bangalore, Karnataka, India;³Critical Care Services Department, Narayana Hrudayalaya Hospital, Bangalore, India

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Summary

Infection from *Aspergillus* results in a wide range of diseases from simple *Aspergillus* pneumonia to fatal invasive Aspergillosis. Though the fungus is known to predominantly affect the immunocompromised host, it has also been known to cause acute pneumonia in immunocompetent hosts which is invariably fatal. It presents as an acute pneumonia with bilateral chest infiltrates on radiograph. Early clinical suspicion and microbiological identification by measures such as broncho alveolar lavage and initiation of therapy with voriconazole significantly increase the chances of survival. In this article the authors discuss a case of acute community acquired *Aspergillus* pneumonia in an immunocompetent host who survived due to early identification and prompt treatment with appropriate antifungal medication.

BACKGROUND

Aspergillosis is an illness caused by any member of the genus *Aspergillus*. The spectrum of human illness ranges on the one hand from allergic reactions and colonisation of preexisting pulmonary cavities to invasion and destruction of lung tissue with dissemination to various organs eventually leading to death.

Members of the genus *Aspergillus* are ubiquitous in nature. They are saprophytic and live in decomposing organic matter. More than 100 species have been identified, but over 95% of human illness is caused by *Aspergillus fumigatus*. Other rare species that cause human disease are *A niger*, *A terreus*, *A flavus* and *A nidulans*.

Five distinguishable clinical types of *Aspergillus* infection have been recognised. (1) Tracheobronchial aspergillosis, often a localised infection of bronchial anastomosis in lung transplant recipients (2) allergic bronchopulmonary aspergillosis, which affects patients with asthma and bronchiectasis (3) mycetomas, or fungus balls, in which the fungus colonises existing pulmonary cavities such as cavities resulting from tuberculous infections (4) chronic necrotising pulmonary aspergillosis, in which the fungus locally invades abnormal lung and adjacent pleura; and (5) invasive aspergillosis, which occurs in patients with defects in phagocyte number, function or both.

Even though *Aspergillus* predominantly causes infection in immunocompromised hosts cases have been reported where *Aspergillus* has caused serious and often fatal pneumonia in immunocompetent hosts. Here we report a case of acute invasive pulmonary aspergillosis in an immunocompetent patient with no underlying lung disease. We have reviewed the diagnostic and treatment options available.

CASE PRESENTATION

A 21-year-old previously healthy woman presented to the emergency room with fever, breathlessness and abdominal

pain for 5 days. She did not give any history suggestive of illnesses that could compromise the immune system and was not taking any medications. She is non-smoker and there was no recent travel or exposure to pets.

On presentation she had a low-grade temperature. There was no finger clubbing and no significant lymphadenopathy. Respiratory system examination revealed tachypnea and lower zone crackles. She was haemodynamically stable but significantly hypoxemic (PaO₂-43 on room air).

INVESTIGATIONS

Initial lab investigations revealed normocytic normochromic anemia and thrombocytopenia. There was no leukocytosis (table 1). Chest radiograph showed bilateral lower and mid zone interstitial infiltrates (figure 1). The gram stain of the sputum showed abundant inflammatory cells with polymorphonuclear cells with no specific organism

Figure 1 Day 1-Chest x-ray: showing bilateral mid and lower zone interstitial infiltrates in the lung.

Table 1 Investigations

S.No	Lab parameter	Day 1	Day 3	Day 6
1.	Hb (g/dl)	10.3	10.0	8.3
2.	WBC count (cells/cu mm)	8100	12800	8500
3.	Platelet count (cells/cu.mm)	<150 on smear with giant platelets	<150 on smear with giant platelets	<150 on smear with giant platelets
4.	ESR	11	-	-
5.	Creatinine (mg/dl)	0.7	0.7	0.8
6.	Procalcitonin	2.98	33.14	104.84
7.	Dengue IgM	Negative		
8.	Leptospira IgM	Negative		
9.	INR	1.28	1.07	
10.	LDH	312		
11.	HIV 1 and 2	Negative		
12.	Hbs Ag	Negative		
13.	Anti HCV antibody	Negative		
14.	CSF cell count	16cells-98% lymphocytes, 2% polymorphs		
15.	HSV PCR in CSF			Negative
16.	HSV 1 and 2 IgM in CSF			Positive
17.	Blood culture			Acinetobacter
18.	Urine culture		Negative	
19.	BAL culture		<i>A fumigatus</i>	<i>A fumigatus</i>
20.	CD4 count (cells/mm)	614		
21.	CD8 count (cells/mm)	1025		
22.	2D echo			Normal. No right atrial, right ventricular dilation. No PAH. LVEF 55%

BAL, broncho alveolar lavage; CSF, cerebrospinal fluid; ESR, erythrocyte sedimentation rate; HCV, hepatitis C virus; HSV, herpes simplex virus; INR, international normalised ratio; LDH, lactate dehydrogenase; WBC, white blood cell.

being isolated and the sputum for Zeil neilson stain was also negative. She was started on cefaperazone and moxifloxacin after appropriate cultures were taken. Her throat swab for H1N1 DNA PCR was negative. Sputum cultures were sterile. ELISA for HIV 1 and 2 was negative. CD4 and CD8 counts and ratio were normal (table 1).

TREATMENT

Patient was non-invasively ventilated for respiratory distress. On the third hospital day patient's respiratory status deteriorated with progressive hypoxemia. Her chest x-ray showed worsening bilateral infiltrates. At this time patient required mechanical ventilator support with 100% oxygen and a positive end-expiratory pressure of 12 cm H₂O. CT thorax showed bilateral extensive air space consolidation predominantly involving middle and lower lung zones (figure 2). Fiber optic bronchoscopy showed copious amount of purulent secretions and inflamed mucus membrane. Heavy growth of *A fumigatus* was reported from the broncho alveolar lavage (BAL) specimen (figure 3). BAL cultures for bacteria were negative. BAL PCR for tuberculosis and cytomegalovirus were negative. Methanamine silver stain for *Pneumocystis jirovecii* was also negative. Patient was started on intravenous voriconazole at 6 mg/kg body q 12 hourly × two doses followed by 200 mg q 12 hourly orally. On day 6 of hospital stay she developed status epilepticus and this was managed effectively with antiepileptics levetirecetam, sodium valproate and phenytoin. MRI of the brain was normal. Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis. CSF cultures were negative for bacteria and fungi. CSF analysis showed herpes simplex virus (HSV) IgM to be positive, but HSV PCR was negative. On clinical grounds patient was given 5 days of acyclovir.

Figure 2 CT thorax showing bilateral extensive consolidation and interstitial infiltrates.

OUTCOME AND FOLLOW-UP

On day 6, post status epilepticus, her condition deteriorated requiring pressors support. Blood culture grew *Acinetobacter* for which she was started on tigecycline. Following sepsis control patient improved clinically and was weaned off the ventilator on the 10th day. Chest x-ray showed progressive improvement (figure 4) and patient could be taken off oxygen completely after 2 weeks in hospital. On follow-up after 2 weeks from discharge, she had normal chest radiograph and normal oxygenation status, with no new episodes of seizures.

DISCUSSION:

Acute invasive *Aspergillus* infection in immunocompromised hosts has been well recognised. The classic presentation of *Aspergillus* pneumonia in immunocompromised host recognised over 60 years ago is usually a chronic

Figure 3 *Aspergillus* isolated from the BAL fluid.

necrotising pneumonia, which progresses over months to years. However, cases of acute aspergillus pneumonia have been reported in immunocompetent hosts but the diagnosis in these cases was not made early enough in their illnesses and hence the outcome of these patients was uniformly fatal.¹

Previous case reports of acute *Aspergillus* pneumonia have described in patients with a history of alcohol consumption and with previous history of flu infection.^{2–3} In some patients there was a history of inhalation of heavy inoculum of aspergillus in farming related exposures and exposure to manure. The unique nature of this presentation is that our patient had a diagnosis of *Aspergillus* pneumonia made very early in the course of the disease and was started on the appropriate treatment promptly. We strongly believe this made the difference in the final outcome.

Radiological features in *Aspergillus* pneumonia can range from bilateral interstitial and alveolar infiltrates to cavitary lesions.⁴ Progressions of infiltrates to cavitary lesions have been described. CT scan findings of nodular lesions have also been reported.

Previous case reports of aspergillus pneumonia describe confirmation of diagnosis by either transbronchial biopsy antemortem or pathological demonstration of the fungus in the autopsy samples.¹ Our patient had a heavy growth of aspergillus from the BAL sample and this in the setting of a rapidly progressive pneumonia is in our belief a fairly confirmatory evidence of aspergillus pneumonia. Voriconazole has become the drug of choice for invasive aspergillosis, though other antifungals (liposomal amphotericin B and caspofungin) have also been described in literature as second line antifungal antibiotics. But, the usage the later antifungals is advocated only in cases of inability to use voriconazole in view of drug toxicity or adverse effects to voriconazole. In our patient clearance of the fungus was also demonstrated in the repeat BAL specimen done 5 days after starting the medication. We believe that patient developed seizures secondary to viral encephalitis, probably herpes simplex encephalitis. Although HSV PCR in CSF was negative, the HSV IgM was positive and hence we treated the patient with acyclovir. It should also be mentioned that there were no symptoms or signs of meningitis until the onset of status epilepticus. To our

Figure 4 Chest x-ray after treatment – completely resolved pneumonia.

knowledge there have not been case reports of dissemination of aspergillus to the central nervous system without positive microbiological or MRI results, even though it is tempting to speculate that this might also have been the cause of encephalitis in our patient.

Use of serum galactomannan and β glucan in the early diagnosis of patients with *Aspergillus* pneumonia in immunocompromised hosts has been described in the literature.^{5–6} Their role in this regard in immunocompetent host is debatable with no conclusive results.⁵

Learning points

- Invasive aspergillosis should be considered as a possibility in acute community acquired pneumonias even in immunocompetent individuals presenting with bilateral chest infiltrates.
- In such patients who end up on the ventilator BAL should readily be undertaken to improve the diagnostic yield.
- Early initiation of antifungal antibiotic will make a significant difference in the outcome of these patients.

Competing interests None.

Patient consent Obtained.

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