Invasive Aspergillosis in a patient with Asthma post H1N1 Pneumonia

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Introduction

Aspergillus species have emerged as an important cause of life-threatening infections in immunocompromised patients like patients with prolonged neutropenia, advanced HIV infection, and inherited immunodeficiency and patients who have undergone allogeneic hematopoietic stem cell transplantation (HSCT) and/or lung transplantation. Invasive Aspergillosis (IA) has been shown to complicate SARS, but often when steroids have been given1.

We present a case of IA in an atypical patient group - a patient with asthma admitted to our Intensive Care Unit with H1N1 pneumonia. Treatment with systemic corticosteroids (which might have been very hazardous or fatal in the presence of untreated mycosis) was avoided but she still developed IA.

In October 2009, a 46 year old female attended the emergency department with increasing shortness of breath and two weeks history of flu-like symptoms. She was complaining of non-productive cough, aches and sweats, tight chest, sore throat and back pain. She had received amoxicillin from her GP with no improvement. There was no acute pain, calf swelling or history of previous clots.

She was known to have mild asthma and depression and was on citalopram, salbutamol and seretide.

On examination, she was febrile and tachycardic with BP of 106/65. Her respiratory rate was 28 and her SaO2 39% on air which improved to 89% on 15L O2. Her airway was patent and she was able to speak in full sentences. She had a wheeze and crepitations all over her chest. Her GCS was 15/15. She was admitted to ITU for tracheal intubation..

Throat swabs for H1N1 and full septic screen including blood cultures were taken. She was started on coamoxiclav and clarithromycin.

Findings

Admission H1N1 throat swabs and bacterial screens were negative. She was on antibiotics and oseltamivir was added. Her WCC was 2.3x 10^6 and CRP 179mg/L. Four days after admission her sputum culture grew *Aspergillus fumigatus* and *Candida albicans*. Six days after admission her bronchial lavage specimen was H1N1 positive and also grew *A.fumigatus* and *Candida* spp. in multiple samples. She was started on liposomal amphotericin B (L-AMB) and antibiotics changed to Tazocin and clarithromycin.

Her chest radiograph showed diffuse consolidation throughout the lungs, suggestive of ARDS. (Fig. 1)

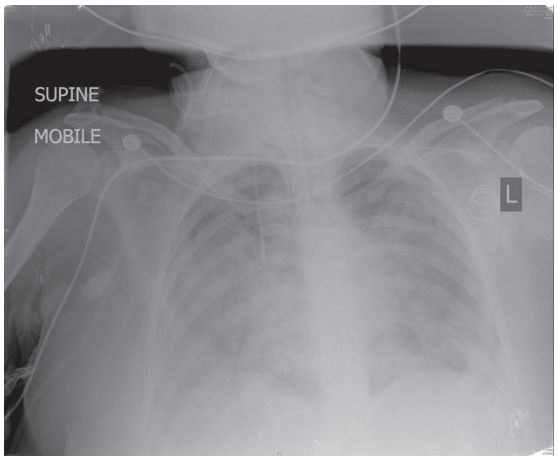

Fig. 1

CT thorax showed bilateral multiple lung cavities with extensive ground glass opacification and consolidation, compatible with infection; possibly fungal, atypical or tuberculosis.(Fig. 2)

Due to worsening markers and chest signs, there was some concern about whether this was bronchiolitis obliterans and discussion about starting steroids. However expert advice sought from the National Aspergillus Centre in Manchester indicated that the combination of cavities, ground glass consolidation and positive

cultures of *A. fumigatus* was more likely to represent IA.

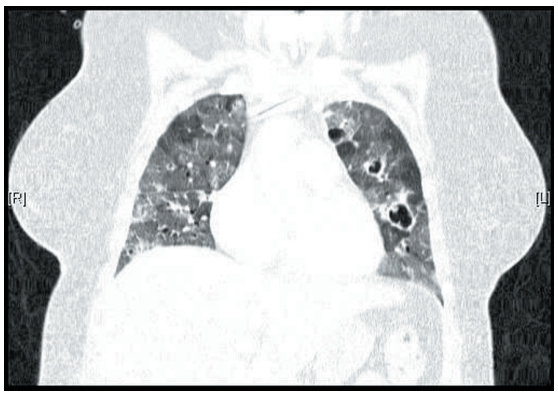

Fig. 2

She remained critically ill and caspofungin was added. Further rise of markers led to her antifungals being changed to voriconazole and caspofungin. The patient showed slow and steady improvement from this point, monitored by serial CT and voriconazole levels. CT done 4 weeks after start of Voriconazole showed more peribronchial organising changes in the anterior segments of the upper lobes, middle and lingular lobes and some less severe ground glass changes in the lower lobes. Fig. 3

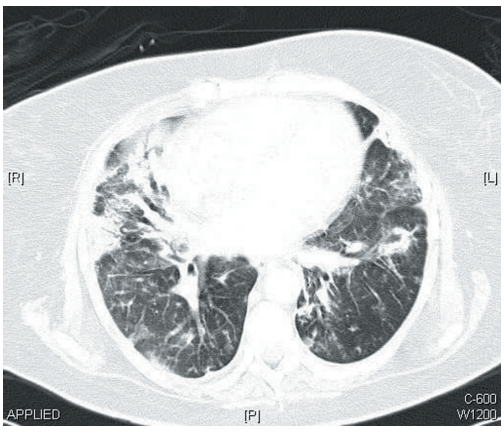

Fig. 3

She had caspofungin for three weeks, Voriconazole for 10 weeks followed by six weeks Itraconazole. She reported severe hair loss while on voriconazole treatment; however we were not sure if this was a direct side-effect of the drug or telogen effluvium.

Her Aspergillus precipitins at the time of acute infection were strongly positive (++++) and gradually reduced while on voriconazole and then itraconazole.

Discussion

A broad group of patients who are admitted to intensive care units (ICUs) may also be susceptible to IA. Estimates about the incidence of IA among critically ill patients are sparse and variable. First, with cultures positive for *Aspergillus* species, discriminating between colonization and infection remains challenging. Second, very few institutions perform post-mortem examinations routinely, although in most cases, this is the only way to prove the definite nature of the diagnosis. Third, characteristic radiological signs of IA are usually absent in the non neutropenic ICU patient[2]. Invasive aspergillosis may develop in ventilated asthmatic patients with no prior history of broncho-pulmonary aspergillosis or any known risk factors for aspergillus infection[3].

Our case was known to have mild asthma and although she was taking seretide, she was not considered to be at high risk for developing IA.

Voriconazole is recommended for the primary treatment for IA in most patients[1,4]. Fear of interactions and atypical presentation led to liposomal amphotericin being used as first line in our case, with change to voriconazole when she deteriorated. In a comparative analysis of clinical outcomes, Marr et al observed a survival advantage in patients treated with the combination of voriconazole and caspofungin, compared with voriconazole alone[5]. We used caspofungin as combination agent with L-amb initially and then voriconazole as our case showed signs of clinical failure.

Conclusion

Lessons learnt from this case of IA in an atypical patient group-

1. IA can occur in non-immunocompromised hosts in patients on ntensive care support. Diagnosis is often difficult and missed. Early diagnosis and appropriate treatment is key for survival.
2. Voriconazole is a preferred primary therapy.
3. We believe that by seeking expert opinion on appropriate antifungals and avoiding steroids in her acute phase of illness, this patient survived the IA.

References

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