CASE REPORT

A fatal case of disseminated aspergillosis caused by a non-sporulating strain of *Aspergillus fumigatus*

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This report describes the case of a 38 year old pregnant woman with fatal disseminated aspergillosis and multiorgan failure, which was preceded by a long history of allergic bronchopulmonary aspergillosis. Postmortem revealed massive infarction and abscess formation in both lungs. Histology revealed a focal granulomatous response. Fungal infiltration with areas of necrosis were also seen in the liver, spleen, and paratracheal, mediastinal, para-aortic, and hilar lymph nodes. Culture of tissue samples produced a non-sporulating, beige coloured fungus that developed green pigmentation only after three weeks of incubation. Nucleotide sequencing of the D1-D2 region of the large ribosomal subunit revealed 100% homology with *Aspergillus fumigatus*. Minimum inhibitory concentrations for amphotericin B and itraconazole were both 0.25 mg/litre (susceptible). Further work is urgently required to determine the prevalence of such non-sporulating strains and their relevance to clinical infection.

A 38 year old pregnant woman was diagnosed with allergic bronchopulmonary aspergillosis on the basis of a deterioration in her asthma control, radiographic evidence of pulmonary infiltration, a raised total IgE concentration (5000 U/ml), a strongly positive IgE radio-allergosorbent test to aspergillus specific antigens, and visualisation of fungal hyphae in her sputum.¹ She was treated initially with high dose inhaled corticosteroids (fluticasone 100 µg twice daily). After delivery, itraconazole (200 mg daily) was added, although this was later discontinued. Seventeen months later, she developed right upper lobe consolidation and a peripheral blood eosinophilia (23.8×10^9 /litre). Oral corticosteroids were added but she failed to recover completely. Two months later, she was admitted with a left sided pneumothorax, hepatosplenomegaly, and widespread lymphadenopathy. Blood tests on admission revealed a white blood cell count of 33.64×10^9 /litre (eosinophil count, 16.54×10^9 /litre), bilirubin of 220 mg/litre, alkaline phosphatase of 505 U/ml, and γ -glutamyltransferase of 670 U/ml. A chest drain was inserted, but a bronchopleural fistula developed and the lung failed to re-expand despite placement of further intercostal drains and the application of suction. An empyema subsequently developed on the same side and *Streptococcus pneumoniae* and *Haemophilus influenzae* were cultured from pleural fluid. At that stage, she had profound leucocytosis (84.4×10^9 /litre), which was composed largely of neutrophils and myelocytes. A computed tomography scan of the thorax and abdomen confirmed hepatosplenomegaly, widespread lymphadenopathy (mediastinal, para-aortic, and around the porta hepatis), and bilateral pulmonary infiltrates. Bone marrow trephine and cytogenetics were normal. She was treated empirically with oral steroids, broad spectrum antibiotics, and liposomal amphotericin B. As a result of failure of the bronchopleural

fistula to resolve with tube drainage, she was transferred to a cardiothoracic centre, where an open decortication and repair were performed. The initial recovery was uneventful. However, later the same day she developed an acute abdomen and presumed septic shock. She was resuscitated and an explorative laparotomy performed, which was unremarkable. Her condition deteriorated over the following 48 hours and the patient subsequently died of septic shock and multiple organ failure.

Postmortem examination revealed large areas of infarction, active chronic inflammation, organising pneumonia, and focal abscess formation in both lungs. Within these areas fungal hyphae invaded the tissue, eliciting a focal granulomatous response. Fungal infiltration with areas of necrosis were also seen in the liver, spleen, and paratracheal, mediastinal, para-aortic, and hilar lymph nodes. The fungal hyphae were septate, branching, focally irregular, and swollen. This is an atypical appearance, which may reflect either degenerative change or a reaction to the surrounding granulomatous inflammation (fig 1).

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Unfixed samples of lung (n = 5) and liver (n = 1) tissue cultured on routine plate and liquid media, including Sabouraud's agar, yielded growth of a non-sporulating, beige coloured, fungal colony that was unidentifiable in routine laboratory tests. This colony was approximately 2 mm in diameter after two weeks of incubation and did not develop green pigmentation until three weeks of incubation. Despite prolonged incubation on Sabouraud's agar, malt agar, and

Figure 1 A Grocott stain shows abundant focally branching septate hyphae with a bulbous appearance to many of the hyphae.

Take home messages

- We report a fatal case of disseminated aspergillosis and multiorgan failure, preceded by a long history of allergic bronchopulmonary aspergillosis
- Fungal infiltration with necrotic areas was also seen in the liver, spleen, and lymph nodes
- Culture produced a non-sporulating, beige coloured fungus, which was confirmed as *Aspergillus fumigatus* by nucleotide sequencing of the large ribosomal subunit
- The organism was susceptible to amphotericin B and itraconazole
- Further work is urgently needed to determine the prevalence of such non-sporulating strains and their relevance to clinical infection

potato sucrose agar and exposure to diurnal patterns of light and dark, the isolate failed to produce sporing structures by which it could be identified. However, sequencing of the D1–D2 region of the large ribosomal subunit revealed 100% homology with *Aspergillus fumigatus*.² Minimum inhibitory concentrations for amphotericin B and itraconazole were both 0.25 mg/litre (susceptible) using broth dilution methodology.³

To our knowledge, the phenomenon of non-sporulation in clinically relevant strains of *A fumigatus* has not been reported previously. Because plate contamination with aspergillus species is a relatively common clinical laboratory problem, there is a danger that the clinical relevance of strains of *A fumigatus* with atypical sporulating characteristics may be underestimated. It is worth noting that most clinical strains

of *A fumigatus* are thermotolerant and grow at temperatures greater than 40°C. This characteristic may assist the clinical microbiology laboratory in the identification of a non-sporing strain of *A fumigatus*. Further work is required to determine the prevalence of such strains and their relevance to clinical infection.

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