Case Report

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Received 7 November 2008

Accepted 28 March 2009

Cutaneous infection caused by *Aspergillus terreus*

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Aspergillus species are widely distributed in nature, and more than 30 species have been reported to be involved in human and animal infection. Cutaneous infections due to *Aspergillus terreus* are particularly rare. In this report, we describe a case of cutaneous infection caused by *A. terreus* in a paediatric patient who underwent surgical treatment for an open tibial fracture secondary to an agricultural accident.

Introduction

Aspergillus species are widely distributed in nature; they have been predominantly isolated from soils, decaying vegetation and on a wide variety of organic matter (Sigler & Verweij, 2003). More than 30 species have been implicated in different human and animal infections (Sigler & Verweij, 2003). Patients who are immunocompromised or who are receiving immunosuppressive drugs, notably bone marrow and organ transplant recipients, and those with haematological malignancies, are particularly susceptible to these kinds of fungal infections (Richardson, 2005). The most important species of *Aspergillus* are *Aspergillus fumigatus*, *Aspergillus flavus* and *Aspergillus niger*; and infections due to *Aspergillus terreus* are increasingly being reported (Lass-Flörl *et al.*, 2005; Cooke *et al.*, 2003). Cutaneous infections are rare in aspergillosis. Primary cutaneous infection caused by *Aspergillus* may present as macules, papules, plaques or haemorrhagic bullae, which may progress into necrotic ulcers with an elevated border that is covered by a black eschar (Walmsley *et al.*, 1993; Lucas *et al.*, 1999). These infections have been described in immunocompromised children, in neonates and after traumatic injuries, with varying treatment options (Lucas *et al.*, 1999; Richards & Mancini, 2000; Amod *et al.*, 2000). Cutaneous infections due to *A. terreus* are particularly rare (Lass-Flörl *et al.*, 2005; Steinbach *et al.*, 2004). In this report, we describe a case of cutaneous infection caused by *A. terreus* in a paediatric patient who underwent surgical treatment for an open tibial fracture secondary to an agricultural accident.

Case report

A 7-year-old boy was admitted to Mustafa Kemal University Research Hospital, Hatay, Turkey, on 13 August 2007. Nine days before, he visited another hospital after an accident. His left lower extremity was crushed under a tractor in an arable field. He underwent an operation for a contaminated grade III open tibial fracture. He had been referred to Mustafa Kemal University Research Hospital for further follow-up. Additional surgical operations (debridement and wound closure) were planned and he was hospitalized. On admission, laboratory tests showed leukocytosis (white cell count 13 500 cells μl^{-1}) with 51.7 % polymorphs, 35.6 % lymphocytes and 7.5 % eosinophils. His erythrocyte sedimentation rate was 67 mm at 1 h. A chest X-ray was normal. Other investigations like C-reactive protein, blood sugar, renal and liver function tests were normal. On examination, a large open wound with crusts covering the anteromedial aspect of the lower leg, extending from just below the knee to both malleoli, was observed (Fig. 1a).

The appearance of the wound and the green colour of the exudate suggested that it was an infected wound. Cultures were taken after multiple and meticulous debridements of the wound, which were carried out in the surgical theatre and under general anaesthesia by orthopaedic surgeons. The culture of the exudate from the lesion was subcultured on 5 % sheep blood agar plate (bioMérieux), in eosin methylene blue agar (bioMérieux), in brain heart infusion broth and in thioglycolate broth (Merck), and incubated at 35 °C. Direct microscopic examination of the Gram stained exudate revealed polymorphonuclear leukocytes and occasional fungal hyphae (Supplementary Fig. S1 available with the online journal). No bacteria were isolated, but cultures yielded numerous identical fungal colonies. These colonies were taken and subcultured on Sabouraud dextrose agar (Merck) and incubated at 35 °C

Images of the fungus are available as supplementary data with the online version of this paper.

Fig. 1. Clinical photographs of the wound before (a) and after (b) treatment.

in a CO₂-free incubator. Cinnamon-brown colonies with granular to velvety textures were observed on the agar (Supplementary Fig. S2a available with the online journal). Microscopically, the colonies showed smooth conidiophore, subglobose vesicle, metulae and phialides bearing small, smooth conidia in a columnar fashion (Supplementary Fig. S2b available with the online journal), and the fungus was identified as *A. terreus*.

In order to rule out contamination, repeated debrided tissue samples were taken. Gram staining of the samples revealed polymorphonuclear leukocytes and fungal hyphae. *A. terreus* was grown in the repeated cultures.

The patient had an initial surgical debridement, which was followed up by wound dressings that were changed daily. A final operation was done on 19 September 2007, and the lesion was covered with an appropriate graft. After this operation the patient had wound dressings with povidone iodine antiseptic solution changed daily until his condition had improved (Fig. 1b) and he was discharged from the hospital on 1 October 2007.

Discussion

Aspergillus infections are the most common cause of human opportunistic fungal infections after yeast infections. These infections have increased dramatically in recent years (Steinbach *et al.*, 2004). Although the genus *Aspergillus* contains over 150 species, only a few are considered to be pathogenic for humans (Lipovsky & Hoepelman, 1999). The majority of *Aspergillus* infections are caused by *A. fumigatus*, *A. flavus*, *A. niger* and *A. terreus*. *A. terreus* infections used to be uncommon, but they have become a growing concern in the past few years (Wald *et al.*, 1997; Iwen *et al.*, 1998; Silva *et al.*, 2000; Park *et al.*, 2000).

An important increase in the rates of infection caused by *A. terreus* has been observed. In a study conducted by Iwen *et*

al. (1998), a 12-year retrospective study was done to identify and evaluate cases of infection caused by *A. terreus*. In that study, it was determined that 13 cases of invasive aspergillosis were caused by *A. terreus*, of which 11 were primary pulmonary infections and 2 cases were primary peritoneal infections, and all patients had malignancy (Iwen *et al.*, 1998). In another study, 83 cases of *A. terreus* infection (1997–2002) from three medical centres were reported by Steinbach *et al.* (2004). There were also some cases of infective endocarditis, myocarditis, meningitis, osteomyelitis, discitis, lymphadenitis, mycotic aortic aneurysm and peritonitis due to *A. terreus* reported elsewhere (Silva *et al.*, 2000; Park *et al.*, 2000; Drexler *et al.*, 1980; Russack, 1990; Stein *et al.*, 1982; Glotzbach, 1982; Mahgoub *et al.*, 1969; Verghese *et al.*, 2008).

Cutaneous infections caused by *Aspergillus* species commonly are due to haematogenous seeding from a primary focus of infection, most often the lungs, which occurs in highly immunocompromised patients. These lesions may be single or multiple, may not be tender and are most commonly found in the extremities. Cutaneous infections caused by opportunistic fungi have been described by Wald *et al.* (1997). Cutaneous infections due to *A. terreus* are quite rare (Lass-Flörl *et al.*, 2005; Iwen *et al.*, 1998).

We present here a primary case of cutaneous aspergillosis caused by *A. terreus*. Such cases occur usually as a result of trauma or colonization. The patient in this report neither was immunosuppressed, nor had a pulmonary source of infection; the cutaneous infection occurred after the trauma he suffered. It is likely that the spores of *A. terreus* that were present at the site of the accident directly invaded the patient's skin as it was disrupted by the trauma. The patient was primarily under the care of an orthopaedic surgeon and was referred to us only after the greenish exudate was observed. An infected rather than a colonized wound will cause such an exudate, and requires multiple daily dressing changes. So this cutaneous infection was

managed by surgical debridements and daily wound dressing with povidone iodine, which is known for its antifungal effect. It was thought that the side effects of systemic antifungal therapy may deteriorate the hepatic function of a patient who undergoes multiple sedation and general anaesthesia, which is known for its hepatotoxic effects.

In summary, we have reported this case because *A. terreus* is infrequently detected as a human pathogen. Hence, *A. terreus* should be considered as a rare but potential pathogen that is able to produce cutaneous infections in patients who have open wounds.

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