A rare cutaneous fungal infection complicating bacterial necrotising fasciitis

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We report a case of bacterial necrotising fasciitis complicated by the rare fungus *Absidia corymbiferia*. Although this fungal infection is rare, the prognosis is poor and it therefore requires attention. Only 30 cases have been reported since 1874, and we are the first group to report this clinical scenario in our locality. Using a comprehensive journal review, we discuss the expected clinical course and optimal management.

Introduction

*Absidia* spp are filamentous fungi found in soil and decaying vegetation worldwide. They belong to the class Zygomycetes. Of the genus *Absidia*, *Absidia corymbiferia* is the only pathogenic species in humans.1,2 Cutaneous necrotising infections are characterised by rapidly progressive, widespread necrosis of the skin, subcutaneous tissue, and superficial fascia.3 Most cases are bacterial in origin and are commonly associated with severe systemic toxicity and high mortality rates. *Zygomycetes* may also be responsible for this life-threatening necrotising infection.4

Case report

In October 2006, a 71-year-old woman, who was living in a public estate with her husband, was admitted to our hospital with left leg pain. She had a history of carcinoma of the stomach managed with a subtotal gastrectomy in 2004. There was no history of recurrence and she was otherwise healthy. A clinical examination performed on admission showed left leg swelling, erythema, and tenderness on her left leg and an elevated body temperature. There was no crepitus over the left leg. Blood tests showed a normal white cell count and a metabolic acidosis. An X-ray of the left leg was unremarkable and showed no evidence of any subcutaneous gas collection. The initial clinical diagnosis was cellulitis and intravenous ampicillin and cloxacillin were started. She went into circulatory and respiratory decompensation 5 hours after admission and was transferred to the intensive care unit (ICU) with ventilatory support.

Soon after admission to ICU, she developed progressive discolouration with blister formation on her left ankle up to mid calf level. There was also pitting oedema up to the lower thigh. She still had a normal white cell count but this might have been due to fulminant sepsis causing immunosuppression. Necrotising fasciitis was strongly suspected and an urgent above-knee amputation was performed. The patient remained stable after the operation and was transferred back to ICU for postoperative monitoring.

The condition of her stump wound was not satisfactory and three more surgical debridements were performed on days 1, 4, and 9. Wound healing remained suboptimal with gapping and serous discharge. All the intra-operative specimens grew no organisms. A histopathological examination of the amputated leg was consistent with necrotising fasciitis with the presence of both Gram-positive and -negative rods. The antibiotic treatment was upgraded to meropenem.

The patient developed acute renal failure requiring haemodialysis. She had a persistent fever and a rising white cell count. Sputum, urine, and blood cultures grew *Candida albicans* so oral fluconazole was started. Her clinical condition improved and she was extubated on postoperative day 16.

The wound further deteriorated, with necrosis and a turbid discharge (Fig 1). A culture of the wound swab grew *A corymbiferia* on day 22 (Fig 2). Amphotericin B was started. Radical surgical debridement of the wound was planned but the patient deteriorated quickly and died the next day. The cause of death was disseminated fungal infection.

The patient was given antibiotics before blood was taken for cultures; this may explain why the blood grew no organisms. The pathologist responsible for reviewing the histology...
slides found no hyphae in the initial samples, which may have provided a diagnosis of fungal infection at an earlier stage.

Discussion

Fungi of the genus *Absidia* belong to the class Zygomycetes in the order Mucorales. They are distributed worldwide and commonly found in plant debris and soil. They have also been isolated from food and indoor air. Human infections by members of the order Mucorales are called mucormycosis and are most commonly caused by the *Absidia*, *Rhizopus*, and *Rhizomucor* species. Mucormycosis usually affects immunocompromised hosts, such as people with haematological malignancies, human immunodeficiency virus infection, on steroids, transplantations, extensive burns, polytrauma, renal failure, and diabetes mellitus. Various clinical forms of mucormycosis have been described, including rhinocerebral, pulmonary, cutaneous, gastrointestinal, renal, cardiac, and disseminated types. The mortality rate ranges from 30 to 96%, depending on the site of infection. *Absidia corymbifera* is one of the least common pathogens in the order of Mucorales, and is responsible for no more than 2% of cases of mucormycosis. Only 30 cases have been reported since Hiller described the first case of *Absidia* infection in 1874. Of these cases, more than half were the cutaneous form of mucormycosis. Though rare, it runs a fulminant clinical course with high mortality rates.

After invading the human body, especially if inside traumatised tissue, *Absidia* will proliferate rapidly. They have a peculiar affinity for blood vessels and will invade the perivascular structures with their hyphae, resulting in vessel damage. Their hyphae will also cause formation of emboli, infarcts, and tissue necrosis. Systemic factors like acidosis, hyperglycaemia, acute renal failure, and prolonged antibiotic usage will facilitate systemic spread of the fungal infection.

Because of the drastic clinical course and high mortality, a high index of suspicion, rapid diagnosis, and appropriate treatment are key elements of successful management of *Absidia* infection. As illustrated in our case, all of the culture specimens were negative for bacteriology, yet the wound deteriorated with increasing tissue necrosis. In the presence of an immunocompromised state, an opportunistic fungal infection should be considered. It is possible that the use of fluconazole to manage the systemic candida infection may have masked the situation in our patient because her clinical condition improved temporarily; however there is only one report of successful management of *Absidia* with fluconazole. The standard treatment for *Absidia* infection is amphotericin B using a minimum dose of 1 mg/kg/day. Aggressive surgical debridements are necessary to control the infection. Hyperbaric oxygen therapy may be helpful as supportive treatment.

*Absidia* infection is confirmed by finding broad non-septate hyphae in a histological specimen or a positive culture from infected material. There is currently no serologic test available for diagnosing systemic *Absidia* infection. One recent study suggested that nucleic acid detection methods like fungal-specific and broad-range fungal polymerase chain reaction (PCR) followed by DNA sequencing...
of the amplified fragment may be a useful tool for early diagnosis of *Absidia* infection. This could have a significant impact on patient outcomes.

We report the first Hong Kong case of necrotising fasciitis complicated by a cutaneous necrotising infection caused by *A. corymbifera* in a 70-year-old woman. The initial cause of the necrotising fasciitis of her lower limb was probably bacterial. Fungal infection is a likely cause of persistent unsatisfactory wound healing and multiple negative bacteriology cultures. Although we finally identified *Absidia* as the causative organism, we could not salvage the patient. The combined effect of acute renal failure, a suboptimal wound condition, and the prolonged use of antibiotics further complicated the picture and were major contributing factors to her demise.

Cutaneous necrotising mucormycosis remains a medical challenge. Its rarity requires a high index of suspicion if a diagnosis is to be made successfully. Its aggressiveness requires prompt appropriate surgical and antifungal treatment. Broad-range PCR may be applicable for early identification of the infective fungal organism when bacterial cultures are negative.

**References**