CASE REPORT

A rare cutaneous fungal infection complicating bacterial necrotising fasciitis

CK Chen 陳志健
SH Wan 尹少豪
SK Kou 高兆祺

We report a case of bacterial necrotising fasciitis complicated by the rare fungus *Absidia corymbifera*. 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 corymbifera* 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 corymbifera* 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

Key words
Absidia; Fasciitis, necrotizing; Mucormycosis

Hong Kong Med J 2008;14:314-6

Department of Orthopaedics and Traumatology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong
CK Chen, MB, BS, MRCS
SH Wan, MB, BS, MRCS
SK Kou, FHKCOS, FHKAM (Orthopaedic Surgery)

Correspondence to: Dr CK Chen
E-mail: danickchen@yahoo.com.hk

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.[5] Various clinical forms of mucormycosis have been described, including rhinocerebral, pulmonary, cutaneous, gastro-intestinal, renal, cardiac, and disseminated types. The mortality rate ranges from 30 to 96%, depending on the site of infection.[6,7] *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.[8] Only 30 cases have been reported since Hiller described the first case of *Absidia* infection in 1874.[9] Of these cases, more than half were the cutaneous form of mucormycosis.[5] 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.[2] 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.[10]

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.[11] 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.[12,13] Hyperbaric oxygen therapy may be helpful as supportive treatment.[14]

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

罕見的皮膚真菌感染併發菌性壞死性筋膜炎

本病例報告描述一宗由一種罕見的真菌——傘枝犁頭霉(*Absidia corymbifera*)併發的菌性壞死性筋膜炎。雖然這種真菌感染極為少有，但預後不良，所以要多加留意，自1874年，至今只有30宗病例，而本院所處理的病例更是本地首宗同類病症報告。本文全面討論預期的臨床治療過程及理想的治療方案。

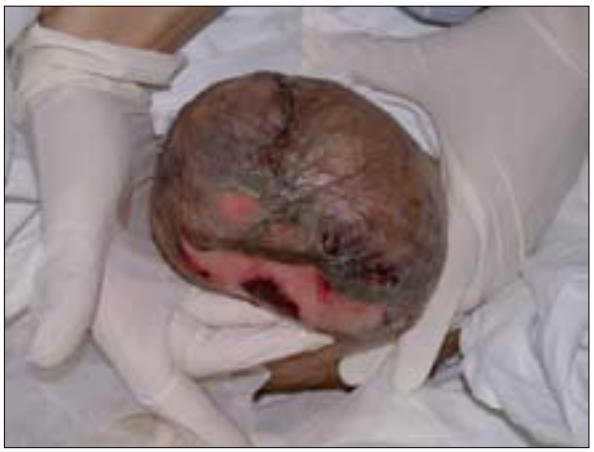

FIG 1. Wound condition on postoperative day 18

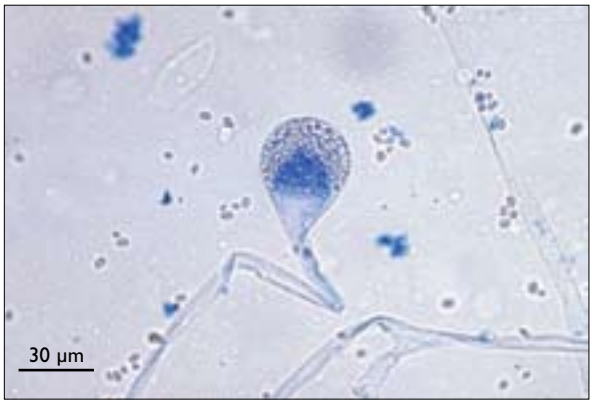

FIG 2. Microscopic morphology of *Absidia corymbifera* showing a typical pyriform-shaped sporangium with a characteristic conical shaped columella and pronounced apophysis

of the amplified fragment may be a useful tool for early diagnosis of *Absidia* infection.[15] 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

1. Richardson MD, Shankland GS. Rhizopus, Rhisomucor, Absidia, and other agents of systemic and subcutaneous zygomycoses. In: Murray PR, editor. Manual of clinical microbiology. Washington DC: ASM Press; 1995:809-24.
2. Mandell G, Bennett J, Dolin R. Agents of mucormycosis and related species. In: Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Vol 2. 5th ed. Philadelphia: Churchill Livingstone; 2000:2685-95.
3. Thami GP, Kaur S, Bawa AS, Chander J, Mohan H, Bedi MS. Post-surgical zygomycotic necrotizing subcutaneous infection caused by *Absidia corymbifera*. Clin Exp Dermatol 2003;28:251-3.
4. Stone DR, Gorbach SL. Necrotizing fasciitis. The changing spectrum. Dermatol Clin 1997;15:213-20.
5. Ribes JA, Vanover-Sams CA, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev 2000;13:236-301.
6. Kitabayashi A, Hirokawa M, Yamaguchi A, Takatsu H, Miura AB. Invasive pulmonary mucormycosis with rupture of the thoracic aorta. Am J Hematol 1998;58:326-9.
7. Concanour CS, Miller-Crotchett P, Reed RL 2nd, Johnson PC, Fischer RP. Mucormycosis in trauma patients. J Trauma 1992;32:12-5.
8. Espinel-Ingroff A, Oakley LA, Kerkering TM. Opportunistic zygomycotic infections. A literature review. Mycopathologia 1987;97:33-41.
9. Marchevsky AM, Bottone EJ, Geiler SA, Giger DK. The changing spectrum of disease, etiology, and diagnosis of mucormycosis. Hum Pathol 1980;11:457-64.
10. Ingram CW, Sennesh J, Cooper JN, Perfect JR. Disseminated zygomycosis: report of four cases and review. Rev Infect Dis 1989;11:741-54.
11. Koszyca B, Ellis D, Toogood I, Byard RW. Fluconazole in the treatment of pulmonary zygomycosis. Mycoses 1995;38:277-80.
12. Ribeiro NF, Cousin GC, Wilson GE, Butterworth DM, Woodwards RT. Lethal invasive mucormycosis: case report and recommendations for treatment. Int J Oral Maxillofac Surg 2001;30:156-9.
13. Scalise A, Barchiesi F, Viviani MA, Arzeni D, Bertani A, Scalise G. Infection due to *Absidia corymbifera* in a patient with a massive crush trauma of the foot. J infect 1999;38:191-2.
14. Seguin P, Musellec H, Le Gall F, Chevrier S, Le Bouquin V, Malleddant Y. Post-traumatic course complicated by cutaneous infection with *Absidia corymbifera*. Eur J Clin Microbiol Infect Dis 1999;18:737-9.
15. Ritz N, Ammann RA, Aebischer CC, et al. Failure of voriconazole to cure disseminated zygomycosis in an immunocompromised child. Eur J Pediatr 2005;164:231-5.