

CASE REPORT

SUBCUTANEOUS PHAEOPHYCOMYCOSIS BY *Exophiala jeanselmei* IN A CARDIAC TRANSPLANT RECIPIENT

Maria do Rosário R. SILVA(1), Orionalda de FL. FERNANDES(1), Carolina R. COSTA(1), Aíçar CHAUL(2), Luciano F. MORGADO(2), Luis Fernando FLEURY-JÚNIOR(2) & Maurício B. COSTA(3)

SUMMARY

We report a case of phaeohyphomycosis caused by *Exophiala jeanselmei* in a cardiac transplant recipient maintained on immunosuppressive therapy with mycophenolate mofetil tacrolimus and prednisone. The lesion began after trauma on the right leg that evolved to multiple lesions with nodules and ulcers. Diagnosis was performed by histological examination and culture of pus from skin lesions. Treatment consisted of itraconazole (200 mg/day) for three months with no improvement and subsequently with amphotericin B (0.5 mg/Kg per day to a total of 3.8 g intravenously). After four months of treatment, the lesions showed marked improvement with reduction in the swelling and healing of sinuses and residual scarring.

KEYWORDS: *Exophiala jeanselmei*; Phaeohyphomycosis; Subcutaneous infections.

INTRODUCTION

Phaeohyphomycosis is a term introduced by AJELLO *et al.*¹ in 1974 and it is used to describe subcutaneous and systemic diseases caused by a variety of dematiaceous fungi that develop in the form of darkly pigmented yeast-like cells, hyphae and pseudohyphae in infected tissue^{6,10}.

Several species of *Exophiala*, *Cladosporium*, *Alternaria* and other genera of fungi have been recognized as agents of subcutaneous phaeohyphomycosis^{4,8,13}. The genus *Exophiala* is widely distributed in the environment and may cause infections in both immunocompromised and immunocompetent patients^{11,12}. We report a case of subcutaneous phaeohyphomycosis caused by *Exophiala jeanselmei* in a patient with a cardiac transplant.

CASE REPORT

A 48 year-old man, was admitted to “Hospital de Doenças Tropicais de Goiânia”, with a nodule on the right lower leg. The lesion began after trauma on the right leg that evolved to nodules and ulcers (Fig. 1). He had undergone cardiac transplantation eight months before immunosuppressive therapy included mycophenolate mofetil (3 mg/day), tacrolimus (5 mg/day) and prednisone (20 mg/day).

Direct examination of the pus from lesion revealed branched pale-

brown hyphae and rounded thick-walled vesicles. Histopathological examination of tissue sections of a skin biopsy from the lesion showed mild hyperplasia of the epidermis and suppurative granulomatous inflammation in dermis with budding yeasts and dematiaceous hyphae (Fig. 2a). Cultures obtained on Sabouraud dextrose agar, produced dark, moist, olive to black yeast-like colony (Fig. 2b). Microscopically, the long mycelium, thick-walled septate conidiophores with a ball of conidia (annelophores) at the tip were visualized (Fig. 2c).



Fig. 1 - Suppurating lesion aspect of right leg with nodules discharging sinuses and ulcers.

(1) Departamento de Microbiologia, Imunologia, Parasitologia e Patologia, IPTSP/UFG, Goiânia, Goiás, Brasil.

(2) Departamento de Medicina Tropical, IPTSP/UFG, Goiânia, Goiás, Brasil.

(3) Departamento de Patologia e Imagenologia, Faculdade de Medicina/UFG, Goiânia, Goiás, Brasil.

Correspondence to: Maria do Rosário R. Silva, Rua 15 n° 108, Setor Oeste, 74140-090 Goiânia, Goiás, Brasil. E-mail: rosario@iptsp.ufg.br

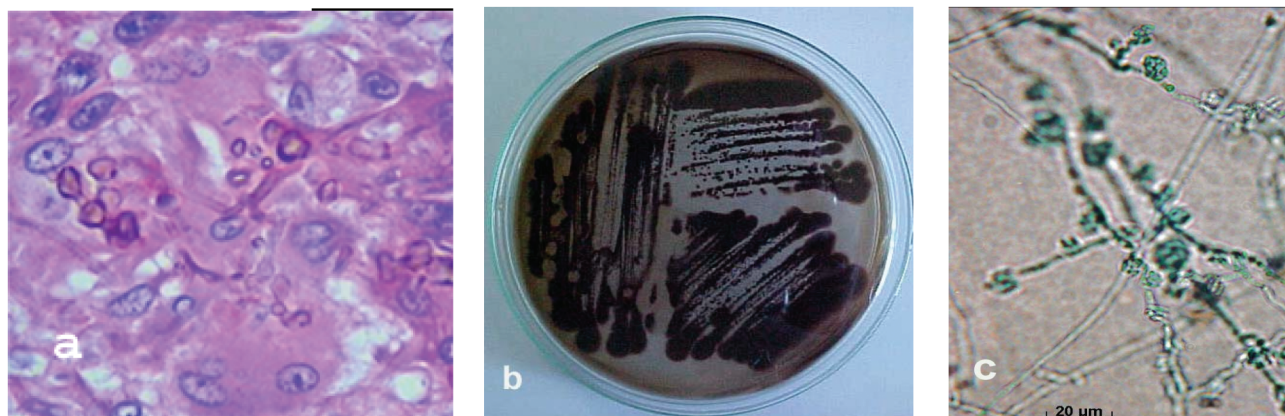


Fig. 2 - (a) Hematoxylin-Eosin (HE-400X) stain of a biopsy specimen from the lesion of the right foot showing many yeast, single or in short chains, and hyphae in the tissue. (b) Culture on Sabouraud dextrose agar, produced dark, moist, olive to black yeast-like colony at room temperature. (c) Conidia gathered in clusters at the apexes of the tapered annelids and long, thick-walled, septate conidiophores (Slide culture of *E. jeanselmei*).

The patient received oral itraconazole (Sporanox), 200 mg daily for three months, but no improvement was noted. Antifungal susceptibility testing of the isolate was accomplished by Etest method. Minimal Inhibitory Concentration (MIC) were 1 µg/mL for amphotericin B (Fungizone, Squibb, US) and 64 µg/mL for itraconazole. Antifungal treatment with amphotericin B was started. The dose regimen was 0.5 mg/Kg per day (alternate days) to a total of 3.8 g intravenously. After four months of treatment, the lesion showed marked improvement with reduction in the swelling and closure of sinuses and residual scarring of the tissue.

DISCUSSION

Dematiaceous fungi can produce three different types of infection, i.e. phaeohyphomycosis, chromoblastomycosis and mycetoma. Unlike chromoblastomycosis or mycetoma, there are no muriform cells nor grains in phaeohyphomycosis^{3,10}. Phaeohyphomycosis is a mycosis that usually presents as single cyst or abscess on exposed area. This infection is most common in patients with underlying problems and has been reported after trauma to the skin⁹. In 54 cases of dematiaceous infections caused by *Exophiala jeanselmei*, underlying diseases were identified in 23 cases⁷. The present patient showed multiple nodules and ulcers on the right leg and a history of local trauma months before the appearance of the lesion. This patient had undergone cardiac transplantation and its immunosuppressive regimen included mycophenolate mofetil, tacrolimus and prednisone, suggesting that the main reason for this disease in this case was the immunodeficiency.

Diagnosis and identification were made by direct examination with KOH, histopathological examination of tissue specimens and culture. Dematiaceous hyphae were seen in our patient specimens. These characteristics are essential to confirm phaeohyphomycosis.

Isolates of *E. jeanselmei* grow up as a yeast-like colony, later on changing to a mould⁵. In the present case, cultures produced dark, a moist, olive to black yeast like colony that did not change after two months of incubation.

No improvement was observed with the administration of oral itraconazole, however marked reduction in the swelling and closure of

sinuses was obtained after treatment with amphotericin B. This drug was used because susceptibility test showed high sensibility to this drug (MIC = 1 µg/mL). Both antifungal agents, either alone or in combination, have been reported with variable cure rates².

RESUMO

Feohifomicose subcutânea por *Exophiala jeanselmei* em um transplantado cardíaco

Este trabalho relata um caso de feohifomicose subcutânea causado por *Exophiala jeanselmei* em um paciente que havia recebido transplante de coração e mantinha terapia com micofenolato mofetil, tacrolimus e prednisona. As lesões tiveram início após trauma na perna inferior direita que evoluíram produzindo múltiplos nódulos e úlceras. Diagnóstico foi realizado através de avaliação histológica e de características macroscópicas e microscópicas da cultura das lesões da pele. O paciente fez uso de itraconazol em concentração de 200 mg/dia durante três meses, não se observando no entanto, melhora das lesões. Após este período, o paciente foi tratado com anfotericina B a uma concentração de 0,5 mg/Kg/dia totalizando 3,8 g. Após quatro meses de tratamento as lesões mostraram melhora evidente, verificando-se fechamento das fístulas e cicatrização das lesões.

REFERENCES

1. AJELLO, L.; GEORG, L.K.; STEIGBIGEL, R.T. & WANG, C.J. - A case of phaeohyphomycosis caused by a new species of *Phialophora*. *Mycologia*, **66**: 490-498, 1974.
2. CLANCY, C.J.; WINGARD, J.R. & HONG-NGUYEN, M. - Subcutaneous phaeohyphomycosis in transplant recipients: review of the literature and demonstration of *in vitro* synergy between antifungal agents. *Med. Mycol.*, **38**: 169-175, 2000.
3. FADER, R.C. & MCGINNIS, M.R. - Infections caused by dematiaceous fungi: chromoblastomycosis and phaeohyphomycosis. *Infect. Dis. Clin. N. Amer.*, **2**: 925-938, 1988.
4. GUGNANI, H.C.; SOOD, N.; SINGH, B.M. & MAKKAR, R. - Case report. Subcutaneous phaeohyphomycosis due to *Cladosporium cladosporioides*. *Mycoses*, **43**: 85-87, 2000.

5. HEMASHETTAR, B.M.; PATIL, C.S.; NAGALOTIMATH, S.J. & THAMMAYYA, A. - Mycetoma due to *Exophiala jeanselmei*. A case report with a description of the fungus. **Indian J. Path. Microbiol.**, **29**: 75-78, 1986.
6. KWON-CHUNG, K.J. & BENNETT, J.E. - **Medical Mycology**. Philadelphia, Lea & Febiger, 1992.
7. MURAYAMA, N.; TAKIMOTO, R.; KAWAI, M. *et al.* - A case of subcutaneous phaeohyphomycotic cyst due to *Exophiala jeanselmei* complicated with systemic lupus erythematosus. **Mycoses**, **46**: 145-148, 2003.
8. ROMANO, C.; FIMIANI, M.; PELLEGRINO, M. *et al.* - Cutaneous phaeohyphomycosis due to *Alternaria tenuissima*. **Mycoses**, **39**: 211-215, 1996.
9. RONAN, S.G.; UZOARU, I.; NADIMPALLI, V.; GUITART, J. & MANALIGOD, J.R. - Primary cutaneous phaeohyphomycosis: report of seven cases. **J. cutan. Path.**, **20**: 223-228, 1993.
10. ROSSMANN, S.N.; CERNOCH, P. & DAVIS, J.R. - Dematiaceous fungi are increasing cause of human disease. **Clin. infect. Dis.**, **22**: 73-80, 1996.
11. SARTORIS, K.E.; BAILLIE, G.M.; TIERNAN, R. & RAJAGOPALAN, P.R. - Phaeohyphomycosis from *Exophiala jeanselmei* with concomitant *Nocardia asteroides* infection in a renal transplant recipient: case report and review of the literature. **Pharmacotherapy**, **19**: 995-1001, 1999.
12. SUDDUTH, E.J.; CRUMBLEY, A.J. & FARRAR, W.E. - Phaeohyphomycosis due to *Exophiala* species: clinical spectrum of disease in humans. **Clin. infect. Dis.**, **15**: 639-644, 1992.
13. XU, X.; LOW, D.W.; PALEVSKY, H.I. & ELENITSA, R. - Subcutaneous phaeohyphomycotic cysts caused by *Exophiala jeanselmei* in a lung transplant patient. **Derm. Surg.**, **27**: 343-346, 2001.

Received: 16 July 2004

Accepted: 30 November 2004