Clinical resolution of *Scedosporium prolificans* pneumonia associated with treatment with liposomal amphotericin B in a patient with acute leukemia

Juan Carlos García-Ruiz[1], Elena Amutio[1], Itziar Hernández[1], Carmen Alvarez[1], Filomena Floristán[1], Iñaki Zuazúa[1], Alfonso Álvarez-Blanco[2] and José Pontón[3]

[1] Servicio de Hematología, [2]Servicio de Medicina Interna, Hospital de Cruces, Baracaldo, Vizcaya; and [3]Departamento de Inmunología, Microbiología y Parasitología, Facultad de Medicina y Odontología, Universidad del País Vasco, Bilbao, Vizcaya, Spain

Summary

Scedosporium prolificans is a filamentous fungus which has been recently identified as the aetiologic agent of severe infections in patients with haematological malignancies. Due to the resistance of *S. prolificans* to all known antifungals there are very few patients recovering from invasive infections. We describe the case of a patient with acute leukaemia who developed a *S. prolificans* pneumonia successfully treated with liposomal amphotericin B and who underwent autologous peripheral blood stem cells transplantation. The patient is in good health and has shown no evidence of reactivation of *S. prolificans* infection over one year after the transplant. Liposomal amphotericin B may be an effective treatment of pneumonia caused by *S. prolificans* in haematological patients.

Key words *Scedosporium prolificans*, liposomal amphotericin B

Resolución clínica de una neumonía por *Scedosporium prolificans* tratada con anfotericina B liposomal en un paciente con leucemia aguda

Resumen

Scedosporium prolificans es un hongo filamentoso que ha sido recientemente identificado como el agente etiológico de infecciones graves en pacientes con neoplasias hematológicas. La resistencia que *S. prolificans* muestra a todos los antifúngicos conocidos hace que sean escasos los casos conocidos de supervivencia a esta infección. En esta nota describimos el caso de un paciente con una leucemia aguda que desarrolló una neumonía por *S. prolificans* y que fue tratado con éxito con anfotericina B liposómica y posteriormente sometido a un trasplante autólogo con células progenitoras de sangre periférica. El paciente se encontraba bien y sin mostrar evidencia de la infección un año después de la realización del trasplante. La anfotericina B liposómica puede representar un tratamiento efectivo de neumonías producidas por *S. prolificans* en pacientes hematológicos.

Palabras clave *Scedosporium prolificans*, anfotericina B liposómica

Scedosporium prolificans, which was previously named *Scedosporium inflatum* [1], is a filamentous fungus that has been recognised as an emerging pathogen in haematological patients where it causes systemic infections [2-4]. The neutropenia and the *in vitro* resistance of the fungus to all known antifungals may explain the high mortality rate observed in haematological patients with systemic *S. prolificans* infections [5]. However, the clearance of the infection following administration of fluconazole or granulocyte colony-stimulating factor have been recently reported in two patients [6,7]. In the case of patients with fungal infections previous to the transplantation we must be sure the patient has cleared the infection before starting the transplantation to avoid a reactivation of the infection. We report a patient with acute leukemia (AL) who developed a pneumonia by *S. prolificans* successfully treated with liposomal amphotericin B. Later on he underwent autologous peripheral blood stem cells (PBSC) transplantation and showed no evidence of reactivation of *S. prolificans* infection.

Case report. A 33-year-old man was diagnosed with AL in November 1996. During the induction therapy

Dirección para correspondencia:
Dr. Juan Carlos García-Ruíz
Servicio de Hematología, Hospital de Cruces, Plaza de Cruces s/n, 48903 Baracaldo, Vizcaya, Basque Country, Spain.
Tel.: +34-94-4850086, Ext. 2209
Fax: 34-94-4992945; E-mail: oipposaj@lg.ehu.es

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he developed erythematous skin lesions which resolved with the addition of amphotericin B (0.5 mg/kg per day, for 20 days) to the empiric broad spectrum antibiotics used and the recovery of neutropenia. The total accumulated dose was 1 g. The patient presented evidence of nephrotoxicity due to the amphotericin B treatment and achieved complete remission.

One month later, during profound neutropenia caused by his second cycle of chemotherapy, he again developed skin lesions in the chest, arms and legs as well as bilateral pneumonia which required supplementary O_2 (inspirated fraction, 50%) for adequate oxygenation. Despite treatment with broad spectrum antibiotics (ceftazidime, imipenem, amikacin, TMP-SMZ and teicoplanin), the patient's condition did not improve and a presumptive diagnosis of fungal pneumonia was made. Liposomal amphotericin B therapy (3 mg/kg per day) was initiated due to the nephrotoxicity caused by conventional amphotericin B used during induction therapy. The treatment was maintained for 16 days and the total accumulated dose was 4.8 g. A bronchoalveolar lavage from the upper left lobe yielded a filamentous fungus identified as *S. prolificans*. Fever persisted until the time the patient's neutrophil count recovered. The fungus was resistant *in vitro* to conventional amphotericin B, 5-fluorocytosine, ketoconazole, miconazole, clotrimazole, fluconazole and itraconazole by a microdilution method [8].

Four months later, the patient was transplanted with autologous PBSC. Recombinant human granulocyte colony-stimulating factor at 5 µg/kg/day was given intravenously from the day after transplantation until the absolute neutrophil count >1000, a situation that was observed at day +10. A follow-up bronchoalveolar lavage performed just before the transplant was negative and the patient had no evidence of recurrence of *S. prolificans* infection during the rest of his hospitalisation.

Several cases of systemic infections by *S. prolificans* have been described in two institutions in Spain [2,9], although in one of them they were epidemiologically unrelated [10]. The management of these infections is difficult since the fungus is highly resistant *in vitro* to all known antifungals. However, it has been recently described the cure of two infections with granulocyte colony-stimulating factor or fluconazole [6,7]. In our patient, the recovery of the neutrophil count and the use of high dose liposomal amphotericin B controlled the *S. prolificans* infection and allowed the performance of the transplant. Liposomal amphotericin B has been shown to be more active *in vitro* against several *Aspergillus* and *Candida* species than conventional amphotericin B [11] and it allows the administration of higher doses than conventional amphotericin B. Liposomal amphotericin B may be an effective treatment of pneumonia caused by *S. prolificans*

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