Enferm Infecc Microbiol Clin. 2018;36(4):246–248

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Diagnosis at first sight

Cutaneous lesions and hemiparesis in a kidney transplant recipient

Lesiones cutáneas y hemiparesia en una receptora de trasplante renal

Jara Llenas-García[a,b,*], Iván Prats Sánchez[c], Vladimir Ospino[a], Ana Alastruey-Izquierdo[d]

[a] Infectious Diseases Unit, Hospital General Universitario de Elche, Alicante, Spain
[b] Foundation for the Promotion of Health and Biomedical Research in the Valencian Region (FISABIO), Valencia, Spain
[c] Microbiology Department, Hospital General Universitario de Elche, Alicante, Spain
[d] National Centre for Microbiology, Instituto de Salud Carlos III, Madrid, Spain

Case description

A 75-year-old kidney transplant patient developed left hemiparesis and hemihypesthesia and nodular cutaneous lesions on day +72 after transplantation. Her medical history was remarkable for hypertension, hypothyroidism, steroid-induced diabetes mellitus, permanent atrial fibrillation and a myocardial infarction. In September 2015, she received a deceased-donor kidney transplantation. After induction with thymoglobulin 250 mg, she was on tacrolimus 3 mg/day, mycophenolate mofetil 4000 mg/day, prednisone 30 mg/day and prophylactic valganciclovir and trimethoprim/sulfamethoxazole. Seven weeks after transplantation she was admitted for ultrasound-guided drainage of a 8.1 cm × 6.2 cm lymphocele compressing the urinary tract; all microbiological cultures of the liquid drained were negative. On the day +72 after transplantation, she developed left hand paresis and hypoesthesia. An urgent brain CT-scan was informed as suggestive of subacute middle cerebral artery stroke; anticoagulation was then restored. An echocardiogram was negative for endocarditis. The following days she developed left hemiparesis and hemihypesthesia and stupor. A cerebral magnetic resonance was performed (Fig. 1A) showing multiple supratentorial space-occupying-lesions with peripheral contrast enhancement surrounded by edema. Two 0.5 cm diameter nodular abscessified cutaneous lesions were noted in her left thigh (Fig. 1B). *Aspergillus* and cryptococcal antigen test in serum were both negative. Empiric treatment was then initiated with meropenem, linezolid, amphotericin B and trimethoprim/sulfamethoxazole and her immunosuppressive treatment was cut down to prednisone. A cutaneous biopsy of a left thigh lesion showed septal panniculitis; no bacteria nor fungi were seen on histology. A Gram stain from the material drained was performed (Fig. 2A). Two days later, some colonies started to grow on the Sabouraud Medium (Fig. 2B and C). What is your diagnosis?

Diagnosis

Cutaneous and cerebral abscesses caused by *Scedosporium apiospermum.*

Progress

Skin abscess Gram stain showed hyphae (Fig. 2A) and in solid and liquid culture medium grew fungal colonies (Fig. 2B) that, when stained with lactophenol cotton blue, revealed typical ovoid conidia suggestive of *Scedosporium spp.* (Fig. 2C). It was preliminarily identified by Maldi-TOF as *S. apiospermum* (score = 1.5); antifungal therapy was then changed to voriconazole and terbinafine. Two days later, a stereotaxic biopsy and drainage of a cerebral abscess was performed; cultures also grew *S. apiospermum* (Fig. 3). A PCR done at the Mycology Reference Laboratory of the National Center for Microbiology confirmed gender and specie identification. Antifungal susceptibility tests showed MIC of 4 μg/ml to amphotericin B, 2 μg/ml to voriconazol, 0.03 μg/ml to miconazole and anidulafungin, >16 μg/ml to terbinafine and >8 μg/ml to itraconazole and posaconazole. Antifungal therapy was changed to voriconazole plus anidulafungin. Adjunctive neurosurgical intervention was dismissed. Patient's level of consciousness progressively deteriorated, cerebral abscesses progressed, she developed several complications and passed away 25 days after the diagnosis.

Discussion

S. apiospermum is an ubiquitous filamentous fungus present in soil, sewage and polluted waters.[1] Human infection often results from inhalation of spores or through direct inoculation. Transmission from nearly-drowned donors to solid organ allografts has been reported.[2] In our case, the donor died of a penetrating ocular traumatism with a wooden stick; all donor routine cultures were reviewed and confirmed to be negative for fungal pathogens. Main risk factor for scedosporiosis is neoplasia, especially hematological malignancies with prolonged persistent neutropenia.[3] Scedosporiosis represents approximately 25% of all non-Aspergillus mold

* Corresponding author.
E-mail address: jarallenas@gmail.com (J. Llenas-García).

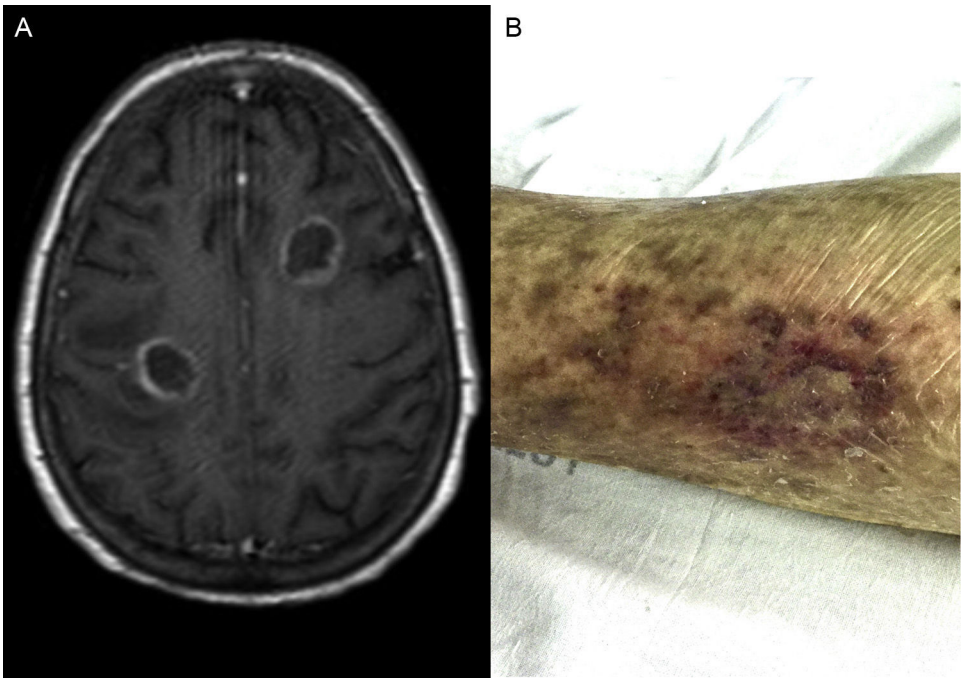

Fig. 1. Magnetic resonance imaging of the brain (A) and cutaneous lesions (B) noted in patient's left thigh.

infections in solid organ transplant (SOT) recipients, affecting more frequently lung transplant recipients.[4] Central nervous system involvement is present in 30% of cases and associated with higher mortality[5,6]; it usually presents as brain abscesses although spinal pachymeningitis, acute or chronic meningitis, intraventricular device-related ventriculitis or epidural abscesses have also been described.[7,8] Microbiological diagnosis is difficult but can be facilitated by the use of real-time PCR assays.[9] Scedosporiosis overall mortality is 54–73% in SOT and goes up to 87.5% in disseminated disease.[5,6] A correct antifungal treatment, surgical debridement and a strong tailored reduction in immunosuppressant drugs are key to success.[3,5] *Scedosporium spp.* are usually amphotericin B resistant; identification to species level is key to direct treatment, as there are species-specific differences in antifungal specificity.[10] The use of prophylaxis or preemptive treatment in high-risk colonized patients or receptors of grafts from nearly-drowned donors, the optimal combination antifungal therapy or the need for secondary chemoprophylaxis are unresolved questions.

In conclusion, physicians should consider *Scedosporium spp.* as a possible cause of brain abscesses in SOT recipients, especially in

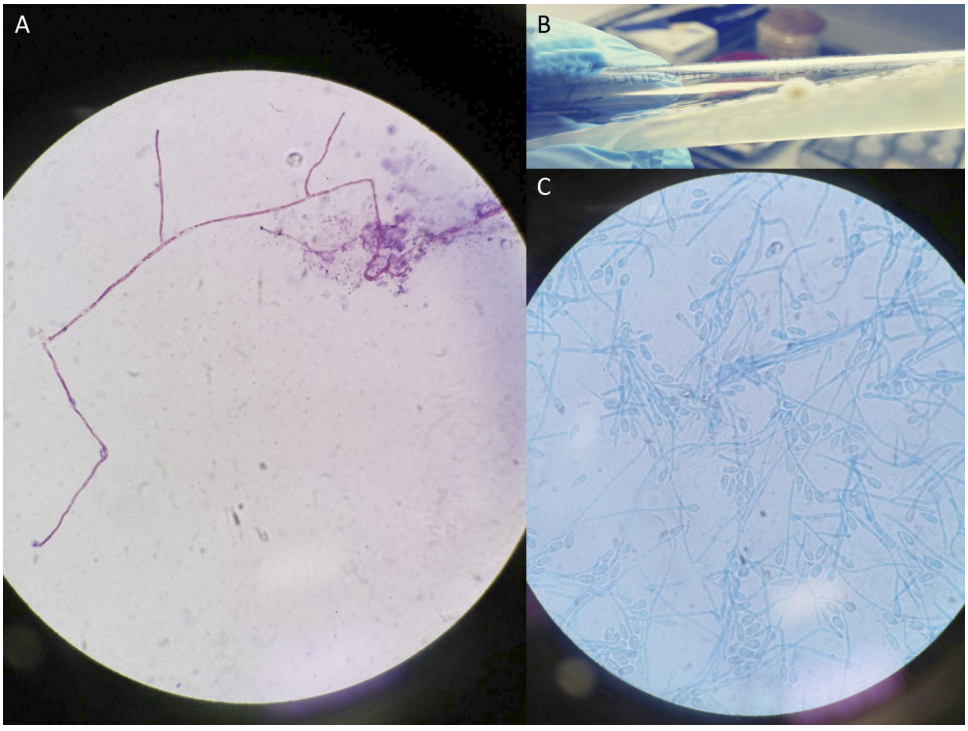

Fig. 2. (A) Gram stain from the material drained from the skin abscess. (B) Sabouraud medium culture and (C) Lactophenol cotton blue wet mount preparation.

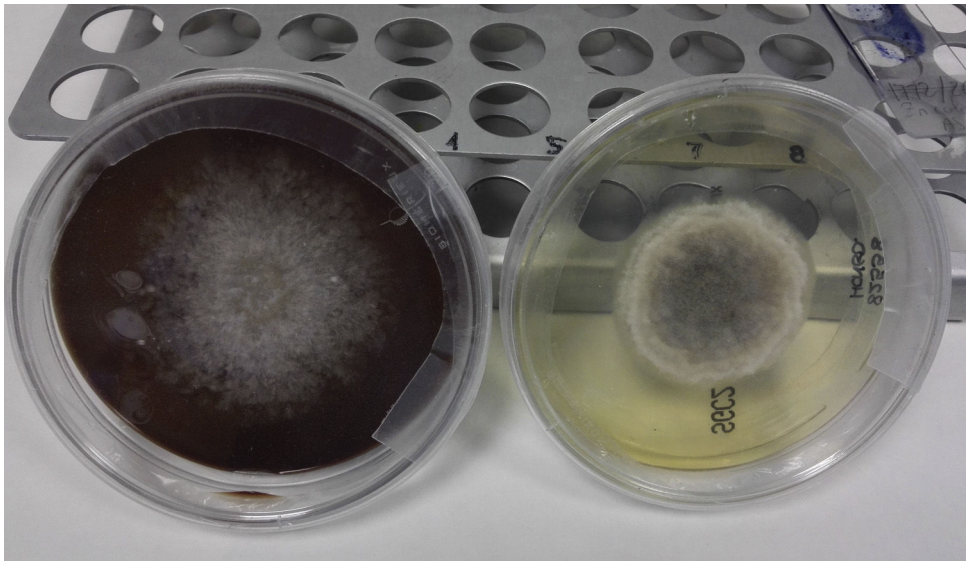

Fig. 3. Agar (left) and Sabouraud agar (right) cultures reverse showing gray-black colonies of *Scedosporium apiospermum*.

those more heavily immunosuppressed and combined antifungal therapy must be promptly started.

Funding

None declared.

Conflict of interest

All authors declare no competing interests.

Acknowledgments

We are in debt with our colleagues from the Intensive Care Unit, Neurosurgery and Nephrology Department for their invaluable collaboration in this case. We want to especially thank Dr. Mar Masiá, from the Infectious Diseases Department who took care of the patient and contributed significantly to this manuscript. We also want to thank Dr. Pilar López García, from the Microbiology Department, for assistance with the microbiological techniques and for her comments that greatly improved this manuscript.

References

1. Cortez KJ, Roilides E, Quiroz-Telles F, Meletiadis J, Antachopoulos C, Knudsen T, et al. Infections caused by *Scedosporium spp.* Clin Microbiol Rev. 2008;21:157–97.
2. Kim SH, Ha YE, Youn JC, Park JS, Sung H, Kim MN, et al. Fatal scedosporiosis in multiple solid organ allografts transmitted from a nearly-drowned donor. Am J Transplant. 2015;15:833–40.
3. Rodriguez-Tudela JL, Berenguer J, Guarro J, Kantarcioglu AS, Horre R, de Hoog GS, et al. Epidemiology and outcome of *Scedosporium prolificans* infection, a review of 162 cases. Med Mycol. 2009;47:359–70.
4. Husain S, Alexander BD, Munoz P, Avery RK, Houston S, Pruett T, et al. Opportunistic mycelial fungal infections in organ transplant recipients: emerging importance of non-Aspergillus mycelial fungi. Clin Infect Dis. 2003;37:221–9.
5. Castiglioni B, Sutton DA, Rinaldi MG, Fung J, Kusne S. *Pseudallescheria boydii* (Anamorph *Scedosporium apiospermum*). Infection in solid organ transplant recipients in a tertiary medical center and review of the literature. Medicine (Baltimore). 2002;81:333–48.
6. Husain S, Muñoz P, Forrest G, Alexander BD, Somani J, Brennan K, et al. Infections due to *Scedosporium apiospermum* and *Scedosporium prolificans* in transplant recipients: clinical characteristics and impact of antifungal agent therapy on outcome. Clin Infect Dis. 2005;40:89–99.
7. Berenguer J, Rodriguez-Tudela JL, Richard C, Alvarez M, Sanz MA, Gaztelurrutia L, et al. Deep infections caused by *Scedosporium prolificans*. A report on 16 cases in Spain and a review of the literature. *Scedosporium Prolificans* Spanish Study Group. Medicine (Baltimore). 1997;76:256–65.
8. Montejo M, Muñiz ML, Zárraga S, Aguirrebengoa K, Amenabar JJ, López-Soria L, et al. Case reports. Infection due to *Scedosporium apiospermum* in renal transplant recipients: a report of two cases and literature review of central nervous system and cutaneous infections by Pseudallescheria boydii/*Sc. apiospermum*. Mycoses. 2002;45(9–10):418–27.
9. Castelli MV, Buitrago MJ, Bernal-Martinez L, Gomez-Lopez A, Rodriguez-Tudela JL, Cuenca-Estrella M. Development and validation of a quantitative PCR assay for diagnosis of scedosporiosis. J Clin Microbiol. 2008;46:3412–6.
10. Lackner M, de Hoog GS, Verweij PE, Najafzadeh MJ, Curfs-Breuker I, Klaassen CH, et al. Species-specific antifungal susceptibility patterns of Scedosporium and Pseudallescheria species. Antimicrob Agents Chemother. 2012;56:2635–42.