Medical Mycology Case Reports 6 (2014) 62–65

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Mucor irregularis-associated cutaneous mucormycosis: Case report and review

Blandine Rammaert [a], Cécile Angebault [b], Anne Scemla [c], Sylvie Fraitag [d], Nathalie Lerolle [a], Marc Lecuit [a,e,f], Marie-Elisabeth Bougnoux [b], Olivier Lortholary [a,g,*]

[a] Université Paris-Descartes, Sorbonne Paris Cité, APHP, Service des Maladies Infectieuses et Tropicales, Hôpital Necker-Enfants Malades, Centre d'Infectiologie Necker-Pasteur, Institut Imagine, 75015 Paris, France
[b] Université Paris-Descartes, Sorbonne Paris Cité, APHP, Service de Microbiologie, Unité de Parasitologie-Mycologie, Hôpital Necker-Enfants Malades, 75015 Paris, France
[c] Université Paris-Descartes, Sorbonne Paris Cité, APHP, Service de Transplantation Rénale, Hôpital Necker-Enfants Malades, 75015 Paris, France
[d] Université Paris-Descartes, Sorbonne Paris Cité, APHP, Département de Pathologie, Hôpital Necker-Enfants Malades, 75015 Paris, France
[e] Institut Pasteur, Unité de Biologie des Infections, 75015 Paris, France
[f] Inserm U1117, 75015 Paris, France
[g] Institut Pasteur, Unité de Mycologie Moléculaire, CNRS URA 3012, 75015 Paris, France

ARTICLE INFO

Article history:
Received 23 June 2014
Accepted 10 July 2014

Keywords:
Invasive fungal disease
Mucorales
Solid organ transplantation
Mucormycoses
Amphotericin B

ABSTRACT

Solid organ transplant recipients are at risk for invasive fungal diseases, and are also exposed to healthcare-associated mucormycosis. Mainly causing localized cutaneous mucormycosis, *Mucor irregularis* infection is reported for the first time in a kidney-transplant recipient. A healthcare-associated origin was highly suspected in this case. We performed a literature review and highlight the characteristics of this very rare fungus.

1. Introduction

Cutaneous localizations are frequently observed in healthcare-associated mucormycosis [1]. In this setting, highly immunosuppressed patients such as those with hematological malignancy or transplantation are particularly at risk. In one study mucormycosis accounted for 2.3% of invasive fungal diseases in solid organ transplantation (SOT), with a mortality rate often approaching 50% [2]. While the highest incidence rate was observed in liver transplant recipients, the estimated mucormycosis incidence in kidney transplant recipients ranged from 0.2% to 1.2% [3]. In a large cohort of patients with invasive fungal diseases from 23 US transplant centers, cutaneous localization accounted for 13% of the 28 mucormycosis cases [2]. The diagnosis of mucormycosis is often delayed in SOT [4], but this is highly dependent on the infected site. However, even though skin localizations can be easily documented by skin biopsies, species identification remains difficult. In fact, in healthcare-associated mucormycosis, more than 30% of *Mucorales* species responsible for cutaneous involvement were unidentified [1].

We report a subacute cutaneous mucormycosis in a kidney transplant recipient due to a very rare *Mucorale* species. It is possible that the infection was healthcare-associated. To our knowledge, this is the first reported case of *Mucor irregularis* infection in a solid organ transplant recipient. However, the management of mucormycosis in the SOT population differs from treatment in hematological patients, and the management of this specific *Mucorale* species is discussed.

2. Case

A 69 year-old woman was admitted in March 2012 for subcutaneous nodular lesions on the back of the left hand and left elbow (Fig. 1). She had chronic renal failure secondary to a hemolytic uremic syndrome and had received two kidney transplants from cadaveric donors in 1987 and 1993. Her baseline creatinine serum level was 150 μmol/L. Her current immunosuppressive therapy was cyclosporine 50 mg b.i.d., azathioprine 50 mg/d and prednisolone 5 mg/d. One year earlier, she was diagnosed with an epidermoid carcinoma on the right leg, which was treated with radiation therapy. She also had a history of gout.

* Corresponding author.

http://dx.doi.org/10.1016/j.mmcr.2014.07.005

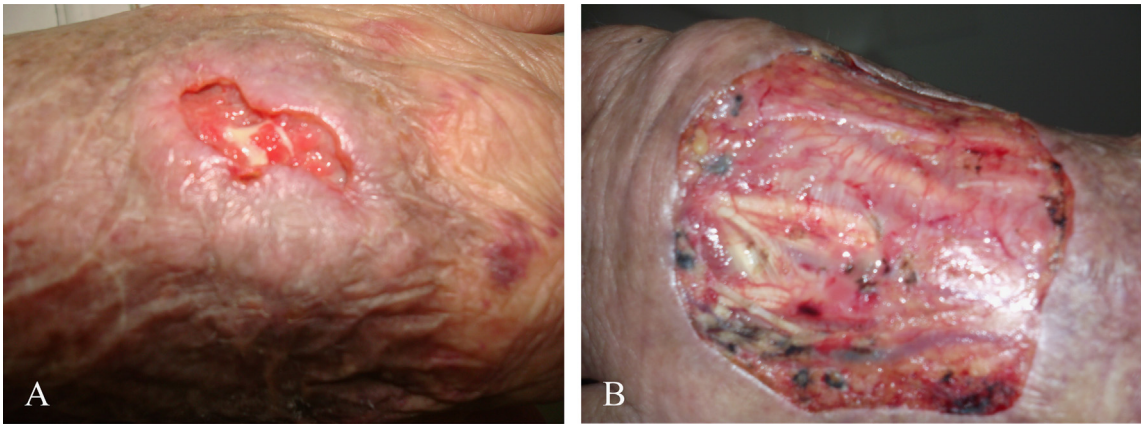

Fig. 1. Cutaneous mucormycosis due to *Mucor irregularis* in a kidney-transplanted recipient. (A) Cutaneous lesions before liposomal amphotericin B treatment. (B) After large debridement on day+13 of liposomal amphotericin B.

At the end of January 2012, she had corticosteroid infiltrations on the left radiocarpal and right metacarpus-phalangeal joints for a gout flare-up. Three weeks later, five-millimeter white subcutaneous nodules appeared, first on the left hand and then on the left elbow. The patient did not report previous injury to the left arm. She mentioned that she applied a moisturizer on both arms daily, but did not recall any contact with plants or animals.

On admission (day 0), the hand nodules had become ulcerated and purulent (Fig. 1A). Overall, the lesions were painless and the patient had no fever. No sign of arthritis or neurological abnormality were noted. Blood test results showed 6000 leukocytes/mm^3, 800 lymphocytes/mm^3, 200,000 platelets/mm^3, hemoglobin 10.8 g/dL, C-reactive protein 6 mg/L, creatinine 195 μmol/L, glucose 16.4 mmol/L with HbA1c 8.1%, iron level 14 μmol/L, ferritin 774 μg/L, and LDH 548 UI/L. A skin biopsy was performed and histopathologic findings showed non-caseating eosinophilic necrosis, granulomatous histiocytic infiltrate, and multinucleate giant cells in the dermis and subcutis. Necrotic areas were surrounded by large, irregular, non-septate, wide-angle branching hyphae on periodic acid–Schiff and Grocott stainings (Fig. 2).

Cultures of biopsy specimens on Sabouraud chloramphenicol agar slants (BioRad Laboratories, Marnes-La-Coquette, France) incubated at 30 °C and 35 °C were positive (day+5) with profuse fluffy whitish colonies presenting a lemon-yellow reverse. The identification was performed by sequencing of the ITS1-5.8S-ITS2 region of the ribosomal DNA using the universal primers ITS1-ITS4 [5]. The nucleotide sequence (deposited in Genbank under accession number KJ472786) had 100% identity over 451 bp for *M. irregularis* (formerly *Rhizomucor variabilis* var. *variabilis* [6]), compared to the nucleotidic sequences of strains CMFCCC B 50 m and CBS 654.78 published under GenBank accession numbers JX976252 and JX976261 [7]. Minimal inhibitory concentrations, measured by the *E*-test agar diffusion method (bioMérieux SA, Marcy l'Etoile, France), were respectively 0.094, 12, 8 and >32 μg/ml to amphotericin B (AmB), itraconazole, posaconazole and voriconazole, respectively.

To assess whether mucormycosis was localized to the skin or disseminated, we performed sinus, chest and abdominal computed tomography, as well as plain films of the left arm, and a cerebral magnetic resonance. All were normal. Cyclosporine and prednisolone were tapered and azathioprine was discontinued. Concurrent type 2 diabetes was balanced with oral medication. Liposomal amphotericin B (L-AmB) was immediately introduced at 3 mg/kg/day, and then increased at 5 mg/kg/day (day +9) due to progression of the lesions. During the course of therapy, the patient showed signs of L-AmB nephrotoxicity with serum creatinine increasing up to 380 μmol/L and respiratory distress due to pulmonary edema. Dialysis was performed twice. Given the severe nephrotoxicity to L-AmB, the drug was discontinued (day +21). The patient received a total of 1.1 g of L-AmB over 3 weeks. Extensive surgical debridement of the left hand and elbow was performed on day+13 (Fig. 1B). Progressive local improvement was noted in the following weeks. One month post-surgery (day+30), a skin graft was successfully performed. No mucormycosis relapse was noted 2 years after treatment discontinuation.

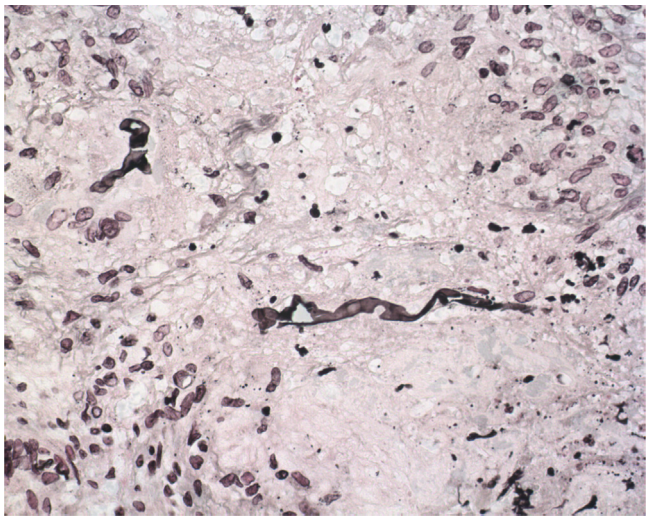

Fig. 2. Histopathological examination of skin biopsy in a cutaneous mucormycosis due to *Mucor irregularis*. Within the dermis is a heavy mixed granulomatous and suppurative infiltrate extending to the subcutis. Fungi are located within histiocytic granulomas showing a large number of giant multinucleate cells. *Mucor irregularis* hyphae are very broad, non-septate and branch at 90°. They appear often twisted (Gomori-Grocott staining; ×400).

Suspecting a healthcare-associated infection, we attempted to look the presence of fungi in the corticosteroid vial, but it unfortunately could not be analyzed. However, no mucormycosis in patients receiving steroids infiltration was reported to the French National Institute for Health Surveillance (InVS) during the same period. In addition, the patient's skin moisturizer was also cultured on Sabouraud agar slants but no fungus was isolated.

3. Discussion

In 1999, Voigt et al. reported that *R. variabilis* was misplaced in the *Rhizomucor* clade and would be better positioned within