Clinical and microbiological efficacy of micafungin on Geosmithia argillacea infection in a cystic fibrosis patient

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Auteur: Marguet, Christophe [1], Favennec, Loïc [2], Matray, Olivier [3], Bertout, Sébastien [4], Giraud, Sandrine [5], Couderc, Laure [6], Zouhair, Rachid [7], Gargala, Gilles [8], Bouchara, Jean-Philippe [9]

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Ville: Angers
Cystic fibrosis are at risk of colonization by a number of fungi, including Geosmithia argillacea which appears to be an emerging pathogen in these patients. This pathogen has been recently reported as a cause of invasive/systemic mycosis in immunocompromized patients such as colonized patients who are immunosuppressed for lung transplantation. In this context, we report here a case of clinical and microbiological efficacy of micafungin in a French cystic fibrosis patient chronically colonized with G. argillacea. O.D., a female F508Del-CFTR homozygous patient was diagnosed at birth with cystic fibrosis in January 1996. She was found chronically colonised with multi-resistant Staphylococcus aureus (MRSA) from 1997 to 2011, and with Aspergillus fumigatus from 2001 to 2006. She was treated alternatively with oral voriconazole and itraconazole from 2004 to 2008, and with posaconazole since February 2008. Geosmithia argillacea was first diagnosed in May 2007, and chronic colonisation was persistent from this date to August 2010 with 23/28 fungus positive sputum samples, in spite of posaconazole therapy. For an isolate obtained in October 2008, minimal inhibitory/effective concentrations (MIC/MEC, mg/ml) determined using the Eucast method were 2.0, 2.0, 16.0, 2.0, 0.25 and 0.015 for amphotericin B, itraconazole, voriconazole, posaconazole, caspofungin and micafungin, respectively. The FEV1 predicted value was 73% at the time of first fungus isolation and was decreased to 47% in October 2009. She then was given caspofungin for 21 days (70 mg/day, later reduced to 50 mg) which resulted in clinical improvement (FEV1 = 64% in January 2010) without eradication of G. argillacea. In June 2010, treatment with micafungin (75 mg, 21 days) was realized owing to deterioration of the respiratory function (FEV1 = 56%), without clinical improvement (FEV1 = 47% in August 2010). O.D. was then treated from September, 23 to November 3, 2010 with micafungin (100mg bid for 21 days and 100mg/day for the following 21 days) which resulted in clinical and microbiological improvement. FEV1 predicted ranged 67-68% in October and December 2010, and February and May 2011, and from the end of treatment to December 2010, 5/6 sputum samples were found negative for G. argillacea. The positive sample contained fungus of the same genotype as previous isolates. The present case is to our knowledge the first description of G. argillacea eradication in a chronically colonized cystic fibrosis patient. Similar to previous studies, G. argillacea colonization was detected in the presence of chronic MRSA after A. fumigatus eradication. Since no change in bacterial colonization was observed before, during, and after G. argillacea colonization, the present case is consistent with a pathogenic role of the fungus in cystic fibrosis patients. In vitro antifungal susceptibility assays suggested that echinocandins are most effective agents against this fungus with a lowest MEC for micafungin (7 isolates studied, MEC range: 0.015-0.03), although eradication could only be obtained with high dose micafungin for a long time (6 weeks).

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