



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

Submitted by Emmanuel Lemoine on Wed, 05/13/2015 - 11:18

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

Type de publication Communication

Type Communication sans actes dans un congrès

Année 2011

Langue Anglais

Date du colloque 01-02/09/2011

Titre du colloque Second Meeting of the ECMM/ISHAM Working Group Fungal respiratory infections in Cystic Fibrosis (Fri-CF)

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]

Pays France

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

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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, 21days) 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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