This observation clearly indicates that *N. meningitidis* is capable of acquiring/possessing more than one capsular gene. These will have important implications on the long-term efficacy of capsular polysaccharide-based vaccines.

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A Multidrug, Including Voriconazole, Resistant Oral Candida Infection in an AIDS Patient Effectively Treated with Echinocandin

Sir,

Before the era of highly active antiretroviral treatment (HAART), oral and oropharyngeal candidiasis were a frequent complication in immune deficient HIV infected patients. Often, these infections were recurrent and tended to become resistant to antifungal agents.[1]

With the use of HAART since 1996, the incidence of these candida infections considerably decreased, and consequently, infections with azole resistant strains.[2] However, there are still HIV-infected patients with low CD4+lymphocyte counts, even in the developed world. They include people diagnosed in an advanced stage of disease who never received HAART, people who do not adhere to their antiretroviral treatment regimen, and people infected with resistant HIV strains.

Today several new antifungal agents including voriconazole and echinocandin have demonstrated potent *in-vitro* activity against fluconazole resistant Candida species,[3] but so far very little has been published concerning their activity *in vivo*.[4,5] We report a case of an AIDS patient with a multidrug resistant candida infection who responded clinically well to intravenous echinocandin (caspofungin acetate) treatment.

A 40-year-old AIDS patient was diagnosed to be HIV infected in 1995 when he presented with a *Pneumocystis carinii* pneumonia and oral candidiasis. The candida infection was treated successfully with oral fluconazole. Despite HAART (initially indinavir, lamivudine and stavudine and later combinations of all other commercially available antiretrovirals), his CD4+ lymphocyte count always remained below 20/μl and his viral load never decreased below 30 000 copies/ml plasma. He was treated for recurrent oral candidiasis and candida oesophagitis with different antifungal agents including fluconazole, miconazole, itraconazole, nystatin and ketoconazole for a period of 5 years, but none of these antifungals were able to suppress the infection. In May 1999, due to a very severe persistent form of oral candidiasis, amphotericine B, 0.5 mg/kg/day was started intravenously four times a week. The oral candidiasis regressed but did not disappear completely. In June 1999, amphotericine B had to be given on a daily basis with doses reaching up to 1 mg/kg/day to control the candida infection. As his renal function deteriorated, the amphotericine B had to be discontinued. In December 1999 a throat swab showed the presence of a *Candida glabrata* and *Candida albicans* infection. Oral voriconazole 400 mg bid was started and initially the candida infection disappeared. In September 2000, despite the voriconazole treatment, the candida started to grow extensively all over the mouth mucosa. At this time his CD4+lymphocyte count was 0/μl and his viral load 190 000 copies/ml plasma. A throat swab revealed once again a *Candida albicans* infection. Amphotericine B was given but the 0.5 mg/kg starting dose immediately caused high fever. End of October 2000, echinocandin (caspofungin acetate) was started intravenously 50 mg/day. Within 24 h the candida lesions started to disappear and after 5 days no more lesions were seen. A new throat swab did not reveal any candida infection. He received echinocandine during 10 days. The drug was well tolerated. However, 7 days after stopping the echinocandine, the oral candidiasis reappeared. Again, echinocandine cured the candida infection within 5 days, but the treatment was finally discontinued after 15 days, because of thrombocytopenia. The echinocandin was stopped for safety reasons because it remains an experimental drug.

There were many potential causes for thrombocytopenia in this patient, including the HIV infection itself and other drugs he had been taking such as pyrimethamine. In the weeks following the stop of the echinocandin, the candida infection reappeared. Meanwhile the patient's general condition deteriorated and he died early January 2001.

Echinocandine exhibits *in-vitro* fungicidal activity against a number of clinically important fungi including candida.[6] Due to its unique mechanism of action (inhibitor of β–(1,3)-D-glucan synthesis), it remains active against candida isolates resistant to other antifungal agents including fluconazole, flucytosine, and amphotericine B.[5] This case report suggests that echinocandine may prove to be a promising drug for the treatment of multidrug (including voriconazole) resistant oral candidiasis in persons with HIV infection.

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