Phenotypic Switching and Genetic Diversity of Cryptococcus neoformans

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Abstract
Niger seed agar was used as a primary plating medium for the isolation of Cryptococcus neoformans from cerebrospinal fluid specimens from AIDS patients with untreated primary cryptococcosis. The medium was used as the primary means to detect variations in the colony morphology of the yeast. To search for phenotypic and genetic variations, nine patients individually harboring two or three types of colony morphology were studied. Intraindividual isolates from nine patients had minor variations in the API 20C profile, and the MICs of one or more antifungal agents (amphotericin B, fluconazole, and itraconazole) for isolates from three patients were significantly different. Intraindividual isolates from three patients had minor karyotype differences, and one showed a dramatic chromosomal length polymorphism. In addition, three serial isolates from a patient with two episodes of infection showed similar karyotypes, confirming persistent infection by the same strain. Random amplified polymorphic DNA products were identical for all isolates (including three isolates from a relapse case). Our results provided evidence suggesting that (i) in humans, C. neoformans may undergo phenotypic and genetic changes during early infection prior to antifungal agent administration; (ii) dramatic variations in electrophoretic karyotypes and in phenotypes, as demonstrated during the early infection of one patient, may be due to infection by different strains; and (iii) the use of niger seed agar as a primary plating medium is useful for studying antifungal susceptibility, phenotypic switching, genetic diversity, and multiple strain infections.