

TITLE: VIRULENCE STUDY OF SEQUENTIAL *SPOROTHRIX BRASILIENSIS* ISOLATES OBTAINED FROM A PATIENT WITH DISSEMINATED SPOROTRICHOSIS OF CHRONIC EVOLUTION AND ACQUIRED IMMUNODEFICIENCY SYNDROME

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ABSTRACT

Sporotrichosis is a subcutaneous mycosis that affects humans and other animals and *Sporothrix brasiliensis* is the most prevalent agent of the disease in Rio de Janeiro. Immunocompromised patients with a TCD4⁺ cell count lower than 200 cells/ μ l usually develop severe disseminated forms. These patients have a difficult clinical management with multiple hospitalizations. Our group previously described a case where *S. brasiliensis* increased its virulence after five years of infection in a patient with controlled diabetes and negative HIV serology. In this study we evaluated the virulence of four *S. brasiliensis* strains recovered between 2016-2018 from a 38-year-old male patient with acquired immunodeficiency syndrome and chronic sporotrichosis. He worked on a carpentry where a cat with cutaneous lesions used to live and had a persistent TCD4⁺ cell count lower than 100 cells/ μ l due to irregular antiretroviral therapy. The following putative virulence factors were evaluated using *in vitro* approaches: hemolysin, esterase, aspartic-protease, urease, resistance to oxidative and nitrosative stress, melanin production, and thermotolerance. In general, there was an increase of the majority of the studied putative virulence factors in most recent isolates, that is, isolates with a higher time interacting with the host. Increases in hemolysin, melanin, aspartic-protease, and esterase production, as well as in fungal thermotolerance and resistance to nitrosative stress were observed. Oxidative stress response remained stable among the studied strains, whereas urease production decreased. As previously described in the literature, the oxidative stress tolerance seems to be stable along the infection and high urease levels are associated to cases with a better prognosis and spontaneous regression of lesions, which may explain the results observed in the present study. In conclusion, the *in vivo* enhancement of *S. brasiliensis* virulence previously observed by our group appears to occur in other patients with chronic sporotrichosis, and the immunosuppression caused by the HIV infection may decrease the time necessary for the selection of more virulent strains within the host. The increased expression of *S. brasiliensis* virulence factors also appears to alter the sporotrichosis course, yielding more refractory cases.

Keywords: Sporotrichosis; *Sporothrix brasiliensis*; Virulence factors; HIV.

Development Agency: Fundação Oswaldo Cruz (Fiocruz) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).