Zoonotic sporotrichosis in Brazil: An update

Sporotrichosis is a subcutaneous mycosis caused by the dimorphic fungus previously described as a single species, *Sporothrix schenckii*, now understood as a complex of different species of clinical interest. This mycosis is widely distributed all over the world, especially in tropical and temperate climates, and is considered the most prevalent subcutaneous mycosis in Latin America. Traditionally, this subcutaneous mycosis is known as “gardeners´disease”, usually associated with puncture injuries. However, the natural history of sporotrichosis has been changing gradually in frequency, mode of transmission, and demographic and geographic distributions. The zoonotic transmission has been sporadically associated with scratches or bites from animals in several regions of Brazil, but the role of felines in the transmission of the mycosis has gained attention in the southeast region of our country. The metropolitan region of Rio de Janeiro is an endemic area of zoonotic sporotrichosis transmitted by cats since 1998, occurring mainly in areas with underprivileged socioeconomic conditions and precarious health services. The individuals most frequently affected were housewives taking care of cats with sporotrichosis. In such epidemic peculiar aspects were reported. Clinically, it has been characterized by unusual clinical presentations, manifestations of hypersensitivity and an increasing number of patients coinfected with HIV. Spontaneous regression of the mycosis, as well chronic cases and recurrences were also observed, although it has been rarely reported in the literature. It was found that acute dacryocystitis (4 cases between 2008 and 2010) is a manifestation of sporotrichosis which evolves with complications (fistula and chronic dacryocystitis) requiring surgical repair. Sweet syndrome was observed in three patients until 2010 and should be incorporated as a manifestation of hypersensitivity of sporotrichosis, along with erythema nodosum and erythema multiforme. The 12 pregnant women with sporotrichosis between 2005 and 2010 presented a good evolution with local thermotherapy. In the clinical and therapeutic analysis of the 21 cases of sporotrichosis and HIV, the clinical forms varied with the immunological status of the patients, and a good therapeutic response was seen in 81% of the cases. The diagnostic investigation of systemic disease in immunosuppressed patients (CD4+ < 200 cells/µL) is required. In the historical series evaluated, with 48 patients with sporotrichosis and HIV, and 3,570 with sporotrichosis, it was seen that patients with HIV evolved with more disseminated pictures, hospitalization and death. Several factors, such as inoculums load, immune status of the host, virulence of the inoculated strain, and depth of traumatic inoculation may influence the different clinical forms of sporotrichosis.

 In the cats evolved in this endemia sporotrochosis usually range from an unique skin lesion that can progress to multiple skin lesions and fatal systemic involvement. Nodules and ulcers are the most frequent skin lesion. Extracutaneous signs, particularly respiratory manifestations and lesions of mucosa are also common.

The hospital database of patient records and the stock strains of the Laboratory of Mycology of Instituto de Pesquisa Clínica Evandro Chagas (IPEC) has been routinely evaluated. The gold standard for the diagnosis of sporotrichosis is culture; however, serologic, histopathologic and molecular approaches have been recently adopted for the diagnosis of this mycosis. Up to now, more than 250 *Sporothrix* spp were identified by phenotypic and genotypic identification. Also, classical laboratory tools have been applied for determination of some virulence factors in of some fungal isolates. *Sporothrix brasiliensis* is the main species identified, and was associated with unusual aspects and cases of hypersensitivity. Sporotrichosis caused by this species require a shorter time of itraconazole treatment (median 12 weeks) when compared to *S. schenckii* (median 24 weeks). The study of five isolates collected over five years in a patient with disseminated sporotrichosis demonstrated increased virulence of the isolate obtained after 11 years of infection (5 years of treatment at IPEC), when *Galleria mellonella* was used as an *in vivo* model, suggesting an adaptation of the fungus to the host within this period. Melanin production analysis showed that, besides the already known DHN melanin, the *S. brasiliensis* and *S. schenckii* are able to produce other two types of melanin, using L-DOPA or L-tyrosine as substrate. In addition, it was demonstrated that *S. globosa* is also able to produce pyomelanin using L-tyrosine as substrate.Urease production was also differentiated between *S. brasiliensis* and *S. schenckii*, with a higher expression of this enzyme by *S. brasiliensis*. Strains of *S. brasiliensis* isolated from patients with spontaneous regression of lesions produced large amounts of urease, and this factormight be related to the high number of spontaneous regression cases of this mycosis in Rio de Janeiro. In conclusion, sporotrichosis in Rio de Janeiro is related to the emergence of rare and novel aspects. On the same way, it has affected HIV-infected patients, with morbimortality, and should be incorporated as an opportunistic infection on its disseminated form. *S. brasiliensis*, the species involved in almost all cases of this region, in both human beings and cats, may have an increase in virulence over the years, favoring its survival and hindering the healing of the patient. However, it was not possible to correlate any specific virulence factor, thermotolerance or antigens of *Sporothrix* spp. with the clinical manifestations of sporotrichosis, suggesting that they are the result of a combination of factors involving the virulence of the fungus and host immunologic status.

 In other Brazilian cities, such as São Paulo, Rio Grande, and Pelotas, sporotrichosis outbreaks related to cat transmission are also being described, but in these locations, authorities were aware of the Rio de Janeiro sporotrichosis scenario and specific actions for disease control were adopted, restricting the number of cases.