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# Cutaneous disseminated sporotrichosis in immunocompetent patient: Case report and literature review

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ABSTRACT

Sporotrichosis is a global occurring implantation (subcutaneous) mycosis, caused by *Sporothrix* species, usually affecting the skin and the lymphatic vessels, from where it can disseminate. Nowadays, the vast majority of sporotrichosis infections in Brazil are caused by zoonotic transmission of *S. brasiliensis* which is the main etiologic agent. We report a cutaneous disseminated case of this disease, observed in an immunocompetent farmer living in southern Brazil, the *Sporothrix schenckii*-infection was successfully treated with itraconazole.

## 1. Introduction

Sporotrichosis is the most prevalent implantation mycosis in the world, considered a neglected endemic mycosis, with a global estimate of 40,000 new cases per year [1,2]. For more than a century, this disease was believed to be caused by a single species, *Sporothrix schenckii*. The disease can be caused by several species of *Sporothrix*, a thermodimorphic fungus. However, according to molecular phylogenetic methods, this fungus depicts a large genetic diversity with several sibling species that have different virulence profiles, mode of transmission, and clinical manifestations. In humans, all species causing humans infections are sensitive to standard therapy, including itraconazole, terbinafine and potassium iodine solution [3].

In the sapronotic route, the infection occurs by traumatic inoculation or inhalation of propagules from mycelial phase, by subproducts of plant origin. In this transmission route, the species most frequently involved are *Sporothrix schenckii* and *Sporothrix globosa* [3]. In Brazil, in the 1990s, a new and more virulent specie emerged, *Sporothrix brasiliensis*, with a zoonotic transmission route [3]. In this form of transmission, the infection occurs directly by the yeast phase of the fungus through traumatic inoculation, usually through a bite or scratch, or even contact with secretions of the infected cat (*Felis catus*), which have a high fungal load. This characteristic allows *Sporothrix brasiliensis* to have the potential to cause epidemics and to expand geographically [4].

Most patients present with the cutaneous form of sporotrichosis that include fixed cutaneous (25%) and lymphocutaneous (55%) involvement, but other systems can be affected [3]. Cutaneous Disseminated Sporotrichosis (CDS) is infrequently reported in immunocompetent patients, but occasionally in the immunosuppressed individuals, notably cat-transmitted infections among HIV-AIDS, uncontrolled diabetes, alcoholism, TNF-$^{\alpha}$ and steroid therapy, organophosphorus pesticide exposition, solid organ transplant and hematologic malignancies [5–7].

We report a case of an immunocompetent patient with CDS who had a favorable response to itraconazole.

## 2. Case

A 52-year-old male Caucasian farmer with a four-year history of various ulcerated nodules on the left hand after a minor occupational injury, which progressed subsequently like a wrapping around the arm.

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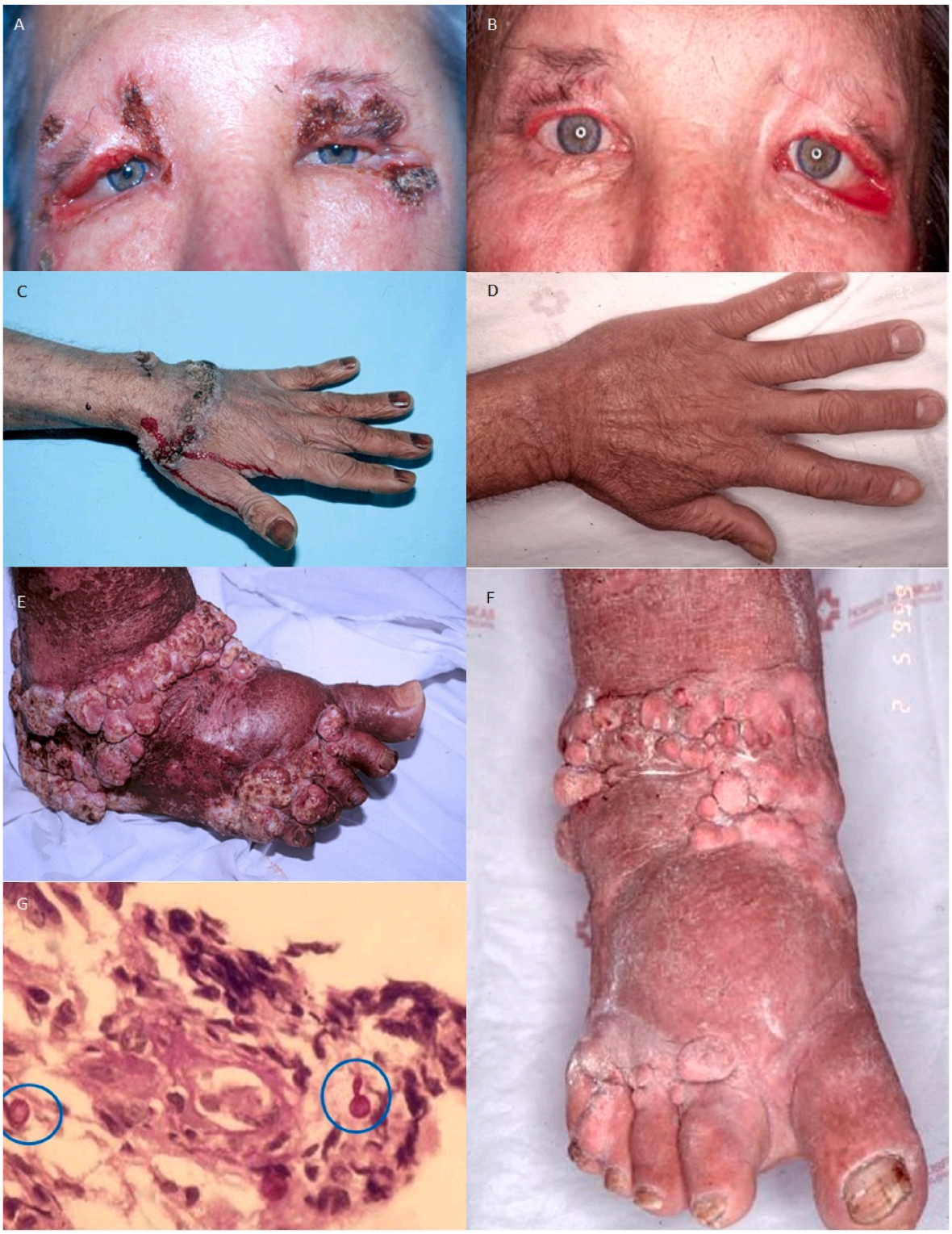


**Fig. 1.** Polymorphic cutaneous lesions caused by *Sporothrix schenckii*.

He denied alcohol intake and he had no diabetes history. At that time, the had not sought medical care. The patient presented multiple ulcerated lesions in the right hand, right forearm and conjunctival mucosa of both eyes as well as several nodular ulcerated, warty and crustose lesions on feet, distal legs (Fig. 1, panel A, C, E) and buttocks. The lesions were painful, with fetid secretion.

There were no significant biochemical or hematological abnormalities, except for leukocytosis. HIV-testing was negative. Histopathology of skin lesions revealed the presence of intense pseudoepitheliomatous hyperplasia and several micro-abscesses. Both skin and conjunctiva biopsies showed numerous ovoid to elongated yeast-like cells (Fig. 1, panel G), the culture yielded *Sporothrix* spp. colonies.

Molecular identification was performed by sequencing of internal transcribed spacer (ITS) of the ribosomal DNA and calmodulin (*CAL*). Obtained ITS and CAL sequences (GenBank accession numbers ITS, KX274433; CAL, KX274447) had 99–100% similarity with *Sporothrix*

**Table 1**
Summary of reports about CDS in immunocompetent patients.

| Report | Patient's Characteristics | Risk Factors and/or Inoculation entry | Clinical Manifestations | Onset of the disease | Diagnostic Method | Molecular identification | Treatment |
|---|---|---|---|---|---|---|---|
| Seow et al., 2022 [10] | Male, 50 years old, Malasian | Gardening and contact with feces from cats | Multiple nodules and fever | 1 month | Direct exam/ Histopathology + culture | Not performed | Amphotericin B deoxycholate 0.7 mg/kg/day/ Itraconazole 200mg twice daily |
| Garcia et al., 2021 [11] | Female, 37 years old, USA | Gardening | Multiple nodules and arthralgias | 2 months | Culture | Not performed | Itraconazole 200mg twice daily |
| Martínez-Herrera et al., 2021 [12] | Male, 21 years old, Mexican | None | Multiple ulcerated nodules | 2 years | Culture | *Sporothrix schenkii* | Potassium iodide 3.5 g day |
| Valeriano et al., 2020 [19] | Female, 26 years old, Brazilian<br>Female, 46 years old, Brazilian | Cat bites<br>Cat scratches | Multiple nodules<br>Multiple ulcerated nodules | 40 days<br>2 months | Direct exam/ Histopathology + culture<br>Direct exam/ Histopathology + culture | *Sporothrix brasiliensis*<br>*Sporothrix brasiliensis* | Itraconazole 200mg day<br>Itraconazole 100mg day |
| Medeiros et al., 2016 [14] | Female, 59-year-old, Brazilian | Contact with cats | Multiple nodules, conjunctivitis | 2.5 months | Culture | Not performed | Itraconazole 200mg day |
| Yap, 2011 [15] | Female, 70 years old, Malasian | Gardener and 2 pets | Papular lesions on lower limbs | 6 months | Direct exam/ Histopathology + culture | Nor performed | Itraconazole 400mg day |
| Romero-Cabello et al., 2011 [16] | Male, 36 years old, Mexican | Long term farmer | Multiple ulcerated nodules on skin of dorsum and anterior abdomen | 3 years | Culture | *Sporothrix schenkii* | Itraconazole + Potassium iodide + Amphotericin B 0.5 mg/kg/day |
| Cullen et al., 1992 [17] | Male ,71 years old, USA | None | Multiple ulcerated nodules and fever | 3 months | Culture | Not performed | Ketoconazole 200mg day |
| Boehm et al., 1982 [18] | Male, 50 years old, USA | None | Multiple ulcerated nodules on skin of forearm and lung involvement | 5 months | Direct exam/ Histopathology + culture | Not performed | Amphotericin B |

*schenckii* when pairwise aligned to strain data in the ISHAM-ITS and NCBI GenBank databases.

Antifungal susceptibility testing was performed by broth microdilution method according to the CLSI protocol M38-A2 [8]. The *S. schenckii* isolate showed minimal inhibitory concentration (MIC) of 0.5 μg/mL for itraconazole. patient was treated with itraconazole, 400mg daily for six months. All skin lesions and mucous membranes healed, but scars remained post-treatment (Fig. 1, panel B, D, F), the patient had bilateral ectropion and lymphedema as sequelae. Ectropion was treated surgically. After two years of follow up, the patient showed no clinical signs of relapse.

Legend: Chronic ulcerative and verrucous palpebral, periorbital and conjunctival lesions (A) with scaring and ectropium after itraconazole therapy (B). Hyperkeratotic nodule ulcerative hemorragic lesions of the hand, before (C) and after itraconazole therapy (D). Nodular and tumorous lesions associated to chronic lymphedema of the right foot, before (E) and after six months of continuous itraconazole treatment, showing fibrotic nodules and residual lymphedema (F). Skin biopsy of the foot with yeast-like cells, circled (G). PAS 600 × .

## 3. Discussion

Sporotrichosis has different clinical forms, which can be divided in two categories, cutaneous and extracutaneous [5]. The CDS form corresponds to 1–5% of cases, characterized by multiple skin lesions, generally in immunocompromised patients, mostly in HIV/AIDS and in immunosuppression conditions, such chronic alcoholism, diabetes mellitus, hematological malignancies [6,7,9]. Cutaneous disseminated sporotrichosis in immunocompetent hosts is a rare condition with a few anecdotal cases reported globally (Table 1) [10–18]. For analysis, cases in which patients had some predisposing factors like diabetes mellitus and alcoholism, were excluded.

Among the 10 published cases of CDS in immunocompetent hosts included in the review, half of them were female and half were male, average age of 46.6 years old (range 21–71 years old), three patients were from Brazil, three from United States of America (USA), two from Mexico and two cases from Malaysia. In all cases, patients had multiple nodular lesions, which could be ulcerated or accompanied by fever. It is interesting that in the cases that were described in Brazil, they occurred from 2016 onwards and possibly the transmission occurred through a zoonotic route, since all the patients claimed to have had contact with cats, and in this route the etiological agent involved is *Sporothrix brasiliensis*, which has caused outbreaks in the country and it's a more virulent specie, associated with atypical manifestations [3,4]. In the other cases, the transmission route was possibly sapronotic and in some cases molecular identification was performed and *Sporothrix schenkii* was the etiological agent. It is important to note that the mean time of onset of the disease when appropriate diagnosis was 251 days (range 30 – 1095 days), probably due to the rare condition and difficulty in the differential diagnosis with other diseases. The gold standard for the diagnosis of sporotrichosis remains the fungal culture which can be time consuming [3].

Despite the antifungal *in vitro* susceptibility of *Sporothrix*, there are no breakpoints or epidemiological cut-offs values for *Sporothrix* species to define susceptible/non-susceptible or wild-type/non-wild-type isolates. Therefore, the results should be interpreted with caution since these findings are not observed *in vivo*, including animal models and human patients [2–5]. Itraconazole, amphotericin B and the combination of itraconazole and terbinafine are the most useful therapy for patients presenting CDS.

I summary, CDS it is an uncommon clinical form, even rarer in immunocompetent hosts. Due to the increased incidence of the disease, especially in hyperendemic regions, it is necessary to maintain a high degree of suspicion in the presence of similar lesions as reported here, and conduct appropriate mycological cultures to diagnose sporotrichosis, in order to initiate therapy early, reducing morbidity and mortality and reduce duration of treatment. Although amphotericin B has been used in CDS, itraconazole is a safe and effective therapy as showed

in the current case as well as in another's reports [11,14,15,19].

## Declaration of competing interest

None of the authors declared a conflict of interest.

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