

# Sporotrichosis with cutaneous and pulmonary involvement in a patient with diabetes

Esporotricose com acometimento cutâneo e pulmonar em paciente diabético



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## ABSTRACT

Sporotrichosis is an endemic, fungal, zoonotic infection that is a notifiable disease in Brazil. It can occur in an atypical and serious manner, such as in its disseminated or systemic form, easily confused with other infectious diseases. Herein, we present a case of a patient with diabetes who, in addition to skin ulcers and cold abscesses on the arms, developed consumptive febrile syndrome and respiratory symptoms attributed exclusively to systemic sporotrichosis, after excluding other differential diagnoses. The treatment comprised amphotericin followed by itraconazole; a good clinical and radiological response was observed. This form of presentation is rare and mimics pulmonary tuberculosis and other systemic mycoses. The initial suspicion of the disease is as essential as is adequate treatment with antifungal drugs.

**Headings:** Skin Ulcer; Sporotrichosis; Invasive Fungal Infections; Diabetes Mellitus. Case Report.

## RESUMO

A esporotricose é uma doença fúngica endêmica de transmissão zoonótica e de notificação compulsória no Brasil que pode cursar de maneira atípica e grave, como por exemplo na sua forma disseminada ou sistêmica, facilmente confundida com outras doenças infecciosas. Apresentamos o caso de um paciente diabético que, além de úlceras cutâneas e abscessos frios em membros superiores, evoluiu com síndrome febril consumptiva e sintomas respiratórios atribuídos exclusivamente à esporotricose sistêmica, depois de excluídos demais diagnósticos diferenciais. O tratamento foi realizado com anfotericina seguida de itraconazol, com boa resposta clínica e radiológica. Esta forma de apresentação é pouco comum e pode mimetizar a tuberculose pulmonar e outras micoses sistêmicas, sendo sua suspeição inicial tão essencial quanto o tratamento adequado com antifúngicos.

**Descritores:** Úlcera cutânea; Esporotricose; Infecções Fúngicas Invasivas; Diabetes Mellitus; Relato de Caso.

## INTRODUCTION

Sporotrichosis is caused by a thermomorphous fungus of the genus *Sporothrix* spp (most commonly the *schenckii* species), and is an infection classically related to contact with domestic animals, specifically cats, or certain activities such as gardening<sup>1,2</sup>. Most cases are observed in the tropical and subtropical regions around the world, whereas the disease is considered hyperendemic in Brazil, where another species, *Sporothrix brasiliensis*, accounts for approximately 90% of cases in the south and southeast of the country<sup>3</sup>.

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The main route of transmission is inoculation of the pathogen into the skin, causing the presentation most commonly observed in clinical practice, which is the lymphocutaneous form<sup>2</sup>. In addition to potential hematogenous dissemination, there is also the possibility of systemic dissemination from aerosolization and direct inhalation of fungal particles that initially cause pulmonary granulomatous reactions similar to tuberculosis<sup>2</sup>. Other reports of disseminated sporotrichosis include osteoarticular involvement, central nervous system infection, and ocular lesions<sup>4</sup>.

In this report, we present the case of a patient with diabetes with skin ulcers and cold abscesses associated with pulmonary involvement, presumptively attributed to sporotrichosis, which was challenging due to the clinical presentation and differential diagnoses.

## CASE REPORT

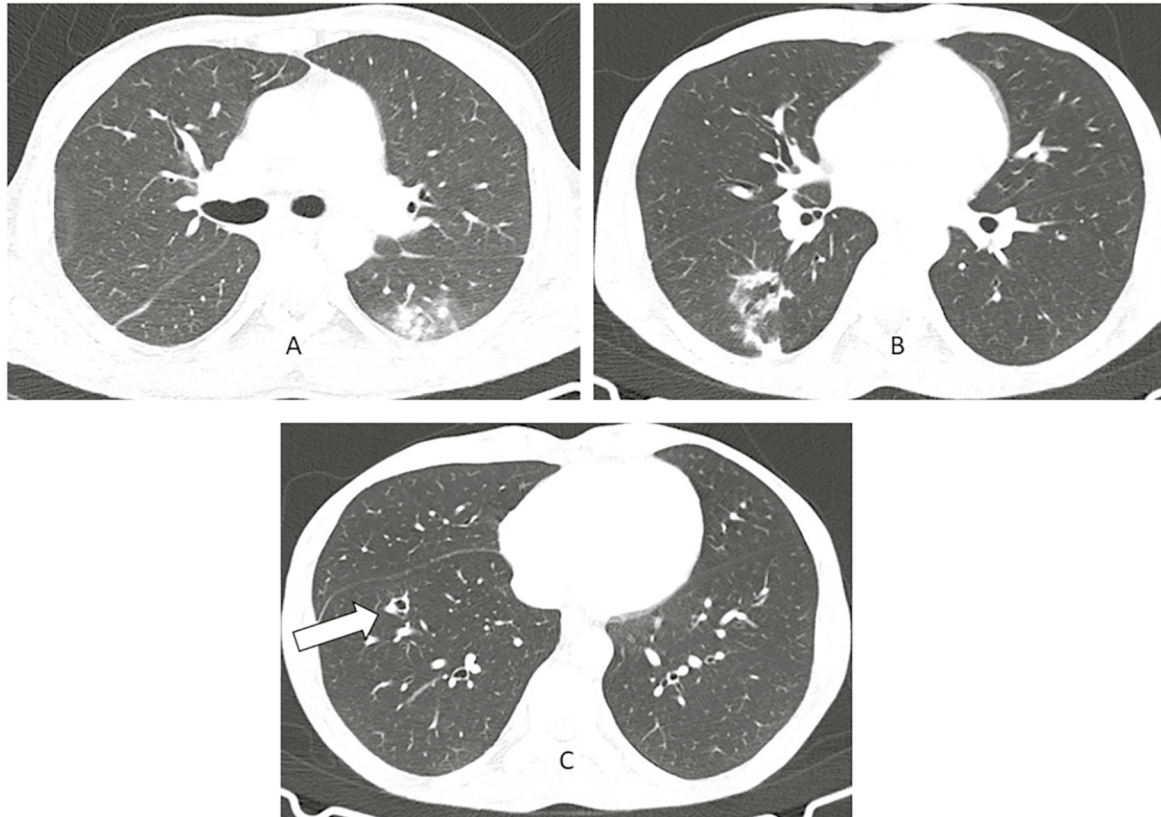
A 35-year-old man was admitted to the emergency department with complaints of unexplained weight loss of 14 kg over the past 4 months as well as intermittent irregular fever. He also reported the appearance of subcutaneous nodules on his left arm during the same period, which were initially painful but gradually ulcerated with spontaneous drainage of pus. He knew he had type 1 diabetes mellitus for the past 8 years and used NPH insulin 10 IU regularly in the morning. He consumed hard liquor four times a day and mentioned he had previously used crack and marijuana, without clarifying whether or how long he had been abstinent. He also reported having gotten a tattoo on his back approximately 3 years ago. He was born in Bahia and lived in Guarulhos, where he worked as a bricklayer's assistant (but denied trauma to the skin) and did not live with pets. More recently, he began to have nonproductive cough and sweats without dyspnea, as well as diarrhea and hematochezia. He was admitted to another service for 9 days where he received amoxicillin and azithromycin for pneumonia and, on discharge, he was referred to primary care for investigation of tuberculosis, which he did not follow up.

Upon physical examination, he had seven ulcers on his left arm (Figures 1A and 1B) and areas of fluctuation (masses with poorly defined borders and a soft consistency) on the right arm, which were not very painful on palpation and presented with discreet local hyperemia (Figure 1C). Laboratory blood tests revealed anemia and absence of leukocytosis; moreover there was an increase in the levels of canalicular enzymes, but no increase in pancreatic enzymes was observed. Glycated hemoglobin



**Figure 1.** (A) Ulcerated lesions on the posterior surface of the left arm with well-defined borders, hyperchromic margins, and granulomatous and hypertrophic background, with the largest lesion being 5-cm wide; (B) skin ulcer with subcutaneous tissue and tendon exposure; (C) masses with undefined limits and soft consistency in the deltoid region and forearm of the right arm, with the largest one being 9-cm wide (arrows).

was 12.2% (reference value: 4.1%–6%). Serologies were also requested for HIV; hepatitis B and C; and syphilis, with all results being negative. Computed tomography (CT) of the chest was performed to examine the lungs, revealing scattered centrilobular opacities in both lower lobes, some in clusters forming a “tree-in-bud” pattern (Figures 2A and 2B), and a single cavitary nodular opacity with a diameter of approximately 1 cm in the anterior basal segment of the right lower lobe (Figure 2C). CT scans of the abdomen and pelvis showed signs of chronic pancreatitis and lymph node enlargement in the periaortic and interaortocaval retroperitoneum measuring 11 mm in its shortest axis. Soft tissue ultrasound of the right arm showed small collections measuring  $5.1 \times 4.8 \times 0.7 \text{ cm}^3$  on the extensor surface of the proximal forearm,  $5.1 \times 4.8 \times 1.8 \text{ cm}^3$  on the lateral aspect of the arm, and  $2.9 \times 3.0 \times 0.6 \text{ cm}^3$  in the deltoid region, while the puncture of a larger abscess in the left arm allowed draining brownish pus that was sent for bacterioscopy (Gram stain), culture of aerobic bacteria, direct mycological examination (PAS and Grocott stains and testing for acid-fast bacilli) and



**Figure 2.** Computerized tomography scans showing scattered centrilobular opacities in both lower lobes, with some grouped together forming a “tree-in-bud” pattern (A and B), and a single isolated nodular opacity with a diameter of approximately 1 cm and a cavitary appearance (arrow in C) in the anterior basal segment of the right lower lobe.

polymerase chain reaction (PCR) for the detection of DNA of *Mycobacterium tuberculosis*, all of them were negative. The histological study of one of the ulcerated skin lesions revealed a diffuse lymphomonocytic infiltrate overlaid by a suppurative inflammatory process with reactional angiogenesis. After 17 days, the growth of filamentous fungi was observed in the pus samples cultured on Sabouraud agar, which were compatible with *Sporothrix* spp, but the species was not identified. Other results of interest were as follows: negative serum PCR for *Histoplasma* sp and negative serology for *Paracoccidioides*, negative direct examinations (and cultures) of mycobacteria and fungi in the sputum, and negative interferon gamma release assay (IGRA).

Specific treatment was then initiated with amphotericin B deoxycholate 50 mg/day for 10 days, followed by its lipid formulation 5 mg/kg/day for another 10 days owing to hydroelectrolytic issues and renal dysfunction. Given the significant improvement in the systemic condition and regression of the skin lesions, the antifungal treatment was switched to itraconazole at a dose of 400 mg a day,

and the acute renal failure was reversed. New CT scans revealed nearly complete resolution of the pulmonary opacities and a reduction in the size of the retroperitoneal lymph nodes, but the patient escaped from the hospital after a stay of 1 month.

## DISCUSSION

Most cases of sporotrichosis detected in humans in Brazil are due to contact with cats<sup>5</sup>, an epidemiological link that is present in >90% of cases in the metropolitan region of São Paulo<sup>6,7</sup>. There has been a steep increase in the number of cases (more than 50% annually) over the past decade<sup>7</sup>, and there is also a tendency for more diagnoses to be made during the coldest and driest periods of the year<sup>6</sup>, remembering that this data may be underestimated do to the fact that notification of the disease became mandatory on a national level only from 2020 onwards<sup>5</sup>.

The most recent clinical classification of sporotrichosis comprises the cutaneous (which includes lymphocutaneous), mucosal, osteoarticular, systemic, immunoreactive, and mixed localized forms<sup>8</sup>. These

presentations are determined based on various factors, including the host's immune status, the extent of fungal inoculation, thermotolerance, and other virulence factors of the species<sup>9,10</sup>. The systemic forms are associated with higher death rates and the predisposing factors include malnutrition; alcoholism; use of immunobiologicals; and comorbidity with AIDS, diabetes, hematological tumors, and organ transplantation<sup>11</sup>. A recent study conducted in Brazil evaluated retrospectively 80 patients with disseminated sporotrichosis and found that a history of diabetes was present in 17% of cases<sup>12</sup>, while alcoholism was observed in 22% of patients and appeared to be more associated with the formation of collections (cold abscesses)<sup>8</sup>.

The cutaneous form of sporotrichosis usually affects the parts of the body that are most exposed to trauma (face, extremities of arms and legs) and then spreads through the regional lymphatic chains in an upward direction<sup>8</sup>, forming new nodules and ulcers, as depicted in Figure 1. Pulmonary involvement can be explained either by hematogenous dissemination (more common in immunosuppressed individuals) or by direct inhalation of the fungus, which leads to the primary pulmonary form<sup>13</sup>. The most common radiological manifestations are reticulonodular infiltrates with the formation of fibrosis and cavitary nodules, which is partly consistent with the CT findings in our case, with the exception of the nodules being preferentially located in the lung apices<sup>13</sup>. However, this presentation is very similar to other diseases that are the main differential diagnoses of sporotrichosis: the initial hypotheses were mainly tuberculosis (or even a nontuberculous mycobacteriosis) and deep mycoses such as histoplasmosis and paracoccidioidomycosis. In this context, some vasculitis, autoimmune diseases, lymphoproliferative disorders with atypical presentations, and tumors are also worth mentioning<sup>14</sup>.

Histopathological and direct mycological examinations usually offer little help for the diagnosis owing to the scarcity of fungal elements in the tissue<sup>5</sup>. The ideal diagnostic method is isolation and identification of *Sporothrix* spp in cultures obtained from purulent secretions and tissue samples (e.g., skin or lymph node aspirate) plated on Sabouraud medium<sup>8,15</sup>. Fungal culture in sputum is positive in up to 80% of cases, but repeated samples or bronchoalveolar lavage are necessary<sup>14</sup>, which, unfortunately, was not performed in this case. In a series of 5,264 Brazilian patients with sporotrichosis,

pulmonary involvement was present in only 17 of them<sup>14</sup>. The disease was mostly diagnosed by the identification of *S. brasiliensis* in sputum culture. Notably, in 42% of these cases there were no imaging changes in the lungs, and in 21% the images were cavitary<sup>14</sup>. Molecular methods (available in commercial kits) can also be used to detect the fungus<sup>8</sup> in routine laboratory diagnosis in clinical samples, to define the species by genetic sequencing followed by phylogenetic analysis, and in ecological investigations with the aim of detecting *Sporothrix* spp. in environmental samples<sup>5,8</sup>. *S. brasiliensis* causes more atypical forms in animal models, and therefore, there is a tendency to replicate this observation in humans, which is what happened in all the unusual forms of sporotrichosis in 1,563 patients from a study conducted in Rio de Janeiro, although only four were of the disseminated form<sup>10</sup>.

The recommended treatment for cutaneous forms is based on the use of itraconazole, with other options being potassium iodide; terbinafine; and auxiliary therapies such as thermotherapy or cryosurgery<sup>8</sup>. In case of systemic presentation, amphotericin is an option for more severe forms of disseminated sporotrichosis (like in the present case) or when oral treatment is not possible<sup>8</sup>. There is no clear consensus on the dose and duration of treatment for pulmonary involvement but early replacement of amphotericin with itraconazole is recommended, with the aim of achieving a prolonged total period of 6 to 12 months of treatment<sup>16</sup>. Specific serology for the diagnosis of sporotrichosis is not an option available in routine care in Brazil, but it can be useful for therapeutic monitoring of the infection, helping to indicate failure, relapse, or discontinuation of treatment<sup>13</sup>. The need for surgical drainage of an abscess is not uncommon, given the low local penetration of the drugs<sup>17</sup>. Some authors advocate surgical lung resection and adjuvant therapy before or after surgery in advanced cavitary disease<sup>14,18</sup>, but these options were deemed dispensable given the small size of the cavity and the good progress observed in the first month of treatment reported here.

## CONCLUSION

This case report is an example of an unusual presentation of sporotrichosis in a diabetic and alcoholic patient, mimicking other more prevalent diseases, specifically tuberculosis. Although pulmonary involvement was not proven with certainty, the radiological (and clinical) response observed reinforced this presumptive diagnosis.



*"This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies. This Open Access article is distributed under the terms of the Creative Commons Attribution License (CC-BY), which allows immediate and free access to the work and permits users to read, download, copy, distribute, print, search, link and crawl it for indexing, or use it for any other lawful purpose without asking prior permission from the publisher or the author, provided the original work and authorship are properly cited."*

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