CASE REPORT

Cutaneous Disseminated Zoonotic Sporotrichosis in Immunocompetent Person

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ABSTRACT

A subacute to chronic fungal illness, sporotrichosis is brought on by the dimorphic species *Sporothrix*. A growing number of cases involve infected wounds exposed to the spore, leading to persistent ulcers that are frequently connected to regional lymphadenopathy. The disseminated form always complicates the infection, but it is rare in immunocompetent persons. Zoonotic transmission of sporotrichosis is on the rise. In this report, we present a case of cutaneous disseminated sporotrichosis in an immunocompetent individual who contracted the infection from an infected cat. The patient exhibited numerous nodules on the hands and lower limbs for four weeks, with an absence of associated symptoms. The diagnosis was confirmed through culture methods and matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) systems and treated with 10 days of intravenous amphotericin B and 12 months of oral itraconazole 200 mg BD. We also emphasized the importance of molecular techniques in accurate identification.
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INTRODUCTION

The main cause of sporotrichosis is a thermally dimorphic fungus called *Sporothrix schenckii*, commonly found in soil and decomposing plant matter. Activities such as landscaping, rose gardening, and other tasks involving the inoculation of soil through the skin are linked to the development of sporotrichosis. Cats are considered the primary reservoir hosts and can harbor and shed the fungus on their skin and claws, potentially transmitting the infection (1). While the infection usually affects the skin and subcutaneous tissues, it can occasionally spread to other areas, especially in immunocompromised individuals. Rarely, it can spread hematogenously, resulting in disseminated cutaneous sporotrichosis (1). *S. schenckii* is present globally, thriving in climates ranging from temperate to tropical regions with focal areas of hyperendemicity. Sporotrichosis predominantly affects individuals between 31 and 60 years of age (1).

CASE REPORT

A female patient in early adolescent age, not on any steroid therapy or prolonged medication previously, presented to the Dermatology Unit, reporting alleged cat scratches attributed to contact with her cat over the past month. Initially, a lesion appeared on the dorsum of her left hand, persisting for two weeks without responding to the initial medication prescribed by her own general practitioner. Itraconazole 200 mg BD was then prescribed for two weeks, but unfortunately, the condition deteriorated leading to the development of painful and pruritic erythematous nodular lesions on her limbs and developed fever during admission. Prior to this, the patient did not exhibit typical symptoms of immunosuppression, such as recurrent or severe infections, persistent fatigue, unexplained weight loss, frequent respiratory infections, skin lesions or infections, loss of appetite, or delayed wound healing. Further history examination upon admission revealed that the patient possessed seven cats, whereby one of them succumbed to sporotrichosis a month prior to the onset of the lesions.

Upon examination, the dermatologist observed an ulcerated plaque measuring 3cmx2cm on the left dorsum of the hand (Figure 1a). In addition to an erythematous nodular lesion near the wrist measuring 2cmx1cm (Figure 1b). Panniculitis of the bilateral lower limbs (Figure 1c) was also noted. No lymphadenopathy is palpable, and examinations of other body systems are

unremarkable. Vital signs were within normal limits.

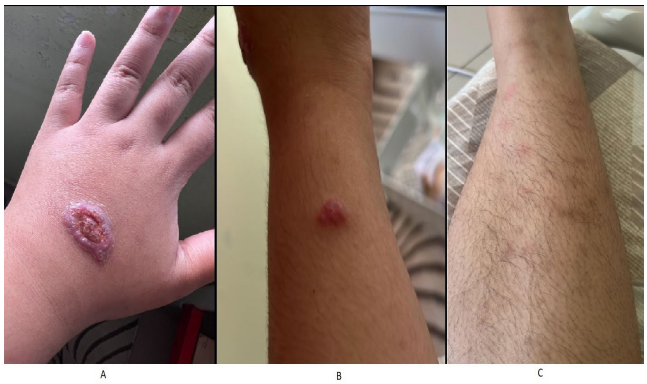

Figure 1: Clinical presentation. An ulcerated plaque measuring 3cmx2cm on the left dorsum of the hand (A). An erythematous nodular lesion near the wrist measuring 2cmx1cm (B). Panniculitis at lower limb (C).

Laboratory investigations revealed an elevated erythrocyte sedimentation rate (ESR) of 35 ml/hr, mild normochromic normocytic anaemia, and mild thrombocytosis. Coagulation tests within normal limits. Given the patient's medical history and clinical presentation, a provisional diagnosis was formulated to investigate disseminated sporotrichosis, with a differential diagnosis including Subacute panniculitis-like T-cell lymphoma and erythema nodosum leprae. Empirical treatment with intravenous amphotericin B and oral itraconazole (200 mg BD) was initiated.

A skin biopsy of the lesion was sent for histopathological examination and cultures. The histopathological assessment revealed necrotizing granulomatous inflammation (Figure 2). Despite using Periodic Acid Schiff (PAS) and Gomori-methenamine silver stains, no fungal bodies were identified. Cultures from tissue specimens on Potato dextrose agar at 30°C yielded black fungal colonies, characterized by a moist, wrinkled appearance often darkening to salt and peppery brown or black, with a narrow white border (Figure 3). Microscopic examination of the colonies with lactophenol cotton blue preparation demonstrated septate hyphae with conidiophores and numerous microconidia, some arranged in clusters resembling a daisy flower—features consistent with *Sporothrix* (Figure 4). Through the use of matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) systems, MALDI Biotyper (Bruker Daltonics GmbH, Bremen, Germany) the species identity of *Sporothrix schenckii* was verified.

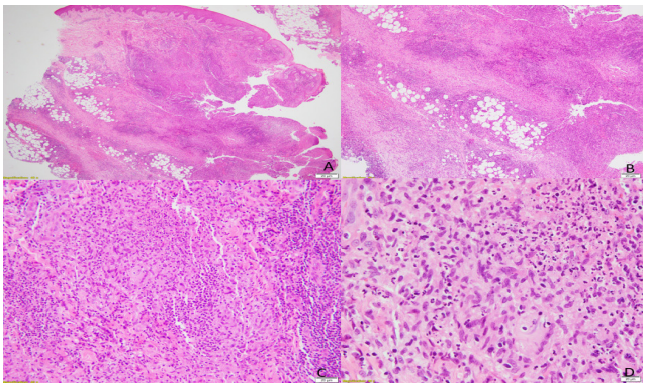

Figure 2: Low power magnification of hematoxylin and eosin stained of skin biopsy shows epidermis, dermis, and subcutaneous layer. The underlying dermis area shows necrotizing granulomatous inflammation with areas of necrosis seen (H&E, 20x and 40x) (A, B). On high power magnification, aggregates of epithelioid histiocytes and neutrophils observed forming necrotizing granulomatous inflammation admixed with lymphocytes, eosinophils, and plasma cells (H&E, 200x and 400x) (C, D).

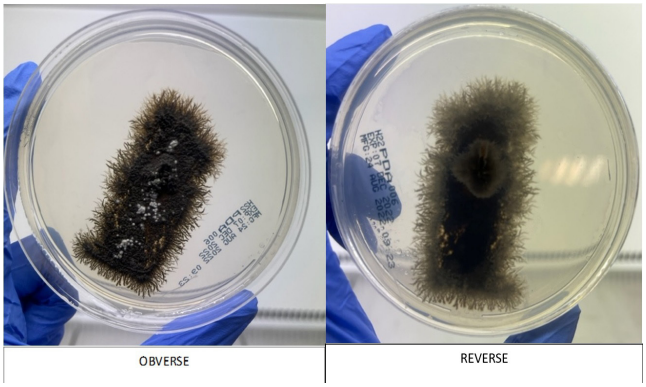

Figure 3: Mold phase on Potato dextrose agar (PDA) at 30°C. The colony is wrinkled, appears black with a narrow white border on both obverse and reverse of the plate.

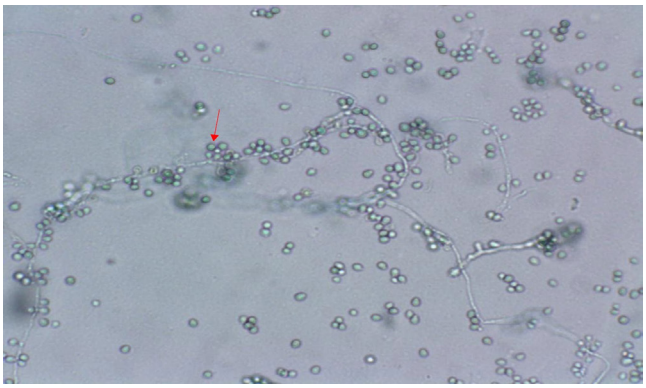

Figure 4: *Sporothrix schenckii* in mold phase showing conidiophores and clustering of microconidia, forming daisylike appearance (red arrow) in Lactophenol cotton blue.

Skin biopsy cultures for Mycobacterium tuberculosis were negative, and latent TB quantiferon was non-reactive. Blood cultures for aerobes, anaerobes, and fungi showed no growth. Additionally, tests for Hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab), and human immunodeficiency virus (HIV) were non-reactive. Abdominal ultrasound revealed no intraabdominal collection.

While hospitalized, the patient developed hypokalemia after ten days of receiving intravenous amphotericin B. Consequently, the intravenous amphotericin B was discontinued, and the treatment protocol was transitioned to oral terbinafine and itraconazole, effectively addressing the hypokalemia concern. Subsequently, the patient recovered after completing 12 months of treatment.

DISCUSSION

Transmission of sporotrichosis related to felines is a significant concern in the context of zoonotic diseases. There are six distinct phylogenetic species associated with sporotrichosis, each concentrated in different geographic regions. *Sporothrix schenckii* is a prevalent human pathogen worldwide, whereas *Sporothrix brasiliensis* is recognized for its significant virulence, notably linked to a major zoonotic outbreak involving cats in Rio de Janeiro. *Sporothrix globosa* is found globally but causes fewer infections. *Sporothrix mexicana* is prevalent in Mexico and other Latin American countries. *Sporothrix luriei* and *Sporothrix pallida* are less frequently responsible for human infections (1).

Diagnosing sporotrichosis poses challenges due to its variable clinical presentation, limited presence of causative organisms in biopsy specimens, and slow growth rate (1). While most cases involve skin or subcutaneous tissue infections, cutaneous disseminated sporotrichosis, which primarily affects immunocompromised individuals, is rare (1). In our patient's case, the presence of an infected cat was significant. Sporotrichosis, particularly when presenting atypically or lacking characteristic nodular lymphangitis lesions, may evade diagnosis. The lesion initially appeared as a single wound in this patient, evolving into a granulomatous plaque rather than the typical nodular lymphangitis, leading to delayed suspicion of sporotrichosis. Notably, the disease progressed into a cutaneous disseminated form without underlying immunosuppression.

Definitive diagnosis relies on fungal culture of tissue specimens, even culture taking a few days to grow (1). Successful isolation depends on a proper sample collection (2). The histopathologic appearance, characterized by a mixed granulomatous and pyogenic process, is supportive but not diagnostic, with yeast forms visualized in only a small percentage of cases (1). This is due to low fungal burden in humans compared to cats (2). In situations where cultures are negative, other alternative methods such as MALDI-TOF MS and molecular identification of *S. schenckii* become crucial for timely diagnosis (1).

Identification of species within the genus *Sporothrix* has become crucial due to the variations in pathogenicity, virulence, geographic distribution, and antifungal susceptibility profiles displayed by the various species (2). The MALDI-TOF MS is an identification tool that analyzes the expression of intrinsic proteins using mass spectrometry within a minute. This mass spectrum, which is species-specific for many microorganisms, represents a 'molecular fingerprint' and is compared to a database in the filamentous fungi library to identify the unknown organism. A score value between 2.00 and 3.00 indicates a high-confidence identification up to the species level. In this case, species identification of *Sporothrix schenckii* was confirmed by the MALDI-TOF MS system, MALDI Biotyper® (Bruker Daltonics GmbH, Bremen, Germany), as accurate identification is important. Relying solely on phenotypic characteristics for identification can be inconclusive at times (1).

Olievera et al. demonstrated that MALDI-TOF MS can distinguish *Sporothrix* species with 100% accuracy in clinical samples, providing a reliable, fast, and streamlined method for clinical mycology labs (1). It offers excellent sensitivity, high throughput, simple operation, and low cost, despite the high expense of the spectrometer (3). The identification results from MALDI-TOF MS matched 100% with those from calmodulin gene sequencing (2). This technology represents a significant advancement in identifying human fungal pathogens, revolutionizing diagnostic mycology workflows, and potentially reshaping molecular diagnostics and patient care (4). However, it is crucial to ensure credibility in diagnosing fungi using MALDI-TOF, especially considering the inherent challenges in analyzing mold compared to yeast forms. Adequate training and practice are essential to effectively utilize this technology.

The treatment protocol for disseminated sporotrichosis typically consists of a two-week regimen of intravenous amphotericin B, followed by approximately 12 months of oral itraconazole. Amphotericin B is recognized as an effective and well-tolerated therapy for severe sporotrichosis, especially when diagnosis and treatment begin promptly. Despite the lack of clear therapeutic response guidelines, it is generally recommended to continue treatment until achieving a favorable response. In this case, amphotericin was stopped due to hypokalemia, a known side effect. Studies show that combining itraconazole with terbinafine is more effective than either drug alone for nasal sporotrichosis, with excellent outcomes and no complications over 8 months (5). For our patient, 12 months of combination treatment

effectively managed disseminated sporotrichosis.

To address the limited awareness of this fungal pathogen, particularly in regions with low cat-to-human transmitted sporotrichosis, a One Health approach should be undertaken. This approach aims to improve health outcomes by considering the connections between humans, animals, plants, and the environment. It requires collaboration among veterinarians, physicians, epidemiologists, microbiologists, and environmental scientists to control outbreaks among high-risk workers and epidemics linked to common infection sources (1).

CONCLUSION

Early recognition and prompt treatment are crucial for improving outcomes in disseminated cutaneous sporotrichosis. Using advanced diagnostic technologies like MALDI-TOF MS and molecular methods along with traditional methods increases accuracy and speeds up treatment. A One Health approach is essential to manage environmental factors contributing to zoonotic disease transmission. Recent studies highlight the efficacy of combination therapy with oral terbinafine and itraconazole for dermatophytosis and nasal sporotrichosis, but treatment responses vary across fungal infections. Further research is needed to optimize treatment regimens and deepen our understanding of sporotrichosis management.

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