



Case report

A rare case of disseminated *Sporothrix schenckii* with bone marrow involvement in a patient with idiopathic CD4 lymphocytopenia



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ABSTRACT

Sporothrix schenckii is a pathogen with a predilection for dissemination in immunocompromised individuals, often with HIV.

We report a case of disseminated sporotrichosis in an unfortunate 25 year old male (without HIV) who was originally treated for presumed pneumonia. The patient continued to worsen clinically and further work-up eventually revealed *Sporothrix schenckii* species with involvement of multiple organs including the skin, heart, lungs and bone marrow. Despite treatment with multiple antibacterials and antifungals, he ultimately passed away.

This case illustrates the aggressive nature of this disease along with the importance of early/proper diagnosis and treatment.

Introduction

Sporotrichosis is a subacute to chronic infection [1], which involves the cutaneous and subcutaneous tissues, with dissemination occurring primarily in immunocompromised patients. It is caused by *Sporothrix schenckii*, a dimorphic fungus. It is associated with activities involving mucosal penetration, such as rose gardening or farming with traumatic injury [1]. It is found worldwide and outbreaks have been reported in countries with temperate or tropical climates such as Peru, South Africa, and Brazil [2]. Lymphocutaneous sporotrichosis is the most common form (observed in up to 75% of cases) [1], and usually involves papule development at the site of infection, followed by ulceration of the lesion and other lesions developing along the lymphatic channels proximal to the lesion. A fixed localized skin form can occur in 20% of cases [1]. Other forms of sporotrichosis include pulmonary, osteoarticular, meningeal, and in very rare cases (less than 5%), disseminated sporotrichosis can occur [1], which is characterized by disseminated cutaneous lesions and involvement of multiple visceral organs. Disseminated sporotrichosis, along with other forms of sporotrichosis with a predilection for a specific organ is rare in immunocompetent patients and is usually associated with immunosuppression such as HIV, diabetes, and alcoholism; very few cases have been documented in immunocompetent patients.

Case presentation

A 25 year old african american male with a history of asthma, hypertension and CD4 T lymphocyte deficiency presented to an outside facility with complaints of shortness of breath and musculoskeletal chest pain. He initially was found to have a pneumonia due to *Pseudomonas aeruginosa* and received a complete course of meropenem. His dyspnea did not resolve, for which he returned to the outside facility. He underwent a VATS (video assisted thoracoscopic surgery) lung biopsy to get a definitive diagnosis. His lung biopsy showed a necrotizing granuloma and tissue cultures isolated yeast. He was treated with 2 weeks of fluconazole and was started on a steroid taper for presumed sarcoidosis. Unfortunately, he returned again to the outside facility shortly thereafter with worsening dyspnea, productive yellow cough, vision changes, night sweats, 30 pound weight loss, and fevers as high as 102 F. He developed presumptive candidemia (positive blood cultures for yeast with identification pending). The patient was started on vancomycin, aztreonam, levofloxacin, and micafungin prior to being transferred to our tertiary care hospital.

Upon admission to our hospital, further history revealed that he was employed as a customs official at an international airport and had a recent trip to the Caribbean for a cruise. He had a skin biopsy due to a papular rash on his face and chest (Fig. 1), and a high resolution CT

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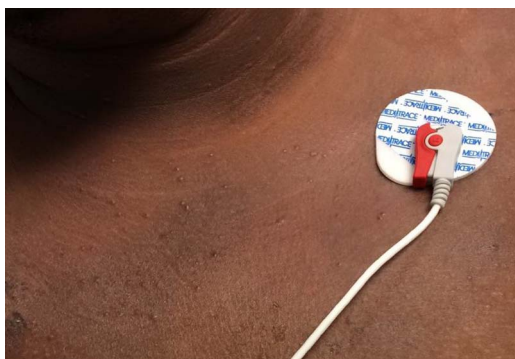


Fig. 1. Papular rash on chest.

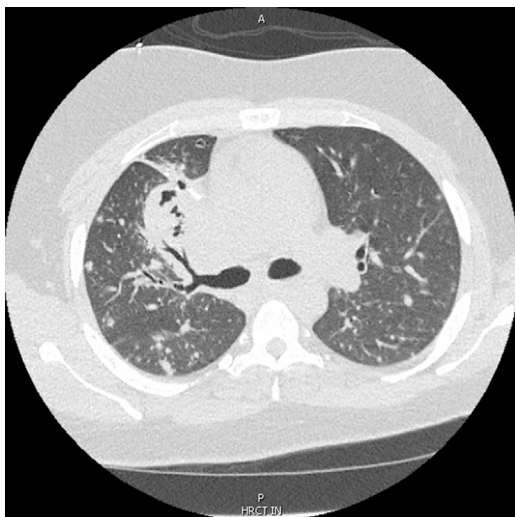


Fig. 2. Cavitory lesion on high-resolution CT Chest.

chest showed cavitary consolidations in the right upper and lower lobe with diffuse bilateral lymphadenopathy (Fig. 2). Infectious and autoimmune workup was ordered (HIV testing by protocol was negative), and he also underwent bronchoscopy and bone marrow biopsy. Immunodeficiency differential included idiopathic CD4 lymphoma, common variable immune deficiency (CVID), systemic lupus erythematosus (SLE), HIV, and other vasculitides. His antibacterial therapy was discontinued, his steroid dose was decreased, and he was continued on micafungin. His clinical course worsened and he became tachycardic, tachypneic, and his lactic acid was increasing despite intravenous fluids, requiring transfer to the intensive care unit. Transesophageal echocardiogram (TEE) showed multiple 1 mm densities on the mitral valve. Fundoscopic examination showed 3 focal white lesions on left optic disc. Intravitreal tap was deferred and his micafungin was switched to amphotericin B.

While awaiting speciation of yeast in blood cultures, results of skin biopsy (Fig. 3), bone marrow biopsy (Fig. 4), and bronchoalveolar lavage on bronchoscopy (all preliminary results showing fungal elements), he was persistently febrile to over 102 F, for which voriconazole was added to amphotericin B. Tuberculosis, strongyloidiasis, cryptococcosis, histoplasmosis, blastomycosis, coccidiomycosis, and cytomegalovirus infection were negative. He had low IgG (456 mg/dL) and IgM (30 mg/dL), and elevated IgA (705 mg/dL). He developed diarrhea due to *Clostridium difficile* (C. difficile PCR positive), and was started on oral vancomycin and metronidazole. Given his progressive worsening clinical status as well as suspicion for a combined immunodeficiency with his T-cell lymphocytopenia and immunoglobulin deficiency, he was given a dose of intravenous immunoglobulin (IVIG), after which he developed respiratory decompensation requiring intubation. He developed worsening acidemia (pH 6.9), hypotension

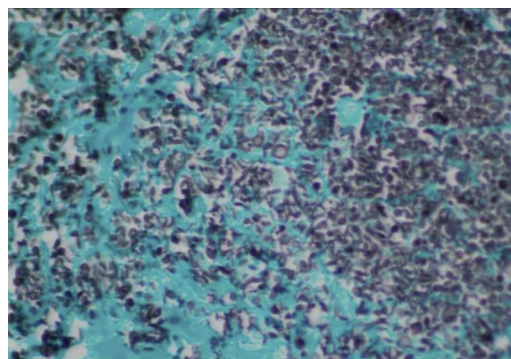


Fig. 3. Skin biopsy (GMS stain) showing fungal forms.

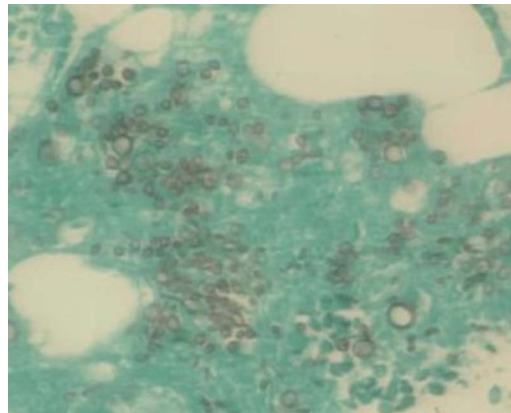


Fig. 4. Bone marrow biopsy (GMS stain) showing hypocellular bone marrow with fungal elements present .

requiring multiple pressors, severe hypoglycemia despite dextrose IV infusion, worsening lactic acidosis (> 20 mmol/L), and severe hypoxemia despite maximal ventilator support. His family opted to pursue comfort care and the patient passed away peacefully. The fungus/yeast was later identified as *Sporothrix schenckii* complex.

Discussion

Disseminated sporotrichosis is extremely rare and most often occurs in immunocompromised patients [1]. It has mostly been documented in HIV patients and there are very few case reports of this disease in immunocompetent or non-HIV positive patients. Multiple cases of disseminated sporotrichosis have been reported in patients with HIV [2–9]. Even more rarely, this has been seen in patients without HIV who were otherwise immunocompromised, including diabetes [7], alcoholism [7,8], and undergoing immunosuppressive therapies [10]. A comprehensive literature search reveals no cases of disseminated sporotrichosis in completely nonimmunosuppressed patients.

Our case is unique because based on a review of the literature, this is the first documented case of disseminated sporotrichosis in a CD4-penic patient without HIV. CD4-lymphocyte deficiency is characterized by a persistently diminished CD4-lymphocyte count (absolute count less than 50) without serological evidence of human immunodeficiency virus infection, and may not have a history of opportunistic infections [11]. Our patient was mostly healthy prior to this disease. He was physically active, with good oral intake, and unfortunately the aggressive nature of this infection lead to his death.

It is still unknown how our patient contracted the disease however he did have an immunodeficiency and worked in a high risk career with recent travel (providing possible exposure to the fungus). His disease was likely worsened after receiving steroids at the outside hospital before he was transferred to our institution. At our institution, the

patient's disease worsened after getting IVIG, which likely set his immune system into overdrive and he had an immune reconstitution inflammatory syndrome-type picture leading to further deterioration. Despite being started on empiric antifungals and then escalation of antifungals, he continued to quickly worsen due to the aggressive nature of the disease and this demonstrates the importance of early and appropriate recognition and treatment.

The diagnosis of sporotrichosis is often delayed when patients present with atypical presentations. Culture is the gold standard and is the most sensitive method of diagnosis. Aspirated material from a skin lesion, or a sample of tissue biopsy, should be inoculated onto dextrose agar and allowed to grow at room temperature; growth usually appears in 5 days, however it can sometimes take several weeks. Treatment of sporotrichosis depends on the severity of disease. Localized, cutaneous disease is usually treated by itraconazole (100–200 mg/day for 3–6 months). However in the case of life-threatening, disseminated, or visceral involvement, the use of intravenous Amphotericin B (3–5 mg/kg per day) is often required. If the patient responds, then the treatment can be switched oral itraconazole. Total duration of therapy is usually at least 1 year and sometimes may require longer duration [9].

Conclusion

In conclusion, disseminated sporotrichosis is a rare human pathogen which occurs in patients who are immunosuppressed, and has often been associated with HIV. Our patient had a CD4 T-lymphocyte deficiency, placing him at increased risk for such opportunistic infections. While it is unclear how he initially contracted the fungus, this case shows that despite early antifungal therapy, this is a disease with very high mortality in this selected patient population.

Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

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