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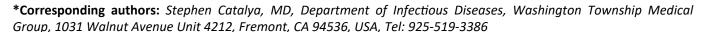
CASE REPORT

COVID-19 with Sporotrichosis (aka *Sporothrix schenckii*) and Fusobacterium Bloodstream Infections (BSI)

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Abstract

We present a case of COVID-19 complicated by sporotrichosis and fusobacterium blood stream infections - no known prior cases of sporotrichosis fungemia nor polymicrobial fusobacterium bloodstream infections in COVID-19 patients. Severe COVID-19, uncontrolled diabetes mellitus (DM), and prolonged corticosteroid use contributed to immune dysregulation, increasing the patient's vulnerability to blood stream infection. This highlights the importance of vigilance regarding risks and complications of steroid use in COVID-19 patients.

Keywords

COVID-19, Sporothrix schenckii, Fusobacterium, Corticosteroids

Introduction

Prior COVID-19 case series discussed patients complicated by candidemia [1] or fusobacterium bacteremia [2]. Disseminated sporotrichosis is associated with HIV and immunocompromised conditions including corticosteroid use and DM [3,4]. Fusobacterium bacteremia is rare, accounting for less than one percent of bacteremia [5]. Our case is the first known case of COVID-19 with fusobacterium bacteremia and sporotrichosis fungemia concomitantly.

Case

Patient is a 54-year-old undomiciled male who presented for dizziness. His history was significant for uncontrolled DM (a1c 11.5%) and being a custodian in an

animal hospital.

He was hypoxic with nadir O_2 saturation 65% on room air and was placed on a non-rebreather mask. COVID-19 PCR testing was positive - patient had contact with his COVID-19 positive nephew three days earlier.

He was given remdesivir (200 mg on day one and 100 mg per day for days two thru five) and dexamethasone 6 mg IV daily - following Infectious Diseases Society of America guidelines and institutional pharmacy protocol. Blood cultures from admission were negative. Patient remained isolated on the general medical floor until hospital day nine when he developed respiratory failure, was transferred to the Intensive Care Unit, and intubated. HS-CRP increased from 153.79 mg/L on arrival to > 160 mg/L.

Dexamethasone was changed to high dose solumedrol at time of intubation; taper ended on hospital day nineteen. Given progressive COVID-19 infection and vasopressor dependent shock, dexamethasone was resumed on day twenty-seven and changed to stress dose hydrocortisone on day twenty-eight and was continued on this for pressor dependence.

Repeat blood cultures taken on hospital day nine were positive for *Sporothrix schenckii*; confirmed by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). Patient was started on amphotericin B with susceptibility tests sent to an outside reference laboratory.



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Figure 1: Left hand wound.

Blood cultures would be repeated for different reasons: Bacteremia, fever, leukocytosis, or increased pressor requirements. Blood cultures taken on hospital days 11, 16, 17, 28, and 34 were negative. Blood cultures taken on hospital days 14 and 23 were positive for *Sporothrix schenckii*. The culture on hospital day 23 also grew fusobacterium species (beta-lactamase negative, not further identified by microbiology lab). Piperacillin-tazobactam was added to amphotericin B to treat a now polymicrobial blood stream infection.

Extensive work up was done to locate the source of infection. Our leading suspect was the left hand wound (Figure 1).

However, no purulence was elicited on exam. Computerized Tomography (CT) scan of the left arm/hand showed subcutaneous edema, but no abscess. Plastic Surgery consult deemed no intervention was indicated.

Fungal endocarditis was considered but transesophageal echo was negative for vegetations and endocarditis. Another possible cause was a yet to be identified abscess. CT abdomen/pelvis showed a "2.3 cm low-attenuation mass in the right lobe of the liver" and head/neck MRI showed "Moderate mucosal thickening in the sphenoid sinuses and lesser mucosal thickening in the maxillary sinuses and ethmoid air cells." CT chest showed "Mosaic attenuation of both lungs, most likely representing severe viral pneumonia. Pulmonary edema is less likely given lack of pleural effusion" ruling out fungal pneumonia. A 4th generation HIV antigen/antibody test was negative on hospital day seventeen effectively ruling out HIV.

Biopsy of the liver mass revealed a previously undiagnosed hepatocellular carcinoma, but no signs of infection. ENT felt sinusitis noted on MRI was due to prolonged intubation and nasogastric tube placement; surgical intervention was not warranted.

Patient remained ventilator and vasopressor dependent, developing acute renal failure. On hospital day thirty-seven care was withdrawn and the patient died.

Two days later, minimum inhibitory concentration (MIC) data returned with amphotericin MIC 4 mcg/ml and itraconazole 0.5 mcg/ml.

Discussion

Sporothrix schenckii is a dimorphic fungus found in plant material, soil, and animal feces [4]. It is associated with rose gardeners presenting with local, cutaneous lesions [4]. Disseminated cases have been documented in immunocompromised patients and immunocompetent patients [3,4].

There is no societal/association guideline for management of *Sporothrix schenckii* fungemia. Historically, potassium iodide was used, but now itraconazole is favored in limited/cutaneous infections and amphotericin B in disseminated cases [4]. Epidemiologic cutoff values of MIC 4 μ g/ml for amphotericin and 2 μ g/ml for itraconazole have been proposed but not adopted by Clinical and Laboratory Standards Institute [6].

Our case stands out given the unique presentation and clinical course. While having risk factors for sporotrichosis including uncontrolled DM, animal exposures, and being without a home, the presentation of dizziness and hypoxia with positive COVID-19 test were atypical. This with initially negative blood cultures creates a unique presentation that is different from prior cases.

Initial source of infection remains unclear. Left hand was a prime suspect given risk factors and nature of Sporotrichosis. However, surgical evaluation and imaging deemed no infection there. Remaining testing (including imaging from the head to the pelvis) was negative for infection. Skin exam had no concerning findings in his legs. Though autopsy wasn't done, we hypothesize that living and employment conditions exposed the patient to *Sporothrix schenckii*. Systemic inflammation from severe COVID-19 and prolonged use of corticosteroids likely predisposed to a disseminated infection.

Another concern is the choice of antifungal agent. Patient was started on amphotericin B, preferred for disseminated *Sporothrix schenckii*. However, the patient's blood cultures would remain intermittently positive, raising the question of resistance. Based off the MIC data, it is possible that itraconazole (though with bioavailability issues) may have been more efficacious.

The risk of concomitant infections [7] and candidemia [1] associated with COVID-19 has been discussed.

However, this appears to be the first case of COVID-19 with *Sporothrix schenckii* fungemia. Therefore: Should clinicians consider antifungal prophylaxis in select COVID-19 patients who are immunocompromised, especially those on a prolonged corticosteroid course? Research including controlled trials should occur before formal recommendation can be made.

Fusobacterium species are anaerobic, gram negative rods implicated in abscesses and wounds [8]. They are rarely associated with bacteremia, accounting for less than 1% of all bacteremias [5]. The Fusobacterium species commonly associated with being pathogenic is F necrophorum [9] - causing oral infections, abscesses, and jugular vein thrombophlebitis [9]. Extensive work up failed to reveal a source in this case. Etiology of translocation due to inflammation has been discussed in COVID-19 patients [2], this could be the case here given ongoing severe illness from COVID-19 and increasing HS-CRP. However, those cases were not associated with a polymicrobial bsi - further distinguishing our case from the literature.

Conclusion

As the COVID-19 pandemic continues, clinicians need to be aware of infectious complications associated with prolonged systemic inflammation and corticosteroid use. Our case highlights potential infectious complications and stands out given their polymicrobial nature. Further research is required to determine if anti-fungal prophylaxis is warranted in severely ill COVID-19 patients who are receiving prolonged steroids and also to determine the optimal antifungal regimen for disseminated sporotrichosis.

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Authors Contribution

All authors contributed equally to this article.

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