First Case Report of an Unusual Fungus (*Sporopachydermia lactativora)* Associated with a Pulmonary Infection in a Drug Injection User

Clinical Pathology
Volume 14: 1–4

DOI: 10.1177/2632010X211029970

Hiba A Al Dallal[1*], Siddharth Narayanan[2*], Christopher M Jones[2], Shawn R Lockhart[3] and James W Snyder[1]

[1]Department of Pathology and Laboratory Medicine, University of Louisville, Louisville, KY, USA. [2]Department of Surgery, University of Louisville, Louisville, KY, USA. [3]Mycotic Disease Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA.

ABSTRACT: In contrast to a robust literature on known pathogenic fungi such as *Cryptococcus* and *Aspergillus* species that cause pulmonary infections, reports of the uncommon genus *Sporopachydermia* causing infections are very limited. We present the first case report describing the fungus, *Sporopachydermia lactativora* as a likely cause of pneumonia in a patient with a history of polysubstance abuse and injection drug use (IDU). The patient recovered following antifungal treatment. The organism was recovered from a blood culture, 3 days post collection. Although CHROMagar was of little value, only yeast-like organisms were observed on cornmeal agar. The organism was not in the matrix-assisted laser desorption/ionization—time of flight (MALDI-TOF) mass spectrometry database. Definitive identification was achieved using the ribosomal DNA (rDNA) sequence analysis by targeting the *ITS1* (internal transcribed spacer 1) region. This case report is intended to promote awareness of this fungus as a potential pathogen, by providing new information that has not yet been reported in the literature, and prompts physician awareness to suspect a fungal infection when managing patients with a history of IDU as a potential source of unique environmental organisms not previously encountered, warranting more comprehensive diagnosis and treatment options.

KEYWORDS: Fungus, pathogenesis, *Sporopachydermia*, pneumonia, infection

RECEIVED: October 9, 2020. **ACCEPTED:** June 10, 2021.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: James W Snyder, Department of Pathology and Laboratory Medicine, University of Louisville, 530 South Jackson Street, Louisville, KY 40202, USA. Email: james.snyder@louisville.edu

Introduction

Fungal species are commonly isolated as contaminants from respiratory secretions. However, they can also be rare or emerging causes of severe opportunistic infections in immunocompromised individuals, with the most consistent presentations being life-threatening pulmonary and cerebral granulomatous lesions.[1] Prompt recognition of pulmonary fungal infections, particularly those caused by unusual species, and appropriate therapy are indispensible in reducing morbidity and mortality.

While *Candida*, *Cryptococcus*, and *Aspergillus* species are well-identified causes of infection, reports that document *Sporopachydermia* species (*S. cereana*, *S. lactativora*, and *S. quercuum*), a genus often associated with cacti, as a human pathogen are rare. Of the 3 known species in this genus, clinical data on human infection is only available for *S. cereana*. There have been reports from 5 patients, 4 of whom died either directly from the pathogen or from other complications of immunosuppression,[2-4] and a fifth patient who survived.[5] We present the first case of the yeast-like fungus, *S. lactativora*, highly suspicious and likely causing pneumonia in a patient with polysubstance abuse who improved after administration of antifungal medication and was discharged.

* Joint first authors.

Case

A 29-year-old female with a past medical history of polysubstance abuse (methamphetamine/heroin), chronic hepatitis C, and seizures presented to the emergency room in September 2019, with a complaint of full body aches, fever, chills, diffuse chest pain, shortness of breath, and yellow to bloody sputum production for 3 days before admission. Three weeks prior to presentation, she had a cardiorespiratory arrest after a heroin overdose and required cardiopulmonary resuscitation with chest compressions. She was previously in drug use (naltrexone) remission which was discontinued due to elevated liver enzymes. The last time she used methamphetamine was 3 days prior to admission, without having withdrawal symptoms. She used sterile needles obtained from an exchange clinic, did not share or lick them but admitted sharing the water used to mix drugs. Her lactic acid levels were moderately elevated (2.17 mmol/L) but her other lab work-ups including the WBC count, were normal. A trans-esophageal echocardiogram was negative for vegetation. Chest X-ray and computerized tomography (CT) scan of the chest (Figure 1) confirmed multifocal pneumonia. The chest CT (Figure 1A) showed bilateral airspace opacities throughout the right upper, middle, and lower lobes, including the lingula. No cavitation or pleural effusions were seen to suggest septic emboli. Mediastinal and hilar structures demonstrated no filling defects within the pulmonary arteries to suggest pulmonary emboli. Patient vitals remained stable.

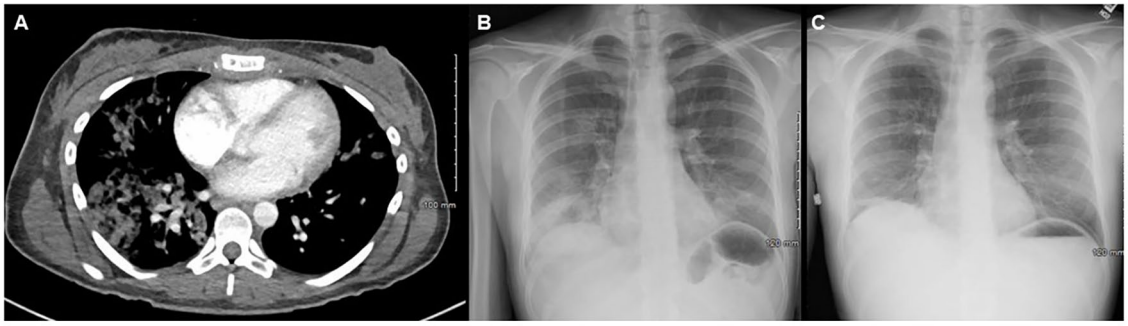

Figure 1. Lung imaging confirming pneumonia in our patient: A computerized tomography (CT) of the chest (A) showing bilateral airspace opacities predominantly throughout the right, upper-middle, and lower lobes as well as the lingula. The opacities appear confluent in the right lower lobe with no cavitation observed. The location is perihilar and likely peripheral in the right. No pleural effusions or endobronchial lesions are seen, (B) a chest X-ray showing patchy airspace opacities at the lung bases with additional multifocal opacities predominantly evident in the right upper and left lower lung zone. No pleural effusion or no pneumothorax was observed. Cardiac and mediastinal borders were within normal limits, and (C) a follow-up X-ray image (day 6 after admission) showed improvement of the infection post antifungal administration.

Two sets of blood cultures were collected and incubated at 35°C in the BACTEC FX system (Becton Dickinson, Sparks Maryland) and the patient was started on vancomycin (1500 mg, intravenous (IV), every 12 hours) plus piperacillin/tazobactam (3.375 g, IV, every 8 h). Despite antimicrobial therapy, she continued complaining of diffuse chest pain and cough. The second blood culture became positive at 3 days of incubation. The blood culture was sub-cultured onto blood, potato flake, Sabouraud's, CHROMagar, and corn meal agar plates and incubated at 30°C. Azithromycin (500 mg, IV, every 24 hours) and micafungin (100 mg, IV, every 24 hours) were added to the therapeutic regimen. A wet preparation showed narrow-necked budding yeast-like fungus (Figure 2A) primarily consisting of round to oval cells, and the Gram stain revealed budding yeast-like cells (Figure 2B). Growth was observed after 24 to 48 hours of incubation on all agar mediums and characterized as smooth, pinpoint small white colonies (Figure 2C and D). Appearance on CHROMagar did not identify any *Candida* species while morphological assessment on corn meal agar was suggestive of a yeast-like fungus predominately, round to oval in appearance. Matrix-assisted laser desorption/ionization—time of flight (MALDI-TOF) mass spectrometry analysis (Bruker Daltonic, Billierica, MA, USA using Bruker flexAnalysis and flexControl software version 3.4), performed 3 independent times, failed to identify the organism. Yeast within the genus *Candida* and, *Cryptococcus* due to the observation of narrow neck budding, were in the differential but was pending confirmation. Symptoms subsided after antifungal administration and a chest X-ray showed relative improvement. Additional tests (HIV, TB, and Legionella) were unremarkable. The sputum culture was predominately indigenous oral flora.

The yeast-like colonies were sent for molecular testing (ARUP Laboratories, Salt Lake City, Utah). The rDNA sequencing, targeting the *ITS1* (internal transcribed spacer 1) region, identified the organism as *Sporopachydermia lactativora* (NCBI #, AF202900.1 (%ID = 100%; hits (444/444)). Antifungal susceptibility testing (YeastOne, Sensititre, Thermo Fisher) was performed and MIC values were provided to the treating clinician with no interpretations for sensitivity or resistance, as there are no interpretive criteria for this species.[6] The reported antifungal MIC values for this species were as follows: Micafungin (8 µg/mL), AmphotericinB (0.5 µg/mL), Itraconazole (0.06 µg/mL), Anidulafungin (2 µg/mL), Capsofungin (4 µg/mL), Fluconazole (≤0.12 µg/mL), Flucytosine (≤0.06 µg/mL), Posaconazole (0.06 µg/mL), and Voriconazole (≤0.008 µg/mL). The patient continued on intravenous micafungin (100 mg, IV, every 24 hours) for the duration of her hospital stay. Her clinical condition improved and she was discharged 13 days after admission, with micafungin (100 mg, IV, every 24 hours) as part of her continuing treatment. Micafungin was discontinued when she showed no further respiratory symptoms on her follow-up visit (11 days after her discharge). Her lungs were clear on auscultation.

Discussion

Sporopachydermia species are rarely identified as a cause of infection in humans. While a few cases of *S. cereana* infection have been described, the current report, to our knowledge, is the first to associate *S. lactativora* as a likely cause of human infection.

The genus *Sporopachydermia* was proposed in 1978, after 2 *Cryptococcal* species with extraordinary thick spore walls and ultrastructures different from other yeast genera were observed.[7] Unlike *Cryptococcus*, *Sporopachydermia* are ascomycetes in the saccharomycetales. Cells of *Sporopachydermia* species are ovoid, ellipsoidal or elongate, and occasionally curved.[8,9] All species grow at 30°C or higher (vitamins required, but amino acids are not), and are resistant to cycloheximide. *Sporopachydermia* species are cactophilic yeasts found in decaying cactus stems.[10] *S. cereana* is known in the context of necrotic cacti in the Americas and Australia, but all previous case-patients denied contact with cacti or other rotting organic material, suggesting an alternative environmental source of this yeast. However, no publications have yet identified other sources.

The value and importance of obtaining tissue for histological examination and demonstrating fungal elements is essential

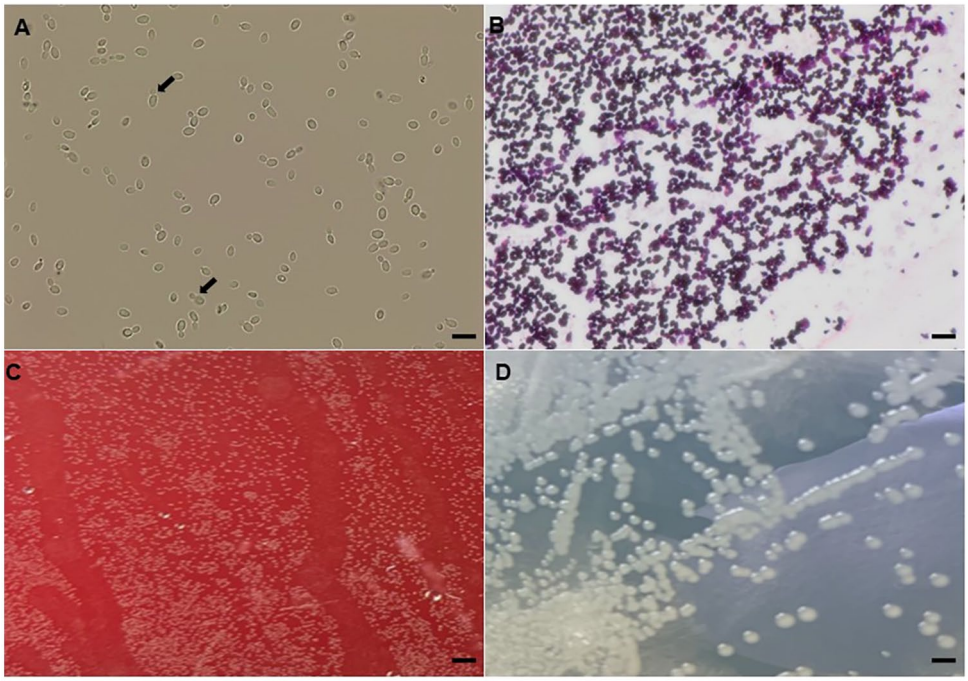

Figure 2. Sporopachydermia lactativora morphology: Wet preparation (A) showing multiple true, narrow-necked budding yeast resembling Cryptococcus (the black arrows showing the "bud connection" between a mother and daughter cell), (B) Gram's stain showing large budding yeasts. Magnification (A and B) = 100×, oil immersion. Scale bar (A and B) = 20 µm, (C) blood agar, incubated at 30°C for 24 hours, show pin-point small white creamy colonies, and (D) larger, creamy round colonies observed at 48 hours on Sabouraud's agar. Scale bar = 1 mm.

in correlating laboratory results with clinical manifestation. The goal of this case report is to promote awareness of this fungus, particularly in patients with a history of injection drug use (IDU). One of the key limitations of our study is the absence of a lung biopsy or bronchial alveolar lavage (BAL) to confirm the presence of the fungus. Previous reports on *S. cereana* infection also lacked confirmatory evidence. Such limitations serve as learning tools for any subsequent studies that place emphasis on determining an organism's clinical relevance and of how it can be essential for diagnosis. It helps to highlight the optimal laboratory diagnosis of fungal infections and the importance for the ordering physician and laboratory personnel to adhere to these principles; that is (i) collect an appropriate specimen (in our case, a BAL or tissue sample); (ii) submit the specimen for both histological and cultural analysis (not to be performed independently but rather as a complete sample analysis); and (iii) further assessments to help confirm a fungal mediated disease process (once awareness of a fungal infection is determined).

In our case, only the differential diagnosis, confirmatory tests, and successful antifungal treatment with significant clinical improvement provide corroborative evidence that this organism was not a contaminant but most likely the agent causing fungemia. Our patient denied having any recent exposure to cacti. Antibacterials (vancomycin/azithromycin) were immediately administered after the venipuncture but did not result in clinical improvement. It was only after the antifungal administration that the patient started showing clinical improvement thus confirming our suspicion of a potential fungal infection. Candidemia was a likely differential, but the rDNA sequencing (*ITS1* region) confirmed *S. lactativora* as the agent most likely responsible for the patient's pneumonia.

Micafungin, an echinocandin, shows potent in vitro inhibitory activity against *Aspergillus* species but none against basidiomycetous yeasts, *Cryptococcus neoformans*, or *Trichosporon* species.[11] Traditional prophylactic measures to treat fungemia include the use of echinocandins. However, no CLSI interpretive guidelines have been established for antifungals for the treatment of *Sporopachydermia* species. Based on our susceptibility testing, voriconazole was most effective, as also identified in a previous report with *S. cereana* infection.[3] Therefore, as per susceptibility testing results from previous reports describing *S. cereana* infections,[2-4] including our report, the echinocandin class may not be an ideal antifungal therapy. New studies are warranted to establish antifungal susceptibility guidelines for this species.

Yeast species should not be regarded as contaminates when recovered from blood cultures. Several studies have suggested that *Cryptococcal* infections should always be considered to represent a fungemia when isolated from blood culture.[12-15] There has been a recent trend toward increasing cases of candidemia in IDU patients.[16] While no cases of candidemia resulting from a concomitant pneumonia have been reported, it is certainly seen with *Cryptococcus* and *Histoplasma*.[17] A report suggests that when yeast are detected in blood cultures from patients with profound neutropenia who do not respond to treatment with an echinocandin, pose a high degree of suspicion toward rare yeasts.[5] All reported *S. cereana* infections have been opportunistic in nature, occurring in immunocompromised neutropenic individuals.

Interestingly, the patient, despite her polysubstance abuse, was immunocompetent (lab work-ups, including WBC count, were normal) further suggesting that the organism *S. lactativora* could behave as a primary pathogen. The injection of non-sterile water may likely have been the source of the infection.

The winter season and, patients being kept in high efficiency particulate air filtered rooms have been suggested to accelerate *S. cereana* fungemia,[2,3] but neither was significant for our patient. Further research is warranted to determine whether *S. lactativora* occurs in nature in sources other than cacti, identify its mode of transmission, and human infection risk. *S. cereana* species have been associated with sepsis and death but the majority of patients had other underlying risk factors that may have contributed to mortality.[2-4] As yeasts are often considered colonizing organisms from respiratory specimens, a slow growing yeast like *S. lactativora* may either be unrecognized in the presence of faster growing bacteria, or seen but not identified as a pathogen.

This organism grew within 72 hours in blood culture (at 35°C), which delayed its rapid identification and subsequent effective treatment of the patient. Our report suggests the need to consider empiric fungal coverage when dealing with infections in IDU patients. *Sporopachydermia* species are notoriously difficult to identify using conventional mycological identification techniques.[2] Three attempts to identify the organism using MALDI-TOF mass spectrometry analysis was also unsuccessful. Expansion of the database to include organisms not previously thought to be pathogens may be warranted. With improved diagnostics, particularly ones associated with increased availability of rapid DNA-based tests, infections with rare yeasts may be diagnosed more often in the future.

Conclusions

Though uncommon, it has been shown that yeasts in the genus *Sporopachydermia* can cause human infection. This report highlights and increases awareness of a rare, never before detected yeast-like fungus as a likely cause of pneumonia in a patient with a history of IDU. It also helps to emphasize to physicians and laboratory personnel the importance of ordering the appropriate tests for confirmatory purposes. As IDU puts an increasing burden on the healthcare system, it should be recognized that this may be a source of unique environmental organisms that may have not previously been identified as potential pathogens.

Author's Note

The findings and conclusions in this manuscript are those of the authors alone and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Author Contributions

H.A. collected the data. S.N. analyzed the literature and wrote the manuscript; C.J., S.L., and J.S. reviewed and edited the manuscript. All authors read and agreed to the final version of the manuscript.

Statement of Ethics

The informed consent was obtained, including consent to publish the case study.

ORCID iD

James W Snyder https://orcid.org/0000-0002-0719-8246

REFERENCES

1. Pundhir P, Tuda C, Vincentelli C, Morlote D, Rivera C. Scolecobasidium granulomatous pneumonia and abscess – an emerging opportunistic fungal pathogen: a case report. *Int J STD AIDS*. 2017;28:94-96.
2. Anoop P, Riley U, Ethell ME, et al. First report of fatal human infections with the cactophilic yeast Sporopachydermia cereana. *J Infect*. 2011;62:311-313.
3. Zamora A, Payne CA, Hansen D, et al. Sporopachydermia cereana sepsis in a patient with acute myeloid leukemia: first reported case in the United States. *Infect Dis Clin Pract*. 2015;23:152-154.
4. Chan TS, Hwang YY, To KK, Kwong YL. Sporopachydermia cereana fungaemia in refractory leukaemia presenting as breakthrough infection during micafungin therapy. *Infection*. 2013;41:715-717.
5. Kingston C, Medinger M, Banderet-Uglioni F, et al. Fungemia and necrotic lymph node infection with Sporopachydermia cereana in a patient with acute myeloid leukemia. *Int J Infect Dis*. 2017;61:103-106.
6. CLSI. *Performance Standards for Antifungal Susceptibility Testing of Yeasts*. CLSI supplement M60. Clinical and Laboratory Standards Institute; 2017.
7. Rodrigues de Miranda L. A new genus: Sporopachydermia. *Antonie Van Leeuwenhoek*. 1978;44:439-450.
8. Lachance M, Phaff H. Sporopachydermia Rodrigues de Miranda. In: *The Yeasts*. Elsevier; 1998:395-399.
9. Yamada Y, Maeda K, Nagahama T, Banno I, Lachance M-A. The phylogenetic relationships of the genus Sporopachydermia Rodrigues de Miranda (Saccharomycetaceae) based on the partial sequences of 18S and 26S ribosomal RNAs. *J Gen Appl Microbiol*. 1992;38:179-183.
10. Lachance MA, Kaden JE, Phaff HJ, Starmer WT. Phylogenetic structure of the Sporopachydermia cereana species complex. *Int J Syst Evol Microbiol*. 2001;51:237-247.
11. Chandrasekar PH, Sobel JD. Micafungin: a new echinocandin. *Clin Infect Dis*. 2006;42:1171-1178.
12. Kashef Hamadani BH, Franco-Paredes C, McCollister B, Shapiro L, Beckham JD, Henao-Martinez AF. Cryptococcosis and cryptococcal meningitis: new predictors and clinical outcomes at a United States academic medical centre. *Mycoses*. 2018;61:314-320.
13. Wilson A, Wilkie M, Rae N. Fungal diseases at the medical front door. *Br J Hosp Med*. 2019;80:157-161.
14. Hall KK, Lyman JA. Updated review of blood culture contamination. *Clin Microbiol Rev*. 2006;19:788-802.
15. Enoch DA, Yang H, Aliyu SH, Micallef C. The changing epidemiology of invasive fungal infections. *Methods Mol Biol*. 2017;1508:17-65.
16. Zhang AY, Shrum S, Williams S, et al. The changing epidemiology of Candidemia in the United States: injection drug use as an increasingly common risk factor—active surveillance in selected sites, United States, 2014-17. *Clin Infect Dis*. 2020;71:1732-1737.
17. Salimnia H, Brown P, Lephart P, Fairfax MR. Hyphal and yeast forms of Histoplasma capsulatum growing within 5 days in an automated bacterial blood culture system. *J Clin Microbiol*. 2012;50:2833-2834.