

Fungus or Parasite or Both: A Diagnostic Challenge

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ABSTRACT

Protothecosis is a rare opportunistic infection caused by achlorophilic algae *Prototheca wickerhamii*, mainly in immunocompromised hosts. Due to their morphologic appearance in routine culture media, they can often mimic yeast-like opportunistic pathogens such as *Pneumocystis jirovecii*. This can delay the identification of other culprit organisms. We present a fatal case of protothecosis in a 74-year-old immunosuppressed male with concomitant *Pneumocystis jirovecii* pneumonia (PJP). The presence of a coinfection along with resemblance in routine culture media and microbiological and histopathological staining can prove to be a diagnostic challenge and delay appropriate care of an immunosuppressed patient.

Key words: Immunocompromised host, *Pneumocystis jirovecii*, *Prototheca wickerhamii*

INTRODUCTION

Prototheca species are spherical unicellular algae (3-30 μm in diameter) that form large nonbudding cells with prominent cell walls in the tissues.^[1] Each cell appears spherical or oval, and the lack of characteristic endospores makes this organism difficult to differentiate from other nonsporulating fungi such as *Cryptococcus* and *Blastomyces*, and parasites such as *Pneumocystis jirovecii*.^[2] There have been reports in the literature of localized protothecal infections of skin, bursae, or postoperative wounds, as well as a few cases of systemic infections such as peritonitis and nasopharyngeal infections.^[1] In immunosuppressed patients, disseminated protothecosis has also been described.^[2] With the advent of advanced immunosuppressive therapies, it may not be unusual to diagnose hitherto uncommon multiple opportunistic infections in the same host. We describe an interesting case of an immunocompromised patient with protothecosis and bilateral ground-glass opacities, which proved to be a diagnostic challenge.

CASE REPORT

A 74-year-old male presented with history of fever and skin rash on the extremities for 1 week. Additionally, he complained of chronic diarrhea. There was no history of night sweats, cough, chest or joint pain, oral lesions, drug use, and tick bites. He lived on a farm and mowed his lawn regularly. He had recently travelled to Florida 1 month prior to admission. His past medical history was significant for previously diagnosed T-cell large granular lymphocytic leukemia, crohn's disease, rheumatoid arthritis, cytomegalovirus (CMV) colitis, and monoclonal gammopathy of uncertain significance (MGUS). He had received multiple immunosuppressive agents in the past, and was taking tofacitinib and daily prednisone at the time of presentation, in addition to valganciclovir. On admission, he was febrile (temperature 39.6°C). Bilaterally symmetrical desquamative, erythematous skin rash was seen on his hands, thighs, and lower legs in the background of generalized pitting edema. The rest of his physical examination was unremarkable.

Initial laboratory data demonstrated normocytic, normochromic anemia (hemoglobin 8.5 g/dl); normal white blood cell count (WBC 5.6 k/ul) including differentials and normal serum chemistries. His C-Reactive protein (CRP) was elevated at 29.6 mg/dl (normal = 0-1). Other

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relevant tests included negative blood cultures, negative fungal antibody panel in blood, negative blood CMV DNA by the polymerase chain reaction (PCR), negative Parvovirus B19 by serologies and PCR tests, and negative serum West Nile virus immunoglobulin G (IgG); and serum cryptococcal antigen, urinary histoplasma, and Legionella antigen. A subsequent computerized tomography (CT) scan of the chest demonstrated multifocal ground-glass and consolidative opacities with air bronchograms predominantly in the left upper lobe (LUL) [Figure 1a and Figure 1b]. The skin rash was biopsied; initial tissue cultures from the biopsy grew spherical unicellular yeast-like fungal organisms. On the second day of his hospital stay, the patient developed significant hypoxia and confusion, requiring endotracheal intubation and mechanical ventilation. The patient underwent bronchoscopy with bronchoalveolar lavage (BAL) from the LUL and broad-spectrum antimicrobial therapy in the form of vancomycin and piperacillin/tazobactam was initiated. The final cultures from both the skin biopsies, taken from upper and lower extremities, as well as later blood cultures were positive for *Prototheca wickerhamii*, a rare opportunistic yeast-like alga. The BAL smear was also positive for yeast-like organisms morphologically similar to *Prototheca wickerhamii*. However, typical morula forms were not observed in BAL, so the likelihood of a fungal-mimic could not be ruled out. *Prototheca wickerhamii* is known to mimic yeast-like fungus on routine media.^[3] Given the patient's immunosuppressive state, lung lesions, and the sudden hypoxia with widened A-a gradient, the possibility of coinfection with *Pneumocystis jirovecii* was entertained. The antimicrobial coverage was broadened to include amphotericin B and trimethoprim-sulfamethoxazole with prednisone. A PCR, performed on the BAL, confirmed the presence of *Pneumocystis jirovecii*. A long-term course of amphotericin B and trimethoprim-sulfamethoxazole was planned to treat the concomitant systemic protothecosis and *Pneumocystis jirovecii* pneumonia (PJP). Eventually, the patient succumbed to a bacterial ventilator-associated pneumonia, and the family decided to transition him to comfort care.

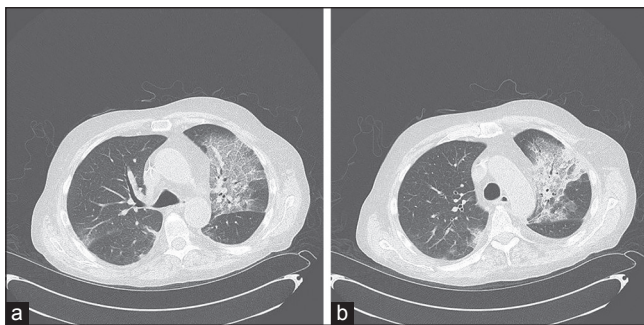


Figure 1: (a) CT chest showing ground-glass opacities in the left upper lobe (b) CT chest showing ground-glass opacities with air bronchograms in the left upper lobe

DISCUSSION

Prototheca species are ubiquitous aerobic, achlorophyllic saprophytic fungi known to colonize under human nails, on the skin, and in the respiratory tract and digestive system.^[4] The most common species affecting humans are *Prototheca wickerhamii* and *Prototheca zopfii*.^[3] Typical human infections involve cutaneous tissue or bursae. However, disseminated infections with *Prototheca wickerhamii* occur only rarely in immunosuppressed hosts.^[1,2] Pulmonary infections are even rarer, and only a few cases have been reported in immunosuppressed patients.^[1,5] The *Prototheca* cell walls lack glucosamine, a specific fungal cell wall component, and the life cycle of *Prototheca* is similar to that of other algae although it lacks chloroplasts.^[2] This organism grows well aerobically on routine bacterial and fungal culture media. The diagnosis of *Prototheca* by histopathology can be challenging. The appearance is similar to yeast-like forms and mimics *Pneumocystis jirovecii*.^[3] As a result, in BAL, *Pneumocystis* cysts can be easily confused for *Prototheca*, the former being more uniform in size and the latter being more variable. Careful examination of the presence of “morula” on Gomori’s methenamine-silver (GMS) stain helps to distinguish it from the similar-appearing yeast-like fungus [Figure 2a and b].^[3] Even though the initial BAL in the present case was suspicious for fungal cysts, the clinical suspicion for *Pneumocystis* was high on the basis of acute decompensation and radiographic requirement. Thus PCR was requested, which was diagnostic. Very few previous reports have presented this diagnostic challenge.^[3] The administration of amphotericin B appears to be the most effective treatment in immunocompromised hosts with protothecosis,^[4] whereas PJP is being treated with

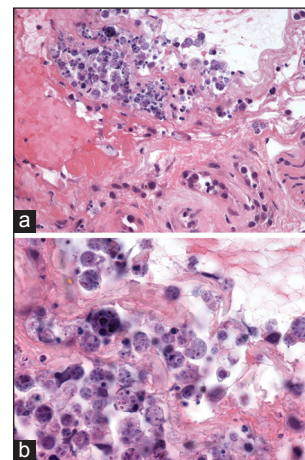


Figure 2: (a) H&E stained section of skin biopsy showing characteristic moruloid appearance of sporangia in the dermis with minimal associated inflammation (high power view) (b) H&E stained section of skin biopsy showing moruloid sporangia filled with thick walled endospores (high power view)

trimethoprin-sulfamethoxazole. A high index of suspicion needs to be maintained, especially for immunosuppressed and/or cancer patients who may be susceptible to multiple opportunistic pathogens at the same time. Any delay in initiating treatment in this situation may have catastrophic consequences.

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