Case Report

Disseminated Prototheca Caused by *Prototheca zopfii* in a Liver Transplant Recipient

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Abstract

Prototheca is a genus of achlorophyllic algae present ubiquitously in the environment. Human infections are rare affecting immunocompromised individuals. We report a case of fatal algaemia caused by *Prototheca zopfii* in a patient who underwent liver transplant. Tissue diagnosis is mandatory for diagnosing rare entities in seriously ill, immunocompromised individuals.

Keywords: Algae, disseminated, fatal outcome, liver transplantation, *Prototheca*

Introduction

Human protothecosis is an infection caused by members of the genus *Prototheca*. These organisms are achlorophyllic, unicellular, spherical, 3–30 mm algae that are ubiquitous in nature and exist in the environment as detritus inhabitants and contaminants of various substrates.[1,2] Human infections are rare. We hereby report a case.

Case Report

A 36-year-old male underwent deceased donor liver transplantation for alcoholic liver disease. He had acute cellular rejection 2-month posttransplant, for which he received intravenous immunoglobulin and plasmapheresis. Eighteen months posttransplant, he had an episode of late cellular rejection and was treated with plasmapheresis, rituximab, and antithymocyte globulin, followed by maintenance immunosuppression with sirolimus, tacrolimus, and prednisolone 5 mg. He was on prophylaxis with valganciclovir and trimethoprim/sulfamethoxazole (TMP-SMX).

He presented 20-month posttransplant with right leg cellulitis, persistent cough, and chest pain. The patient could not recollect a traumatic event to his leg. Blood cultures grew a sensitive strain of *Klebsiella pneumonia* and computed tomography (CT) chest was suggestive of septic emboli. He was treated with intravenous ceftriaxone and discharged on oral ciprofloxacin. He was readmitted 1 month later with right-sided facial weakness, altered mental status, and hemiparesis. Hemogram and chest X-ray were normal. Creatinine was 1.9 mg/dl, bilirubin – 35.6 mg/dl, aspartate transaminase (AST) – 118 IU/L, alanine transaminase (ALT) – 65 IU/L, albumin – 2.4 mg/dl, and gamma-glutamyl transpeptidase-129 IU/L. Magnetic resonance imaging brain showed multiple enhancing lesions. Brain biopsy could not be done in view of elevated prothrombin time and activated partial thromboplastin time. He was started on empiric meropenem, TMP-SMX, liposomal amphotericin-B, and fluconazole. CSF analysis showed no cells with normal sugar and proteins. CSF cryptococcal antigen, XpertMtb, Gram-stain, Ziehl–Neelsen stain and fungal stains were negative. Blood cultures (BacTALERT, bioMerieux, Marcy L'Etoile, France) and mini-bronchoalveolar lavage, on subculture, grew cream colored, nonmucoid "*Candida*-like" colonies on sheep blood agar (bioMerieux), and Sabouraud's Dextrose Agar [Figure 1]. Gram stain of the colony showed Gram-positive large spherical cells of varied sizes. The organism was identified as *Prototheca zopfii* by MALDI-TOF (Vitek MS, bioMerieux,) and Vitek 2 Compact (bioMerieux). A diagnosis of disseminated protothecosis was made and amphotericin-B and fluconazole were continued. However,

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Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/jgid.jgid_55_17

How to cite this article: Rao PV, Sethuraman N, Ramanathan Y, Gopalakrishnan R. Disseminated protothecosis caused by *Prototheca zopfii* in a liver transplant recipient. J Global Infect Dis 2018;10:228-9.

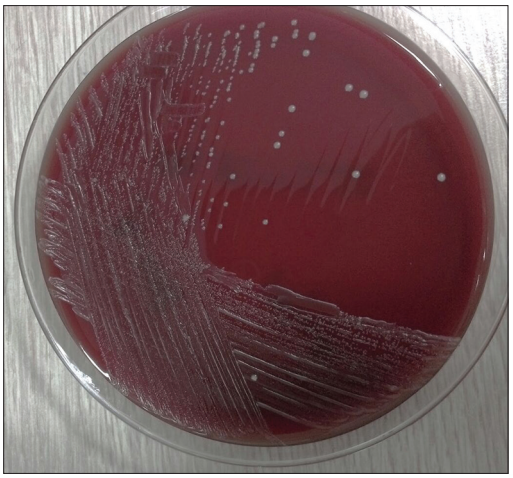

Figure 1: Blood agar showing medium-sized cream colored, nonmucoid colonies of *Prototheca zopfii*

the patient's mental status and oxygenation progressively worsened and he expired 7 days after admission.

Discussion

Protothecosis typically occurs in cattle as bovine mastitis. Even though the first description of human infection was given by Davies *et al.* as early as 1964,[3] human infections are extremely rare and difficult to suspect clinically. *P. zopfii* and *Prototheca wickerhamii* are the two species incriminated in human infections although most human infections are caused by *P. wickerhamii*.[1] Most infections are probably caused by traumatic inoculation into subcutaneous tissues.

Clinically, human protothecosis can present in three forms; cutaneous lesions, olecranon bursitis, and disseminated infection.[4] Olecranon bursitis and localized cutaneous infections are more commonly seen in immunocompetent patients, whereas dissemination and visceral involvement are associated with compromised host immunity.[4] Disseminated protothecosis occurs in individuals undergoing cancer chemotherapy,[5] or immunosuppression related to solid organ transplantation (SOT),[6,7] or in those with advanced AIDS.[8] The organs most commonly affected in dissemination are the skin, subcutaneous tissue, gut, peritoneum, blood, and spleen. Our patient presented with septic pulmonary emboli and multiple ring-enhancing lesions in the brain following cellulitis in the background of severe T-cell immunosuppression. The route of entry may have been the right leg cellulitis site. The presence of severe immunosuppression for underlying rejection appears to be the key reason for dissemination of disease.

Previously, 12 cases have been reported in the literature of protothecosis following SOT.[7] Of these, 6 were localized and 6 were disseminated infections. Most common organ transplanted was kidney (in 7 out of 12 cases). Only one each of liver and combined liver/kidney transplant recipients has been reported to have protothecosis previously.[6,7] The present case is the 13th case of protothecosis in SOT and third case associated with liver transplant in published literature. It is also the first case of disseminated *P. zopfii* in SOT recipients.

Mortality rates are as high as 75% overall and 100% in disseminated protothecosis in SOT recipients even with appropriate therapy with amphotericin B.[7] The underlying immunosuppression along with coinfections contributes to the increased mortality, as was seen in our patient who had an associated *Klebsiella* bacteremia.

There are no standard guidelines for treatment, but most *Prototheca* have *in vitro* sensitivity to amphotericin B and variable sensitivity to azoles. Amphotericin B therapy is recommended as the first-line therapy in cases of dissemination and for patients with severe underlying illness or with immunosuppression.[4]

Organism identification was done by Vitek 2 Compact (bioMerieux) and confirmed by MALDI-TOF (Vitek MS, bioMerieux). Molecular identification was not feasible in our setup. However, MALDI-TOF has been shown to be a robust tool for highly confident identification of this organism.[9] Our case illustrates the importance of obtaining a tissue diagnosis and cultures in seriously ill immune-compromised patients, to diagnose rare entities like protothecosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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