Short Communication

**Prototheca** Algaemia: a Rare but Fatal Opportunistic Infection among Immunocompromised Individuals

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**SUMMARY:** Infections due to *Prototheca* spp. are ubiquitous in nature, occurring in both immunocompetent and immunocompromised patients. The study cohort consisted of 14 cases of *Prototheca* algaemia reported over the past 5 decades and 2 recent cases from study hospitals. *Prototheca wickerhamii* was the most common species. The overall mortality rate was 62.5%. *Prototheca* algaemia, a healthcare-associated infection, was observed in immunocompromised patients and was associated with a poor prognosis.

*Prototheca*, an achlorophyllous alga that is ubiquitous in the natural environment, has been found to colonize in the fingernails, skin, respiratory tract, and digestive system of humans (1–4). In the genus *Prototheca*, *P. wickerhamii*, *P. zopfii*, and *P. cutis* sp. nov. are potential human pathogens, with *P. wickerhamii* playing the predominant role (5–10). The first reported case of algaemia was published by Cox et al. in 1974 (11). Till date, more than 100 cases of human protothecosis have been reported, with a predominance of cutaneous involvement (9). Local or systemic steroid use, hematological malignant disease, diabetes mellitus, AIDS, and organ transplantation have been considered to be the main risk factors. However, *Prototheca* algae-mia has rarely been reported. Here, we summarize the clinical features, antimicrobial therapy, and outcome of 16 cases of *Prototheca* algaemia.

To identify the reported cases, we searched the PubMed database using key words, including “*Prototheca*,” “protothecosis,” and “algaemia” and found 14 cases reported to have *Prototheca* algaemia. We also included 2 cases of algaemia from 2 hospitals in southern Taiwan. Under ethical review of the Institutional Review Board in Chi Mei Medical Center, the committee concluded that the review of a case report is not necessary (application number: 10206-E01).

A 57-year-old man (Case 15) who presented with severe numbness in his lower left leg for 1 day. He had type 2 diabetes mellitus and secondary hypothyroidism due to a prior I-131 therapy for hyperthyroidism. Later, Cushing syndrome due to ectopic adrenocorticotropic hormone (ACTH) syndrome was diagnosed from laboratory data and imaging results. During hospitalization, a small wound (8 × 8 mm) was observed on his left index finger due to repeated pinpricks for blood sugar measurement. A local incision was made, and pus culture was performed on day 24 after admission. Six days later, he developed respiratory failure, requiring ventilator support. Empirical broad-spectrum antibiotics were prescribed. On day 33, the pus culture was positive for *P. wickerhamii*. Despite amphotericin B therapy, he died on day 40. Three days later, blood cultures were positive for *P. wickerhamii*.

A 75-year-old woman (Case 16) with type 2 diabetes mellitus and hypertension presented to the emergency department because of accidental ingestion of a detergent-containing acid. Emergent transhiatal esophagectomy, total gastrectomy, Roux-en-Y jejunojuno-denostomy, and jejunojejunostomy were performed. Empirical parenteral flomoxef and fluconazole were prescribed. On day 9 after admission, she went into shock, and blood cultures were obtained. Due to evolving multiple organ failure, she died on day 16. Later, blood cultures were positive for *P. wickerhamii*.

Retrospective analysis of 16 published cases, including the 2 aforementioned cases, was conducted (Table 1). Steroid therapy was prescribed upon diagnosis of protothecosis in 6 cases. *P. wickerhamii* was the predominant pathogen (13 cases). Amphotericin-B therapy was used in 11 cases, 5 (45.5%) of which died; however, when antifungal therapies other than amphotericin B were used or no antifungal therapy was used, all 5 cases died ($P = 0.09$, Fisher’s exact test). Therefore, a total of 10 cases died of algaemia, leading to a mortality rate of 62.5%.

Nine (56%) cases exhibited various skin lesions. Among these, *Prototheca* spp. were isolated wounds or
Prototheca-specific skin lesions could be identified as a predictor of experienced cytomegalovirus viremia (16,19,21). Concurrent or recent steroid use was observed in 6 cases solely treated with an azole (2 cases) or echinocandin (1 case) survived. Therefore, amphotericin B may play a crucial therapeutic role for Prototheca infections. No evidence of ventilator-associated algaemia was found in the 5 cases with ventilator support. Among 10 cases with detailed hospital information, the onset of algaemia after admission ranged from 9 to 63 days, except for 1 case (Case 14). Preceding Enterococcus (8,15,16) or Escherichia coli (15,17) bacteremia, and Candida glabrata fungemia (12,18,19) were commonly observed. In addition, 3 cases experienced cytomegalovirus viremia (16,19,21).

To identify the possible sources of infection, we observed various skin lesions in 9 cases. Although no specific skin lesion could be identified as a predictor of algaemia, Prototheca spp. were isolated from the skin lesions of 6 cases. Thus, the skin was the potential portal of entry; however, the primary focus remained obscure in majority of the cases. Microbial translocation from the intestine is another possibility, just as candidemia, and the skin lesions may be secondary features.

Concurrent or recent steroid use was observed in 6 cases (37.5%). Among the 6 cases of algaemia with preceding cutaneous protothecosis, 3 had prior steroid use or ectopic ACTH syndrome. Accordingly, steroid use or ectopic ACTH syndrome could be an important factor in precipitating cutaneous Prototheca infection to algaemia.

Among 10 cases with detailed hospital information, 9 were regarded as healthcare-associated infections. CVC tip cultures were performed in 3 cases (12,16,22) and 1 of our cases (Case 15); and all were negative for Prototheca spp. Thus, the possibility of catheter-related algaemia was low. Despite the fact that Prototheca spp. have been found to colonize the respiratory tract (6), no protothecal organisms were isolated from sputum samples. Thus, no conclusion could be made regarding the sources or reservoirs of Prototheca spp. in the cases of healthcare-associated algaemia.

Among the 16 cases of algaemia, the mortality rate of those treated with amphotericin B was lower than that of the cases without amphotericin B therapy, although the statistical difference was not significant. None of the cases solely treated with an azole (2 cases) or echinocandin (1 case) survived. Therefore, amphotericin B may play a crucial therapeutic role for Prototheca algaemia.

Concurrent or preceding bacterial, fungal, or viral infections and prior exposure to multiple antimicrobial agents were common. Given the limited number of cases, no specific pathogen or antimicrobial agent could be identified as being related to Prototheca algaemia.

In conclusion, Prototheca algaemia often occurs in immunocompromised individuals and can be inferred to be a healthcare-associated infection. The skin is a possible portal of entry for Prototheca spp., although the possibility of other routes cannot be ignored. If protothecosis is suspected, amphotericin B should be promptly administered to achieve a favorable outcome.

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Conflicts of interest None to declare.

REFERENCES

Table 1. Clinical characteristics of 16 cases of Prototheca algaemia

<table>
<thead>
<tr>
<th>Case no. (ref.)</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Underlying disease</th>
<th>Steroid therapy1</th>
<th>Prototheca spp.</th>
<th>Other sites of infections</th>
<th>Antifungal agent</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (11)</td>
<td>29</td>
<td>M</td>
<td>Cell-mediated immunity deficiency</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>Skin</td>
<td>AmB</td>
<td>Survival</td>
</tr>
<tr>
<td>2 (18)</td>
<td>7</td>
<td>M</td>
<td>Hodgkin’s disease</td>
<td>Yes</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>AmB</td>
<td>Survival</td>
</tr>
<tr>
<td>3 (21)</td>
<td>59</td>
<td>F</td>
<td>Lung transplant recipient</td>
<td>NA</td>
<td>P. zopfii</td>
<td>Urinary tract</td>
<td>No</td>
<td>Death</td>
</tr>
<tr>
<td>4 (22)</td>
<td>32</td>
<td>M</td>
<td>Acute myeloid leukemia</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Itraconazole, AmB</td>
<td>Survival</td>
</tr>
<tr>
<td>5 (12)</td>
<td>75</td>
<td>M</td>
<td>Myasthenia gravis</td>
<td>Yes</td>
<td>P. wickerhami</td>
<td>Skin</td>
<td>AmB, liposomal AmB</td>
<td>Survival</td>
</tr>
<tr>
<td>6 (8)</td>
<td>19</td>
<td>M</td>
<td>Acute myeloid leukemia-BMT, GVHD</td>
<td>Yes</td>
<td>Prototheca spp.</td>
<td>NF</td>
<td>Liposomal AmB</td>
<td>Survival</td>
</tr>
<tr>
<td>7 (13)</td>
<td>56</td>
<td>M</td>
<td>HSCT-GVHD</td>
<td>Yes</td>
<td>P. wickerhami</td>
<td>Skin</td>
<td>AmB</td>
<td>Death</td>
</tr>
<tr>
<td>8 (20)</td>
<td>58</td>
<td>M</td>
<td>Osteomyelofibrosis, acute leukemia, BMT</td>
<td>NA</td>
<td>P. zopfii</td>
<td>Heart, lung, liver, kidney</td>
<td>Voriconazole, caspofungin, liposomal AmB</td>
<td>Death</td>
</tr>
<tr>
<td>9 (14)</td>
<td>58</td>
<td>M</td>
<td>MDS, BMT, chronic GVHD</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>Skin, bilateral choroid</td>
<td>AmB</td>
<td>Death</td>
</tr>
<tr>
<td>10 (16)</td>
<td>61</td>
<td>M</td>
<td>Liver transplant recipient, DM</td>
<td>Yes</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Miacafungin, AmB</td>
<td>Death</td>
</tr>
<tr>
<td>11 (17)</td>
<td>79</td>
<td>M</td>
<td>Chronic lymphocytic leukemia</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Voriconazole</td>
<td>Death</td>
</tr>
<tr>
<td>12 (15)</td>
<td>49</td>
<td>F</td>
<td>Acute myeloid leukemia</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Voriconazole, caspofungin</td>
<td>Survival</td>
</tr>
<tr>
<td>13 (19)</td>
<td>69</td>
<td>F</td>
<td>Cardiac allograft recipient, DM</td>
<td>Yes</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Caspofungin</td>
<td>Death</td>
</tr>
<tr>
<td>14 (23)</td>
<td>61</td>
<td>M</td>
<td>Renal transplant recipient</td>
<td>NA</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>No</td>
<td>Death</td>
</tr>
<tr>
<td>15b)</td>
<td>57</td>
<td>M</td>
<td>Ectopic ACTH syndrome</td>
<td>No</td>
<td>P. wickerhami</td>
<td>Skin</td>
<td>Fluconazole, AmB</td>
<td>Death</td>
</tr>
<tr>
<td>16b)</td>
<td>75</td>
<td>F</td>
<td>Corrosive injury, DM</td>
<td>No</td>
<td>P. wickerhami</td>
<td>NF</td>
<td>Fluconazole</td>
<td>Death</td>
</tr>
</tbody>
</table>

1: Systemic steroid therapy before the diagnosis.
2: Two cases reported in the present study.

BMT, bone marrow transplantation; GVHD, graft versus host disease; HSCT, hematopoietic stem cell transplant; MDS, myelodysplastic syndrome; DM, diabetes mellitus; ACTH, adrenocorticotropic hormone; NF, not found; AmB, amphotericin B.

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