Cutaneous protothecosis: a new case and review of Brazilian patients

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Abstract

Protothecosis is a rare but emerging infectious disease, caused by algae from the genus *Prototheca*. It presents predominantly as cutaneous lesions and poses a diagnostic challenge owing to its diverse clinical presentation. Typically, it occurs in exposed areas of the skin, associated with trauma. Diagnosis relies mainly on histopathology and culture. This article presents an elderly diabetic woman with cutaneous protothecosis from Rio de Janeiro, Brazil. We emphasize clinical features, histopathology, and successful treatment with itraconazole, along with a brief review of the 12 previously reported cases from Brazil.

Keywords: algae, itraconazole, Prototheca, protothecosis

Introduction

Protothecosis is a rare algae infection caused by *Prototheca* spp, that predominantly presents as cutaneous lesions and may affect both immunocompetent and immunocompromised individuals [1]. These organisms, ubiquitous in the environment, are commonly found in sources such as plants, soil, water, food, and even on human fingernails [2]. Infection generally takes place via traumatic inoculation into the skin [1].

The diverse range of clinical presentations that have been described, which may mimic bacterial infections, fungal infections, and eczemas, make the diagnosis challenging [1]. Protothecosis is an emerging disease with a growing global incidence [3]. Enhancing awareness is crucial for facilitating early detection and ultimately ensuring effective treatment.

Case Synopsis

An 81-year-old woman from the state of Rio de Janeiro, Brazil with a history of type 2 diabetes treated with metformin, presented with a painful, well-demarcated, erythematous-to-violaceous patches on the upper chest and shoulders, with areas of erosions and crusting (**Figure 1**). The lesions had appeared one year earlier, with no history of prior trauma. However, she reported frequent contact with garden plants. The patient denied any systemic symptoms and besides her diabetes had no history of other diseases or immunosuppression.

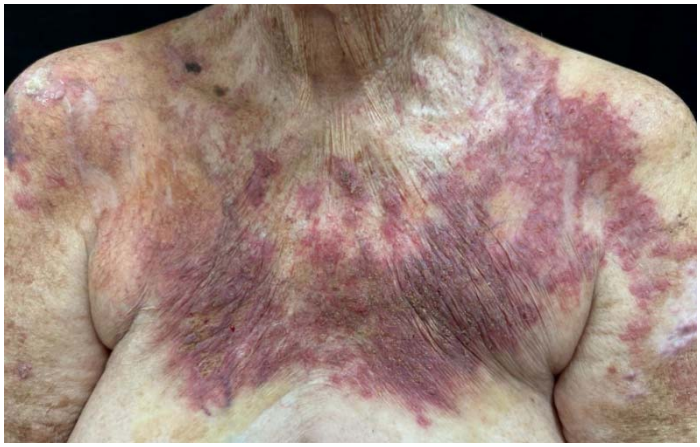

Figure 1. *Well-demarcated, erythematous to violaceous patches and plaques of the upper chest and shoulders with areas of erosion and crusts.*

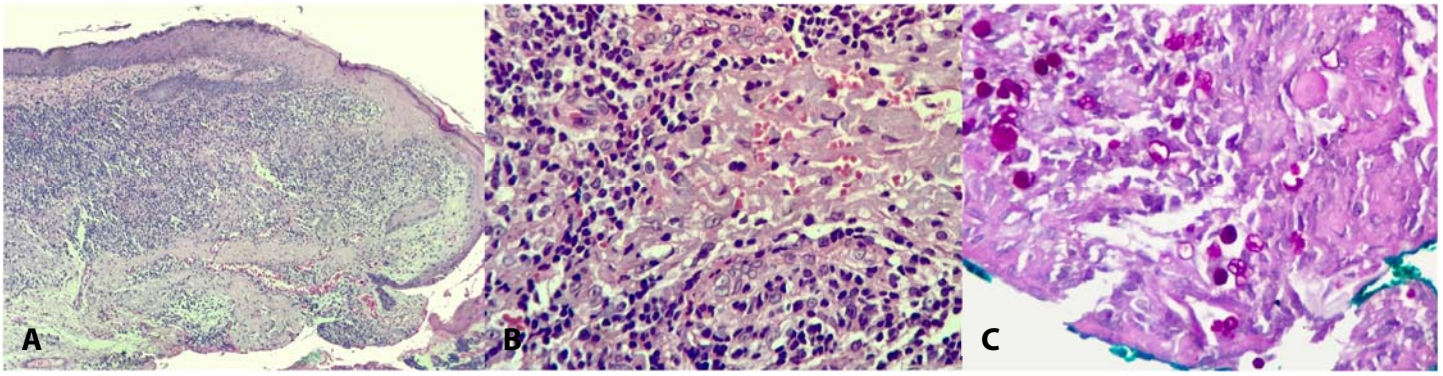

Figure 2. ***A)*** *Focal epidermal hyperplasia and a diffuse dermal infiltrate with extravasated erythrocytes in the interstice; H&E, 10×.* ***B)*** *Extravasated erythrocytes in the interstice and among inflammatory cells; H&E, 40×.* ***C)*** *Spherical organisms of variable size, some of them with endosporulation in a daisy-like pattern; periodic acid-Schiff, 40×.*

Histopathological examination revealed a mixed inflammatory infiltrate in the upper dermis consisting mostly of lymphocytes, macrophages, and plasma cells, along with vascular congestion and extravasation of red blood cells (**Figures 2A**, **B**). Giant cells or granulomas were not observed. Silver stain and PAS reaction confirmed the presence of spherical bodies of variable size, some of them with endospores in a cartwheel or daisy-like pattern, consistent with protothecosis (**Figure 2C**). Culture results were negative, owing to bacterial overgrowth. Subsequently, treatment with itraconazole 200mg/day was initiated, leading to a satisfactory improvement after six months (**Figure 3**).

Case Discussion

Prototheca spp. are unicellular, achlorophyllous microalgae that inhabit various natural environments. Five of the 18 *Prototheca* species currently recognized have been associated with human infections: *P. wickerhamii, P. blaschkeae, P. cutis, P. miyajii,* and *P. bovis*. The most commonly involved species is *P. wickerhamii* [1]. These microorganisms are found in diverse habitats, such as plants, soil, fresh water, saltwater, sewage, and food items, especially dairy products [2]. *Prototheca* is recognized as a major cause of bovine mastitis and infections have also been reported in other animals [3]. Furthermore, *Prototheca* have the capacity to colonize human skin and nails [2].

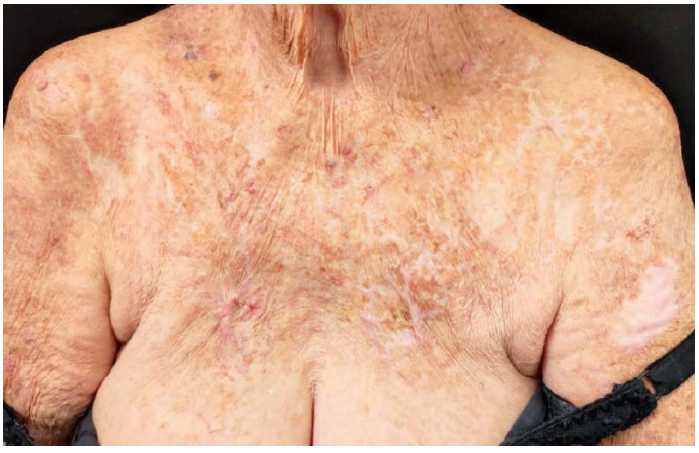

Figure 3. *Significant improvement six months after initiating treatment with itraconazole, 200mg/day.*

Human protothecosis primarily presents as cutaneous disease, with less common manifestations including soft tissue rheumatic involvement (bursitis, fasciitis, tenosynovitis, and most notably olecranon bursitis) or disseminated systemic infection. It affects both sexes equally with a predilection for older individuals. Risk factors include immunosuppression, diabetes, organ transplantation, corticosteroid use, and malignancies, but it may occur in patients without underlying conditions [4]. Occupations with a higher exposure risk include fishermen, farmers, gardeners, and aquarists [2].

Infection typically occurs through traumatic inoculation in the skin. Lesions can present as plaques, nodules, vesiculobullae, ulcers, verrucous plaques, herpetiform lesions, or lesions resembling eczema [2,4,5]. This broad spectrum of presentations present a significant diagnostic challenge. Our patient presented with a striking erythematous-purpuric appearance, which has not been previously

described in the literature to our knowledge, with additional areas of erosion and crusting that could potentially be mistaken for several inflammatory diseases.

Diagnosis confirmation depends on identification of the organisms through histology, culture, and/or molecular tests. Histopathological examination often shows a mixed inflammatory infiltrate and necrotizing granulomatous inflammation. The hallmark finding is that of morula-like structures that have a cartwheel-like appearance and exhibit a distinct cell wall [6]. *Prototheca* may be noted on hematoxylin-eosin staining but are best visualized with Grocott methenamine silver or PAS stains [2].

Cultures should be obtained from fresh samples. The organism easily grows within days on various media, but may be difficult to isolate if overgrown by bacteria or fungi [6]. Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry and various molecular methods have also been used for the identification of *Prototheca* [3].

Although protothecosis remains rare, there has been a global increase in the number of cases [1]. In Brazil, there have been 12 reported cases (**Table 1**). These cases primarily involved cutaneous lesions, often attributed to factors like trauma and gardening; some had comorbidities like diabetes. The most frequently identified species was *P. wickerhamii*. The patients were distributed across different states, emphasizing the potential presence of *Prototheca* throughout various environments. Notably, half the cases were reported in the last four years, which could indicate either a potential increase in the incidence of protothecosis or an improved recognition and reporting of the condition. Further studies may be needed to confirm this trend.

Treatment of protothecosis lacks established protocols or monitoring guidelines, relying primarily on empirical approaches. Research on drug sensitivity remains limited [1]. Disseminated infections typically require treatment with amphotericin B, whereas localized infections are managed with azole antifungals or surgical excision [2]. However, treatment remains a challenge owing to the general low susceptibility of algae to antimicrobial agents, leading to inconsistent clinical responses [7].

Conclusion

This case report underscores the importance of considering protothecosis in the differential diagnosis of atypical or treatment-resistant cutaneous infections, especially when conventional microorganisms cannot be identified. Although treatment lacks standardization, our report demonstrates a successful response to itraconazole. Awareness and recognition of protothecosis can lead to more timely diagnosis and appropriate treatments, ultimately improving patient outcomes.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *Summary of reported protothecosis cases in Brazil [5,8-17].*

	Author	State	Sex/age	Comorbidity or risk factor	Site	Type	Species	Treatment
1	Agostini et al. (1983), [8]	Rio Grande do Sul	M/72	None reported	Arm	Cutaneous + Olecranon bursitis	*Prototheca sp.*	Surgical excision
2	Follador et al. (2001), [9]	Bahia	F/72	Trauma	Arm	Cutaneous	*P. wickerhamii*	Fluconazole 150mg/day for 30 days and then weekly (150mg/week) for 60 days
3	Leimann et al. (2004), [10]	Rio de Janeiro	F/59	Trauma; Gardening	Hand	Cutaneous	*P. wickerhamii*	Itraconazole 400mg/day for 6 weeks Fluconazole 200mg/day for 1 year
4	Zaitz et al. (2006), [11]	São Paulo	F/70	Gardening	Leg	Cutaneous	*P. wickerhamii*	Itraconazole 200mg/day for 30 days and then 100mg/day for 60 days
5	Carneiro et al. (2007), [12]	Distrito Federal	M/78	Rural worker; Pemphigus foliaceus; Corticosteroids	Hand	Cutaneous	*P. wickerhamii*	Itraconazole 200mg/day for 180 days
6	Silva et al. (2013), [5]	Rio de Janeiro	F/61	Trauma; Diabetes; Corticosteroids	Leg	Cutaneous	*P. wickerhamii*	Itraconazole 200mg/day for 90 days
7	Godofredo et al. (2019), [13]	São Paulo	M/60	Kidney transplant	Leg	Cutaneous	*Prototheca sp.*	Fluconazole 150mg/day for 90 days
8	Góes et al. (2021), [14]	Amazonas	F/79	Diabetes	Back	Cutaneous	*P. wickerhamii*	Itraconazole 200mg/day
9	Melo et al. (2022), [15]	Rio de Janeiro	M/65	Gardening; Fishing	Arm	Cutaneous + olecranon bursitis	*Prototheca sp.*	Surgical debridement amphotericin B
10	Rodrigues et al. (2023), [16]	Rio de Janeiro	M/40	Aquarist; Reactive arthritis; Imunossupressor	Hand	Cutaneous	*Prototheca sp.*	Itraconazole 200mg/day for 90 days
11	Rodrigues et al. (2023), [16]	Rio de Janeiro	M/68	Fishing	Penis	Cutaneous	*Prototheca sp.*	Itraconazole 400mg/day for 180 days
12	Santos et al. (2023), [17]	Maranhão	M/76	Trauma	Arm	Cutaneous	*P. wickerhamii*	Itraconazole 400mg/day Liposomal amphotericin B 4mg/kg/day for 45 days Voriconazole 400mg/day for 180 days