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# An exuberant case of protothecosis: an emergent disease in tropical dermatology

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## Abstract

Protothecosis is a rare condition caused by the achlorophylated algae of the genus *Prototheca*. We described an exuberant case treated as sporotrichosis with prolonged course which evolved to arm deformation. Itraconazole treatment for 8 months was ineffective.

*Keywords: algal, diseases, harmful, infectious, medicine, protothecosis, proliferation, skin, tropical*

## Introduction

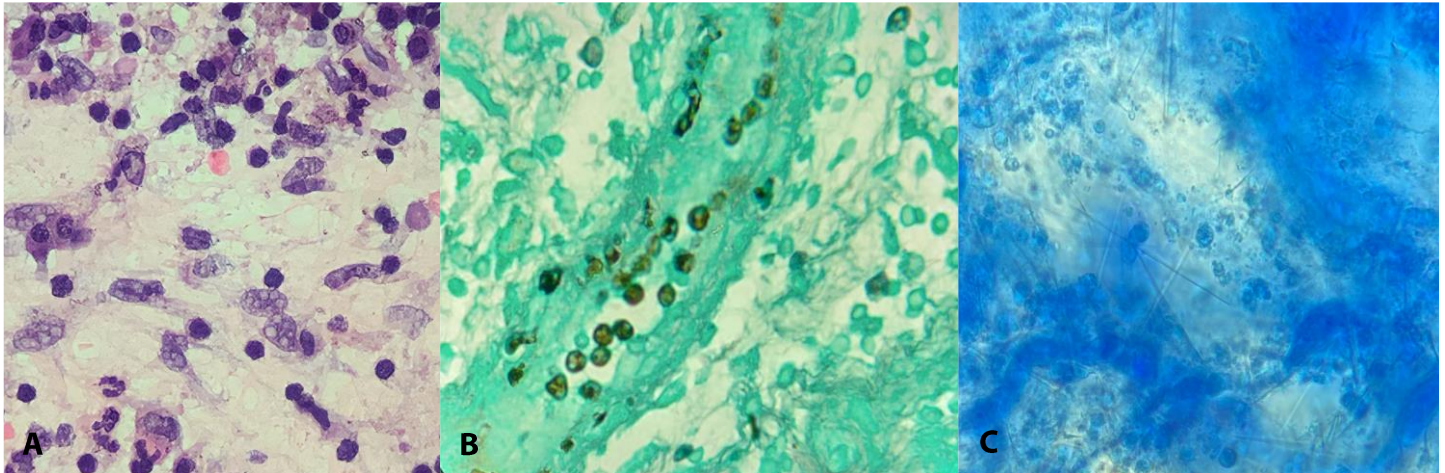
Protothecosis is a rare infection caused by unicellular achlorophyllic algae of the genus *Prototheca*. The species most commonly involved in humans and animal diseases are *P. wickerhamii* and *P. zopfi*. They are present in the soil, plants, animals, and water bodies, such as lakes and swimming pools. *Prototheca* algae were first implicated in bovine mastitis in 1952. The algae mostly affect the skin in humans, especially immunocompromised individuals, such as those with kidney failure, diabetes, HIV, or those who use corticosteroid and monoclonal antibody therapies. The diagnosis of protothecosis is very challenging. It is an indolent infection with three primary clinical presentations: cutaneous lesions, olecranon bursitis, and disseminated systemic disease. The cutaneous form can present as erythematous plaques, vesiculobullous lesions, nodules, ulcers, and pyoderma-like lesions [1-3].

## Case Synopsis

A 65-year-old immunocompetent man from Rio de Janeiro, Brazil, was referred to our dermatology department. He was otherwise healthy with a previous history of vitiligo and no comorbidities. He complained about multiple erythematous papules on his right arm that had appeared about 2 years prior. These lesions evolved to diffuse infiltrated erythematous plaques and then to multiple nodules. Eventually this became a raised tumoral mass with



**Figure 1. A)** Right arm lesions showing erythematous nodules and plaques with ulcers. **B)** Erythematous nodule exhibiting vitiligo Koebnerization around the mass.



**Figure 2.** **A)** H&E histopathology showed morula-like structures, typical of *Prototheca* species, colored red, 400 $\times$ . **B)** The sporangia are detected by Grocott stain, 400 $\times$ . **C)** Lactophenol cotton blue stain showing morula form of *Prototheca*, 100 $\times$ .

ulcerated areas that released purulent exudate, deforming the patient's arm (**Figure 1**). Regarding the epidemiologic history, the patient stated that he often did the gardening at home, and he had traveled for a fishing trip to a countryside lagoon 5 years before the symptoms. Several tissue samples of the lesion were studied and tested negative for fungal, bacterial, and other microbial agents. IgG test for sporotrichosis was positive; thus, itraconazole therapy was initiated at 200mg/day for 12 months. However, no improvement was observed with the treatment. The patient was subsequently referred to the dermatology department of this hospital, where the diagnosis of protothecosis was suspected. The diagnosis were confirmed by direct observation of the structures resembling *Prototheca* species on lactophenol cotton blue stain and histopathologic findings on Grocott and H&E staining that showed typical sporangial structures internally containing

sporangiospores. Culture samples on Sabouraud dextrose agar were negative (**Figure 2**). The patient subsequently underwent surgical debridement, including removal of inflammatory collections on the olecranon bursa and administration of amphotericin B on interspersed days, until the total dose administered amounted to 2.8g (**Figure 3**).

### Case Discussion

This condition was difficult to diagnose as it could be easily confused with deep-tissue fungal infections, given the positive serological result for sporotrichosis as a confounding factor. The receipt of this patient from another tertiary hospital, the indolent evolution with negative bacterial and fungi cultures, and non-remission of the lesions after 12 months of itraconazole use, led us to think of a rare disease such as protothecosis. Other items in the differential diagnosis to be considered in tropical dermatology include cutaneous mycobacteriosis and resistant sporotrichosis. The key to the diagnosis depends upon histopathological findings; most patients exhibit a chronic granulomatous reaction with a predominance of lymphocytes, giant cells, some eosinophils with or without suppurative change, and areas of necrosis. *Prototheca* presents itself as spherical structures called sporangia, which have a thin cell wall containing several endospores inside, forming structures with the appearance of morula [4-5]. Two hundred cases of protothecosis



**Figure 3.** Aspect of the arm after amphotericin cycle and surgical debridement.

**Table 1.** Description of *Protothecosis* cases published in Brazil.

Author	Age	Comorbidities/immunosuppressant drug use	Type and site of lesion	Agent identification	Treatment
Agostini et al. 1983 [6]	No data	No data	Arm	No data	No data
Follador et al. 2001 [7]	72	Topical corticosteroids chronic use	Erythematous plaque, arm	Positive culture and histopathology	Successful treated with fluconazole for 3 months
Zaitz et al. 2006 [8]	70	Without comorbidities	infiltrated eczema-like plaque, arm	Positive culture, carbohydrate assimilation, and histopathology	Successful treatment with itraconazole for 3 months
Leimanm et al. 2004 [9]	59	Without comorbidities	Erythematous plaque, finger	Positive culture and histopathology	Unsuccessful treatment with itraconazole 6 weeks, successful treatment with fluconazole for 3 months
Zaitz et al. 2006 [10]	60 years-old	Without comorbidities	Yellowish nail coloration, nail	Positive culture, carbohydrate assimilation and histopathology	Successful Topic oxiconazole 8 months
Carneiro et al. 2007 [11]	78	Pemphigus foliaceus and chronic use of corticoid	Infiltration, leg	Positive culture, carbohydrate assimilation and histopathology	Unsuccessful treatment with itraconazole for 2 months
Da Silva et al. 2013 [1]	61	Systemic corticoid chronic use and Mellitus Diabetes	Erythematous plaque, arm	Positive culture, carbohydrate assimilation and histopathology	Successful treatment with itraconazole for 3 months
Godofredo et al. 2019 [12]	60	Kidney transplant and prednisone and sirolimus use	Erythematous nodule, leg	Negative culture, positive histopathology	Successful treatment with fluconazole for 3 months
Góes et al. 2021 [13]	79	Mellitus Diabetes	Erythematous plaque, shoulder	Negative culture, positive histopathology	Successful treatment with fluconazole for 3 months

have been reported globally, nine of which were from Brazil. This case is the first, at least in Brazil, to be reported with a clinical presentation of ulcers, deformation of the arm, and olecranon bursitis. We present a review of previous Brazilian protothecosis cases in **Table 1** [6-13].

In our case, we were unable to observe the growth of *Prototheca* species in Sabouraud medium despite two attempts, even with samples taken from deep tissue. This may be explained by the previous use of

itraconazole for 6 months. No consensus has been established on the treatment of protothecosis, but the use of itraconazole and amphotericin B for weeks-to-months is recommended. In some cases, itraconazole administration fails to produce an adequate clinical response. Although the *in vitro* effect of itraconazole is good, *Prototheca* species show marked variability in their susceptibility to imidazoles. Voriconazole seems to be a good alternative drug for such cases. Nevertheless, the effects of drug interactions and mistakes in the daily

administration of the prescribed drug on prolonged use can lower the clinical value of itraconazole [14-16].

## Conclusion

Protothecosis is an emerging and often neglected disease. Our case demonstrates a possible serologic cross-reaction between sporotrichosis and protothecosis. Differential diagnosis should include

this disease along with mycobacteriosis and deep mycoses, especially when the treatment administered is ineffective. If itraconazole treatment is insufficient in treating protothecosis, surgical debridement, amphotericin B, and voriconazole can be alternatives for such cases.

## Potential conflicts of interest

The authors declare no conflicts of interest.

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