Cutaneous protothecosis: report of a case with emphasis on histopathology

Luz Ángela Castro[1], María Inés Álvarez[2], María Teresa Ramírez[3]

SUMMARY

Protothecosis is a rare infection caused by algae of the *Prototheca* genus. Its diagnosis is based on microbiological studies and on the identification in biopsies of the characteristic structures of the algae. We present the histopathological findings of protothecosis in a 72 year-old woman with the presumptive diagnosis of chronic actinic dermatitis. The pathological study of a skin biopsy revealed structures with internal septa typical of *Prototheca*. A review of all reports on this disease in Colombia is also presented.

KEY WORDS

Achlorophyllous Algae; Prototheca

RESUMEN

Prototecosis cutánea: presentación de un caso con énfasis en la histopatología

La prototecosis es una infección infrecuente causada por algas del género *Prototheca*. Su diagnóstico se hace mediante estudios microbiológicos o por la identificación del alga en biopsias por su morfología característica. Se presenta el hallazgo histopatológico de prototecosis en una mujer de 72 años con diagnóstico presuntivo de dermatitis actínica crónica; en el estudio anatomopatológico de una biopsia de piel se observaron estructuras con septos internos típicas de *Prototheca*. Se hace una revisión de todos los registros de esta enfermedad en Colombia.

PALABRAS CLAVE

Algas Aclorofílicas; Prototheca

[1] Associated Professor, School of Bacteriology and Clinical Laboratory, Universidad del Valle, Cali, Colombia.
[2] Professor, Department of Microbiology, Universidad del Valle, Cali, Colombia.
[3] Auxiliary Professor, Department of Pathology, Universidad del Valle. Pathologist, Ángel Laboratories, Cali, Colombia
Mail to: María Inés Álvarez; maria.alvarez@correounivalle.edu.co

Recibido: octubre 03 de 2013
Aceptado: octubre 17 de 2013

INTRODUCTION

Ubiquitous and opportunistic algae without chlorophyl of the genus *Prototheca* cause protothecosis, a rare disease that affects both humans and animals (1). Only two species are known to cause disease in humans: *P. wickerhamii,* which is responsible for the majority of infections, and *P. zophii* (2). Neutrophils are considered the main cell defense against *Prototheca,* and the disease has been associated with their defective functioning (3). Both immune-competent and immune-suppressed individuals may develop the disease (1).

On Sabouraud agar *Prototheca* colonies macroscopically resemble those of yeasts, but microscopic examination permits an accurate differentiation that is important for proper treatment.

So far, only six cases of protothecosis have been reported in Colombia (4-7). The finding of *Prototheca* in a skin biopsy, and a review of the previously published Colombian data with emphasis on the histopathological diagnosis are presented.

CASE REPORT

A 72 year-old woman was referred to the Dermatology department because she had suffered for the past six months from erythematous, echimotic plaques with burning and itching sensations in the sun-exposed areas of the neck and upper limbs. With a presumptive clinical diagnosis of chronic actinic dermatitis, a 0.6 x 0.4 x 0.2 cm skin biopsy was taken of the left forearm and, subsequently, an additional 0.4 x 0.3 x 0.2 cm specimen was taken from the scar area.

Histological examination with hematoxylin eosin identified skin including the reticular dermis. Epidermis was normal. In the entire thickness of the dermis, granulomas with epithelioid histiocytes and large multi-nucleated cells containing internal structures similar to fungi were found (figure 1A). For confirmation, staining was carried out with periodic acid-Schiff (PAS) (figure 1B) and Gomori methenamine silver (figure 1C and 1D), which showed organisms with multiple septa in the cytoplasm. A few presented morula-like characteristics of the *Prototheca* algae.

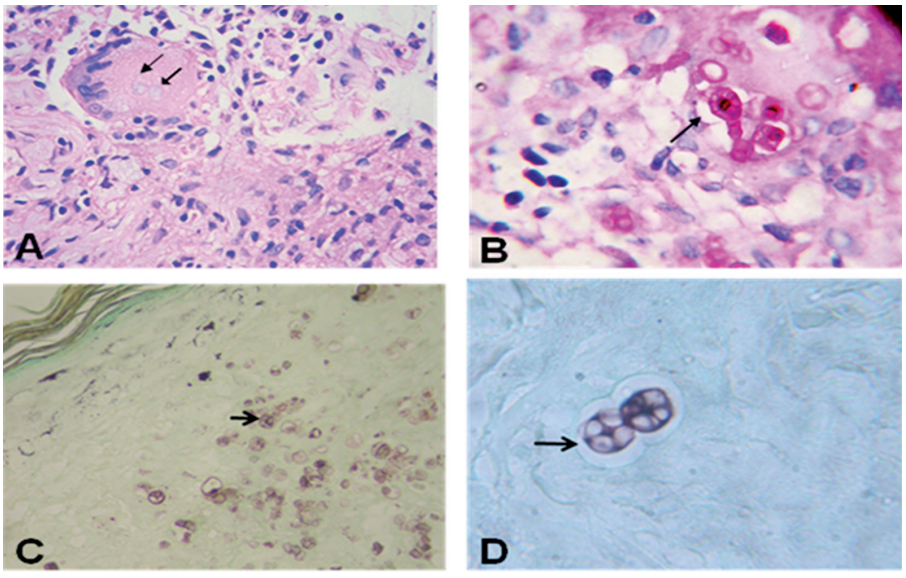

Figure 1. A. Cutaneous protothecosis. Giant multi-nucleated cell with endospores. HE x400. **B.** Morula-like structure with internal septa. PAS x1.000. **C.** Numerous sporangia with endospores located in the dermis. Silver methenamine x 400. **D.** Sporangium with internal septa-forming endospores. Methenamine silver x 1.000.

DISCUSSION

The first human protothecosis case was reported in 1964 in Sierra Leone in a rice farmer with foot lesions (8). Since then about 160 cases have been reported in 34 countries (1). In Colombia, there have been few reports of *Prototheca* infections. In the review by Todd (1) only one case was included from this country, but a national literature search revealed five additional cases (4,6,7); skin presentation was the predominant type (table 1). In the literature skin involvement has also been the most frequent followed by olecranon bursitis (1).

Table 1. Data on the protothecosis cases reported in Colombia

Case	Sex/Age (years)	Site of lesion	Immunocompromised	Diagnostic procedures	Ref/year
1	ND[1]	Skin	No	Histopathology	5/1970
2	Male/40	Olecranon	No	DE[2] and culture	4/1983
3	Female/32	Fingernail	No	Histopathology	4/1983
4	Male/48	Olecranon	No	Hist.[3] and culture	4/1983
5	Male/50	Elbow-subcutaneous	Yes (steroids)	Histopathology	5/1992
6	Male/43	Skin	Yes (drug addict)	Histopathology	6/2001
Current	Female/72	Skin	No	Histopathology	Current

[1]ND: No data, [2]DE: direct exam, [3]Hist.: histopathology

Definitive diagnosis of this condition depends upon the morphological identification of the organism in culture or in tissues based on the presence of sporangia containing multiple endospores (morula). In the present case, the histopathological study that demonstrated these structures was the sole diagnostic procedure (figures 1C, 1D). If a morula is not present, professionals with little experience can confuse the endospores with the fumagoid cells of chromoblastomycosis, *Blastomyces dermatitidis*, *Cryptococcus neoformans* or *Paracoccidioides brasiliensis* (2).

Differentiation from other organisms that produce sporangia with endospores, such as *Coccidioides immitis/C. possadassi* or *Rhinosporidium seeberi,* is based on the size of the sporangia (those of *Prototheca* are generally smaller and contain fewer endospores), typical characteristics that allow the diagnosis without isolation of the agent. Staining procedures that allow a better visualization of the sporangia with the endospores (morula) include periodic acid-Schiff (PAS) and Gomori (2).

In the culture media used in mycology, the appearance of *Prototheca* colonies is similar to that of yeast colonies; however, microscopic observation allows the differentiation. For species identification it is necessary to carry out sugar assimilation tests. One of the most commonly used systems is API 20C Aux (BioMérieux, Marcy l'Etoile, France). Instruments that offer automated identification based on a biochemical profile may also be used, such as the Vitek 2 Compact (BioMérieux, Marcy l'Etoile, France), MicroScan (MicroScan Systems, Inc, Renton, USA) or Phoenix (Becton Dickinson, Franklin Lakes, USA) among others.

To date there is no standard treatment for protothecosis, and its management is still very controversial. Several drugs have been used but no consistent clinical responses have been obtained. Some authors have used amphotericin B, ketoconazole, fluconazole and itraconazole with good results, as well as some antibacterial drugs (2,9,10). The susceptibility to the aforementioned antifungals is due to the fact that *Prototheca* spp., possesses a cell membrane with 4% ergosterol;

on the other hand, it is resistant to echinocandins due to the absence of glucans in the cellular wall (11). Unfortunately, in this case the treatment given to the patient was unknown.

It is still true that ideally the diagnosis of infectious diseases should be established using direct examination and isolation of the causal agent, but sometimes anatomopathological examination is the only method available for diagnosis. Although it is difficult to establish specific infectious etiologies with biopsies, in the case of *Prototheca* it is easy as this organism has morphological characteristics that differentiate it from other agents.

REFERENCES

1. Todd JR, King JW, Oberle A, Matsumoto T, Odaka Y, Fowler M, et al. Protothecosis: report of a case with 20-year follow-up, and review of previously published cases. Med Mycol. 2012;50(7):673–89.
2. Mayorga J, Barba-Gómez JF, Verduzco-Martínez AP, Muñoz-Estrada VF, Welsh O. Protothecosis. Clin Dermatol.2012;30(4):432–6.
3. Hillesheim PB, Bahrami S. Cutaneous protothecosis. Arch Pathol Lab Med. 2011 Jul;135(7):941–4.
4. Guzman M, Ramirez G, Buitrago B. Prototecosis: Informe de tres casos. Biomedica. 1983; 3(4):140-5.
5. Linares G, Baker RD. Prototecosis cutánea: Infección causada por algas. Arch Col Med El Salvador. 1970; 23:194-8.
6. Palacios V, Rodríguez G, Chalela JG. Prototecosis subcutánea en un paciente inmunosuprimido. Rev Soc Col Dermatol. 1992; 1:159-61.
7. Rodríguez G, Ordonez N. Haga usted su diagnóstico. Biomedica. 2001; 21(1):83-5.
8. Davies RR, Spencer H, Wakelin PO. A case of human protothecosis. Trans R Soc Trop Med Hyg. 1964; 25:72-4.
9. Leimann BCQ, Monteiro PCF, Lazéra M, Candanoza ERU, Wanke B. Protothecosis. Med Mycol. 2004;42(2):95–106.
10. Lu S, Xi L, Qin W, Luo Y, Lu C, Li X. Cutaneous protothecosis: two new cases in China and literature review. Int J Dermatol. 2012;51(3):328–31.
11. Min Z, Moser SA, Pappas PG. Prototheca wickerhamii algaemia presenting as cholestatic hepatitis in a patient with systemic lupus erythematosus: A case report and literature review. Med Mycol Case Rep. 2012;2:19–22.