Cutaneous acanthamebiasis infection in immunocompetent and immunocompromised patients

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Tropical medicine rounds

Cutaneous acanthamebiasis infection in immunocompetent and immunocompromised patients

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Abstract

Background Cutaneous acanthamebiasis is a rare infection and few patients have been reported worldwide.

Methods Observational and descriptive study carried out from March 1996 to February 2006 in patients with diagnosis of cutaneous free-living amebic infection caused by *Acanthamoeba* spp. The patients were diagnosed at the Dos de Mayo National Hospital (Lima-Peru) where skin biopsies, histopathologic studies and cultures were performed. The clinical and epidemiologic characteristics, diagnosis, treatment and evolution were recorded in a survey.

Results Five patients with cutaneous free-living amebic infection caused by *Acanthamoeba* spp. were identified. Skin lesions were ulceronecrotic (four patients), an infiltrative bluish plaque (one patient), and a periorbital tumor (one patient). Three patients were positive for human immunodeficiency virus (HIV), had only cutaneous involvement, and died of opportunistic infections. The two immunocompetent patients developed *Acanthamoeba* granulomatous encephalitis and meningoencephalitis that progressed to intracranial hypertension and death.

Conclusion The clinical manifestations of cutaneous free-living amebic infection caused by *Acanthamoeba* spp. appear to vary according to the underlying immunologic status.

Introduction

Free-living amebae (FLA) are amphizoic protozoa. The three genera of medical importance are *Acanthamoeba*, *Naegleria*, and *Balamuthia*, but *Sappinia* cerebral infection has also been reported.[1] These organisms have been classified under two supergroups: Amoebozoa and Excavata.[2] The life cycle of FLA has two stages: trophozoite and cyst. *Naegleria* has an additional, flagellar stage.[3] In 1958, Culbertson *et al*.[4] found that FLA were pathogenic in experimental animals. Fowler and Carter[5] subsequently reported the first human case of amebic meningoencephalitis; the etiologic agent, first thought to be *Acanthamoeba*, was later identified as *Naegleria*. The first human infection with *Acanthamoeba* was described by Jager and Stamm[6] in 1972. Patients with *Balamuthia*[7] and *Sappinia diploidea*[1] infection have since been reported. FLA can affect the central nervous system and typically produce two types of lesion: *Acanthamoeba*, *Balamuthia*, and *Sappinia* cause amebic granulomatous encephalitis (AGE); *Naegleria* induces primary amebic meningoencephalitis (PAM).[8] The entry point for *Acanthamoeba* infection is the skin or upper respiratory tract via airborne cysts.[3] The organism has been isolated from contact lens solutions[3] and from secretions of healthy individuals.[9]

Acanthamoeba and *Balamuthia* cause ocular abnormalities, such as keratitis[10] and corneal ulcers, as well as primary cutaneous lesions.[3] *Acanthamoeba* produces AGE, cutaneous infections, sinusitis, and amebic keratitis. In contrast with PAM, which is characterized by sudden onset, the clinical presentation of AGE is insidious (weeks, months, or years).[11] Involvement of the central nervous system develops after hematogenous spread from a primary cutaneous or respiratory tract lesion.[8–14,16–21] PAM caused by *Naegleria fowleri* usually affects healthy children and young adults with a recent history (7–10 days) of exposure, particularly during the summer months, to contaminated water in lakes, swimming pools, ponds, streams, or mud.[8]

Options for treatment of PAM, AGE, cutaneous infections, nasopharyngeal infections, and amebic keratitis include combinations of antimicrobials and azoles. *Naegleria fowleri* is highly sensitive to antifungal agents, such as amphotericin B. Nevertheless, because of the insidious onset of the disease and typically delayed diagnosis, the mortality rate is high. The use of multiple antimicrobials is recommended to avoid resistance;[12] however, recovery depends not only on antimicrobial therapy, but also on the underlying host defense, virulence of the amebic strain, and early diagnosis and therapy.

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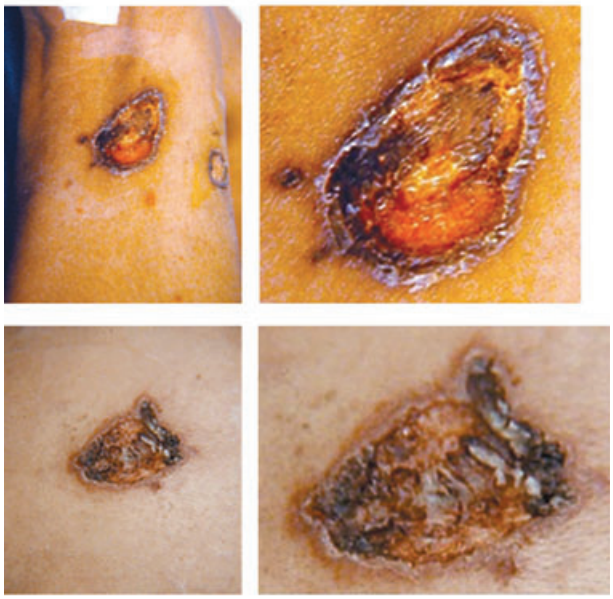
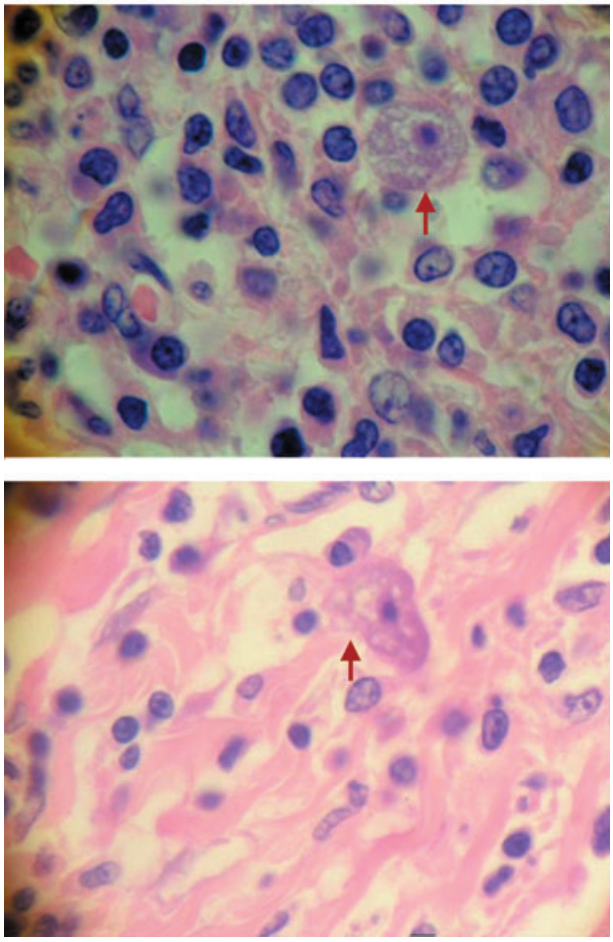
(a)



(b)



Our study sought to determine the clinical, epidemiologic, and histopathologic characteristics of cutaneous free-living amebic infections in immunocompetent and immunocompromised patients at the Dos de Mayo National Hospital, Lima, Peru.

Materials and Methods

Patients with cutaneous acanthamebiasis infection, who were seen at the Dos de Mayo National Hospital by the Teaching Division of Dermatology from March 1996 to February 2006, were studied. Patients were evaluated by a multidisciplinary medical group. Skin biopsy specimens were obtained for histopathologic examination and culture. Specimens were processed by the Institute of Tropical Medicine of the Universidad Nacional Mayor de San Marcos, Lima, Peru. If abnormal neurologic signs or symptoms were detected, fundoscopy and computed tomography (CT) (with and without contrast) of the brain were performed. All patients had human immunodeficiency virus (HIV) testing by enzyme-linked immunosorbent assay; when positive, HIV infection was confirmed by Western blot.

Results

Five patients with FLA infection caused by *Acanthamoeba* spp. were identified during the 11-year period. Cutaneous involvement was mainly in young adult men (four of five patients; average age, 28.4 ± 5.4 years) with an illness lasting for 4.8 ± 2.2 months. Only two patients gave a history of exposure to pond or swimming pool water, which occurred during the year prior to the onset of their disease. Two patients were from outside the capital (Arequipa and Madre de Dios) (Table 1).

Three patients were HIV positive and were thus considered to be immunocompromised. The cutaneous lesions had the following features: ulceronecrotic (four patients), an infiltrative bluish plaque (one patient), and a cellulitis/abscess-like periorbital tumor (one patient) (Fig. 1a). Four patients presented with multiple lesions that predominantly involved the lower limbs (three patients) and upper limbs (two patients). Skin lesions were also located in the thoracic, abdominal, and periorbital areas. Two patients (one immunocompetent and one immunocompromised) had lymphadenopathy. None had amebic keratitis. In all cases, histopathologic

Figure 1 (a) Ulceronecrotic cutaneous lesions caused by free-living *Acanthamoeba* spp. in patients with human immunodeficiency virus (HIV). (b) Histologic description: ulcerated epidermis, necrosis of keratinocytes. The dermis shows an intense inflammatory reaction with a predominance of histiocytes, plasmocytes, and neutrophils. Presence of *Acanthamoeba* spp. trophozoite. Light microscopy; hematoxylin and eosin stain, ×400

Table 1 Characteristics of patients with cutaneous acanthamebiasis infection

				Epidemiology			Immune status		Cutaneous lesions				
Pt	Age (years)	Sex	Duration of illness (months)	Origin	Pond/ swimming pool	Previous diagnosis	HIV	Systemic disease	Number/type of lesion	Location	Lymphadenopathy	Course	Histopathology
1	25	M	3	Coast (Lima)	No	Cutaneous tuberculosis	Yes	Pulmonary tuberculosis	Multiple/ ulceronecrotic	Thorax	No	Partial remission	Ulcerated epidermis, necrosis of keratinocytes. Dermis with intense inflammatory reaction with predominance of histiocytes, plasmocytes, and neutrophils. Presence of FLA trophozoite. A few tuberculoid granulomas
2	31	F	4	Coast (Lima)	No	Leukocytoclastic vasculitis	Yes	No	Multiple/ ulceronecrotic	Lower limbs/upper limbs	Yes	Partial remission	Ulcerated epidermis, necrosis of keratinocytes. Dermis with intense inflammatory reaction with predominance of histiocytes, plasmocytes, and neutrophils. Presence of FLA trophozoite
3	22	M	3	Amazonia (Madre de Dios)	No	Leishmaniasis	Yes	No	Multiple/ ulceronecrotic	Lower limbs/upper limbs	No	Remission	Ulcerated epidermis, necrosis of keratinocytes. Dermis with intense inflammatory reaction with predominance of histiocytes, plasmocytes, and neutrophils. Presence of FLA trophozoite
4	28	M	7	Andes (Arequipa)	Yes	Lymphoma	No	No	Single/cellulitis abscess-like	Periorbital area	Yes	*Acanthamoeba* meningoencephalitis	Epidermis: acanthosis with irregular papillomatosis. Dermis: intense inflammatory reaction with lymphocytes, histiocytes, and plasmocytes involving blood vessels. A focal point of tuberculoid granuloma. Presence of trophozoites and some cysts of FLA
5	36	M	7	Coast (Lima)	Yes	Lymphoma	No	No	Multiple/ infiltrative bluish plaque and ulceronecrotic	Abdomen and lower limbs	No	AGE	Flattened epidermis. Dermis with intense mixed inflammatory infiltrate. Focal points of tuberculoid granuloma. A few trophozoites of FLA

AGE, amebic granulomatous encephalitis; F, female; FLA, free-living amebae; HIV, human immunodeficiency virus; M, male; Pt, patient.

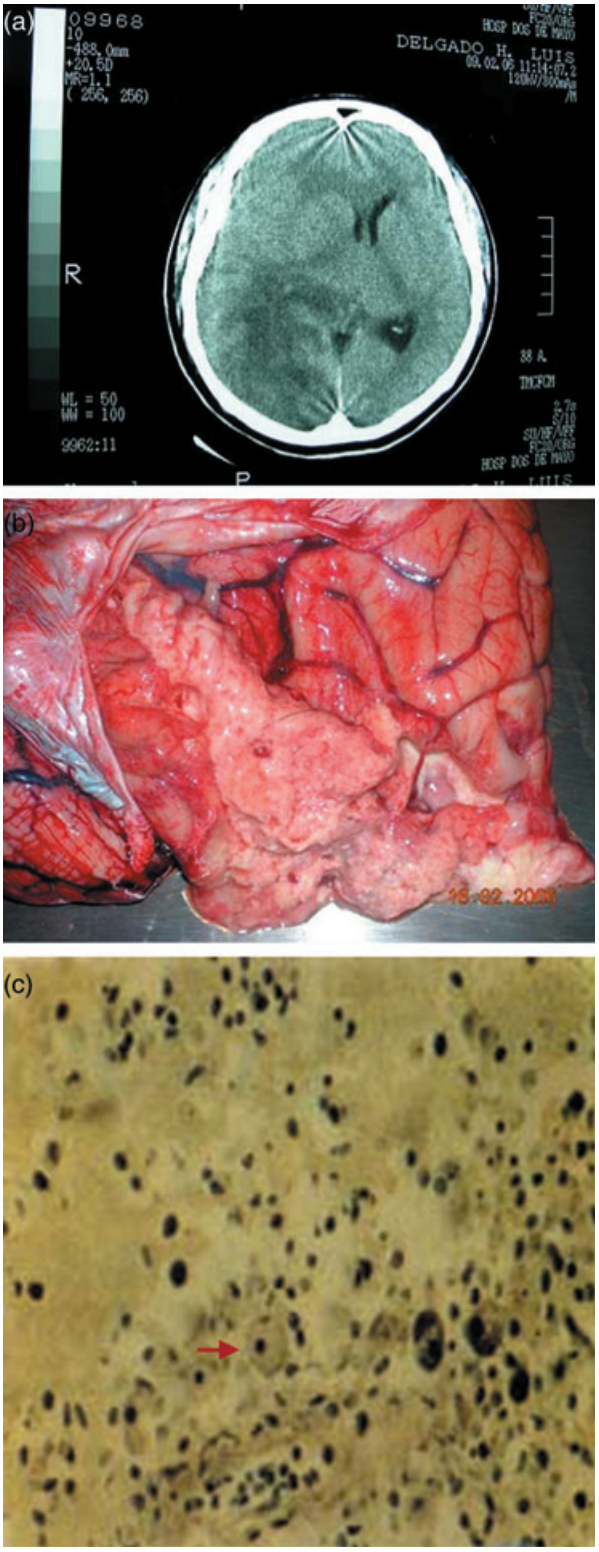


Figure 2 (a) Amebic granulomatous encephalitis (AGE) in an immunocompetent patient. (b) Trophozoites of *Acanthamoeba* spp. in brain tissue. (c) Ferric hematoxylin stain, ×400

study of the cutaneous lesions showed trophozoites and cysts of *Acanthamoeba* spp. (Fig. 1b), and cultures were positive for this organism. The patients had been given a different diagnosis prior to evaluation at our hospital: cutaneous tuberculosis, leishmaniasis, leukocytoclastic vasculitis, and, in two cases, lymphoma. The immunocompromised patients received treatment with itraconazole and amphotericin B, with good clinical response and partial remission of the lesions, but they succumbed to opportunistic infections (disseminated cryptococcosis and miliary tuberculosis). At the time of diagnosis, the two immunocompetent patients had suffered from a longer duration of illness than those who were immunocompromised (7.0 ± 1.4 months vs. 3.3 ± 0.6 months); they developed *Acanthamoeba* AGE (Fig. 2a–c) and meningoencephalitis.

In the patient with AGE, who had a 7-month history of cutaneous lesions and a 1-month history of progressive and intense headache, CT scan showed a cerebral tumor-like mass that shifted the midline. The second patient presented with a papulonodular lesion of the right eyelid that, within 6 months, had evolved into a periorbital tumor and was accompanied by progressive sensory loss, psychomotor agitation, and meningoencephalitis. Both patients developed intracranial hypertension and died despite medical intervention.

Discussion

The present study shows that the clinical characteristics of cutaneous free-living amebic infection caused by *Acanthamoeba* spp. differ according to the underlying immunologic competence. Immunocompromised patients tend to have multiple subacute cutaneous lesions, without central nervous system involvement and with a good response to therapy. In contrast, immunocompetent patients present with an insidious onset of chronic cutaneous lesions, followed by central nervous system compromise and death. In general, cutaneous lesions are late manifestations of disseminated acanthamebiasis, especially in patients with AGE.

Cutaneous lesions are typically papulonodular, exhibit purulent drainage, and ultimately develop into poorly healing/nonhealing ulcers.[13] Papules, pustules, plaques, cellulitis, and intramuscular abscesses have also been described. The lesions may be pruritic, tender, or nontender.[14] The broad spectrum of diseases in the differential diagnosis may be misleading, including other types of infection, pyoderma gangrenosum, and vasculitis.[13] Patients from Amazonia, who have papulonodular and eventually ulcerative lesions, most often are thought to have a deep mycosis. In developing countries, cutaneous tuberculosis or atypical mycobacteria should be considered. The latter is more common in immunocompromised patients. Cytomegalovirus (CMV) and herpes simplex virus (HSV) infection frequently present as chronic periorificial ulceration.[13]

Infection caused by acanthameba is rare, and few patients have been reported from Peru. Worldwide, approximately 200 cases of systemic acanthamebic infection and more than 3000 patients with keratitis have been reported.[3] In Peru, some previously described cases resemble those described here; however, the immunologic condition of these patients was not compared with the clinical manifestations. In 1979, Arce and Asato[15] reported a case of *Acanthamoeba* encephalitis, and, in 1996, Narváez[16] reported four cases of *Acanthamoeba* encephalitis. The Institute of Tropical Medicine of the Universidad Nacional Mayor de San Marcos described 10 patients with isolated cutaneous ulcers caused by acanthamebiasis. In 2000, a patient with cutaneous acanthamebiasis[17] was presented and, in 2002, two with cutaneous involvement and one with ocular compromise were described.[18] In the Peruvian National Institute of Health, from 1995 to the present, three cases of acanthamebiasis have been evaluated, all with ocular involvement (María Beltrán, Coordinator of the Laboratory of Enteroparasites, Instituto Nacional de Salud, personal communication). Between April and May 1999, 15 samples from patients at the Department of Ophthalmology, Cayetano Heredia Hospital, Peru were positive for *Acanthamoeba*.[19] The international literature contains several reported cases[20–25] of *Acanthamoeba* meningoencephalitis, with characteristics similar to those of our patients.

In contrast with the clinical presentation described for *Naegleria* sp. (PAM), we found that *Acanthamoeba* spp. infection presented an insidious course with neurologic signs and symptoms developing 6 months after cutaneous infection of the right eyelid. Only two patients presented with a history of bathing in a pond/pool. Therefore, the absence of such a history should not eliminate the diagnosis if the clinical characteristics are compatible with free-living amebic infection. The clinical characteristics of cutaneous free-living amebic infection caused by *Acanthamoeba* spp. appear to vary according to the underlying immunologic status.

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