South American Cutaneous Leishmaniasis of the Eyelids

Report of Five Cases in Rio de Janeiro State, Brazil

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Purpose: To describe American cutaneous leishmaniasis of the eyelids and highlight the main clinical and diagnostic features of lesions, which are rare in this location.

Design: Retrospective, noncomparative case series

Methods: Leishmanin skin test, touch preparations, histopathologic analysis, and culture in appropriate media were used for clinical confirmation and parasitologic diagnosis. Positive cultures were identified by the iso-enzymes technique. All patients were treated with pentavalent antimony applied intramuscularly.

Results: Leishmanin skin test was positive in all five patients. Touch preparations, histopathologic analysis, and culture were performed in four patients. Touch preparations were positive (presence of Leishman's bodies) in two patients; histopathologic analysis showed a granulomatous infiltrate in four patients and parasite was present in two patients; culture was positive in three patients, and in two the parasite was identified as *Leishmania* (*Viannia*) *braziliensis*. Therapy was effective for all patients.

Conclusions: Cutaneous leishmaniasis of the eyelids is uncommon in the Americas. The disease may present diagnostic difficulties when appearing in nonendemic areas. The clues for diagnosis are the clinical aspect of lesions, the epidemiologic data, and a positive Leishmanin skin test. Demonstration of parasite is not always possible. Pentavalent antimonial compounds are the therapy of choice. Formerly, transmission of leishmaniasis occurred only when humans penetrated forested areas and became an incidental host. Now, eyelid lesions are part of the changing pattern in the transmission of the disease. With the increase in ecotourism, these lesions may begin to be seen in air travelers returning to other parts of the world. *Ophthalmology 2000;107:169–172*

American cutaneous leishmaniasis is endemic in many areas of Central and South America.[1] It is characterized by skin ulcers at the site of the primary inoculation of parasitic protozoa of the genus *Leishmania* (Kinetoplastida: Trypanosomatidae). These parasites possess a unique mitochondrial or kinetoplastic DNA and are highly diverged eukaryotic cells. In nature, all *Leishmania* species are transmitted by the bite of infected phlebotomine sand flies (Diptera: Psychodidae) of the genus *Phlebotomus* in Old World and *Lutzomyia* in the New World. Typically, ulcers appear at the bite site after an incubation period of 3 to 8 weeks and are commonly located in exposed areas of the body. Inferior limbs, superior limbs, and the face are more commonly affected, but eyelid lesions are more rarely seen. Diagnosis is made by the epidemiologic notion, clinical history and aspect of lesions, a positive Leishmanin skin test, and demonstration of parasite by touch preparations, histopathologic sections, culture in NNN (Novy, McNeal, and Nicolle) medium or detection of parasite DNA.

Pentavalent antimonial compounds are the therapy of choice. Antimonial compounds are commercially available in South America as Glucantime (Rhodia Laboratories, Anton, France). In English-speaking countries, the product is sodium stibogluconate or Pentostan (Wellcome Foundation, London, UK). In the United States, the drug can be obtained from the Centers for Disease Control in Atlanta, Georgia. The recommended dosage is 20 mg per kilogram of body weight per day for at least 3 weeks.[2] Side effects are common with pentavalent antimony and include muscular and joint pain, nausea, anorexia, and increase of the Q–T interval in ECG (electrocardiogram).

Materials and Methods

Patients

The studied patients were examined in the outpatient unit of the Evandro Chagas Hospital, Oswaldo Cruz Foundation, Rio de Janeiro,

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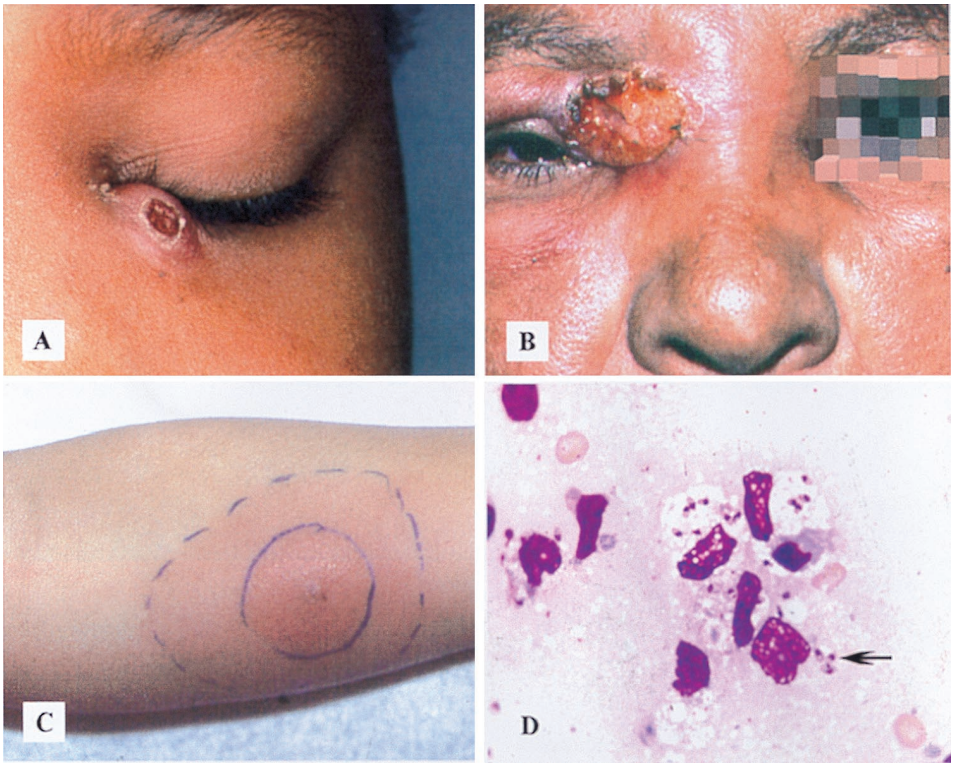

Figure 1. A, Clinical aspect of lesion in patient 1. **B,** Note the vegetating lesion and swelling of right superior eyelid in patient 2. **C,** Strongly positive leishmanin skin test in patient 1. **D,** Touch preparation in patient 2. Numerous amastigotes or Leishman's bodies are present (stain, Leishman; original magnification, ×1000).

Brazil. All patients proceeded from endemic regions of Rio de Janeiro State and patients had only eyelid lesions at presentation.

Diagnostic Methods

Leishmanin Skin Test. The Leishmanin skin test was performed in all patients by intradermal injection of 0.1 ml of the antigen in the volar surface of forearm, and the tests were measured 48 hours later. A positive test showed an indurate nodule 5 mm or more in diameter.[3,4] In patient 5 this was the only diagnostic test used.

Biopsies. Wedge-shaped incisional biopsies were performed in four patients (patients 1, 2, 3, and 4) after local anesthesia with Lidocaine. The resulting fragment was subdivided into two parts. The first was used for touch preparation stained with a Romanowsky-based stain (Leishman dye [Merck, Darmstadt, Germany] 0.15% in methanol) and then fixed in buffered formalin, embedded in paraffin, and stained with hematoxylin–eosin. The second part was used for cultivation in NNN media.[5] When possible, the culture was identified according to species by the isoenzyme technique.[6]

Case Reports and Results

Patient 1. A 4-year-old boy sought treatment 2 months earlier for a small pimple in the left inferior eyelid that slowly increased in size, becoming eroded on top. Dermatologic examination identified an indurate erythematous nodule 0.9 cm in diameter located at the interior angle of left inferior eyelid (Fig 1A). The lesion was painless. Leishmanin skin test was strongly positive, showing an indurate papule 16 mm in diameter (Fig 1C). Skin biopsy revealed a granulomatous infiltrate with few amastigotes. Touch preparation was negative as well as the culture in NNN medium.

Patient 2. A 69-year-old woman reported a small lump in the inner angle of right superior eyelid. In 3 months the lesion increased in size. Clinical examination revealed a symptomless ulcero-vegetating lesion 3 cm in major diameter, an infiltrate base, and raised, erythematous borders. There was considerable edema of the superior eyelid (Fig 1B). Leishmanin skin test was positive, showing an indurate papule 13 mm in diameter. A biopsy was taken and submitted to touch preparation, histopathologic analysis, and culture. Touch preparation was positive for Leishman's bodies (amastigotes) (Fig 1D). Histopathologic analysis revealed a granulomatous infiltrate with numerous plasma cells and no parasites. Culture was positive for *Leishmania* species.

Patient 3. A 12-year-old girl sought treatment 3 months after the appearance of a lesion that initially was a lump at the right superior eyelid that then rapidly increased in size to become ulcerated. The patient reported difficulty opening her eyelid. Clinical examination revealed an ulcer, oval in shape with raised borders and measuring 3 cm in the major diameter (Fig 2A). Leishmanin test was positive, showing an indurate papule 30 mm in diameter. A biopsy was performed and submitted to touch preparation, histopathologic analysis, and culture. Touch preparation was negative for parasites. Histopathologic analysis showed a heavy, mononuclear cell infiltrate with numerous macrophages and granuloma formation, but parasites were not detected (Fig 2B). Culture was positive, and the parasite was identified by isoenzyme technique as *L.* (*Viannia*) *braziliensis*.

Patient 4. A 7-year-old girl sought treatment 4 months after the appearance of a lesion that initially was a small inflammatory papule at the left inferior eyelid and later became enlarged and ulcerated. Two months after the onset, the lesion extended to the superior eyelid. The patient reported an itching sensation in the affected eye. Dermatologic examination showed an ulcerated lesion of the left inferior eyelid and an infiltrate erythematous plaque-like lesion of the superior eyelid (Fig 2C). Leishmanin skin test was positive, showing an induration of 18 mm. A biopsy was performed and touch preparation, histopathologic analysis, and culture were positive for parasite. Subsequent identification of culture by isoen-

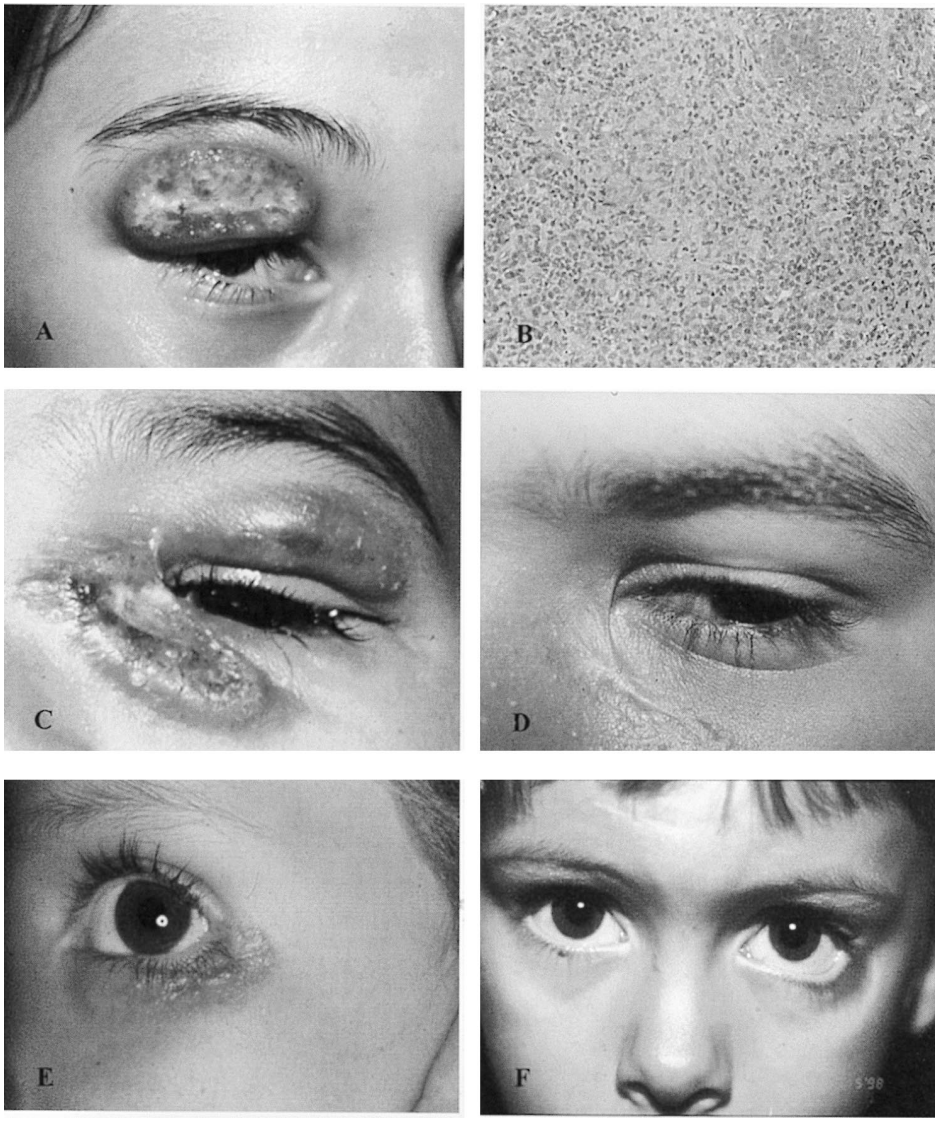

Figure 2. A, A large ulcer of the right superior eyelid in patient 3. **B,** Histopathologic analysis of the lesion in patient 3. Note the heavy inflammatory infiltrate of upper dermis with epithelioid cells granuloma (the more clear zone at center) (stain, hematoxylin–eosin; original magnification, ×100). **C,** Clinical aspect of lesion in patient 4. **D,** Epicanthus developed after healing in patient 4. **E,** A shallow ulcer in left inferior eyelid of patient 5. **F,** After healing, a discrete ectropion could be noted in patient 5.

zyme procedure classified the parasite as *L.* (*Viannia*) *braziliensis.*

Patient 5. A 4-year-old boy sought treatment for a shallow ulceration of left inferior eyelid (Fig 2E) that had appeared 2 months earlier. The lesion was painless, but the child reported an "itching eye." A leishmanin skin test was positive, showing an 18-mm indurated nodule. No further diagnostic procedures were used in this patient.

In all patients the lesions were confined to eyelid skin, but in patients 2, 3, and 4, some irritation of conjunctiva with teary eyes were noted.

Differential Diagnosis

Early papulonodular lesions should be distinguished from other inflammatory conditions such as chalazion or hordeolum. Such nodular, tumor-like lesions, when ulcerated on top (Fig 1A, B), may resemble keratoacanthomas or basal cell carcinomas, especially in older adults. The epidemiologic data and a positive leishmanin test are the clues for a precise diagnosis.

Therapy

The 20 mg/kg per day dosage was used in patient 1. In all other patients, an alternative, smaller dosage of 5mg/kg per day over a 30-day period was used with good results.[7] Cutaneous leishmaniasis usually leaves no sequels other than the occasional anesthetic scar. However, in the case of eyelid lesions, we observed after treatment an epicanthus in patient 4 (Fig 2D) and a slight ectropion in patient 5 (Fig 2F).

Discussion

Parasites are infrequent causes of ophthalmic diseases and include protozoa, helminths, and arthropods. Among protozoa, the more important are *Acanthamoeba*, *Microsporidia*, *Toxoplasma*, and *Leishmania*.[8] At the beginning of the century in this region of Brazil, leishmaniasis was typically a zoonosis with humans becoming an incidental host when they penetrated the forest, usually for professional reasons

(railroad construction) or hunting.[9] The continuous destruction of Atlantic rain forest, mainly for agricultural purposes, has led to the change in the vector of biologic behavior, and sandflies can now be observed around and inside houses, affecting man as well as domestic animals such as dogs and horses.[10,11] With the increased facility in air travel and the increase in "ecologic" tourism and "adventure" holidays, foreign tourists may stay overnight in what seems to be a sheltered place and may experience infected insect bites. When returning home, such individuals may seek diagnosis and treatment in areas where the disease is rare or unknown. The more effective treatment is with pentavalent antimonial compounds, and the dosage recommended by the World Health Organization is 20mg/kg per day over 3 weeks.

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Pseudotumor cerebri

When treating pseudotumor cerebri,
In normal logic you can't rely.
For she won't lose the fat,
No, anything but that!
But serial LP she will try.

Andrea Varner Gray, MD
Roseburg, Oregon