

HTLV-1 - associated infective dermatitis in an adult

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Abstract

Infective dermatitis is a form of chronic, relapsing eczema described as a specific dermatosis associated with HTLV-1 infection. It mainly affects children, and only exceptionally adults; thus, few of the latter cases have been published. We present a case of a 42-year-old woman with generalized eczema of 23 years of evolution, with repeated cutaneous infections exacerbating the dermatosis, and relapses after antibiotic treatment discontinuation. Diagnosis of HTLV-1 and virus-associated infective dermatitis is reached with the patient hospitalized, after ruling out adult T-cell leukemia-lymphoma. Antibiotic treatment is prescribed, with good response (Dermatol Argent 2009; 15(1):49-53).

Key words: *infective dermatitis, HTLV-1.*

Introduction

The HTLV-1 virus is the first human retrovirus wherein oncogenic potential was demonstrated. Infection occurs worldwide, with an estimate of about 20 million infected people, but only 5% develop some pathology.

Various diseases have been associated to HTLV-1 infection. The first one to be identified was adult T-cell leukemia-lymphoma (ATLL), confirmed by demonstration of monoclonal integration of proviral DNA to the neoplastic cell genome. Subsequently, a type of spastic myelopathy known as tropical spastic paraparesis (TSP) was identified, generally considered an expression of an infection acquired in adult life.¹

In the late,² a severe type of eczema known as infective dermatitis (ID) was recognized as a HTLV-1-infection specific dermatosis, usually a marker of early infection (since it appears in children). However, cases of childhood TSP have been published, as well as of ID in adults,³ and both pathologies may appear associated in the same patient.⁴

This report would be the first national adult case of ID.

Clinical case

A 42-year-old female patient from Paraguay.

Personal history: Exclusive sexual partner of same origin, living together for 7 years (from 18 to 25 years of age).

Current disease: She appears at the physician's office owing to the presence of a 23-year-evolution dermatosis, characterized by generalized eczema and poor response to steroid

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and antihistamine treatment. Repeated skin infections exacerbate her dermatosis, with recurrences after discontinuation of antibiotic treatment.

Physical examination. Diffuse, scaling, and exudative eczema almost completely involving the integument. On the cephalic pole, involvement of the scalp covered by furfuraceous scaling, discrete alopecia of eyebrow tails, external ear duct exudate with yellowish crusts (**Figure 1**) and retroauricular fissured and exudating intertrigo (**Figure 2**). On the anterior trunk, multiple erythematous milliar papules aggregated in sectors (**Figure 3**). On the back, marked skin infiltration whereon punctiform erosions. Lichenification of axillary fold, antecubital and popliteal fossae (**Figure 4**). In lower limbs, extended erosive-crusted surfaces alternating with small and irregular hyperpigmented maculae as sequeale, and marked cutaneous infiltration at knee level (**Figure 5**). The dermatologic picture is associated with intense itching, fever, and generalized lymphadenopathies (tough-elastic, painless, not adhered at deep levels).

Laboratory tests:

- Routine laboratory tests: eosinophilia (21.9 percent). Orther tests within normal values/limits.
- IgE Dosage: >1000 IU.
- Electrophoretic proteinogram: polyclonal hyper-gammaglobulinemia.
- Serology for HAV, HBV, HCV, EBV, HIV: (-).
- Bacteriological test: skin biopsy culture: (+) for *methicillin-sensible S. aureus*.
- Skin biopsy: spongiotic dermatitis with eosinophilia (**Figure 6**).

Owing to the torpid and long evolution of dermatosis, studies are done to rule out an associated lymphoproliferative process:

- **HTLV-1 serology, ELISA and Western Blot: reactive.**
- **HTLV-1 PCR (skin biopsy): reactive.**
- CD4/CD8 ratio: 3.3 (normal value: 2).
- Neck/chest/abdomen and pelvis CT: no abnormality discovered (NAD).
- Peripheral blood smear: eosinophilia, remaining tests NAD.
- Axillary/inguinal lymph node biopsy: follicular hyperplasia.
- Axillary lymph node flow cytometry and bone marrow aspiration: NAD. After ruling out a lymphoma, an HTLV-1-associated infective dermatitis diagnosis is suggested.

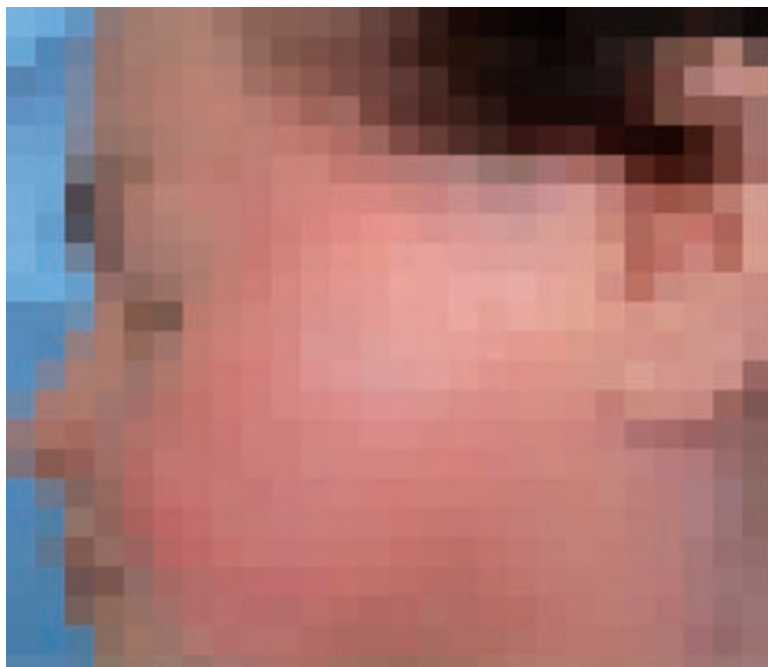


Figure 1. Scalp involvement and yellowish crusts crusting in external ear canal.



Figure 2. Fissured retroauricular intertrigo.

Evolution: parallel course to recurrent infections. The underlying pathology is exacerbated with each infection, and improves with treatment.

Treatment: antibiotic for infectious recurrences, antihistamines, topic emollients-corticoids, and thalidomide 100 mg/d.



Figure 3. Multiple erythematous miliary papules.



Figure 4. Lichenification of popliteal areas.

Comments

HTLV-1 is a cosmopolitan virus, but with higher prevalence in areas such as Asia (especially Japan), Africa, the Caribbean islands, and South America. In the latter, the country with the higher absolute number of infected individuals is probably Brazil, in its northern area.⁵ Cases have also been detected in Paraguay, Colombia, Chile, Peru, Bolivia, and in Argentina, especially in the northwestern provinces (as opposed to HTLV-2, whose seroprevalence is higher in the northeastern provinces). Seroprevalence in blood banks in Jujuy is 1 percent, with high prevalence of TSP.⁶

This led to the passing of a provincial act in the 90's, requiring virus tests in the provincial blood banks. Prevalence in the general population associated with HIV is 8 to 13 percent and higher in intravenous drug addicts.

As with other retroviruses, transmission route may be: a) by sexual contact, with higher prevalence in sex workers (2.8 to 5.7 percent); b) by transfusion (intravenous-drug addiction), and c) vertical (transplacental, through birth canal, and especially by breastfeeding). The longer breastfeeding time and the larger maternal viral burden, the higher probability of transmission.⁷

Once infection occurs, the virus is incorporated to the host cell DNA as a provirus and may remain in latent status or start replicating; a multifunctional viral protein, known as TAX, plays a major role in the physiopathogenicity of infection. This viral capacity to incorporate itself to the cell genome enables it to acquire or transduce genetic material and activate or inactivate cell genes that are essential to the mechanisms of carcinogenesis.⁸ In addition, there may be a cytotoxic effect on CD8 cells, releasing cytokines and immunoglobulins with nervous system effects such as progressive and irreversible demyelination. There is seemingly a contribution to cell immunity deficit with polyclonal immunoglobulin production and activation of the proinflammatory cytokines such as IL-1, IL-6, and TNF- α .

In addition, however, it is likely that other factors inherent to the host are required for disease development (immunogenetic factors). It has been suggested that the presence of certain HLA-haplotypes would increase susceptibility to HTLV-1 infection (association with HLA DRB1 and DQB1 was found in members of infected families).⁹

Diagnosis is by ELISA and Western Blot serology (the latter is confirmatory and enables HTLV-1 and HTLV-2 differentiation). HTLV-1 identifica-

tion requires the presence of antibodies to p24, p19, rgp46-1, and rgp21 proteins.¹⁰ High titers of antibodies would relate to higher probability of developing a disease (prognosis value). Diagnosis is supplemented by PCR in blood, cerebrospinal fluid, or tissue samples (skin, lymph nodes), which is especially useful for indeterminate serology.⁹

Quantitative PCR enables viral burden variation detection at different infective stages; a relation between PCR and risk of developing ATLL, TSP or ID is suggested.¹¹

An interesting aspect of this virus is its skin-tropism.¹² Infection prevalence is higher in patients with a dermatosis. The virus has been identified by PCR in the skin of seropositive patients, even in the absence of skin lesions (43 percent); postulating that this finding could have a predictive value.¹³

Infective dermatitis was first described in 1966 by R. Sweet in a group of Jamaican children; it is a special type of chronic and relapsing eczema.¹⁴ Twenty-four years later, La Grana et al.² recognize a clear association between this new entity and the human lymphotropic retrovirus (HTLV-1).

ID affects mostly children, with shedding, exudating features as distinctive traits, and persisting pyogenic infections. Preferred locations are scalp, folds (retroauricular, axillar, perineal), anterior nares, neck, and umbilicus,^{3,9} and is associated with mild to moderate itching, and adenopathies. Occasionally, it is associated to blepharconjunctivitis. *Staphylococcus aureus* and/or β -hemolytic *Streptococcus* is often re-



Figure 5. Erosive crusty surfaces, and marked skin infiltration.

covered in skin cultures,⁷ (94 percent of cases), and recurrences usually appear after discontinuation of antibiotics. Histopathological examination studies of ID are nonspecific and reveal acanthosis with mild to mode-

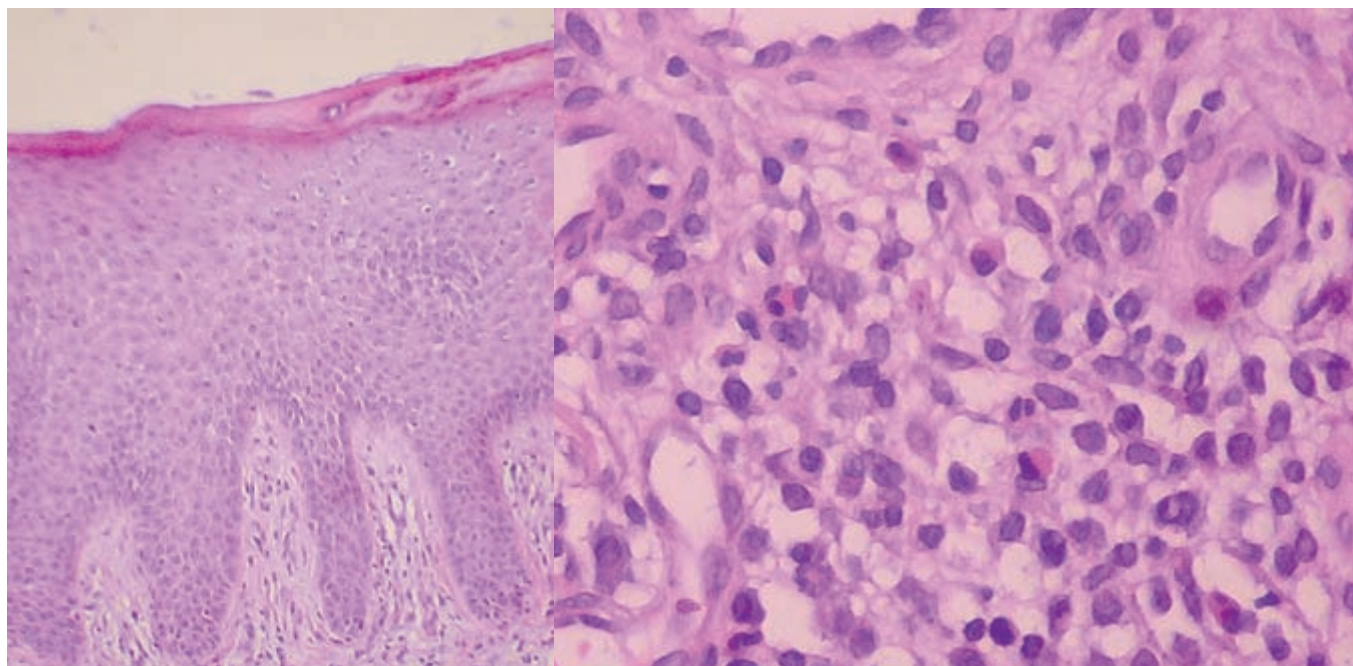


Figure 6. Spongiotic dermatitis with eosinophilia

TABLE 1. INFECTIVE DERMATITIS DIAGNOSIS CRITERIA. LAGRENADE.²

Major criteria
• Eczema of scalp, axillae, groin, external ear, retroauricular area, eyelids, perinasal skin and/or neck.
• Chronic watery nasal discharge without other signs of rhinitis and/or crusting of anterior nares.
• Chronic relapsing dermatitis with prompt response to appropriate antibiotic treatment but prompt recurrence upon discontinuation of antimicrobials.
• Onset typically in early childhood.
• HTLV-1 seropositivity.
Minor criteria
• Positive skin or anterior nares cultures for <i>S. aureus</i> and <i>S. pyogenes</i> .
• Fine, generalized papular rash.
• Generalized lymphadenopathies.
• Elevated ESR.
• IgD and IgE hypergammaglobulinemia.
• Elevated CD4 and CD8, and CD4/CD8 ratio.

rate spongiosis, and occasionally collections of neutrophils are described in stratum corneum. Dermal lichenoid, or perivascular and perianaxial lymphocyte infiltrate may be found.³ Lymphocyte epidermotropism, with or without atypical lymphocyte collection and dermal lymphocyte aggregations, may be seen in a small number of cases.

Immunohistochemistry reveals greater CD8 and CD57 positivity.¹⁵ These morphological findings, together with CD7 negativity (mature T lymphocytes), are very similar to those found in early stages of ATLL. This leads some researchers to suggest that ID is an early stage of ATLL.⁹

It is suggested that ID could be a marker of more severe associated pathologies, such as ATLL and TSP.^{3,7,9,10}

ID diagnosis is eminently clinical; differential diagnosis is with atopic dermatitis and seborrheic dermatitis. Major and minor criteria are proposed. Four of five major criteria are necessary; and the first, second, and fifth are mandatory (**Table 1**). Our patient showed three major criteria (first, third, and fifth), and all minor criteria. Although ID is a childhood disease, 2 adult cases have been published.³ Dermatoses development occurred in adulthood in our patient, and the presence of HTLV-1 virus was determined in blood and by PCR in skin biopsy.

In regard to the second major criterion, our case did not show rhinorrhea or crusting in anterior nares. However, a series of 15 patients where the absence of this sign did not invalidate diagnosis was recently published. The authors suggest that this criterion may be deemed transient, and thus not mandatory.⁷

In conclusion, we believe it to be of interest to publish this first case in Argentina of an adult patient with unusual presentation of ID associated with HTLV-1 infection.

HTLV-1 infection is an emerging virosis with marked skin tropism, whose understanding should be further explored in the dermatological field.

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