Infective Dermatitis in an Adult Patient With HTLV-1

Beatriz Di Martino Ortiz, MD,* Rosalba Riveros, MD,* Raquel Medina, MD,* and Maida Morel, MD†

Abstract: Infective dermatitis is a chronic exudative eczematous eruption presenting in human T-lymphotropic virus type 1 (HTLV-1)-infected people. It presents with relapsing erythematous, scaly, and crusted lesions affecting simultaneously the scalp, external ear, retroauricular area, eyelid, paranasal skin, neck axilla, and groin. Superimposed *Staphylococcus* and *Streptococcus* infection are common. It mainly affects children and exceptionally adults, and there are only a few published cases. The authors present the first reported case in Paraguay of an adult patient who had symptoms of human T-lymphotropic virus type 1-associated progressive tropical spastic paraparesis, and 6 years after the onset of the neurological symptoms, the patient developed infective dermatitis lesions on the skin, with frequent exacerbations since then.

Key Words: spastic paraparesis, tropical paraparesis, HTLV-1, infective dermatitis

(*Am J Dermatopathol* 2015;37:944–948)

INTRODUCTION

Human T-lymphotropic virus type 1 (HTLV-1) was the first human retrovirus with demonstrated oncogenic potential. Its infection exists worldwide, and it is estimated that about 20 million people are infected but only 5% of them developed any pathology. Different diseases have been associated with HTLV-1. The first identified was adult T-cell leukemia–lymphoma (ATLL), confirmed by the demonstration of monoclonal integration of proviral DNA into the genome of neoplastic cells. Later on, a type of spastic paraparesis called tropical spastic paraparesis (TSP) was identified, generally regarded as an expression of acquired infection in adult life.^{1,2}

In 1980, Poiesz et al in the United States identified and isolated the first human retrovirus in a patient with cutaneous T-cell lymphoma. In 1985, Gessain et al³ found antibodies against HTLV-1 in patients with myelopathy and spastic paraparesis who were carriers of the virus, which led to establish the double pathological role of this virus.^{4–6}

In 1966, Sweet⁷ reported in Jamaica the first case of infective dermatitis (ID) in children. In 1967, Walshe documented the clinical and biological features of the disease in 25 Jamaican children, noting its association with malnutrition and infection

by *Staphylococcus aureus* and *Streptococcus* beta hemolyticus with poor response to antibiotic treatment, postulating that malnutrition resulted in immunosuppression. In 1990, LaGrenade et al defined ID as an early marker for HTLV-1. Years later, it was determined that ID does not only belong to children.^{8–10}

We present the first case described in our country of ID and spastic paraparesis in a patient with HTLV-1 infection.

CASE REPORT

A 40-year-old man who is a painter, single, from an urban area of Paraguay with no vicious habits followed by the Neurology service for 10 years for symptoms of HTLV-1-related progressive TSP, treated with prednisone 50 mg once daily and then gradually decreased, and then with pregabalin 75 mg once daily, gabapentin 800 mg once daily, and baclofen 10 mg once daily.

He consulted the Dermatology service for dry skin, markedly predominant in extremities, and generalized itching of 3-month duration.

On physical examination, there are erythematous, scaly, eroded, and crusted patches with jagged edges, fuzzy boundaries spread over face, neck, trunk, and extremities, predominantly in lower back, thighs, knees, and flexures. Lichenification areas are also present (Figs. 1–3).

Histopathology of 3 Skin Sites

1. Epidermal acanthosis with irregular to psoriasiform elongation of rete ridges (ortho and parakeratosis).
2. Epidermal spongiosis with exocytosis of leukocytes (neutrophils and lymphocytes) within it.
3. Collection of subcorneal/intracorneal neutrophils and cellular debris (Figs. 4, 5).

The following tests were requested:

1. Hematology: HB, 11.6 g/dL; WBC, 11,800 cells per cubic millimeter; N, 32%; lymph, 32%; Eos, 44%; Plat, 402,000; ESR, 60 mm; hematocrit, 35. Peripheral blood smear: Eos, 42%. Rest of routine, normal.
2. Blood cultures: positive for MRSA 3/3. Urine culture: negative.
3. Elisa for HIV: nonreactive.
4. HTLV-1: positive (EIA method).
5. Nasal swab sample for *S. aureus*: negative.
6. Coproparasitology: positive for *Escherichia coli* (>10,000 CFU).

Final Diagnosis: ID and Spastic Paraparesis in an Adult Patient With HTLV-1

Evolution

The patient was treated for the dermatological symptoms with emollients, topical corticosteroids, oral antihistamines, and topical and oral antibiotics, plus topical antifungal because of a frequent

From the *Department of Dermatology, Clinicas Hospital, Faculty of Medical Sciences, National University of Asuncion, Asuncion, Paraguay; and †Neurological Center, Clinicas Hospital, Faculty of Medical Sciences, National University of Asuncion, Asuncion, Paraguay.

The authors declare no conflicts of interest.

Reprints: Beatriz Di Martino Ortiz, MD, 1019 Peru Street, Asuncion 1412, Paraguay (e-mail: beatrizdimartino@gmail.com).

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

FIGURE 1. Clinic: patient overview.

association of this entity with intertrigo. The patient had several referrals to the emergency room of our hospital for fever and two episodes of sepsis that started in the skin in October, 2013 and June, 2014. On both times, a MRSA 3/3 was isolated from blood cultures, and in the last episode, the same germ was found in urine culture. He also had a crusted scabies outbreak and intertrigo with good response to systemic antibiotics, ivermectin, and topical and oral antifungal therapy.

COMMENTS

HTLV-1 is a cosmopolitan virus, although its highest prevalence is found in some regions such as Asia (especially Japan), Africa, the Caribbean, and South America (Argentina, Bolivia, Brazil, Colombia, Chile, Ecuador, Peru, Venezuela). In our continent, Brazil, in its northern area, is probably the country with the highest absolute number of infected people. Some cases have also been detected in Paraguay.^{1,4,11,12}

Just like it happens with other retroviruses, transmission can be through (1) sexual contact, with highest seroprevalence in female sex workers (2.8%–5.7%), (2) transfusions (intravenous drug users), with a seroconversion of 40%–60% among exposed subjects in a 60-day period, and (3) vertical transmission (transplacental, birth canal, and especially with breastfeeding). The more the breastfeeding time and maternal viral load are the more the likelihood of transmission is. Children get infected fundamentally through breast milk, unlike with HIV.^{1,2,13,14}

Not all people infected with HTLV-1 will develop complications, and up to 90% of HTLV-1 carriers remain asymptomatic. However, the remaining 10% develop HTLV-1–associated diseases. Some of those associated diseases could be very severe, like ATLL and TSP/HTLV–associated myelopathy.

When function and reproduction of T cells are interfered by HTLV-1, it can cause several diseases, separated in three categories: (1) neoplasms: mainly ATLL, (2) inflammatory syndromes: TSP, uveitis, thyroiditis, and alveolitis, (3) complications: infections, including strongyloidiasis, scabies, tuberculosis, and ID.^{15,16}

ID affects mainly children, and the characteristic feature is the presence of desquamation and exudation, with persistent purulent cutaneous infections. Most common locations include the scalp, skin folds (retroauricular, axillae, and groin), nares, neck, and umbilicus. It has mild-to-moderate pruritus and adenopathy. Sometimes, it can be associated with blepharoconjunctivitis. In skin cultures, *S. aureus* and/or beta hemolytic *Streptococci* are frequently found (94% of cases), and they usually relapse after discontinuation of the antibiotic.^{1,11,13,17,18}

Histopathology study of ID is not specific and it reveals acanthosis, with mild-to-moderate spongiosis, and occasional conglomerates of neutrophils in the stratum corneum. Dermis observation shows lymphocyte infiltrates of liquenoid or superficial perivascular type. A small number of cases could present lymphocytic epidermotropism, with or without atypical lymphocytes. Immunohistochemistry reveals major positivity for CD8 and CD57. These morphological findings, along with negativity for CD7 (mature T cell), are very similar to the ones observed in the early stages of ATLL. This leads some authors

FIGURE 2. Clinic: A, Erythematous, scaly, eroded, and crusted patches with jagged edges, fuzzy boundaries spread on the lower limbs, on the front, and (B) on the back. Lichenification areas are also present.

to suggest that ID could be an early stage of ATLL. It is suggested that ID could be a marker of more severe associated diseases such as ATLL and TSP.^{1,11,13,14,19,20}

ID is primarily diagnosed clinically; differential diagnosis includes atopic dermatitis and seborrheic dermatitis.

There are major and minor diagnosis criteria. Four of 5 major criteria are required, and 1, 2 and 5 are mandatory.^{1,9,13,14,20}

Of the 5 major criteria, 4 are required for diagnosis, being 1, 2, and 5 mandatory. To fulfill the first major criteria, it must be present in at least 2 of the 7 locations.^{1,2,21}

FIGURE 3. Clinic: A, The same lesions in the back. B, An overview of the patch.

FIGURE 4. Histopathology: A, Biopsy number 1 at higher magnification. Epidermal acanthosis with irregular elongation of rete ridges. Orthokeratosis: B, Epidermal spongiosis with exocytosis of leukocytes within it.

FIGURE 5. A and B, The third biopsy shows a nearly psoriasiform hyperplasia with parakeratosis and intra-corneal cell debris and almost no dermal inflammation. Correspond to chronic eczema. No mites were identified at this time.

Major Criteria

Dermatitis of the scalp, external ear, retroauricular area, eyelid margins, paranasal skin, neck, axillae, or groin
 Chronic watery nasal discharge and/or crusting of the anterior nares
 Chronic relapsing dermatitis that responds quickly to antibiotics but relapses promptly after withdrawal
 Onset during early childhood
 Seropositivity for HTLV-1

Minor Criteria

Positive cultures for *S. aureus* and/or beta hemolytic *Streptococci* from the skin or anterior nares
 Generalized fine papular rash
 Generalized lymphadenopathy with dermatopathic lymphadenitis
 Anemia
 Elevated erythrocyte sedimentation rate
 Hyperimmunoglobulinemia (IgE and IgD)
 Elevated CD4 and CD8 T-cell counts

Our patient presented 3 major criteria (1, 3, and 5) and all minor criteria. Although ID is an infancy pathology, there are a few cases in adults published. Our patient developed dermatosis in the adult age, and the presence of HTLV-1 virus in the blood was demonstrated.

In regard to the second major criteria, this case did not present with rhinorrhea or crusting of the anterior nares. However, a series of 15 patients where the absence of this sign would not invalidate diagnosis was recently published.

The authors suggest that this criteria could be considered transient, therefore, not mandatory.^{1,13}

Diagnosis requires serologic confirmation with ELISA, Western blot, Polimerasa chain reaction, or Southern blot, with higher titers having the worst prognosis. The presence of antibodies against proteins p24, p19, rgp46-1, and rgp21 is required. It is complemented with polimerasa chain reaction of blood, cerebro spinal fluid, or tissue sample (skin, lymph node), especially if serology is not conclusive.^{1,4,14}

There is no specific treatment. Antiretroviral schemes such as the use of AZT have not been sufficiently effective. Each clinical presentation has a special approach. For ID, exudative type treatment is used; it includes topical steroids and antistaphylococcal antibiotics.^{1,4,6}

The best way to approach this is with prevention, eliminating transmission factors with blood donor screening, avoiding breastfeeding in infected mothers, using barrier protection during sexual intercourse, educating on how the virus is transmitted, early serologic detection, and elective c-section in seropositive women. There is no specific vaccine.^{1,4,6,14}

We believe that it is important to present the first case of an adult patient with ID and TSP/HTLV-associated myelopathy in the country. HTLV-1 is an emergent virus with marked cutaneous tropism, and knowledge on this subject should be shared among the dermatology field.

REFERENCES

- Olivares L, D'Atri G, Martinetti C, et al. Dermatitis infectiva asociada a HTLV-1, en un adulto. *Dermatol Argent*. 2009;15:49–53.
- Primo JRL, Brites C, de Oliveira M de FSP, et al. Infective dermatitis and human T lymphotropic virus type 1-associated myelopathy/tropical spastic paraparesis in childhood and adolescence. *Clin Infect Dis*. 2005;41:535–541.
- Gessain A, Barin F, Vernant JC, et al. Thé G. Antibodies to human T-lymphotropic virus type-I in patients with tropical spastic paraparesis. *Lancet*. 1985;2:407–410.
- Díaz CJ, Valencia M. Manifestaciones cutáneas asociadas con el HTLV-1. *Rev Asoc Colomb Dermatol*. 2014;22:67–73.
- Poiesz BJ, Ruscetti FW, Gadzar AF, et al. Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T cell lymphoma. *Proc Natl Acad Sci USA*. 1980;77:7415–7419.
- Franco FC, Quijano-Gomero E. Manifestaciones cutáneas de la infección por el virus linfotrópico T humano (HTLV-I). *Dermatología Peruana*. 2009;19:49–58.
- Sweet RD. A pattern of eczema in Jamaica. *Brit J Derm*. 1966;78:93–100.
- Puel L, Ballona R, Cáceres H, et al. Características clínicas y epidemiológicas de la dermatitis infectiva infantil en dos hospitales peruanos, periodo 2000–2002. *Dermatol Pediatr Lat*. 2004;2:109–116.
- LaGrenade L, Hanchard B, Fletcher V, et al. Infective dermatitis of Jamaican children: a marker for HTLV-1 infection. *Lancet*. 1990;336:1345–1347.
- Walshe MM. Infective dermatitis in Jamaican children. *Br J Dermatol*. 1967;79:229–236.
- Nobre V, Guedes ACM, Proietti F, et al. Increased prevalence of human T cell lymphotropic virus type 1 in patients attending a brazilian dermatology clinic. *Intervirology*. 2007;50:316–318.
- Yamaguchi K. Human T-cell lymphotropic virus type I in Japan. *Lancet*. 1994;343:213–216.
- de Oliveira M de FSP, Brites C, Ferraz N, et al. Infective dermatitis associated with the human T- lymphotropic virus type 1 in Salvador, Bahia, Brazil. *Clin Infect Dis*. 2005;40:90–96.
- Pérez L, Villarroel J, Reyes A, et al. Eritrodermia exfoliativa y dermatitis infecciosa en un lactante infectado por el virus linfotrópico humano-I (HTLV-I). *Rev Chil Infect*. 2007;24:142–148.
- Gotuzzo Herencia E, González Lagos E, Verdonck Bosteels K, et al. Veinte años de investigación sobre HTLV-1 y sus complicaciones médicas en el Perú: perspectivas generales. *Acta Med Per*. 2010;27:196–204.
- Verdonck K, González E, Van Dooren S, et al. Human T-lymphotropic virus 1: recent knowledge about an ancient infection. *Lancet Infect Dis*. 2007;7:266–281.
- Farre L, de Oliveira M de FSP, Primo JRL, et al. Early sequential development of infective dermatitis, human T cell lymphotropic virus type 1 associated myelopathy and adult T cell leukemia/lymphoma. *Clin Infect Dis*. 2008;46:440–442.
- Ballona R. Dermatitis infectiva: una revisión. A propósito de la experiencia peruana. *Dermatol Pediatr*. 2009;7:5–10.
- Bittencourt AL, Oliveira M de F, Brites C, et al. Histopathological and immunohistochemical studies of infective dermatitis associated with HTLV-1. *Eur J Dermatol*. 2005;15:26–30.
- Bittencourt AL, Oliveira M de F, Ferraz N, et al. Adult onset infective dermatitis associated with HTLV-1. Clinical and immunopathological aspects of two cases. *Eur J Dermatol*. 2006;16:62–66.
- Tschachler E, Franchini G. Infective dermatitis: a pabulum for human T lymphotropic virus type I leukemogenesis? *Arch Dermatol*. 1998;134:487–488.