Correspondence

First description of bullous lupus associated with cutaneous leishmaniasis: coincidence or trigger?

Dear Editor,

A 70-year-old Creole-Guyanese man consulted for a descending nodulo-crusted rash affecting the photo-exposed areas (scalp, trunk, and limbs) over a week. The lesions secondly became bullous, then erosive, and finally crusted (Fig. 1). He had a history of chronic cigarette smoking and alcohol abuse and unlabeled treated psychosis. There were no recent therapeutic changes or symptoms such as weight loss or fever. He reported frequent trips to the woods. He had a bicytopenia (Hb 9.6 g/dl, platelets 94 g/l) with lymphopenia (0.75 g/l), without hemolysis markers or biological inflammatory syndrome. The bone marrow examination was normal. Syphilis, HIV, and HTLV-1/2 serologies were negative.

Antinuclear antibodies (ANA) were positive at 320 (mixed fluorescence: homogeneous and speckled) as well as SSA/Ro60 antibodies (>8) and p-ANCA (80), but without complement consumption. All anti-epidermal antibodies were negative including anti-collagen VII.

Histological examination of a skin biopsy of the chest showed a blister lesion with dermal-epidermal cleavage, focal keratinocyte necrosis, and perivascular lymphocyte-dominant inflammatory infiltrate. The direct immunofluorescence (IFD) showed linear IgG deposits at the roof of the blister associated with granular deposits of C3. Interestingly, histology also revealed the presence of numerous corpuscles of *Leishmania* in the cytoplasm of histiocytes (Fig. 2). The parasitological culture of the skin biopsy was positive, and mass spectrometry identified *Leishmania guyanensis*, confirmed by PCR and Hsp70 sequencing.

A bullous lupus associated with cutaneous leishmaniasis was diagnosed. The main differential diagnosis was epidermolysis bullosa acquisita in its inflammatory form. It was eliminated mainly due to the absence of mucosal involvement and anti-collagen VII antibodies. Erythema multiforme was ruled out due to the absence of mucosal involvement and target lesions. Skin biopsies of several other body parts were negative for *Leishmania*, ruling out a diagnosis of disseminated leishmaniasis. Intravenous pentamidine for leishmaniasis did not modify the lesions. Plaquenil was started for bullous lupus as Disulone was contraindicated (G6PD deficiency). One month after treatment, he presented infiltrated, crusted, and hypopigmented oblong lesions of both arms evoking a secondary evolution in a discoid form of lupus (Fig. 1).

American cutaneous leishmaniasis is endemic in French Guiana with an annual incidence rate estimated between 15 and 20 new cases per 10,000 inhabitants.[1] To our knowledge, the association of cutaneous leishmaniasis with bullous lupus has never been described so far. The exact etiology of systemic lupus erythematosus (SLE) is still unknown, but infections can

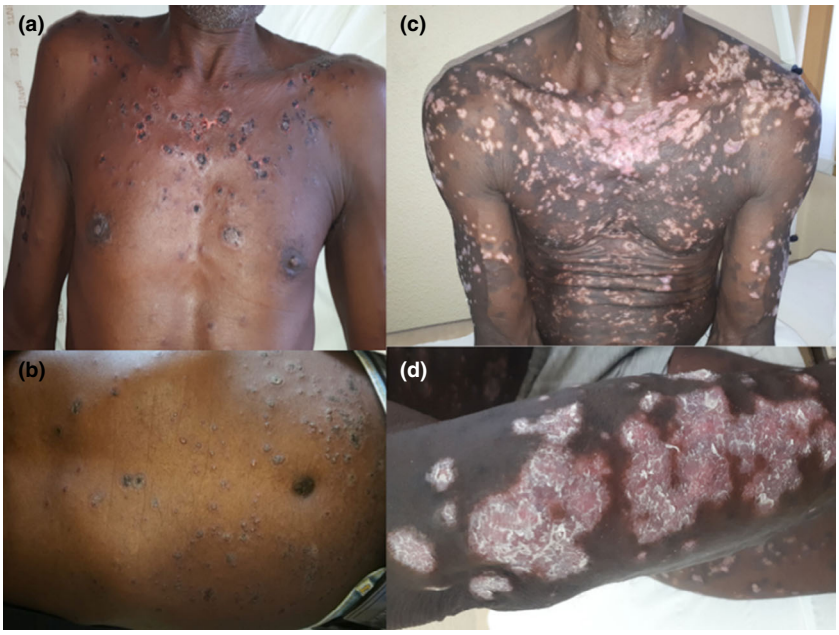

Figure 1 Photographs at diagnosis and at 1 month. Descending rash (a), with bullous abdominal lesions (b) at diagnosis. Hypopigmented evolution (c) with infiltrated and crusted plaques of both arms (d) after 1 month

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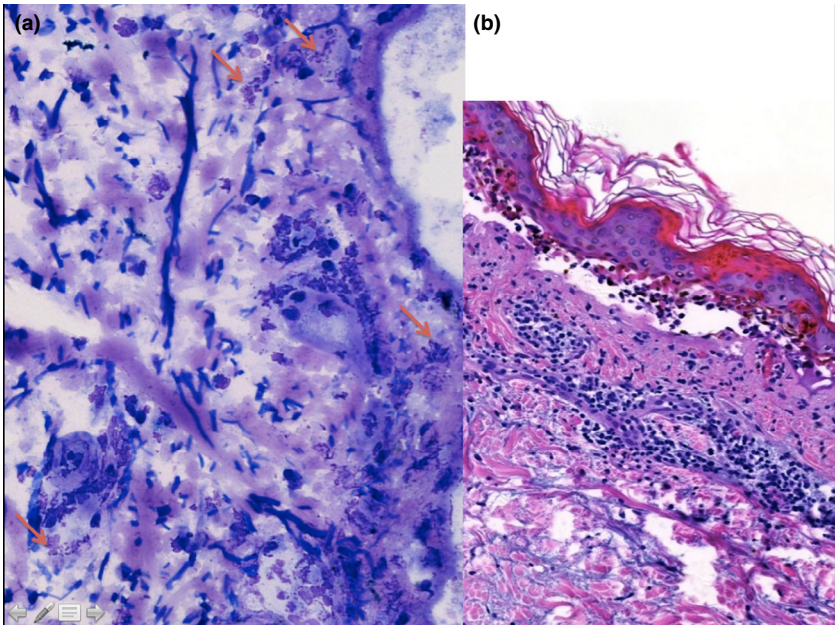

Figure 2 Histological examination of skin biopsy. (a) Frozen section. Light microscopic examination of a Giemsa-stained cutaneous biopsy (×800) showing macrophages containing multiple Leishmania amastigotes (red arrow). (b) Hematoxylin and eosin stain (×600) of a cutaneous biopsy showing a blister lesion with dermal–epidermal cleavage, focal keratinocyte necrosis, and perivascular lymphocyte-dominant inflammatory infiltrate

act as environmental primers, inducing onset and exacerbations of autoimmune response in genetically predisposed individuals. Several viruses, bacteria, and protozoa can cause immune dysfunction by molecular mimicry, epitope spreading, and bystander activation.[2] In contrast, some parasitic infections (primarily protozoan infections like *Plasmodium falciparum*) might confer protection from autoimmunity, depending on the unique interaction between the microorganism and host.[3,4] Therefore, the association of parasitic infections and the development of SLE remains ambiguous.

A link may exist between leishmaniasis and another autoimmune bullous dermatosis endemic of Brazil called foliaceous pemphigus "fogo selvagem" (FS). Patients with parasitic diseases including leishmaniasis possess anti-Dsg1 antibodies which cross-react with the arthropod salivary antigens leading to an early antibody response.[5] A minority of them will develop FS due to an extended immune response by epitope spreading leading to pathogenic antibodies against Dsg1. The autoimmune disease may be perpetuated by continuous exposure to self-Dsg1 and genetic predisposition (expression of HLADRB is linked to FS [RR = 14]).[6]

In our case, a parallel mechanism is suspected. First, sand fly bite may have released a salivary antigen leading to an early antibody response. Second, it induced a leishmaniasis which in itself can trigger an immunological response through antigenic mimicry. These two stimuli in a genetically predisposed patient can lead to the onset of lupus bullosa.

Acknowledgment

The patient has given written informed consent to publication of his case details.

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