Cutaneous sarcoidosis development in a patient with previous disseminated cutaneous leishmaniasis: a manifestation of Immune Reconstitution Inflammatory Syndrome

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Introduction

Immune reconstitution inflammatory syndrome (IRIS) is the term used for the paradoxical clinical deterioration noted in people with human immunodeficiency virus (HIV) after introduction of highly active antiretroviral therapy (HAART) mostly due to the restoration of a dysregulated immune response against pathogen-specific (mycobacteria, virus, fungi, parasites) antigens. A wide range of clinical manifestations have been described within the spectrum of IRIS.

Sarcoidosis has occasionally been reported as a potential complication of IRIS. We describe an HIV-infected man with a previous medical history of disseminated cutaneous leishmaniasis successfully treated who developed cutaneous sarcoidosis coinciding temporarily with increasing CD4 cell counts after HAART.

Case report

A 38 year-old homosexual white man with HIV infection since 1987 was taking HAART (lamivudine, didanosine and efavirenz) since June 2005. In January 2006, when CD4 lymphocyte count was 350 cells/μL (Figure 1), the patient presented a generalized maculopapular rash on the trunk, face (Figure 2A) and palms and soles.

Histologically a dermal granulomatous inflammatory infiltrate with numerous plasma cells, lymphocytes and scattered multinucleated giant cells was observed (Figure 2B). Specific stains for acid-fast bacilli (Ziehl-Neelsen), fungi (Grocott), bacteria (Gram stain) and parasites (Giemsa) failed to detect microorganisms and *Treponema pallidum* serologic tests were negative. Polymerase chain reaction (PCR) for *Leishmania infantum*-specific DNA yielded positive results. No bone marrow involvement was detected and the diagnosis of disseminated cutaneous leishmaniasis was established. Meglumine antimoniate therapy (20 mg Sb/kg/day for 5 weeks; intramuscular) was prescribed and a complete resolution of all his lesions was achieved.

Three and a half years later, when CD4 count was 1070 cells/μL (Figure 1), under treatment with raltegravir, emtricitabine and tenofovir, the patient developed multiple erythematous papules with Koebner phenomenon and nodules located on both hands, feet and elbows (Figure 3A). Histopathological examination showed well-defined sarcoidal granulomas mainly in the papillary dermis (Figures 3B and 3C). Special stains and cultures for acid-fast bacilli and fungi were negative. Immunohistochemical stains for *Leishmania* failed to detect parasites, however, PCR specific for *Leishmania* was positive. Bone marrow aspiration, chest X-ray, thoracoabdominal computed tomography scan and blood tests including angiotensin-converting enzyme ruled out extracutaneous disease. Tuberculin skin test resulted negative (ten years before it had been positive) and the patient had never received treatment for *Mycobacterium tuberculosis* infection. Meglumine antimoniate therapy did not result in remission of the lesions in this episode. Skin lesions resolved spontaneously in a few months.

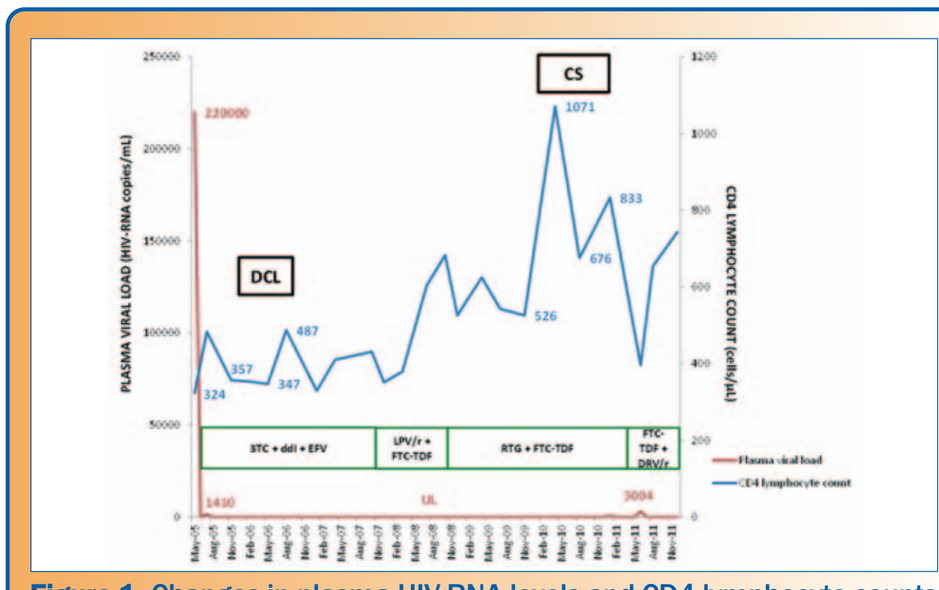

Figure 1. Changes in plasma HIV RNA levels and CD4 lymphocyte counts during antiretroviral therapy.

DCL: Disseminated Cutaneous Leishmaniasis; CS: Cutaneous Sarcoidosis; 3TC: lamivudine; ddI: didanosine; EFV: efavirenz; LPV/r: lopinavir/ritonavir; FTC-TDF: emtricitabine- tenofovir; RTG: raltegravir; DRV/r: darunavir/ritonavir; UL: undetectable levels.

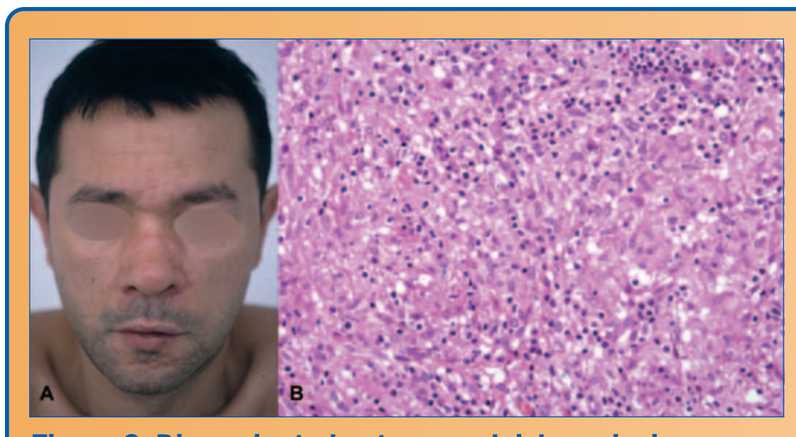

Figure 2. Disseminated cutaneous leishmaniasis.
A Erythematous papules and nodules affecting the face. **B** Dense and diffuse granulomatous infiltrate with histiocytes, lymphocytes and numerous plasma cells in the dermis (haematoxylin and eosin, original magnification x 200).

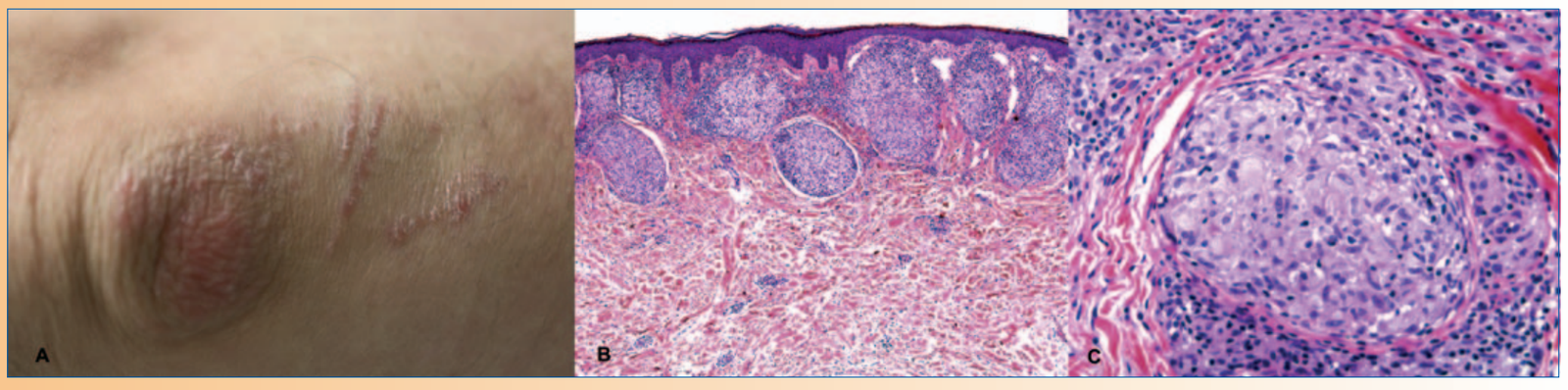

Figure 3. Cutaneous sarcoidosis. A Erythematous and slightly scaly papules with Koebner phenomenon on the right elbow. **B and C** Sarcoidal granulomas with histiocytic cells in the papillary dermis (haematoxylin and eosin, B, low power ; C, higher power).

Discussion

Sarcoidosis is an idiopathic granulomatous disease in which CD4 T lymphocytes play an important role in the pathogenesis. This could explain the small number of reports of patients with sarcoidosis in the presence of HIV infection as CD4 T lymphocyte depletion may attenuate sarcoidal granuloma formation.[1] However, immune restitution after HAART could induce sarcoid-like lesions in tissues (lung, skin, lymph nodes, salivary glands, liver, etc.) suggesting that sarcoidosis is another feature of IRIS.[2,3] In contrast to other typical disorders of IRIS, sarcoidosis seems to develop after a longer delay (several months) after the introduction of HAART.[4] A non-reactive tuberculin skin test may help to differentiate immune reconstitution-associated sarcoidosis from mycobacterial immune restoration disease in which a positive reaction is usually observed.[5]

The observation of a cutaneous sarcoidosis in an HIV-infected patient with a previous disseminated cutaneous leishmaniasis could lead to suggest that poorly degradable *Leishmania* antigens may be the trigger factor of this uncommon cutaneous manifestation of IRIS. An exaggerated immune reaction mediated by CD4 T cells to persistent *Leishmania* antigens may lead to the development of a cutaneous sarcoidosis. The present case seems to illustrate the clinical heterogeneity of cutaneous manifestations observed within the IRIS spectrum.

References

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