



## Case Report

## Adult T-cell leukemia/lymphoma triggered by adalimumab



Achilea L Bittencourt<sup>a</sup>, Pedro D Oliveira<sup>b</sup>, Valeria G Bittencourt<sup>c</sup>, Edgar M Carvalho<sup>c</sup>, Lourdes Farre<sup>d,\*</sup>

<sup>a</sup> Laboratory of Pathology, Complexo Hospitalar Universitário Prof. Edgard Santos, Federal University of Bahia, Rua Dr. Augusto Viana, s/n, Canela, CEP:40.110-060, Salvador, Bahia, Brazil

<sup>b</sup> Dermatology Service, Complexo Hospitalar Universitário Prof. Edgard Santos, Federal University of Bahia, Rua Dr. Augusto Viana, s/n, Canela, CEP:40.110-060, Salvador, Bahia, Brazil

<sup>c</sup> Laboratory of Immunology, Complexo Hospitalar Universitário Prof. Edgard Santos, Federal University of Bahia, Rua Dr. Augusto Viana, s/n, Canela, CEP:40.110-060, Salvador, Bahia, Brazil

<sup>d</sup> Laboratory of Experimental Pathology (LAPEX), CPQGM–FIOCRUZ, Bahia, Rua Waldemar Falcão 121, Candeal, CEP: 40296-710, Salvador, Bahia, Brazil

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## ABSTRACT

Here, we describe a 48-year-old woman infected by the human T-cell lymphotropic virus type 1 (HTLV-1) with spondyloarthritis, uveitis, bilateral episcleritis and neurogenic bladder. She had a history of a probable infective dermatitis associated with HTLV-1 (IDH) in childhood. After the use of adalimumab, she developed lymphocytosis and a cutaneous lymphoma associated with IDH. She had the diagnoses of IDH and of chronic adult T-cell leukemia/lymphoma, supported by the demonstration of proviral integration in the cutaneous lesion.

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## 1. Why this case is important

Rare cases with infective dermatitis associated with HTLV-1 (IDH) have been described associated with adult T-cell leukemia/lymphoma [1]. Here, we describe a case with both diseases triggered by the administration of adalimumab.

## 2. Case report

The patient was a 48-year-old afrodescendent woman, from Salvador, Bahia, with positive serology for the human T-cell lymphotropic virus type 1 (HTLV-1) who had the following diagnoses at the University Hospital of the Federal University of Bahia: spondyloarthritis, uveitis, bilateral episcleritis, and neurogenic bladder. She also had a history of a severe eczema in childhood involving the scalp, the retroauricular areas and the cutaneous folds.

Due to the worsening of the rheumatological clinical picture and poor response to oral immunosuppressants, an anti-TNF- $\alpha$  (adalimumab) was introduced. After this treatment the

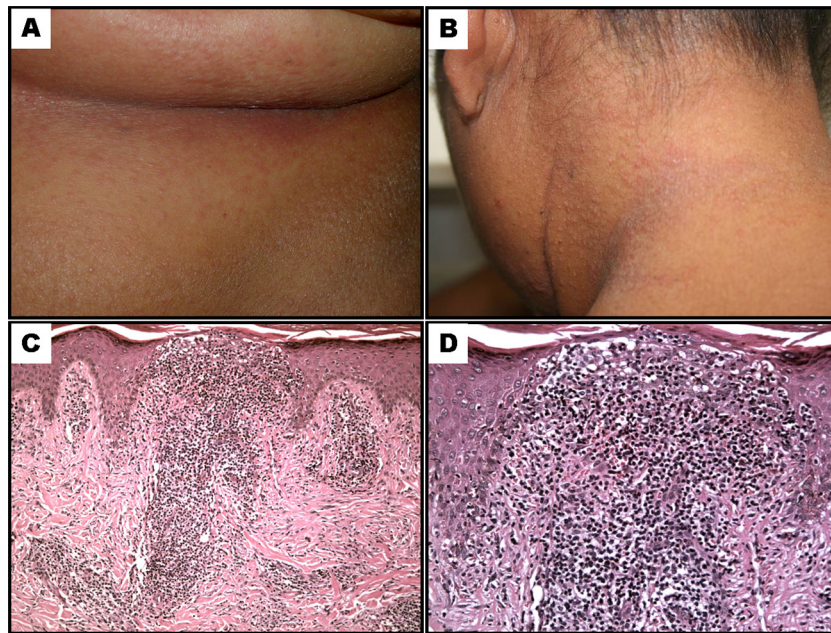
patient progressed with persistent discrete lymphocytosis (5.049 to 5.882 cells/ $\mu$ L) and 27 months later, showed erythematous papules on the limbs, back and breasts (Fig. 1A). Simultaneously erythematous-scaly lesions appeared on the scalp, retroauricular regions, posterior aspect of the neck (Fig. 1B), inframammary folds (Fig. 1A) and axillae associated with numerous follicular papules on the abdomen. At that time, laboratory examinations revealed lymphocytosis (5.168 cells/ $\mu$ L), mild elevated serum lactate dehydrogenase and normal blood calcium level. No infiltration was observed in the biopsy of the bone marrow.

Histopathological examination of a papular lesion showed a pagetoid epidermotropism and patchy areas of dense infiltration of small and medium atypical cells, in the superficial and mid dermis (Figs. 1C and D) showing a classic mycosis fungoides (MF) pattern. By immunohistochemistry the atypical cells were CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>-</sup>, CD20<sup>-</sup>, CD25<sup>+</sup>, CD30<sup>-</sup> and CD68<sup>-</sup>. The proliferative index assessed by Ki-67 was 8%. Monoclonal integration of HTLV-1 was detected by Southern blot [2] in the skin lesion (Fig. 2). Complete staging showed no involvement of other organs. Chronic adult T-cell leukemia/lymphoma (ATL) was diagnosed according to the Shimoyama's classification (1991) [3].

Adalimumab was suspended right after the diagnosis of MF and treatment with phototherapy and topical corticosteroids was initiated, without response. Right after, specific treatment for ATL with interferon- $\alpha$  in combination with zidovudine was introduced with complete disappearance of the skin lesions and lymphocytosis.

\* Corresponding author at: Laboratory of Pathology, Complexo Hospitalar Universitário Prof. Edgard Santos, Federal University of Bahia, Rua Dr. Augusto Viana, s/n, Canela, CEP:40.110-060, Salvador, Bahia, Brazil. Tel.: +557132838016.

E-mail address: [achilea@uol.com.br](mailto:achilea@uol.com.br) (L. Farre).



**Fig. 1.** A, Erythematous papules on the right breast and an erythematous-scaly lesion on the inframammary fold. B, Erythematous-scaly lesions on the scalp and left retroauricular region and many small papules on the posterior aspect of the neck. C, A dense infiltration of small- and medium-sized atypical lymphocytes is present on the upper and mid dermis (hematoxylin and eosin stain; original magnification,  $\times 100$ ). D, A higher magnification of Fig. 1C; see the pagetoid epidermotropism (original magnification,  $\times 200$ ).

Now, after 16 months of treatment, autoimmune diseases are under control.

### 3. Other similar and contrasting cases in the literature

There are no other reports about the development of ATL due to anti-TNF- $\alpha$  treatment. The association of ATL, IDH and HTLV-1

associated myelopathy/tropical spastic paraparesis (HAM/TSP) has been previously described [1].

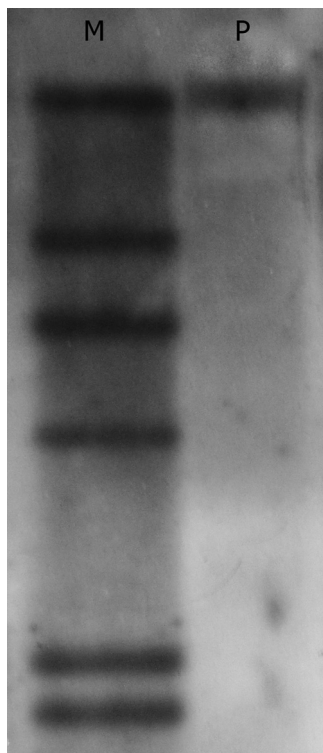
### 4. Discussion

Infection by the HTLV-1 causes several diseases, among them ATL, HAM/TSP, infective dermatitis associated with HTLV-1 (IDH), and is associated with autoimmune diseases such as rheumatoid arthritis, uveitis, and spondyloarthritis [4]. There have been no reports of ATL induction by anti-TNF- $\alpha$ , but TNF- $\alpha$  inhibitors have been associated with the development of lymphomas and, in particular, T-cell lymphomas [5].

This is an uncommon case, due to the combination of several diseases caused by HTLV-1. The ATL lesions appeared concomitantly with a classic pattern of IDH with lesions in the scalp, retroauricular regions and folds [6]. The presence of a neurogenic bladder probably corresponded to an initial form of HAM/TSP [7]. The combination of HAM/TSP and ATL, although considered rare [8], has been commonly observed in Bahia, Brazil, where 19% of the cases of ATL with skin involvement have shown this combination [9]. Even more rare was the association of ATL and HAM/TSP with other HTLV-1 associated diseases, such as IDH [1] and uveitis [10].

Monoclonal viral integration has shown, without a doubt, that it was, in fact, ATL [11]. The presence of lymphocytosis and cutaneous lymphoma, even in the absence of other involvements, led to the diagnosis of chronic ATL. This lymphoma may mimic, histologically, several others lymphomas, including MF [9].

TNF- $\alpha$  pharmacological blockage has been shown to be effective in the treatment of several immunologically mediated diseases, which is why it was used with this patient. However, TNF- $\alpha$  blockers are markedly immunosuppressant, and may even result in the reactivation of infectious diseases [12,13] and B and T-cell lymphomas [14]. In an FDA database, 100 T-cell lymphomas were identified in patients treated only with anti-TNF- $\alpha$ , with 20 showing MF/Sezary syndrome (SS). In a literature review, 10 other cases of MF/SS treated in this way have also been observed [5]. However, no reference was found in the literature of the development



**Fig. 2.** Polyacrylamide gel of long, inverted PCR products. Lane M, DNA molecular weight marker VIII (Roche); lane P, patient with adult T-cell leukemia/lymphoma.

of ATL due to anti-TNF- $\alpha$  treatment. Considering that the patient had had a history of a severe eczema in childhood, certainly the anti-TNF- $\alpha$  also caused a reappearance of the IDH. It is possible that the marked suppression of cellular immune response through medication may have permitted the proliferation of a transformed T-cell clone causing ATL.

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None.

#### Competing interests

None.

#### Ethical approval

Not required.

#### Disclosure

The authors have nothing to disclose.

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