*Rev. Inst. Med. trop. S. Paulo*
*49(4):267-270, July-August, 2007*

## CASE REPORT

# SOFT TISSUE ABSCESS AND LYMPHADENITIS DUE TO *Mycobacterium avium* COMPLEX AS AN EXPRESSION OF IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME AFTER A SECOND SCHEME OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

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**SUMMARY**

Immune reconstitution inflammatory syndrome (IRIS) is an atypical and unexpected reaction related to highly active antiretroviral therapy (HAART) in human immunodeficiency virus (HIV) infected patients. IRIS includes an atypical response to an opportunistic pathogen (generally *Mycobacterium tuberculosis*, *Mycobacterium avium* complex, cytomegalovirus and herpes varicella-zoster), in patients responding to HAART with a reduction of plasma viral load and evidence of immune restoration based on increase of $CD4^+$ T-cell count. We reported a case of a patient with AIDS which, after a first failure of HAART, developed a subcutaneous abscess and supraclavicular lymphadenitis as an expression of IRIS due to *Mycobacterium avium* complex after starting a second scheme of HAART.

**KEYWORDS:** HAART; Immune reconstitution inflammatory syndrome; *Mycobacterium avium* complex.

## INTRODUCTION

The immune reconstitution inflammatory syndrome (IRIS) includes several responses to preexisting opportunistic infections or tumors after the restoration of immune function in human immunodeficiency virus (HIV) infected patients receiving highly active antiretroviral therapy (HAART)[10,12]. Before the HIV pandemic, IRIS was also described in patients with chronic diseases such as leprosy and tuberculosis[2,7,16]. Since the extending use of HAART, numerous papers describing episodes of IRIS have been published in the medical literature[5,17], and IRIS became frequent (29% to 36%) in patients with history of tuberculosis in the HAART era[11].

We describe a patient, which developed a soft tissue abscess and a focal supraclavicular lymphadenitis due to *Mycobacterium avium complex* (MAC) after starting a second scheme of HAART.

## CASE REPORT

A 32-year-old man, seropositive for human immunodeficiency virus (HIV), with history of disseminated histoplasmosis and *Mycobacterium avium* complex disseminated disease, was started on highly active antiretroviral therapy (HAART) based on zidovudine plus lamivudine plus nevirapine. At this moment, his plasma viral load was > 500,000 copies/mL (5.7 $\log_{10}$ copies/mL) and his $CD4^+$ T-cell count was < of 50 cell/µL. He presented an initial good clinical, virological and immunological response to this scheme of HAART. Three months later, his plasma viral load was 32,814 copies/mL (4.52 $\log_{10}$ copies/mL) and the $CD4^+$ T-cell count was 361 cell/µL (21%). Six months later he evidenced a virological failure with a rebound of the plasma viral load (76,222 copies/mL/4.89 $\log_{10}$ copies/mL) and with a loss of $CD4^+$ T-cell count (289 cell/µL 20%).

At this moment, HAART was modified; then, he received a new scheme based on abacavir plus didanosine plus saquinavir boosted with ritonavir.

Two months later, with a plasma viral load of 424 copies/mL (2.63 $\log_{10}$ copies/mL) and $CD4^+$ T-cell count of 348 cell/µL (18%), he presented with fever, supraclavicular lymphadenitis (Fig. 1A) and pain with tender and inflammatory swelling located at the right thigh. Ultrasonography revealed the existence of a hypoechoic soft tissue liquid collection of 79 x 31 x 26 mm of diameters consistent with an abscess (Fig. 2). Aspiration of this mass and the supraclavicular lymphadenopathy showed pus that contained scanty acid-fast bacilli. Culture of this material was negative.

We supported the same scheme of HAART and antimycobacterial

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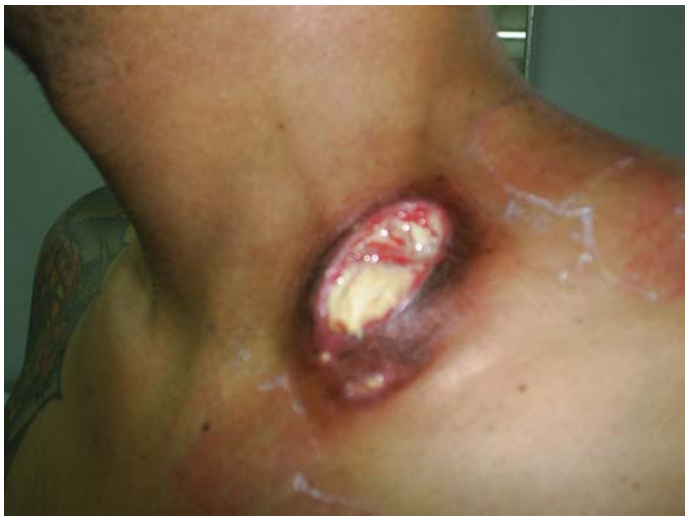

**Fig. 1A -** Left supraclavicular lymphadenitis as a manifestation of immune reconstitution inflammatory syndrome (IRIS) due to *Mycobacterium avium* Complex (MAC) of an HIV-infected patient.

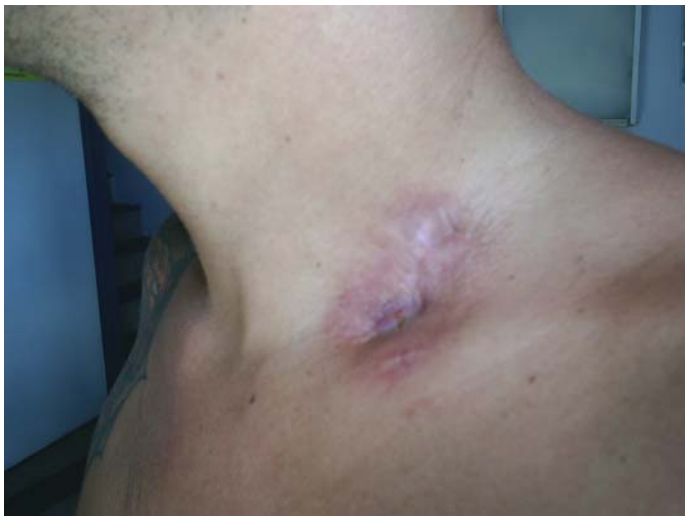

**Fig. 1B -** After four months of antimycobacterial therapy, the patient presented with neck scar.

treatment with ciprofloxacin, ethambutol and clarithromycin plus non-steroid anti-inflammatory was started. Four months later, the patient was in a good clinical condition and the symptoms of lymphadenitis and the soft tissue abscess resolved (Fig. 1B). At this time, the plasma viral load was 168 copies/mL (2.23 $\log_{10}$) and the CD4+ T-cell count was 447 cell/µL (16%).

## DISCUSSION

IRIS has been reported for a limited number of patients with various and previous opportunistic infections and tumors associated with AIDS immunodeficiency despite the adequate control of virologic and immunologic parameters[5,11,17]. IRIS is an inflammatory reaction which appears after initiating or changing of HAART regimens and is

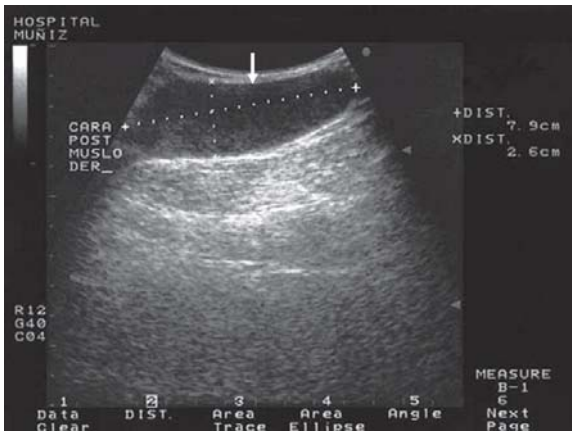


**Fig. 2 -** Ultrasound shows a hypoechoic liquid collection compatible with soft tissue abscess of the right thigh (arrow) of an HIV-infected patient with immune reconstitution inflammatory syndrome (IRIS).

temporally related with an increase in the CD4+ T-cell counts[3,8].

The real incidence of IRIS during HAART is unknown; however, SHELBURNE *et al.*[18] in a cohort of 180 HIV-infected subjects who received HAART observed that 31.7% of these patients developed IRIS. KUMARASAMY *et al.*[9] published an incidence of 15.2 cases/100 patients/year to IRIS related with tuberculosis. NARITA *et al.*[14] published a prevalence of 36% for *Mycobacterium tuberculosis*-associated IRIS.

IRIS appears to reflect an immune response against an active infection by opportunistic pathogens and is associated with delayed-type hypersensitivity responses to mycobacterial antigens[6].

The most frequent manifestations of IRIS published in the medical literature were MAC lymphadenitis, cytomegalovirus uveitis and cutaneous herpes zoster[18]. Major criteria to defining IRIS include the develop of an opportunistic infection or tumor, including an atypical presentation, in patients responding to HAART with a reduction of plasma HIV-RNA level more than one $\log_{10}$ copies/mL, without other explanation and with evidence of immune restoration, as minor criteria[6].

The temporal association between IRIS and the initiation of HAART has not been well established. PHILLIPS *et al.*[15] reported two patients with musculoskeletal disease for whom the intervals between HAART and IRIS were one and two years, respectively. The late onset of IRIS due to MAC has been described in patients with bone involvement[1]. The majority of IRIS cases associated with MAC infections evolve within the three months after starting HAART. In a large series of 51 patients with IRIS related to nontuberculous mycobacterias, the median interval from initiation of HAART to the onset of IRIS symptoms was three weeks (range one to eight weeks), but the median interval since the onset of symptoms to the diagnostic procedure was 10 weeks (range six to 19 weeks)[15].

Generally, patients with diagnosis of IRIS associated with MAC presented with inespecific symptoms as fever, fatigue and lymphadenitis with involvement of major lymph nodes regions: the cervical and

supraclavicular regions, the thoracic including the mediastinum and the abdominal cavity. However, besides the lymphadenitis of different regions, IRIS associated with MAC and other nontuberculous mycobacterias include a variety of clinical presentations such as soft tissue abscesses, monoarthritis, lung cavity, endobronquial lesions, thoracic and spine mass lesion and MAC bacteremia[15]. In the PHILLIPS' serie[15], 17 of 51 patients (33%) presented with peripheral lymphadenopathy; 15 (29%) with pulmonary and thoracic disease and 13 (25%) with abdominal compromise.

Primary or secondary MAC prophylaxis did not protect against the development of IRIS. PHILLIPS *et al.*[15] published a large series of nontuberculous mycobacterial IRIS including 51 patients (43 with MAC infection). Thirty eight (75%) of these patients had no history of mycobacterial disease.

In this serie[15], the median of $CD4^+$ T-cell counts at baseline (pre-HAART) was 20 cell/μL (range 10 to 50) and the median at IRIS diagnosis was 120 cell/μL (range 70 to 180). In the same series, the median of viral load at baseline was 230,000 copies/mL and at the time of IRIS diagnosis was < 500 copies/mL.

IRIS is an inflammatory syndrome that may cause atypical and clinical manifestations with a variety of outcomes ranging from minimal disease to occasionally fatal progression. For example, in a case published by VENDRELY *et al*.[19] about a patient who presented a progressive multifocal leucoencephalopathy as a manifestation of IRIS or in other patients with cryptococosis-associated IRIS[13].

Treatment for this complication of AIDS therapy includes the continuation of primary therapy against the pathogen implicated in the IRIS to decrease the antigenic load, the continuation of HAART and, eventually, the use of non-steroid antiinflammatory agents and corticosteroids[8,17]. IRIS is a condition thought to be caused by the improvement in the host's immune response to several pathogens. IRIS is common among HIV-infected patients and co-infected with MAC, *Mycobacterium tuberculosis* or other pathogens. Diagnosis of IRIS is difficult for clinicians; differential diagnosis includes treatment failure or resistance and other opportunistic diseases[4,13].

This disorder should be suspected in patients who start HAART in close proximity to the diagnosis of an opportunistic infection and have a rapid decline in the HIV viral load and an immune restoration associated with a rapid increase in the $CD4^+$ T-cell counts.

## RESUMEN

### Linfadenitis y absceso subcutáneo por Complejo *Mycobacterium avium* como manifestación de síndrome inflamatorio de reconstitución inmune luego de un segundo esquema de terapia antirretroviral de gran actividad

El síndrome inflamatorio de reconstitución inmune (SIRI) es una reacción atípica e inesperada relacionada con el tratamiento antirretroviral de gran actividad (TARGA) en pacientes infectados por el virus de la inmunodeficiencia humana (VIH). El SIRI representa una respuesta inflamatoria frente a un patógeno oportunista (generalmente *Mycobacterium tuberculosis,* Complejo *Mycobacterium avium*, citomegalovirus y herpes varicela-zóster) en pacientes que responden a la TARGA con una marcada reducción de la carga viral en plasma y evidencia de una recuperación inmunológica expresada por el incremento de los niveles de linfocitos T $CD4^+$. Presentamos el caso de un paciente con síndrome de inmunodeficiencia adquirida que desarrolló un absceso subcutáneo en muslo derecho y una adenitis supraclavicular izquierda como manifestación de SIRI por Complejo *Mycobacterium avium* luego del inicio de un segundo esquema de TARGA.

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Received: 28 June 2006
Accepted: 24 January 2007