

Rheumatic manifestations in Brazilian patients with AIDS

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ACTA REUMATOL PORT. 2014;39:143-145

ABSTRACT

Introduction: Patients with AIDS (acquired immunodeficiency syndrome) may have rheumatic complaints such as arthritis and arthralgia, dry eyes, increased salivary glands, lower back pain, enthesitis etc. Autoantibodies like ANA (antinuclear antibody) and RF (rheumatoid factor) may also be present.

Objective: To study the prevalence of rheumatic complaints in AIDS patients and correlate them with the presence of ANA and RF.

Methods: We studied 69 patients with AIDS (28.9% women and 71.0% men) with a mean age of 40.8 ± 8.9 years, median disease duration of 60 months, for rheumatic complaints, ANA, ENA-6 (anti-Ro, anti-La, anti-Sm, anti-RNP, anti-Scl70 and anti-Jo1) and RF. We collected demographic data, CD4+ and CD8+ cell count and values of viral load.

Results: Arthralgia was present in 39.1%, sicca symptoms in 21.7%, inflammatory lumbar pain in 13.4%, enthesopathy in 6.6%, parotid enlargement in 1.4%, RF in 10.1% and ANA in 8.6%. All patients were negative for ENA-6. ANA was more common in older patients ($p = 0.03$) and in those with higher viral load ($p = 0.006$). No association was found with the presence of RF.

Conclusions: The most common manifestation in this context was arthralgia. ANA presence was associated with age of the patients and viral load.

Keywords: Rheumatoid factor; Arthritis; Autoantibodies; Acquired Immunodeficiency Syndrome.

INTRODUCTION

HIV (human immunodeficiency virus) infected patients may present with rheumatic complaints¹. Arthralgias and arthritis have been associated with HIV infection itself¹. Sicca symptoms may result from diffuse infiltrative lymphocytosis syndrome (DILS) and require differential diagnosis with Sjögren's syndrome². Spondyloarthritis and lupus-like syndrome have also been described in this infection^{1,3}. In these patients the presence of immunological markers such as ANA (antinuclear antibodies) and RF (rheumatoid factor) may create confusion between an associated rheumatic disease and a rheumatic manifestation due to HIV. The prevalence of rheumatic manifestations in HIV may also be associated with the geographical area of the affected population. DILS has been linked to the presence of HLA DR5, DR6, and DR7².

A study in 62 patients from Thailand⁴ found arthralgia in 26%, sicca symptoms in 10% and a positive ANA in 3%. Another study in 98 patients from China⁶ showed that vasculitis was the most common manifestation (20.4%); sicca symptoms were found in 11.2% and ANA in 4%. Another study done in 300 patients from Uganda⁷ revealed a 19.3% prevalence of arthralgia and that no patients had ANA. Thus, the presence of rheumatic complaints in HIV should be investigated taking into account the genetic background of the population.

In the present study the rheumatic manifestations of 69 HIV positive Brazilian patients were evaluated

METHODS

This study was approved by the local Committee of Ethics in Research and all participants signed consent. All 69 included patients were 18 years or older and had the diagnosis of AIDS, i.e. HIV infection with manifes-

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ted disease; pregnant women and those with rheumatic disease prior to HIV diagnosis were excluded. This was a convenience sample of patients from a single Infectious Disease Center included according to appointment order and willingness to participate in the study, from January 2012 to December 2012.

Patients were interviewed and examined for rheumatologic findings such as arthritis and arthralgias, tendinitis, inflammatory back pain, parotid enlargement and sicca symptoms (dry eyes and dry mouth). Inflammatory lumbar pain diagnosis followed ASAS criteria⁸ and sicca symptoms were considered according to those used for American/European Sjögren's classification criteria⁹. Blood was drawn for ANA, ENA-6 profile and RF determination. IgM RF was measured by latex agglutination test (BioSystems, S.A., Barcelona, Spain); values <8UI/ml were considered negative. ANA were screened with indirect immunofluorescence on HEp-2 cells, using the commercially available ImunoCon ANA HEp-2 (Wama Diagnóstica, São Paulo, Brazil). A titer of 1:80 or higher was considered positive. ENA-6 profile (anti-Ro, anti-La, anti-RNP, anti-Sm, anti-Scl70 and anti-Jo1) was searched by ELISA (Orgentec, Germany).

Demographic data, CD4+ and CD8+ cell count and viral load were obtained from chart review.

Acquired data was studied in contingency and frequency tables. Data distribution was studied by Kolmogorov Smirnov test and central tendency was expressed in median values and interquartile range (IQR) for non parametric and mean and standard deviation (SD) for parametric data. Comparisons of nominal data were done by Fisher and chi squared tests; of numeral data by unpaired t test and Mann Whitney. The significance adopted was 5%.

RESULTS

In the 69 studied patients, 28.9% were women and 71.0%, men with mean age of 40.8±8.94 years and median disease duration of 60 months (IQR=9-120 months). The median CD4+ count was 124.5/mm³ (IQR=66.5-287.5) and the mean CD8+ was 753.5±455.0/mm³. Median viral load was 50.0 copies/mL (IQR=50-101 546). HAART (active anti-retroviral therapy) was used in 55.07% of them.

The rheumatologic findings are summarized in Table I.

In the studied sample, the most common arthritis

TABLE I. RHEUMATOLOGIC FINDINGS IN 69 BRAZILIAN HIV POSITIVE PATIENTS

Arthralgia	39.1%
Sicca symptoms (*)	21.7%
Inflammatory lumbar pain	13.4%
Enthesopathy (Acchiles and plantar)	8.8%
Arthritis	8.6%
Parotid enlargement	1.4%
Positive rheumatoid factor	10.1%
Positive antinuclear antibody	8.6%

(*)Sicca symptoms = dry mouth and dry eyes

was in the knees (40%); only one patient had parotid enlargement and concomitant sicca symptoms. Two patients with inflammatory lumbar pain and simultaneous enthesopathy had sacroiliac X ray done and there was sacroiliitis in one of them. None of the patients had clinical evidences of septic arthritis.

All ANA positive patients had fine dense speckled immunofluorescence pattern in titers from 1:80 to 1:160. Comparing ANA positive and negative patients we found that ANA was more common in older patients (p=0.03) and in those with higher viral load (p=0.006).

The comparison of RF positive and negative patients showed no differences (p=ns).

Concerning to the antirretroviral therapy used by these patients, the most used class of drugs are reverse-transcriptase inhibitors (RTIs): Lamivudine (89,7%), Tenofovir (58,9%), Efavirenz (53,8%) and Zidovudine (43,6%).

Protease inhibitors also were found: Lopinavir/ritonavir (23,1%), Atazanavir/ritonavir (17,9%) and Saquinavir/ritonavir (2,6%).

DISCUSSION

Before the widespread implementation of HAART, retrospective studies calculated the rates of musculoskeletal complications up to 72% (10). In the HAART era, rheumatic complications declined significantly but continue to be very prevalent¹⁰.

The most common rheumatologic manifestation in our population with HIV was arthralgia which was found in almost 40% of the sample. Berman et al¹¹ studying 101 HIV infected patients also found arthralgia

as the most common manifestations in 35% of their patients, a number similar to ours. Although common in HIV infected patients, arthralgias are unspecific and usually affect knees, shoulders and elbows¹⁰.

In our sample ANA positivity was 8% and we found that this positivity had a relationship with patient's age (more common in older patients) and with higher viral load. The titers found were low and all had fine dense pattern. ANA with a fine dense speckled pattern is directed against the DFS70 antigen, also known as lens epithelium-derived growth factor (LEDGF) and is usually devoid of any clinical meaning¹³. This pattern may help judge situations in which there is a possibility of association with SLE. Koppelman et al¹⁴ found ANA positivity in 12% in a sample of 151 patients usually at low titer as we did. Kulthanan⁴ found a lower rate, of 3%, without any association with clinical findings. In the present study we found an interesting association between this autoantibody positivity with viral load; antigenic similarities between HIV-gp120 and nuclear antigen⁷ may explain this latter finding.

HIV-associated arthritis mainly manifests itself as a non-erosive oligoarthritis of the lower extremities and is caused by local virus infection¹⁰. It may also belong to larger picture of a spondyloarthritis such as reactive or psoriatic arthritis. In the latter cases it is usually associated with enthesopathy¹⁰. None of our peripheral arthritis patients had concomitant enthesopathy but 2 patients had association of enthesopathy with lumbar inflammatory pain and one of them had sacroiliitis at X Ray. No psoriatic arthritis was found.

One patient had association of sicca symptoms with parotid enlargement, so he could have DILS although we did not perform a Schirmer test or salivary gland biopsy.

The sample size was a limitation of our study and this occurred mainly because of the weak adherence to the research by many patients and the low turnover of patients in the Disease Center where the study was conducted.

Concluding we found a high rate of rheumatic complaints in HIV patients, most commonly arthralgias. ANA and RF were present in low prevalence and at low titers. ANA was found to be associated with age and viral load.

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