

Musculoskeletal Manifestations in Patients Positive for Human Immunodeficiency Virus: Correlation with CD4 Count

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ABSTRACT. Objective. To determine the relationship between the CD4+ lymphocyte count and musculoskeletal manifestations of human immunodeficiency virus (HIV) infection.

Methods. All patients from 1991 to 1998 who were positive for HIV with osteoarticular manifestations were reviewed retrospectively. HIV positivity was confirmed by ELISA and Western blot. CD4 count was performed by flow cytometry.

Results. We studied 74 patients with osteoarticular manifestations. The study group comprised 61 men (82.4%) and 13 women (17.5%) with a mean age of 34.2 years (range 17–62). Fifty-two patients were iv drug users (70.3%). Septic arthritis was present in 20 cases (23.0%), soft tissue infections in 9 cases (12.2%), spondyloarthropathies in 6 cases (8.1%), lymphomas in 9 cases (12.2%), osteomyelitis in 6 (8.1%), and 24 miscellaneous cases (32.4%). The mean CD4 count was as follows: septic arthritis 164.7 cells/mm³, soft tissue involvement 127.1 cells/mm³, spondyloarthropathies 245.8 cells/mm³, lymphoma 132.8 cells/mm³, and osteomyelitis 233.6 cells/mm³.

Conclusion. Osteoarticular manifestations in the setting of HIV infection tend to be predominantly infectious. *S. aureus* is the microorganism most frequently involved. Osteoarticular infections always appeared when the CD4 count was < 200 and pyomyositis and lymphoma appeared when CD4 was < 150. CD4 counts may be useful predictors to determine the type of musculoskeletal manifestation. (J Rheumatol 2001;28:802-4)

Key Indexing Terms:

HUMAN IMMUNODEFICIENCY VIRUS

MUSCULOSKELETAL MANIFESTATIONS

CD4 COUNT

Since the beginning of the human immunodeficiency virus (HIV) epidemic, several musculoskeletal manifestations have been reported in infected individuals¹. Many of these manifestations have been described in small groups of patients but HIV associated arthritis, infectious arthritis, and spondyloarthropathies (SpA) are the best characterized manifestations²⁻⁵.

The number of CD4+ T cells as a predisposing factor for the different musculoskeletal manifestations has not been fully elucidated⁶. We describe musculoskeletal manifestations in patients with HIV infection and their correlation with the CD4 count.

MATERIALS AND METHODS

Patient selection. We retrospectively studied patients seen at the University Hospital over a period of 7 years (January 1991 to December 1998). The

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center is a 553 bed hospital in Badalona, Spain, serving a population of 700,000. All patients positive for HIV with musculoskeletal manifestations were reviewed in the outpatient clinics of the rheumatology and HIV units.

Inclusion criteria. Inclusion criteria for this study included HIV positivity (by ELISA) confirmed by Western blot. All records of patients positive for HIV with evidence of musculoskeletal manifestations who were seen in consultation were reviewed. Data gathered from chart review included age, sex, risk factors for HIV infection, CD4 count (by flow cytometry and FACS scan; Becton Dickinson), isolation of the responsible microorganism from blood or synovial fluid, clinical findings, and diagnosis.

RESULTS

We studied 74 patients with evidence of musculoskeletal manifestations, 61 men (82.4%) and 13 women (17.5%), age range 17 to 62 years (mean 34.2, SD 9.5 yrs). Risk factors for HIV infection included iv drug addiction in 52 patients (70.3%), homosexuality in 8 (10.8%), heterosexuality in 6 (8.1%), unknown etiology in 7 (9.4%), and hemophilia in one patient (1.3%).

We identified 20 cases of infectious arthritis (23.0%), 9 soft tissue infections (12.2%), 6 spondyloarthropathy (SpA) (8.1%), 9 lymphomas (12.2%), 6 osteomyelitis (8.1%), and 24 miscellaneous cases (32.4%).

Infectious arthritis was the commonest musculoskeletal manifestation in patients positive for HIV. In 14 cases (66.7%), a microorganism was identified: *Staphylococcus*

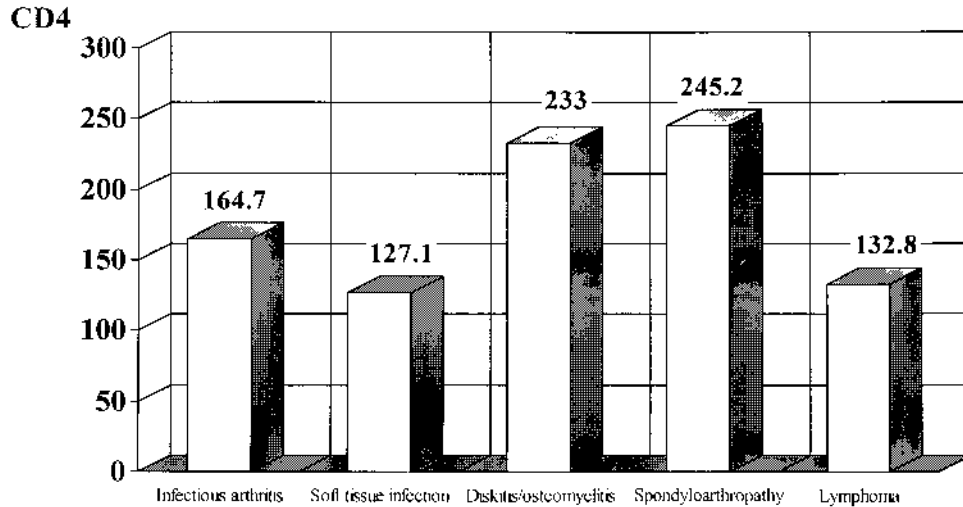


Figure 1. CD4+ lymphocyte count and the relationship with osteoarticular manifestations.

aureus in 11 patients, Group B *Salmonella* in one, and *Mycobacterium tuberculosis* in 2. Nineteen of the patients were iv drug users (95%). The mean CD4 count among those patients with infectious arthritis was 164.7 cells/mm³ (Figure 1).

Soft tissue infection, namely pyomyositis, was present in 9 cases (12.2%). *S. aureus* was responsible for 6 infections and *Aspergillus* species in one. Seven of the patients with soft tissue infections were iv drug users, with a mean CD4 count of 127.14 cells/mm³ (Figure 1).

SpA were uncommon. Psoriatic arthritis was present in 3 patients, Reiter's syndrome in one, and undifferentiated SpA in 2. IV drug addiction was present in 2 patients, homosexuality in one, and heterosexuality in 3. Their mean CD4 count was 245.2 cells/mm³ (Figure 1).

Solid lymphoma was present in 9 cases (12.2%). Known risk factors included iv drug use in 5 cases, homosexuality in 2 cases. There were 2 patients for whom there were no known risk factors. Their mean CD4 count was 132.8 cells/mm³ (Figure 1).

Osteomyelitis was present in 6 cases (8.1%). *S. aureus* was observed in 2 patients, *M. tuberculosis* in 2 patients, and 2 had bone bacillary angiomatosis (mean CD4 count 233 cells/mm³ (Figure 1).

There were other musculoskeletal manifestations (Table 1) that are occasionally described in the setting of HIV infection but are not the focus of our study.

DISCUSSION

Musculoskeletal infections have been reported rarely in studies of musculoskeletal manifestations associated with HIV infection^{1,2}. Berman found no osteoarticular infection in his study of 101 patients². Conversely, studies from Europe reported 20 cases (3.6%) among 556 patients, of whom 86% had a history of iv drug addiction⁷. Louthrenoo

Table 1. Miscellaneous osteoarticular manifestations in the setting of HIV infection.

Arthralgia	1
Unspecified arthritis	5
HCV arthritis related	1
DILS	1
Temporomandibular dysfunction	1
Myalgias	1
Reflex sympathetic dystrophy	1
Gout	2
Metatarsalgia	1
Osificant myositis	1
Osteonecrosis	2
No diagnosis	1
Compartmental syndrome	1
Hypermobility syndrome	1
Tendinitis	2
Soft tissue involvement	1
Vasculitis	1
Total	24

HCV: hepatitis C virus.

reported osteoarticular infections in 30% of patients, but only 5% were iv drug users⁸.

We describe 20 cases of infectious arthritis (27.0% of our study group) caused primarily by *S. aureus*. Our data are similar to the work of Muñoz, *et al*, who described 10 out of 17 cases of infectious arthritis caused by *S. aureus*. As in his work most of our patients were iv drug users. Louthrenoo described *Salmonella* species as the most frequently found microorganism, followed by *S. aureus* and *Penicillium marneffei*. However, most of his patients were heterosexual⁸. Recent work showed that *Streptococcus pneumoniae* was the most commonly isolated agent in HIV positive patients with infectious arthritis; 40% of the patients were iv

drug users⁹. The contribution of a history of iv drug abuse in the pathogenesis of infectious arthritis in patients positive for HIV is unclear although most of the series have it in common. However, there is evidence that infectious arthritis occurs in patients positive for HIV without a history of iv drug use^{6,8}. Further, HIV positivity confers an increased susceptibility to infectious arthritis and SpA^{10,11}.

There is a poor correlation between infectious arthritis and the number of CD4+ cells⁶. The mean CD4 count in our patients with infectious arthritis was 164.7 cells/mm³. Vassilopoulos, *et al*⁹ showed a mean CD4 count in patients positive for HIV with infectious arthritis of 352 cells/mm³. HIV infection is associated with progressive immunosuppression and development of multiple infections. The more advanced the disease, the more depleted the CD4 count¹². In concordance with systemic infections, infectious arthritis appears when the CD4 count is below 200 cells/mm³.

We identified 6 patients with osteomyelitis with a mean CD4 count of 233 cells/mm³. Previous work suggests that patients positive for HIV with osteomyelitis have a mean CD4 count of 149 cells/mm³. Pyomyositis is relatively common in HIV patients, and although the mean CD4 count was only 127.14 cells/mm³, our results are not comparable to a report⁹ that showed a CD4 count below 29.4 cells/mm³.

Patients with SpA were a minority in our study. Our patients are predominantly iv drug users, which might explain the low percentage of this type of arthropathy. Recent reports from Central Africa, where the most frequently seen risk behavior is heterosexuality, showed that SpA are very common in HIV infection¹³. However, infectious arthritis is also present¹⁴.

Our patients positive for HIV with bone lymphoma had very advanced disease, with a mean CD4 count of only 132.8 cells/mm³, and this corroborates earlier observations¹⁵.

Our study shows that infectious arthritis is the commonest musculoskeletal manifestation in a group of patients positive for HIV who were predominantly iv drug users. This suggests that musculoskeletal infections occur when HIV infection is advanced and that CD4 counts may be predictive for particular musculoskeletal manifestations.

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