

## Joint Manifestations in HIV Infection: A Review

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Received date: July 31, 2015; Accepted date: October 17, 2015; Published date: October 23, 2015

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### Abstract

Globally, incidence of HIV is on the rise. The epidemic of HIV infection has also affected the practice of rheumatologists. The increased life span of patients with HIV disease has resulted in emergence of musculoskeletal impairments ranging widely from arthritis to traumatic fractures. Joint disorders are common during the course of HIV infection. They are more prevalent in the late stages of disease. These disorders cause a significant amount of morbidity in HIV-infected patients and may lead to deformities if not treated. Joint involvement in HIV can range from mild pain and arthralgias to other conditions as painful articular syndrome, Reiter's syndrome, reactive arthritis, HIV-associated arthritis, undifferentiated spondyloarthropathy, septic arthritis, avascular bone necrosis, osteomyelitis and hypertrophic osteoarthropathy. Early detection of joint disease and timely intervention is essential to improve quality of life.

**Keywords:** HIV; Joint; Rheumatological; Spondyloarthritis; Psoriasis; Arthralgia; Arthritis

### Introduction

There is a diversity of literature on varying aspects of HIV. Central nervous system, cardio-pulmonary and abdominal complications affecting people living with HIV infection and AIDS.

(PLWHA) have been extensively discussed in the literature. However, research has recently focused on how the disease affects the musculoskeletal system. It is necessary to focus among various joint manifestations in order to diagnose and properly treat various orthopedic, rheumatologic and pain symptoms amongst PLWHA. Musculoskeletal manifestations can occur at any phase of the infection but they are commonly seen in late phases. The incidence of rheumatic manifestations in HIV infection was reported in about 4 to 71.3% cases in different studies [1,2]. Although musculoskeletal abnormalities in PLWHA are not as common as other systemic disorders but a wide variety of osseous, articular, muscular and soft tissue diseases may be seen [3]. Many of these conditions are not specific for HIV infection and AIDS and can be seen in other forms of immunosuppression. However, I will be focusing only on joint disease in this review.

### Epidemiology

Studies show that musculoskeletal conditions affect 72% of HIV-infected individuals during their lifespan [4].

In a prospective study of 74 consecutive HIV +ve patients clinical features of rheumatic manifestations were compared with 72 controls HIV -ve subjects with similar risk factors for HIV. HIV +ve group had more rheumatological manifestations than the HIV -ve group: arthralgias were found in 45%, arthritis in 10%, and Reiter's syndrome in 8%. Thus, the study suggested that rheumatic manifestations more prevalent in HIV +ve patients [2].

In a study of 300 HIV positive patients by Kole et al. [5], musculoskeletal disorders were observed in a total of 190 cases (63.33%). Body ache was seen in 140 (46.7%), arthralgia in 80 (26.7%), mechanical low back pain in 25 (8.3%), osteoporosis in 20 (6.7%), painful articular syndrome in 10 (3.3%), hypertrophic osteoarthropathy in two (0.7%) and avascular bone necrosis in one patient (0.3%). Reactive arthritis was seen in seven (2.3%), septic arthritis in three (1%), acute gout in three (1%), spondyloarthropathy in two (0.7%) and rheumatoid arthritis in two patients (0.7%).

### Etiopathogenesis

The rheumatic manifestations in HIV can be either due to the direct effect of HIV infection or to host immune response to the infection. The effects can be mediated by intact components of the immune system (CD8 cell). Some effects arise because of immunodeficiency with genetic and environmental factors also contributing a key role [6].

HIV detection of HIV RNA/p24 antigen from synovial fluid, muscle cells and within intravascular lesions have proven direct effects of virus in causation of arthritis [7].

In early HIV infection, there is activation of cellular and humoral immune response. There is spontaneous B cell proliferation leading to antibody production which mediates immune response [8].

Joint manifestations in HIV include –

- HIV associated arthralgia
- Painful articular syndrome
- HIV associated arthritis
- Reactive arthritis occurring in HIV infection
- Psoriatic arthritis in HIV
- Undifferentiated spondyloarthritis
- Avascular necrosis of bone
- Hypertrophic pulmonary osteoarthropathy
- Osteopenia and osteoporosis

### HIV associated arthralgia

HIV associated arthralgia is most commonly observed manifestation in HIV patients being reported in upto 45% of HIV positive patients [9]. Arthralgias can be constitutional symptoms of HIV seroconversion. The pathogenesis is unclear but role of cytokines or transient bone ischemia has been postulated [10]. Patients present with joint pain alone which rarely progress to inflammatory joint disease. Treatment consists of non-narcotic analgesics and reassurance.

### Painful articular syndrome

Painful articular syndrome is a self-limited syndrome lasting less than 24 hours. It is characterized by severe bone and joint pain [11]. It occurs predominantly in the late stages of HIV infection. Its cause is unknown. No evidence of synovitis has been found in these patients. The knee is most commonly affected joint. Treatment is symptomatic.

### HIV associated arthritis

HIV-associated arthritis is commonly seen in sub-Saharan Africa, as HIV infection is pandemic in the part of Africa. In countries such as Congo, where the seroprevalence of HIV infection is high, AIDS is the leading cause of aseptic arthritis (60% of cases) [12]. It is usually present as an oligoarthritis, predominantly affecting lower extremities, which tend to be self limiting, lasting for less than 6 weeks [13,14]. However, newer reports say that polyarticular involvement is now seen frequently [15]. Knee is the most common joint involved. Treatment includes Non steroidal anti-inflammatory drugs (NSAIDs). Low-dose glucocorticoids can be used in severe cases. Hydroxychloroquine and sulfasalazine also have been used [16].

### Reactive arthritis occurring in HIV infection

Reactive arthritis in HIV commonly presents as a seronegative lower extremity peripheral arthritis which is generally accompanied by enthesitis (dactylitis, Achilles tendinitis, and plantar fasciitis). Mucocutaneous features especially keratoderma blennorrhagicum and circinate balanitis are commonly seen. Extensive psoriasiform skin rashes can occur. It is difficult to distinguish HIV-associated reactive arthritis from psoriatic arthritis [17].

Among whites, HLA-B27 is found in 80% to 90% of patients with HIV associated reactive arthritis [17]. Some studies suggest that the presence of HLA-B27 antigen may slow the progression to AIDS [18].

Treatment is similar to that for HIV-negative patients with reactive arthritis. NSAIDs are the mainstay of treatment. Sulfasalazine has been shown to be effective in some studies at doses of 2 g/day, and a study showed that it ameliorated HIV infection [19].

Recent studies have suggested a role of methotrexate in the treatment of reactive arthritis and psoriatic arthritis occurring in HIV infection [20].

Hydroxychloroquine has been reported to be efficacious not only in treating HIV-associated reactive arthritis, but also in reducing HIV replication [21]. However, TNF blockers must be used with caution in patients of reactive arthritis in HIV [22].

### Psoriatic arthritis in HIV

Psoriatic arthritis (PsA) is associated with HIV infection and occurs commonly in the late stage of HIV infection.

There can be extensive psoriatic rash – especially in patients not receiving anti-retroviral treatment (ART). The arthritis is predominantly polyarticular and involves lower limbs.

ART has been shown to be effective in treating both HIV associated psoriasis and its associated arthritis. Phototherapy, etretinate, cyclosporine and methotrexate can also be useful [23]. Refractory disease can be treated with tumor necrosis factor blockers, although with caution [24].

### Undifferentiated spondyloarthritis

Sometimes, some HIV-infected patients fail to develop the entire spectrum of clinical manifestations for disease and only develop a few symptoms of reactive arthritis or psoriatic arthritis such as enthesopathy (plantar fasciitis, Achilles tendinitis) [25]. Treatment is symptomatic and may be treated with NSAIDs or intralesional/intra-articular corticosteroid injections.

### Avascular necrosis of bone

The true incidence of osteonecrosis in HIV infected patients is not well known. Hypothetical risk factors peculiar to HIV infected individuals for development of osteonecrosis include –

- Introduction of protease inhibitors and resulting hyperlipidemia
- Anticardiolipin antibodies in serum leading to a hypercoagulable state
- Immune recovery
- Vasculitis

The most common presentation is joint pain.

Patients may give history of steroids intake, HAART therapy, smoking, and alcoholism [26].

### Hypertrophic pulmonary osteoarthropathy (HPOA)

HPOA can develop in HIV-infected patients with *Pneumocystis jiroveci* pneumonia. It is characterized by digital clubbing; arthralgia; nonpitting edema; and periarticular soft tissue involvement of the ankles, knees, and elbows.

Radiography reveals extensive periosteal reaction and subperiosteal proliferative changes in the long bones of the lower extremity. Treatment of *P. jiroveci* pneumonia usually cures the condition [27].

### Osteopenia and osteoporosis

Regardless of ART use, osteopenia and osteoporosis occur more than three times as commonly in HIV-infected patients [28].

Risk factors for the development of osteopenia include use of ART especially protease inhibitors, long duration of HIV infection, high viral load, high lactate levels, low bicarbonate levels, increased alkaline phosphatase levels, low vitamin D levels and lower body weight before ART [29]. Treatment should include vitamin D replacement, calcium tablets and bisphosphonates. Testosterone has been used in patients with HIV wasting syndrome [30].

To date, scarce literature is available on various rheumatological manifestations of HIV. Azmi et al. [31] in his study of 200 HIV patients found that spondyloarthritis was present among 4% of HIV patient, HIV associated arthralgia among 2% and HIV associated arthritis among 0.5% of HIV patients.

## Conclusion

Joint manifestations in HIV are commonly seen. These manifestations must be adequately addressed to improve the morbidity of a HIV patient. Proper and timely treatment will prevent development of deformities and improve quality of life.

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