Reviewer: Dr CH Snyckers
Consultant: Department of Orthopaedics
University of Pretoria

Musculoskeletal manifestations of human immunodeficiency virus infection

Ayaz A Biviji, MD; Guy D Paiement, MD; Lynne S Steinbach, MD.
Journal of the American Academy of Orthopaedic Surgeons Sept/Oct 2002;**10**(5):312-9

Human immunodeficiency virus infection is a reality that orthopaedic surgeons cannot ignore. An estimated 71% of patients with HIV infection will develop bone, joint or muscle involvement and can sometimes be the presenting complaint of the disease.

Certain infections and inflammatory conditions are rarely seen in the general population but are more prevalent in the HIV population. Musculoskeletal manifestations usually occur in the later stages of the infection but can occur in any phase. The literature is awash with new publications and it can sometimes be difficult and confusing to stay informed. This article attempts to give a short overview of the clinical musculoskeletal manifestations that patients with HIV can present with.

The article focuses on:

Acute infection	**Inflammatory arthropathies**
Myopathies	• Reiter's disease
• Pyomyositis	• Psoriatic arthritis
• Polymyositis	• HIV-associated arthritis
• AZT myopathy	• Painful articular syndrome
Skeletal infections	• Acute symmetric polyarthritis
• TB osteomyelitis	• Hypertrophic osteoarthropathy
• Bacillary angiomatosis	**Osteonecrosis (AVN)**
Neoplastic conditions	**Surgical outcome**
• Non-Hodgkin's lymphoma	
• Kaposi's sarcoma	

It is well known that a patient in the acute infection phase is highly infective, although the HIV-Elisa and even the PCR can be negative. It can thus be imperative for the treating surgeon to recognise the symptoms of myalgia, artralgia and paraesthesias that manifest in the early disease, as these complaints may bring the patient to an orthopaedic surgeon. A low-grade fever and a maculopapular rash often accompany these symptoms.

Due to the possible inaccuracy of blood tests in the very early phase of infection post-exposure prophylaxis is still encouraged in all situations.

Pyomyositis, although more common in advanced disease, can often be the first presentation to the orthopaedic surgeon. The first stage is characterised by cramp-like pain and induration along a muscle group (75% in the quadriceps). A high level of suspicion is necessary as these can often be misdiagnosed as muscle strain or contusions. Left untreated this can develop into a fulminating abscess and septic shock. The mortality rate of pyomyositis ranges from 1%–20%. The erythrocyte sedimentation rate is raised but the creatine kinase (CK) is often normal. The MRI shows rim enhancement on T1 weighted images. Blood cultures are only positive in 5%, thus tissue sampling is essential. *Staphylococcus aureus* is responsible for 90% of cases, but any host of organisms can be isolated and swabs should therefore include aerobic, anaerobic, fungal and TB cultures. The treatment is aggressive and early surgical drainage and intravenous antibiotics are essential.

Polymyositis and AZT myopathy both present with symmetrical proximal limb girdle weakness and elevated serum CK levels. The AZT myopathy is dose related and subsides once the AZT is discontinued. The polymyositis on the other hand is possibly due to a direct invasion of the muscle tissue by the virus. On MRI images rim enhancement is not seen and the diagnosis can be confirmed by muscle biopsy. The polymyositis can effectively be treated with anti-inflammatories.

The prevalence of tuberculosis is 500 times greater in the HIV-infected population.

Tuberculosis osteomyelitis develops from haematogenous seeding from a newly acquired or reactivated site. The thoracic and lumbar regions are the most common, followed by the hip and knee. The infection typically starts in the anterior portion of the vertebrae and spreads to the adjacent disc spaces and may spread underneath the longitudinal ligament. These patients can also present with a psoas abscess. In other bones the metaphyseal region is most commonly affected. Radiographs can show calcified cold abscesses. Treatment consists mainly of chemotherapy for periods of one year. Surgery is reserved for refractory cases, progressive neurological deficit or structural instability.

Bacillary angiomatosis is a unique multi-system infection caused mainly by *Bartonella henselae* acquired through cat scratches or bites and is seen exclusively in immunocompromised patients. These patients develop vascular proliferations of the skin (resembles Kaposi's sarcoma), CNS (aseptic meningitis), viscera (peliosis hepatis) and lymph nodes (adenitis). Multi-organ involvement can be fatal. One-third of patients with bacillary angiomatosis have lytic osseous lesions. The organism can be identified with Warthin-Starry silver staining. The osseous lesions can effectively be treated with erythromycin. Therefore any HIV patient presenting with a lytic osseous lesion should undergo a biopsy and receive erythromycin.

Although Kaposi's sarcoma is the most common neoplasm in Aids, osseous involvement is rare. Non-Hodgkin's lymphoma is the second-most common tumour in HIV-infected individuals and tends to be more aggressive. The tumour predominantly affects the lower extremities and often presents with a pathological fracture. The radiographs usually show an osteolytic lesion with cortical destruction and a permeative pattern. MRI images classically show a low signal on T1 and a high signal on the T2 images. Treatment consists of biopsy, chemotherapy and radiation, with surgical debulking in selected cases.

Although certain rheumatic conditions (rheumatoid arthritis, systemic lupus erythematosus) tends to improve with HIV infection due to immune modulation, there are certain specific inflammatory arthropathies known to be prevalent and often more aggressive in HIV patients. Reiter's disease is 100–200 times more prevalent and typically has oligoarticular involvement of the large joints of the lower limb.

The enthesopathies (Achilles tendon, plantar fascia, rotator cuff, etc) are very common and can lead to an 'Aids foot' with painful heels. Inflammatory markers are often raised and HLA-B27 positive (70%–80%). Psoriatic arthritis is 10–40 times more prevalent and patients often have a severe cutaneous disease consisting of silvery-scaled maculopapules on the knee, trunk, scalp and elbow. Nail changes are common and often severe. Radiological changes often show severe destruction with pencil-in-cup digital deformities and osteolytic destruction. Management of these inflammatory arthropathies is problematic as immunosuppressive agents can lead to full-blown Aids and Kaposi's sarcoma. Recognition and anti-inflammatories are the mainstay of treatment although sulfasalazine has been found to be effective.

Surgical outcome in the HIV patient is still debated, especially regarding bone and soft tissue healing and post op infection

HIV-associated arthritis is a subacute oligoarthritis that develops over a period of 1–6 weeks and may last up to 6 months. Patients develop incapacitating joint pain (knee and ankle). Radiographs are essentially normal and biopsy reveals only a chronic mononuclear infiltrate. Rheumatoid factor and HLA-B27 is negative. Intra-articular steroid therapy can be very effective. The painful articular syndrome is seen as often as in 10% of patients. These patients often present with acute, severe arthralgia (knee) that simulate a septic joint. There is no effusion or synovitis and this condition responds well to narcotics. It is self-limiting and usually lasts less than 24 hours. Acute symmetric polyarthritis is a unique rheumatoid arthritis found in HIV patients that resembles rheumatoid arthritis in all aspects apart from the acute onset and negative rheumatoid factor. Again treatment can be difficult. Hypertrophic osteoarthropathy is a systemic disorder seen with pulmonary diseases (TB etc). Patients present with extensive periosteal reaction and subperiosteal proliferation in the long bones of the lower limb. A bone scan will reveal increased uptake along the cortical surfaces. Treatment consists of treating the primary lung condition.

Osteonecrosis (most commonly of the hip) is being seen with more frequency in the HIV population group, although the cause is not yet apparent, but can be either disease or treatment dependent. The main presenting symptom is pain and a high index of suspicion is needed in the HIV patient with hip pain. Other joints can be involved in up to 70% of cases and is often bilateral.

Surgical outcome in the HIV patient is still debated, especially regarding bone and soft tissue healing and post op infection. In elective surgery with an optimised patient and CD4 counts >200 cells/mm there is no higher risk for postoperative infection, but in trauma cases the risk is higher. Even in asymptomatic HIV-positive patients the risk for infection is greater, especially in open fractures. Routine HIV testing in trauma cases do not seem to be beneficial though. Late implant sepsis and bone healing still seems to be a problem, but routine implant removal cannot be supported currently.

Unfortunately no overview article can cover all aspects of musculoskeletal manifestations of HIV as the subject matter becomes too large. Unfortunately there is no mention of the immune restoration inflammatory syndrome (IRIS). This well-known entity of immune reconstitution with the commencement of highly active antiretroviral therapy (HAART) in advanced disease can precipitate a severe immunological response that can 'unmask' subclinical infections (i.e. TB). Furthermore treatment related (HAART) complications (i.e. arthralgia, frozen shoulder, de Quervan's and carpal tunnel, etc) are not elaborated on. There is also no mention made of the osteoporosis associated with HIV infection and HAART therapy and the possible role of bisphosphonates in the treatment of accompanying osteoporosis. It must also be stressed that pyogenic septic arthritis (and osteomyelitis) is very common in HIV patients constituting 23% of musculoskeletal infections. The varied causative organisms found in HIV also need mentioning as this necessitates wide spectrum antibiotic cover while awaiting specimen culture and sensitivity results. Reticuloendothelial blockade (RE-blockade) is very common leading to haemopoietic dysfunction in HIV individuals. Impaired iron regulation leads to a normocytic-normochromic anaemia with low iron stores. This leads to low T1 signal intensity of the bone marrow especially in the vertebrae. These can be mistaken for infiltrating tumour and contrast sequences are necessary.

In conclusion this article, although not a complete summary of all HIV-associated musculoskeletal conditions, provides a concise overview of the subject matter in a well-structured manner. It therefore remains a good review of a large topic that we as orthopaedic surgeons do not often have the time to work through. With the prevalence of HIV in our population, the availability of HAART and the increased life expectancy of our patients, more and more HIV-positive patients will present to orthopaedic surgeons with musculoskeletal complaints, which makes this article invaluable.

Acknowledgement

Dr A Visser, Registrar Clinical Pathology, University of Pretoria, National Health Laboratory Service.

Bibliography

1. Florence E, Schrooten W, Verdonck K. Rheumatological complications associated with the use of indinavir and other protease inhibitors. *Ann Rheum Dis* 2002;**61**:82-4.
2. Harrison WJ. HIV/AIDS in trauma and orthopaedic surgery. *J Bone Joint Surg (Br)* 2005;**87-B**:1178-81.
3. Lawn S, Bicanic T, Macallan D. *C Inf Diseas* (correspondence) 2004:**38** (1Feb):461-3.
4. Lima A, Zumioti V, Camanho G. Osteoarticular complications related to HIV infection and highly active antiretroviral therapy. *Bra Journ Inf Dis* 2007;**11**(4):426-9.
5. Tehranzadeh J, Ter-Oganesyan R, Steinbach L. Musculoskeletal disorders associated with HIV infection and AIDS.Part I Infectious musculoskeletal conditions. *Skeletal Radiol* 2004;**33**:249-59.
6.. Tehranzadeh J, Ter-Oganesyan R, Steinbach L. Musculoskeletal disorders associated with HIV infection and AIDS. Part II Non-infectious musculoskeletal conditions. *Skeletal Radiol* 2004;**33**:311-20.