Musculoskeletal Manifestations of Human Immunodeficiency Virus Infection

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First case of acquired immunodeficiency syndrome (AIDS) was identified nearly 20 years back when healthy individuals were developing unusual and dramatic opportunistic infections and cancers known to occur in an immunosuppressive state.

Following is the spectrum of musculoskeletal diseases associated with HIV infection.

**Conditions Unique to HIV infection**
- Diffuse infiltrative leukocytosis syndrome
- HIV–associated arthritis
- Zidovudine-associated myopathy
- Painful articular syndrome

**Not specific to HIV infection**
- HIV-associated Reiter’s syndrome
- Psoriatic arthritis
- Polyarteritis nodosa
- Giant cell arteritis
- Hypersensitivity angiitis
- Wegener’s granulomatosis
- Schönlein-Henoch purpura
- Behcet’s syndrome
- Infectious arthritis (bacterial, fungal)

**Ameliorated by HIV infection**
- Rheumatoid arthritis
- Systemic lupus erythematosus

Some of the musculoskeletal diseases like diffuse infiltrative lymphocytosis syndrome (DILS), Reiter’s syndrome or inflammatory myopathy if subclinical become clinically manifest or takes on a severe clinical course if already clinically manifest. Whereas few other diseases such as rheumatoid arthritis and systemic lupus erythematosus (SLE) have been reported to improve in proportion to decrease in number of CD4 lymphocytes.

First musculoskeletal manifestation of HIV infection was described in 1987 by Winchester and colleagues in a series of 13 patients from New York city with HIV infection and Reiter’s syndrome. To date questions regarding epidemiology, pathogenesis and therapy remain unanswered. The coexistence of a distinct spectrum of rheumatic disease and HIV has become of great practical importance to both clinician and researcher in the field of rheumatology.

**Epidemiology**

HIV infection is a worldwide, epidemic which grew from an estimated 1,00,000 infections in 1980 to an estimated 30 million in 1996. Reported in over 150 countries, it is prevalent in Africa, Asia and America.

HIV transmission occurs through three routes. First, it is a sexually transmitted disease that is bidirectionally transmitted between men and women, women and men and even rarely women and women. Second, it is a blood-borne pathogen transmitted through the sharing of intravenous needles and syringes among drug users or through contaminated blood or blood products. Third, it can be transmitted perinatally from an infected mother to her unborn child.

**Clinical features**

**Arthralgia**

Arthralgia is a common symptom (45%). It is generally intermittent, mild, and polyarticular. It occurs in later stages of HIV infection. Their significance is difficult to ascertain, as a multiple opportunistic infections are associated. Treatment includes use of non-narcotic analgesics such as acetaminophen or tramadol and reassurance.

**Painful Articular Syndrome**

This is a self limited syndrome, usually lasting less than 24 hours and accompanied by few objective clinical findings. It is characterized by extremely painful bone and joint pains. It has been mainly described in patients from the United States. Aetiology is unknown. There is usually no evidence of synovitis. Treatment is symptomatic.

**HIV-associated Arthritis**

HIV associated arthritis is an oligoarthritis which predominantly affect knees and ankles. It lasts for less than 6 weeks. Synovial fluid leukocyte count is lower than that seen in HIV-associated Reiter’s syndrome. No association with HLA-B27. Synovial fluid white blood cell count often reveals a minimally inflammatory state, with counts in the range of 50 to 2600 cells/mm³. Radiographs of the affected joints are normal.

Treatment includes NSAIDs, low dose glucocorticoids, hydroxychloroquine, oral gold and sulfasalazine.

**Reiter’s Syndrome or Reactive Arthritis**

Typical presentation is seronegative peripheral arthritis predominantly involving lower extremities accompanied by enthesitis. Mucocutaneous features are common, especially keratoderma blennorrhagica and circinate balanitis. Psoriasiform skin rashes are seen. Axial involvement and uveitis appear to be uncommon.

Treatment: Indomethacin is recommended not only for its efficacy, but also for its inhibition of HIV replication. Phenylbutazone may be useful in refractory cases. Sulfasalazine found effective in the doses of 1.5 to 2 g/day and in fact, one study suggested that it ameliorated HIV infection. Methotrexate was not recommended in earlier studies, later studies found methotrexate useful in treatment of these
seronegative arthritis. Hydroxychloroquine has also been reported to be as efficacious not only in treating HIV-associated Reiter’s syndrome but also in reducing HIV replication in vitro and in reducing HIV viral loads in vivo. Both arthritis and cutaneous lesions of HIV-associated Reiter’s syndrome and psoriatic arthritis have been found to respond to etretinate (0.5 to 1 mg/kg/day).

Psoriasis and Psoriatic Arthritis

Skin rash ranges from seborrheic dermatitis at the mild end, through frank psoriasis vulgaris to pustular psoriasis at the severe end.

Arthritis and enthesopathy similar to that described in patient with Reiter’s syndrome are also seen concomitantly with psoriasis. The clinical course is heterogeneous for both skin disease and arthritis ranging from mild to severe, and it is interesting to note that the antiretroviral drug zidovudine (AZT) may frequently be effective for controlling the skin disease but rarely effective for articular disease.

Septic Arthritis

Even though increasing incidence of pyogenic infections in HIV-infected is reported very few cases of septic arthritis have been reported. Organisms responsible are Staphylococcus aureus and Streptococcus pneumoniae. Other organisms Sporothrix schenckii, Cryptococcus neoformans, are also reported.

Osteonecrosis

Knees and hip joints are common sites. Other factors like alcohol, prednisone therapy are also associated. Pathogenesis is unclear at present. Anticardiolipin antibodies of the IgG and IgM isotopes have pathogenic role.

HIV-associated Muscle Disorders

Spectrum of clinical picture ranging from uncomplicated myalgias and fibromyalgia or asymptomatic creatinine kinase elevation to severe disabling HIV-associated polymyositis or pyomyositis has been described.

Myalgia and Fibromyalgia

Occur up to a third of patients. Associated with longer disease duration and history of depression. Treatment is similar for fibromyalgia in non-HIV setting.

Non-inflammatory Necrotizing Myopathy

Non-inflammatory necrotizing myopathy has been described in patients with HIV infection. Despite lack of inflammation, immune-mediated pathogenesis is favoured by most investigators. Corticosteroids restore muscle strength and mass.

HIV-associated Polymyositis

Typically manifests early in the course of HIV infection. Subacute progressive proximal muscle weakness with elevated creatine kinase are prominent features. Electromyogram studies reveal myopathic motor unit potentials with early recruitment and full interference patterns as well as fibrillation potentials, and positive sharp waves. Multiple biopsies reveal interstitial inflammatory infiltrates of variable intensity accompanied by degenerating-regenerating myofibrils. Cause is unclear. Whether HIV virus per se directly contributes to inflammatory myopathy or nutritional factors are contributing is debated.

Treatment is similar to other inflammatory myopathies. Both creatinine kinase elevation and the muscle weakness respond to moderate-dose glucocorticoids. Refractory cases benefit by methotrexate or azathioprine.

Pyomyositis

Important complication of HIV infection in areas most endemic for HIV such as Africa and India. A case-control study from Uganda found a highly significant association of pyomyositis with HIV infection. Organisms identified are Staphylococcus aureus, Salmonella enteritidis, Micsoroporum and Toxoplasma.

Sjogren’s-like Syndrome

Characterised by multiple exocrine gland dysfunction leading principally to keratoconjunctivitis sicca and xerostomia. Some authors suggested the name diffuse infiltrative lymphocytosis syndrome.

Clinical features are parotid gland enlargement, xerostomia or xerophthalmia, generalised lymphadenopathy, lymphocytic interstitial pneumonitis and meningitis.

Zidovudine, moderate dose of corticosteroids (30 to 40 mg prednisolone per day), low dose radiotherapy have been tried.

Vasculitis Associated with HIV Infection

Different types of vasculitis including hypersensitivity vasculitis, polyarteritis nodosa, Henoch Schonlein purpura, giant cell arteritis, isolated CNS angiitis, Behcet’s, Kawasaki diseases have been described.

Corticosteroids remain the mainstay of treatment. Cytotoxic agents have been employed in refractory cases. Painful neuropathy due to vasculitis responds well to high-dose glucocorticoids.

Musculoskeletal manifestations in pediatric HIV infection in same as in adult HIV infection.

REFERENCES


