Rheumatological Manifestations in HIV Infection

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Abstract

The global epidemic of HIV infection has also affected the practice of rheumatologists. Reiter’s syndrome was the first reported rheumatic disorder in patients of HIV infection, and since then, many other rheumatic manifestations have been reported. These conditions include arthralgia, painful articular syndrome, Reiter’s syndrome, reactive arthritis, HIV-associated arthritis, undifferentiated spondyloarthropathy, soft tissue rheumatism, septic arthritis, avascular bone necrosis, osteomyelitis, hypertrophic osteoarthropathy, myalgias like polymyositis, dermatomyositis, Sjögren’s like syndrome - DILS, vasculitits like Schonlein-Henoch purpura, polyarteritis nodosa (PAN), giant cell arteritis(GCA), Wegener’s granulomatosis (WG), Raynaud’s phenomenon and Behcet’s syndrome. HIV-related neoplastic processes namely Kaposi’s sarcoma and non-Hodgkin’s lymphoma can also affect the musculoskeletal system. Musculoskeletal manifestations can occur at any phase of the infection though they are much more prevalent in late phases. There could be involvement of bone, joint, and muscle during the course of HIV infection. A number of rheumatic manifestations have been described in HIV infection. The rheumatic manifestations can be attributed either to direct or indirect effects of HIV virus with genetic and environmental factor also contributing a key role. One of the biggest paradoxes of HIV infection is the finding of certain rheumatic diseases such as the diffuse infiltrative lymphocytosis syndrome (DILS), reactive arthritis, Reiter’s syndrome, or inflammatory myopathy occurring in the face of immunodeficiency. Alternatively, other rheumatic diseases such as rheumatoid arthritis and systemic lupus erythematosus have been reported as improving in the face of the CD4+ lymphocytes depletion associated with HIV infection. Thus, an early understanding and treatment of rheumatic disease will go a long way in reducing physical, mental, social, and economic burden in these miserable HIV infected patients.

Key words: HIV, Rheumatic, Manifestation.

Introduction

Human immunodeficiency virus (HIV-1) infection was reported almost two decade ago. Since then the disease has spread worldwide at an alarming rate. India already has the second highest number of people estimated to be living with HIV/AIDS in the world (5.1 million). The global epidemic of HIV infection has affected the practice of almost every clinician, and rheumatologists are no exception. Earliest reports of rheumatological associations of HIV infection were published in mid-1980s, and since then much interest has been aroused in this topic. Reiter’s syndrome was the first reported rheumatic disorder in HIV infection, and since then many other rheumatic manifestations have been reported ranging from 4 to 71.3% in their prevalence. Various aspects of these rheumatic manifestations in HIV infected patients are discussed in the present review.

Epidemiology

The prevalence and characteristics of the rheumatic and extra-rheumatic manifestations of human immuno-deficiency virus (HIV) infection determined in one of the prospective studies suggested that out of one hundred and one patients with HIV infection, the musculoskeletal system was involved in 72 patients. Thirty-five patients had arthralgias, ten had Reiter’s syndrome, two had psoriatic arthropathy and myositis respectively, and one had vasculitis. Also found were two previously unreported syndromes. The first, occurring in 10 patients, consisted of severe intermittent pain involving less than four joints, without evidence of synovitis, of short duration (two to 24 hours), and requiring therapy ranging from non-steroidal anti-inflammatory drugs to narcotics. The second, occurring in 12 patients, consisted of arthritis (oligoarticular in six patients, monoarticular in three patients, and polyarticular in three patients) involving the lower extremities and lasting from one week to six months. The synovial fluid studied in five patients was sterile and inflammatory.

Similarly, in another prospective study of 74 consecutive HIV +ve patients, clinical and laboratory findings of rheumatic manifestations were compared with 72 control HIV −ve subjects with similar risk factors for HIV. It was found that rheumatic manifestations were more frequently observed...
in the HIV +ve group than the HIV -ve group: arthralgias were found in (45%), arthritis in (10%), and Reiter’s syndrome in (8%). Laboratory findings revealed rheumatoid factor in 21% HIV +ve versus 2% in HIV -ve, antinuclear antibodies in 17% HIV +ve vs 0 in HIV -ve, IgG anticardiolipin antibodies in 94% HIV +ve vs 9% in HIV -ve. Hyperuricaemia was found in 41% HIV +ve patients and hypouricaemia in 5%, compared with none in the HIV -ve group. Neoplasias were identified in 13 HIV +ve patients, and in 7 these were associated with hyperuricaemia, and in 3 with hypouricaemia. Of interest, 2 patients had urate abnormalities before the diagnosis of neoplasia. Thus, the study suggests that rheumatic manifestations and autoantibodies are more prevalent in HIV +ve patients6.

Natural course of the disease

Rheumatoiological manifestations can occur at any phase of the infection, though they are much more prevalent in late phases5, 7. There could be involvement of bone, joint, and muscle during the course of HIV infection.

Rheumatic diseases associated with, or occurring in, patients with HIV infection

A number of rheumatic manifestations have been described with HIV infection. These include arthralgia, painful articular syndrome, Reiter’s syndrome, reactive arthritis, HIV-associated arthritis, undifferentiated spondyloarthropathy, soft tissue rheumatism, septic arthritis, avascular bone necrosis, osteomyelitis, hypertrophic osteoarthropathy, myalgias, polymyositis, dermatomyositis, Sjögren’s like syndrome—DILS, vasculitis like Schönlein-Henoch purpura, polyarteritis nodosa (PAN), giant cell arteritis (GCA), Wegener’s granulomatosis (WG), Raynaud’s phenomenon, and Behcet’s syndrome1811. HIV-related neoplastic processes such as Kaposi’s sarcoma and non-Hodgkin’s lymphoma can affect the musculoskeletal system12.

Aetiopathogenesis of rheumatic manifestations in HIV infection

The rheumatic manifestations can be attributed either to the direct effect of HIV infection or to host immune response to the infection; those mediated by intact components of the immune system (CD8 cell), and those that arise because of immunodeficiency13 with genetic and environmental factors also contributing a key role.

### Table I: Rheumatological consequences of HIV infection.

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<td>HIV-related neoplastic processes</td>
<td>Rheumatic diseases e.g. RA</td>
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Direct effects

Reports of isolation of 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, myositis, and polyarteritis nodosa (PAN)-like vasculitis1416. Many symptoms are attributable to host immune response to infection, mediated by intact components of immune system (CD8) or those arising due to immunodeficiency.

Indirect effects

A. Early HIV infection:

Characterised by chronic activation of host cellular and humoral responses.

1. Involvement of humoral arm is evidenced by presence of a plethora of antibodies in circulation occurring due to spontaneous B-cell proliferation17.

- The commonest laboratory abnormality is polyclonal hyperglobulinaemia in 45% of HIV positive individuals18.
- Autoantibodies are more frequent in HIV positive with rheumatoid factor and ANA being in low titre in 17% of patients19. IgG anticardiolipin antibodies seen in 95% patients with AIDS, more so in
advanced cases in 20 - 30% HIV positive individuals\textsuperscript{20,21}. ANCA (both c-ANCA and p-ANCA) present in approximately 43% of ELISA\textsuperscript{22}.

2. Diffuse infiltrative lymphocytosis syndrome (DILS): Sjogren-like syndrome is now a well established manifestation of HIV infection with unrestricted increase in number of CD\textsubscript{8} T-cells directed against host antigens bearing HLA-DR5 phenotype\textsuperscript{23}.

3. Reiter’s syndrome (RS), psoriatic arthritis and various undifferentiated spondyloarthropathies: It has been postulated that the progressive CD\textsubscript{4} cell depletion occurring in HIV infection may permit persistant gut infection and decreased clearance of streptococcal and staphylococcal infection contributing to the greater severity of spondyloarthropathies and psoriasis respectively. The association between RS and AIDS has been explained by the fact that the acquired immunodefiency heads to bacterial, viral, and parasitic infections caused by micro-organisms with arthrogenic potential\textsuperscript{24}.

4. Vasculitis: Histopathological examination of HIV-associated vasculitic lesions showed perivascular infiltration by CD\textsubscript{8}+ T-cells\textsuperscript{25}. Apart from the direct effect of HIV infection, a host of opportunistic pathogens may contribute to the vasculitis. Although antibodies to neutrophil cytoplasmic antigens (ANCA) have been described in HIV seropositive patients, these antibodies do not appear to be associated with the HIV-associated vasculitides.

5. Inflammatory myopathy: HIV infection is associated with polymyositis like syndrome. The perivascular and interstitial infiltrate chiefly comprises of CD\textsubscript{8} cells\textsuperscript{26}.

B. Advanced stage of HIV infection\textsuperscript{27}

The rapid CD\textsubscript{4} cell depletion occurring in this stage is associated with infectious/septic arthritis and osteomyelitis by conventional and opportunistic pathogens.

Clinical presentation of rheumatological manifestations in HIV patients

HIV-associated arthralgia

Frequency of arthralgias, unexplained in origin, in HIV +ve subjects has been reported to be more than 45% and are the most commonly observed manifestation in HIV infection\textsuperscript{9}. They are mild-to-moderate in severity, and may be transient or intermittent, and are often oligoarticular— affecting large joints such as shoulder, elbow and knee — although any joint can be involved. A polyarticular presentation is now also seen frequently\textsuperscript{28}. The most appropriate treatment alongwith a non-narcotic analgesic such as acetaminophen or tramadol, is reassurance\textsuperscript{8,9}.

Painful articular syndrome

The painful articular syndrome is characterised by bone and joint pain on movement, without evidence of synovitis\textsuperscript{29}. It is a self-limiting syndrome which lasts less than 24 hours. This syndrome is usually observed in the late stage of HIV infection. The exact aetiology of unclear, and treatment is symptomatic\textsuperscript{8,9}.

HIV-associated arthritis\textsuperscript{8,9}

HIV associated arthritis occurs atleast as frequently, and sometimes more commonly, than HIV indirectly associated spondyloarthropathy. It is usually present as an oligoarthritis, predominantly affecting lower extremities, which tend to be self limiting, lasting for less than 6 weeks. Although early reports in western communities reported asymmetrical oligoarthritis as the usual pattern, polyarticular involvement is now seen frequently\textsuperscript{30}. The synovial fluid leucocyte count is lower than seen in HIV-associated reactive arthritis (500 - 2,000/ l). Synovial fluid cultures are typically sterile. Isolation of HIV from one synovial fluid sample, and electron microscopy, show particles resembling retrovirus. No mucocutaneous involvement is observed, and enthesopathy is also absent. The treatment, by and large, includes NSAIDs, and in more severe cases, low dose corticosteroids. Patients may respond equally well to hydroxychloroquine and sulphasalazine. Most of the patients with HIV associated arthritis are in the late stage of infection. The aetiology is still unclear, however recently both HTLV-I and -II have been suggested to induce inflammatory or autoimmune reactions which can increase significantly the incidence of arthritis.

Reactive arthritis

Reactive arthritis occurs more commonly in the setting of HIV infection and perturbation in the CD\textsubscript{4} lymphocyte
count, and CD4 to CD8 ratios may be involved in the pathogenesis of reactive arthritis. The most typical presentation is that of a seronegative peripheral arthritis predominantly involving the lower extremities, usually accompanied by enthesitis and mucocutaneous features. The diagnosis of reactive arthritis (RS) is based on the combination of dermatological and articular alterations. The patient’s cutaneous lesions are characterised by exfoliation and the formation of crusts located on the face, scalp, genitals, hands, and feet; onychodystrophy with opacity; yellowish colouration; and hyperkeratosis of the nails. Articular lesions lead to progressive deformity of phalangeal joints of the hands, and intensive arthralgia, mainly of the larger joints (shoulders, elbows, hips, and knees). The synovial fluid white cell count rises to 2,000 - 10,000/ l, synovial fluid cultures are negative, and the most common microorganism present in the synovial membrane is Chlamydia. Unlike HIV-associated arthritis, HLA-B27 association exists in 70% - 90% of patients8, 9, 31.

Jaccoud arthropathy is a non-erosive, deforming arthropathy reported to occur in cases of chronic rheumatic fever and systemic lupus erythematosus. Only two cases of HIV-associated Jaccoud arthropathy have been reported in the literature so far, both in patients with features of reactive arthritis. Interestingly, a case of HIV-associated Jaccoud arthropathy in a patient without features of reactive arthropathy was presented recently, suggesting that unpredictable presentation, are possible in HIV infection32.

Similarly, psoriasiform dermatitis can present in Reiter’s syndrome associated with AIDS33.

NSAIDs are the mainstay of treatment8, indomethacin, in particular is recommended because of its additional property to inhibit HIV replication, whereas rarely, phenylbutazone is preferred in refractory cases. Sulphasalazine like NSAIDs can ameliorate HIV infection to a little extent. Methotrexate was initially considered contraindicated because of its immunosuppressive action, but recently it has been suggested to have a role in treatment, if careful monitoring of HIV viral load and CD4 counts is done. Hydroxychloroquine also has been reported to be very effective with in vitro reducing action on HIV replication as well. Etretinate34 can be useful for both arthritic and cutaneous manifestations. Research is also on to evaluate the role of infliximab and other TNF blockers.

Psoriatic arthritis (PsA)

PsA is almost universally associated with HIV infection. It occurs most commonly in the late stage, of HIV infection. The psoriatic rash can be extensive – especially in patients not receiving anti-retroviral treatment. The arthritis is predominantly polyarticular, involves lower limbs, and is progressive. Amelioration is noted with onset of AIDS35. The aetologic mechanisms remain unclear, but most likely represent a combination of genetic and environmental factors8.

Antiretroviral treatment has been shown to be effective in treating both HIV associated psoriasis and its associated arthritis. Phototherapy, etretinate, and methotrexate can also be useful. Etanercept37 may play an important role in modulating the inflammatory activity and progression of HIV-associated psoriasis and psoriatic arthritis. Although, both cutaneous and joint manifestations of psoriasis improve dramatically with its use, careful follow-up must be exercised while prescribing etanercept in the setting of HIV infection.

Undifferentiated spondyloarthopathy8, 9

Some HIV-infected patients fail to develop the entire spectrum of clinical manifestations for disease to be called as ankylosing spondylitis, Reiter’s syndrome, or psoriatic arthritis, and are labelled as undifferentiated spondyloarthropathy. The epidemic of HIV infection in sub-Saharan Africa in recent years, however, has been associated with a dramatic upsurge in the prevalence of spondyloarthopathies other than ankylosing spondylitis, primarily reactive arthritis and undifferentiated forms of the disease, and less often psoriatic arthritis. HLA-B27, because of its rarity and virtual lack of association with the observed cases of spondyloarthropathy in this population, cannot be used as an aid in diagnosis of spondyloarthropathy in black Africans. Conversely, HIV infection is increasingly showing such a strong association with reactive arthritis, psoriatic arthritis, and undifferentiated spondyloarthropathies in sub-Saharan African populations that any patient with acute or chronic inflammatory arthritis may need to be tested for possible HIV infection38.

Enthesitis, dactylitis, oligoarthritis, sacroiliitis, nail changes, and conjunctivitis are commonly seen in such patients and they
are usually negative for RA factor, ANA, and HLA B27. The pathogenesis of HIV-associated spondyloarthropathy (SpA) is poorly understood. On magnetic resonance imaging and sonographic imaging, inflamed knees, extensive polyenthesitis, and adjacent osteitis are the frequent findings. The arthritis deteriorates despite conventional anti-rheumatic treatment, but improves dramatically after highly active anti-retroviral treatment, which is accompanied by a significant rise in CD4 T-lymphocyte counts. Otherwise, treatment is symptomatic (NSAIDs); intralesional corticosteroids and sulphasalazine may be used in more extensive disease.

Avascular necrosis (Osteonecrosis)

Osteonecrosis, also known as avascular necrosis, is chiefly characterised by death of bone caused by vascular compromise. The true incidence of osteonecrosis in HIV-infected patients is not well known and the pathogenesis remains undefined. Hypothetical risk factors peculiar to HIV-infected individuals that might play a role in the pathogenesis of osteonecrosis include the introduction of protease inhibitors and resulting hyperlipidaemia, the presence of anticardiolipin antibodies in serum leading to a hypercoagulable state, immune recovery, and vasculitis. The most common presentation is arthralgia. The majority of the patients will give history of receiving steroids, HAART therapy, smoking, and alcoholism. This complication has been reported mostly in adults, but recently, even the case of a 5-year-old child with AIDS (stage 3) who developed osteonecrosis related to the advanced stage of the illness and to HAART is reported without any of the above risk factors. Hence, it is believed that osteonecrosis should be included as a differential diagnosis of every HIV-infected patient who complains of pain of weight bearing joints. Likewise, it seems prudent to rule out HIV infection in subjects with osteonecrosis.

Myopathy

Skeletal muscle involvement can occur at all stages of HIV infection, and may represent the first manifestation of the disease. Myopathies in HIV-infected patients is classified as follows: (1) HIV-associated myopathy and related conditions, including HIV polymyositis, inclusion-body myositis, nemaline myopathy, diffuse infiltrative lymphocytosis syndrome (DILS), HIV-wasting syndrome, vasculitic processes, myasthenic syndromes, and chronic fatigue; (2) muscle complications of anti-retroviral therapy, including zidovudine and toxic mitochondrial myopathy related to other nucleoside-analogue reverse-transcriptase inhibitors (NRTIs), HIV-associated lipodystrophy syndrome, and immune restoration syndrome related to highly active anti-retroviral therapy (HAART); (3) opportunistic infections and tumour infiltrations of skeletal muscle; and (4) rhabdomyolysis. Dermatomyositis, fibromyalgia, and osteomyelitis complicating pyomyositis are a few other rare presentations.

Patients presenting with proximal muscle weakness can show a normal or minor elevation of creatine phosphokinase (CPK), and normal findings on electromyography. Whereas, muscle biopsy can reveal CD4 polymyositis. This illustrates the importance of muscle biopsy in identifying the underlying pathology in HIV infected patients with muscle weakness and little or no abnormality in laboratory investigations.

A severe neuromuscular weakness syndrome may occur in HIV-infected individuals. The association with hyperlactataemia and NRTI exposure supports mitochondrial toxicity as a pathogenesis. In some, the onset of neurological symptoms lag significantly after discontinuation of anti-retroviral therapy, suggesting that different aetiological mechanisms may underlie these cases. The management of HIV-associated polymyositis is similar to that for other inflammatory myopathy.

Diffuse infiltrative lymphocytosis syndrome (DILS):

Definite DILS is found in 3% of the patients, and possible DILS in 3.4%. The prevalence of definite DILS is significantly higher in African Americans (4.5%)47. Diffuse infiltrative lymphocytic syndrome (DILS) is a rare manifestation of human immunodeficiency virus (HIV) disease which is characterised by a diffuse visceral CD8 lymphocytic infiltration, a persistent CD8 lymphocytosis, bilateral parotid swelling and cervical lymphadenopathy48. A role of Epstein-Barr virus (EBV) and HIV, but not CMV, in the pathogenesis of DILS, is suggested by our immunohistochemical findings49. Evidence is also there suggesting that CD8 lymphocytosis represents an immune response to viral infection rather than a malignant disorder, i.e., it is a benign monoclonal expansion50.

The following diagnostic criteria have been suggested:
a. Patient must be HIV seropositive by ELISA and Western blot;
b. Must have bilateral salivary gland enlargement or xerostomia persisting for more than 6 months; and
c. Must have histological confirmation of salivary or lacrimal gland lymphocytic infiltration in absence of granulomatous or neoplastic enlargement.

It is important to differentiate Sjogren syndrome and HIV associated DILS; features similar and different are depicted in Table II and III.

Table II: Comparison of clinical features of Sjogren syndrome and HIV associated DILS.

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<th>Features which are similar</th>
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<tr>
<td>a. Sicca symptoms</td>
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<td>b. Salivary gland swelling (often massive in DILS)</td>
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<tr>
<td>c. Extraglandular involvement (hepatitis, renal tubular acidosis)</td>
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<tr>
<td>d. Lymphocytic infiltration on salivary gland biopsy</td>
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<tr>
<td>e. Neutropenia and/or lymphopenia in peripheral blood</td>
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<tr>
<td>f. Polyclonal hypergammaglobulinaemia.</td>
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Table III: Comparison of clinical features of Sjogren syndrome and HIV associated DILS.

<table>
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<th>Features which are different</th>
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<tr>
<td>Sjogren syndrome</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Lymphadenopathy</td>
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<td>Extraglandular involvement</td>
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<td>Autoantibodies</td>
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<tr>
<td>HLA-DR</td>
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<td>Infiltrating lymphocyte</td>
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In addition, clinicians should be aware that the pulmonary process associated with DILS may mimic clinically and radiographically the pulmonary process caused by *Pneumocystis carinii*. Other manifestations of DILS include a severe form of peripheral neuropathy; lymphocytic infiltration of the liver, evident as hepatitis; myositis; and lymphocytic interstitial nephritis.

Such patients with the syndrome may also be seen in the dental clinics. Recognition and appropriate referral are responsibilities of the dental practitioner. Myositis also has been documented to be one of the presentations of DILS.

Corticosteroids in moderate doses (30 - 40 mg prednisolone per day) might be useful in treating both glandular swelling and sicca symptoms of DILS, without adversely affecting frequency of opportunistic infections, raising viral loads or depressing CD4 counts. Radiotherapy also has been suggested to have a role, and besides, combination anti-retroviral therapy is also effective. Cysts – if refractory – can be managed by aspiration and instillation of 1 ml of a depot steroid into the cyst.

**Vasculitis**

The vasculitides associated with HIV are usually not life-threatening, and present as a single flare rather than a relapsing illness. A wide spectrum with inflammatory diseases has been described in patients of HIV infection. Lesions included in these are hypersensitivity vasculitis, polyarteritis nodosa, and Henoch Schonlein purpura, others being Kawasaki disease, giant cell arteritis, Wegener’s granulomatosis, and isolated angiitis of central nervous system, small-vessel vasculitis, and inflammatory lung disease. Corticosteroids remain the mainstay of treatment, although cytotoxic drugs also have been employed in refractory cases.

**Septic arthritis**

In a prospective study among all new admitted patients with septic arthritis (SA), 79% were HIV-1 seropositive. Gonococcal arthritis was found in four patients, all HIV positive. Non-gonococcal bacterial arthritis was established in 16 patients, of whom 13 were HIV positive. Causative organisms involved in this group were: *Staphylococcus aureus*, *Streptococcus pneumoniae*, Salmonella group B, Streptococcus group D, *Klebsiella pneumoniae*, and mycobacterium. Among atypical mycobacterium species, most commonly implicated are *Mycobacterium avium-intracellular complex*, *M. kanssasii*, *M. haemophilum*, *M. terrae* and *M. fortuitum*. Septic arthritis due to *Haemophilus influenzae* has also been described in a HIV-infected patient. Fungal infections like *Candida albicans* also can manifest with oligoarthritis or polyarthritis.

Thus, HIV-1 infection appears as a risk factor for SA patients, but SA cannot be used as a predictor for HIV-1 infection.
hospitalised patients. SA occurs infrequently, and may present at any stage of HIV infection\textsuperscript{54}.

**Paradoxes of HIV infection**

One of the biggest paradoxes of HIV infection is the finding of certain rheumatic diseases such as the diffuse infiltrative lymphocytosis syndrome (DILS), reactive arthritis, Reiter’s syndrome, or inflammatory myopathy occurring in the face of immunodeficiency. Alternatively, other rheumatic diseases such as rheumatoid arthritis and systemic lupus erythematosus have been reported as improving in the face of the CD\textsubscript{4} lymphocytes depletion associated with this disease\textsuperscript{8}.

**Systemic lupus erythematosus**

Systemic lupus erythematosus (SLE) in patients infected with HIV due to transfusion of either blood or platelet concentrate can show a near remission in the disease and during the course of follow-up\textsuperscript{56}. But contrary to previous findings, it has been suggested that the features of both HIV infection and connective tissue disease (SLE) can co-exist\textsuperscript{57, 58}. Systemic lupus erythematosus (SLE) may be influenced by the treatment of HIV infection also. A person with HIV infection was reported to develop SLE after the initiation of highly active anti-retroviral therapy\textsuperscript{59}.

Thus, generally, HIV-related immuno-suppression improves SLE symptoms, but anti-retroviral therapy may lead to an autoimmune disease flare subsequent to the increase of circulating CD\textsubscript{4} cell count\textsuperscript{60}.

**Rheumatoid arthritis (RA)**

The effects of HIV infection on rheumatoid arthritis (RA) are a matter of debate as there is no agreement on the influence of HIV related immunodeficiency on this disease. Patients with RA with symmetric joint erosions and positive rheumatoid factor (RF) who develop classic acquired immunodeficiency syndrome (AIDS) improve with resolution of bony erosions and disappearance of RF, and reach a complete clinical remission only in the paralytic limbs\textsuperscript{61, 62}.

**Laboratory abnormalities associated with HIV infection**

The commonest laboratory abnormality is polyclonal hyperglobulinaemia in 45\%, whereas rheumatoid factor and ANA occur in low titre in 17\% of HIV patients. IgG anticardiolipin antibodies are seen in 95\% patients of AIDS, moreso in advanced disease. ANCs (both c-ANCA and p-ANCA) are present in approximately 43\% by ELISA. Similarly, false positive results for HIV antibody by ELISA/Western blot may be seen in SLE\textsuperscript{8}.

**Conclusion**

As the epidemic of HIV is increasing, burden of rheumatic disorders would also be a visible cause of morbidity in these patients. The understanding of interface of HIV with the immune system and clinical manifestations of rheumatic and autoimmune disorders is important as HIV infection can alter the clinical presentation and course of the disease. Awareness regarding presence and interpretation of the spectrum of auto-antibodies in these patients is important as presence of auto-antibodies can lead to diagnostic dilemmas. One should entertain the possibility of HIV infection in presence of polymyositis and vasculitis. Early recognition and treatment of opportunistic infections is of paramount importance as they can become the reasons for rheumatological disorders. Anti-viral effects of drugs like indomethacin and hydrochloroquine, and impact of HAART in producing and affecting the clinical spectrum of rheumatic disease has to be kept in mind while treating HIV-infected patients. Early understanding and treatment of rheumatic diseases will go a long way in reducing physical, mental, social, and economic burden in these unfortunate HIV-infected patients.

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