Case Report

Vasculitis with Digital Gangrene in a Patient with HIV Infection

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Abstract

A case of polyarteritis nodosa (PAN) like systemic necrotizing vasculitis in an HIV infected individual, who presented with digital ischaemia is reported. The pathogenesis of PAN in HIV infected patients is not well understood and whether HIV or other agents are directly involved in the vascular injury remains to be established.

INTRODUCTION

A broad array of rheumatic syndromes are associated with HIV infection ranging from arthralgia to reactive arthritis, myopathy and fibromyalgia to more severe necrotizing vasculitis. Vasculitic syndromes have been reported in 0.4% of patients with HIV infection. Calabrese has divided the vasculitides associated with HIV infection into four major categories: polyarteritis nodosa like illness (PAN) and other systemic necrotizing vasculitides, hypersensitivity vasculitis, lymphomatoid granulomatosis and primary angiitis of the CNS.

The PAN like illness presents most commonly as peripheral neuropathy or as ischaemic changes in the limbs. In contrast to the high prevalence of renal involvement in idiopathic PAN, none of the reported cases associated with HIV infection have significant renal disease. Mononeuritis multiplex is a frequent finding in HIV infected patients with vasculitis.

CASE REPORT

A 37 years female presented with complaints of severe and progressively increasing pain, bluish discoloration, numbness and coldness of both hands and feet since four days. She was treated with analgesics and pentoxiphylline by a family physician. As there was no relief of pain and because of brackish discoloration of tips of digits she was referred to our centre. There were no complaint of fever, abdominal pain, nausea, vomiting, giddiness, syncopal attack or history of similar illness in the past. She gave history of episodes of pain, swelling and erythema of small joints of hands and knees since last three years. For this she was treated with analgesics and steroids from time to time.

Patient was married married since 16 years and had three issues. She had never taken oral contraceptive pills and had no known addictions. Tubectomy was done 9 years back. She denied history of extra-marital exposure. Her husband was known HIV positive.

Physical examination revealed a young women in severe pain. Pulse was 114/min regular, BP was 140/90 mmHg. She was mildly febrile. There was no clubbing or lymphadenopathy. Carotid, brachial, radial, femoral and popliteal pulses were well felt on both sides. Left posterior tibial was weak. Dorsalis pedis pulsations were absent on both sides. There was gangrenous change in the toes and fingers on both sides mainly at the tips. Changes were more marked on the right side (Fig. 1). Cardiovascular, respiratory and central nervous system examination was essentially normal. On abdominal examination liver was palpable 4 cms below the right costal margin. There was no tenderness.

Investigations revealed : hemoglobin 10.4 gm/dl, ESR 38 mm/hr (Wintrobe method), total WBC 9000/mm³, P68%, L 30%, E 2%, B 0%, M 0%, platelets adequate, urine sugar and albumin negative, 24 hrs urinary protein 0.162 gm, urine microscopy normal, urinary VMA negative. Blood culture showed no growth. Post-prandial blood sugar was 145 mg/dl, blood urea 24 mg/dl, cholesterol 245 mg/dl, sodium 125 mEq/l, serum potassium 3.6 mEq/L, creatinine 0.8 mg/dl, bilirubin 0.5 mg/dl, uric acid - 4.1 mg/dl, SGPT 12 IU/L. HBsAg and anti HCV were negative. Elisa for HIV was positive thrice with different kits. CD 4 count was 224, CD8 was 1118 and CD4 : CD8 ratio was 0.2. Her HIV viral load was 62912 micro pieces/ml.

X-ray chest PA view, ECG, 2D ECHO, USG abdomen, barium swallow and X-ray both hands were within normal limits.

RF was negative, ANA by ELISA technique was positive 240 units/ml. (Lab reference values < 150 IU/ml - negative, 152 to 200 IU/ml borderline, > 200 IU/ml significant), ANA
blot immunoassay for SmB, SmD, RNP - 70 K, RNP - A, Topo/Scl - 70, Jo - 1/HRS, ribosomal RNP, histones, polyclT, RNP-C, SS-A/RO52, SS-a/RO 60, 55-B/La and cemp B was negative. Antiphospholipid antibody test was negative. Her anti-dsDNA was 4.8 IU/ml (normal range 0.0 to 4.5 IU/ml). There was mild increase in gamma globulins. Cryoglobulins were negative.

Doppler study showed absent digital flow in upper and lower limbs. Angiography of left leg showed block in the left posterior tibial with appearance of few collaterals. Skin biopsy from the site of involvement (digits) showed PAN like vasculitis with superadded thrombosis.

Measures were undertaken to keep the limbs warm. Patient was treated with nifedipine 5 mg tid, tab. pentoxyphylline 400 mg tid, tab. prednisolone 30 mg od, after food. Prednisolone was gradually tapered and stopped, over a period of six weeks. With this treatment burning and pain subsided and there was arrest of progression of disease. Patient wanted to go home and agreed for readmission for further investigations.

One month later she was readmitted with same complaints. There was no progression of gangrene. The previous treatment was continued and prednisolone was restarted. She was also given daily IV low molecular weight dextran. As these measures did not relieve her of pain, cervical and lumbar blockade by epidural catheterisation with tramadol + 2% lignocaine was done. There was significant temporary pain relief. Prednisolone was gradually tapered over four weeks and stopped as patient developed cushingoid features.

Soon after discontinuation of prednisolone, she came back again with pain, discoloration and extension of gangrenous change. Her both radial pulses were feeble. This time, she was put on prednisolone 60 mg od along with lamivudine 150 mg bd and zidovudine 300 mg bd. Steroids were tapered over six weeks. Antiretroviral drugs were continued. The patient’s symptoms of pain improved significantly and there was no further increase in gangrene. A line of demarcation appeared soon after, followed by autoamputation. Few months later, she succumbed to septicaemia following infection at gangrene site.

**DISCUSSION**

One of the unforeseen consequences of infection with human immunodeficiency virus is the appearance of various rheumatic syndromes that traditionally have been thought to result from inappropriate over actively of the immune system. Infection with HIV causes features of immune stimulation expected with any chronic viral infection and later immune deficiency resulting from specific injury to cells that express CD4 receptors such as helper ‘T’ cells and those of monocytes/macrophage lineage specific to this agent. Three different categories of such responses have been identified.

1. Those conditions which arise as a direct result of immuno stimulation caused by the viruses and host response to infection with HIV like diffuse infiltration lymphocytosis syndrome, polymyositis and various vasculitides.

2. Diseases considered to have an immune pathogenesis mediated by residual components of the immune system such as CD8 T cells such as like Reiters disease, psoriatic arthritis and various undifferentiated spondyloarthropathies.

3. Conditions arising as a direct consequence of a deficient helper arm of the immune response associated with depletion of CD4 T cells like infectious arthritis and osteomyelitis due to conventional and opportunistic pathogens. It has now been established that several seronegative arthritis syndromes occur in HIV infections. A new spectrum of disease ranging from small, asymptomatic effusion to a wide spread disabling multisystemic involvement that posses major therapeutic problem is observed.

The incidence of rheumatic syndromes is reported to range from 11 to 70% in different studies. The rheumatological manifestations associated with HIV are:

1. **Articular** : arthralgia, arthritis, enthesisopathy, painful articular syndrome, reactive arthritis, including Reiter’s disease, psoriatic arthritis, lupus like syndrome and septic arthritis.

2. **Muscular** : myalgias, myopathy (HIV, AZT), polymyositis and pyomyositis.

3. **Dermatolgical manifestations** : dermatomyositis and psoriasis.

4. **Vasculitis syndrome and miscellaneous** : diffuse interstitial lymphocytosis syndrome (DILS), fibromyalgias, hypertrophic osteoarthropathy and avascular necrosis of bone.

The incidence of vasculitis is 0.4% in patients with HIV infection. The vessels reported to be commonly affected are arteries of muscles and digits. Recently involvement of coronary artery leading to fatal myocardial infarction has been reported.

Two theories have been proposed to explain the virus-associated vasculitis. The virus may attack the vessel wall directly or cellular or humoral immune mechanisms involved in the disease may lead to the formation of in situ or deposition of circulating immune complexes that subsequently result in the development of vasculitis. The demonstration of vascular deposits of HIV antigens, immunoglobulins and complement components suggest an immune / or complement deposition process. It is also suggested that in patients with HIV disease, the pathogenesis is multifactorial and may result from HIV induced immunologic abnormalities and response to a variety of xenoantigens including HIV, other opportunistic infectious agents and drugs used for the treatment.

Biopsy specimen have documented polyarteritis nodosa, Henoch - Schonlein purpura, drug induced hypersensitivity vasculitis and unspecified vasculitis in patients who are HIV infected with symptoms of autoimmune disease. HIV RNA and P24 antigens have been reported within the vascular
lesions and in some cases CMV inclusions were identified in vascular endothelial cells suggesting a direct or indirect role of other viruses in the development of vasculitis.

In PAN like vasculitis, treatment with systemic corticosteroids may offer relief of symptoms but benefits of long-term use are unknown. Intravenous gammaglobulin may be an effective alternative treatment. PAN occurring in HIV infected patients has been successfully treated by combining plasma exchange with antiretroviral agents. Remission has occurred after treatment with corticosteroids in addition to combination with antiretroviral therapy consisting of two non-nucleoside reverse transcriptase inhibitors and a protease inhibitor. Our patient responded to steroids and an antiretroviral drug combination of lamivudine and zidovudine.

REFERENCES