Case Report

Bilateral lower limb gangrene due to HIV vasculitis – a rare case

D. Majumdar[1], S. Chakraborty[1], S. Pandey[1], S. Bhattacharya[1],
B. Bhattacharjee[1] A. Naskar[1], B. Saha[1]

Sri Lankan Journal of Infectious Diseases 2017 Vol.7 (1):53-57

DOI: http://doi.org/10.4038/sljid.v7i1.8122

Abstract

Human immunodeficiency virus (HIV) positive patients may develop vasculitis, either mediated by immunological factors or by direct vascular injury. It may also be caused by infectious agents or by some nonspecific causes. We describe a patient who developed manifestations suggestive of extremities vasculitis (occlusive variety) with no identifiable risk factors other than HIV. He responded to steroid and combination anti-retroviral therapy.

Keywords: gangrene, vasculitis, HIV

Introduction

Vasculitis is a rare but clinically significant manifestation in a HIV infected patient with an incidence of less than 1%, excluding adverse drug reactions.[1] A wide range of vasculitides can be encountered, ranging from vasculitis resulting from specific infective agents to a non-specific vasculitis. Among the infective causes, cytomegalovirus and tuberculosis are probably the most common.[2] Physicians should be aware that vasculitis may have a heterogeneous presentation and occur associated with HIV infection. Although unusual, this association should be recognized for early proper treatment and prevention of ischaemia.

Case report

A 42 year old male was admitted with a chief complaint of bilateral painful lower limb swelling with multiple fluid filled large blisters involving both feet and the anterior surface of the right lower end of tibia. He was diagnosed as HIV-1 reactive 2 years ago but was lost to follow up and anti-retroviral therapy was not initiated. He gave a history of applying a pain relieving spray (diclofenac-linseed oil-methyl salicylate-menthol) on affected areas of his legs to reduce pain, preceding the development of the blisters and swelling. There was no history of Raynaud's phenomenon, claudication or oral ulcers. There was also no history of cough, shortness of breath or fever. Bowel and bladder function were normal. There was no significant illness in the past.

[1] *Dept of Tropical Medicine, School of Tropical Medicine, Kolkata, India*

Address for correspondence: Dr. Debajyoti Majumdar Department of Tropical Medicine, School of Tropical Medicine, 108, Chittaranjan Avenue, Kolkata, West Bengal, India, Pin 700073 Telephone: +919804330792 ; Email: dr.debajyotimajumdar@gmail.com

Received 6 October 2016 and revised version accepted 6 March 2017

General examination did not reveal any peripheral lymphadenopathy. Bilateral arteria dorsalis pedis pulsation could not be properly appreciated because of the presence of blisters and swelling over the palpating areas. Systemic examination did not reveal any organomegaly or cardiac abnormality. Fundoscopy was also normal. He had a WBC count of 14700/cmm with 90% neutrophils and normal liver and kidney function tests. Urine examination was normal.

The patient was started on intravenous piperacillin and tazobactam and a nonsteroidal anti-inflammatory drug (Ibuprofen) on a provisional diagnosis of cellulitis secondary to contact dermatitis, possibly as a result of using the pain relieving spray. However, despite treatment, there was no improvement in the pain and he developed blackening of both great toe and first toe (Figure 1).

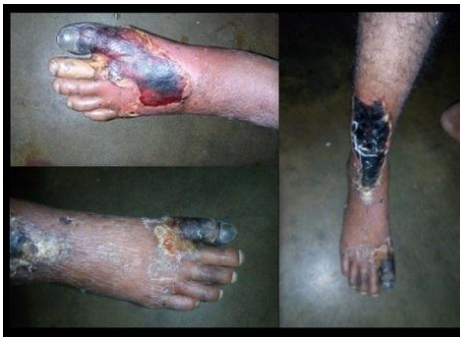

Fig 1: Appearance of legs after 3 days of antibiotics

He was started on vasodilators (pentoxifylline, nifedipine) and aspirin as an antiplatelet agent. His CD4 count was 84/uL. There was no clinical or biochemical evidence (fever, peripheral lymphadenopathy, ESR, tuberculin skin test, ultrasonography of abdomen, Chest X-ray, sputum for Gene Xpert MTB/Rif) suggestive of tuberculosis infection. HBsAg, Anti HCV and VDRL were negative.

A cardiothoracic and vascular surgeon and a general surgeon were consulted, both of whom suggested it may be a case of peripheral vascular disease or an atheroembolic disorder. Echocardiography was normal with no evidence of vegetations.

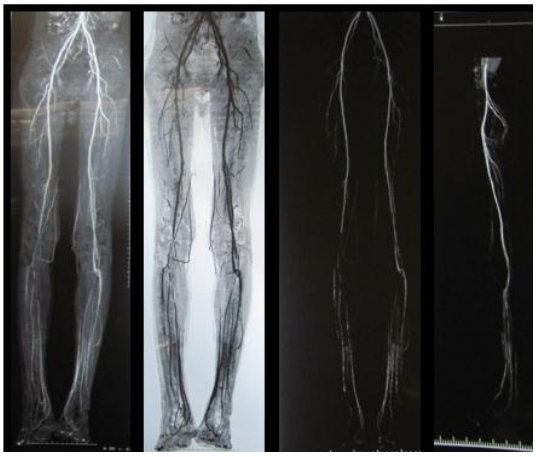

Fig 2: CT Angiography showing popliteal artery narrowing with decreased flow in arteria dorsalis pedis

In the meanwhile, his gangrene started progressing upwards. Bilateral lower limb arterial and venous Doppler scan was done, which showed monophasic flow patterns in the arteria dorsalis pedis, with no evidence of deep vein thrombosis (Figure 2). Fibrin degradation product level was found to be high (582.2 ng/ml: normal value <500ng/ml), but prothrombin time (PT), activated plasma thromboplastin time (aPTT) and platelet count were found to be normal. CMV DNA PCR was also found to be negative. CT angiography of both lower limbs showed popliteal artery narrowing with multiple collaterals bilaterally and decreased flow in arteria dorsalis pedis although renal artery angiography was within normal limits. Although MR angiography of the brain was considered, it was not done due to the financial constraints of the patient.

Skin biopsy from the edge of the gangrenous margin was sent for histopathology and a blood sample was sent for ANA and ANCA profiles and anticardiolipin antibody. Considering the possibility of vasculitis, intravenous methyl prednisolone (1gm/day) was started as limb salvage

therapy after five days of initiation of ART (tenofovir + lamivudine + efavirenz as per NACO guidelines) with intravenous meropenem and oral linezolid (to cover secondary bacterial infection). The gangrene started to regress after 3 doses of corticosteroids, although dry gangrene persisted in both great toes (Figure 3).

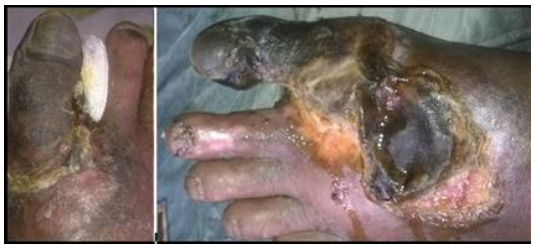

Fig 3: Appearance of legs after 3 doses of IV methyl prednisolone

We continued steroids after 3 doses of IV methyl prednisolone with oral prednisolone 1 mg/kg/day and stopped antibiotics after a course of 10 days. With treatment his pain subsided and the condition of both legs improved. Meanwhile his ANA and ANCA profiles were reported as negative. Skin biopsy showed features of nonspecific vasculitis. Unfortunately the patient left the hospital against medical advice and follow up was not possible.

Discussion

HIV vasculopathy was first described as an entity in 1987[3] and may present with arterial occlusive disease, aneurysmal disease or spontaneous arteriovenous fistula. The incidence of symptomatic vasculitis is in the region of 1% of HIV-infected patients.[4] HIV-associated arterial occlusive disease is recognized as a specific clinical entity. As for aneurysmal disease, young males within a median age of 30-40 years are mainly affected. The underlying cause of occlusive disease is thought to be related to vasculitis.

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.

Various theories have been proposed to explain the virus associated vasculitis.[5] The virus may attack the vessel wall directly. 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 suggests an immune/or complement deposition process. 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 in treatment.[6]

Diagnosis of vasculitis was made on the basis of history (bilateral involvement), clinical findings (absence of distal pulsation and presence of bilateral gangrene), CT angiography findings, biopsy report and dramatic response to steroid, although we could not document the type of vasculitis (depending on size of vessel involvement). Several causes for vascular damage has been described in patients with HIV (Table 1). We couldn't demonstrate on a molecular basis that HIV was responsible for the vasculitic event (demonstration of HIV virus or antigen in vessel wall on biopsy). However, several vasculitic mimics were ruled out as shown in Table 2.

Table 1 Possible causes of vasculitic processes encountered in patients with HIV infection.[6]

Infective	cytomegalovirus, herpes zoster virus, toxoplasma, pneumocystis, salmonella, tuberculosis, direct HIV infection
Necrotizing systemic	polyarteritis nodosa-like, non-specific necrotizing
Hypersensitivity	leucocytoclastic, eosinophilic, Churg-Strauss, Henoch-Schonlein, Behcet's, drug induced, cryoglobulinaemia, relapsing polychondritis, erythema nodosum, erythema elevatum diutinum
Angiocentric immunoproliferative lesions	benign lymphocytic angiitis, lymphomatoid granulomatosis, angiocentric lymphoma
Primary angiitis of the central nervous system	
Large vessel vasculopathy	related to infection or leucocytoclastic vasculitis of vasa vasora
Miscellaneous	non-specific vasculitides not fitting into the above categories

Table 2: Exclusion of vasculitic mimics in diagnostic work-up.

Tuberculosis	Absence of fever, lymphadenopathy, normal Chest X-ray & ultrasonography, low ESR, absence of AFB on sputum by PCR (CBNAAT)
CMV	negative DNA PCR, normal fundoscopy, absence of other clinical features
Bacterial infections	non responsive even after higher generation antibiotics including Gram positive as well as Gram negative Coverage
Other infections	HBsAg, Anti HCV, VDRL negative
Antiphospholipid antibody syndrome	negative for anticardiolipin antibody and male sex
Thrombotic thrombocytopenic purpura	no thrombocytopenia or renal involvement
Sickle cell anaemia	no anaemia or no history of sickle crisis
Collagen vascular disease Rheumatoid arthritis	negative ANA profile with negative ANCA and Anti CCP
Inflammatory bowel disease	no history of pain in the abdomen or altered bowel habit or bleeding per rectum
malignancy and drugs	Exclusion on history, clinical and laboratory findings.

In PAN like vasculitis, treatment with systemic corticosteroids may offer relief of symptoms but benefits of long-term use are unknown.[6] Intravenous gamma globulin may be an effective alternative treatment. Plasma exchange with antiretroviral agents may be another treatment modality. Remission has occurred after treatment with corticosteroids in addition to combination with antiretroviral therapy. Our patient responded to steroids and combination antiretroviral therapy.

Conclusion

HIV can present in varied ways. Vasculitis is one of the rare presentations among those. For diagnosis of HIV associated vasculitis one needs to search thoroughly to exclude other vasculitic mimics and establish HIV as a cause of vasculitis. Early identification and prompt treatment may decrease the morbidity and mortality associated with the disease.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Guillevin L. Vasculitides in the context of HIV infection. *AIDS.* 2008; Suppl 3:S27-33 *doi :10.1097/01.aids.0000327513.53255.17*
2. Chetty R. Vasculitides associated with HIV infection, *J Clin Pathol* 2001;54:275-278 *doi : 10.1136/jcp.54.4.275*
3. Nel D. *2011 www.vasculardiseasemanagement.com/.../hiv-vasculopathy-renal-artery-manifesting-severe hypertension in young female*
4. Mulaudzi T. V. HIV-associated vasculopathy, Vasculopathy is a major feature of HIV disease. *Continuing Medical Education* 2009; 27:(7)320-322 *No doi*
5. Kakrani AL, Anita Basavraj, Madraki R. Vasculitis with Digital Gangrene in a Patient with HIV Infection *J Assoc Physicians India* 2003; 51:299-301 *No doi*
6. O'Grady NP, Sears CL. Therapeutic dilemmas in the case of HIV immunodeficiency virus infected patients with vasculitis. Case report. *Clin Infect Dis* 1996; 23:659-61. *doi : http://dx.doi.org//10.1093/clinids/23.3.659*