Case Report

# Bilateral limb gangrene in an HIV patient due to vasculopathy: Managing the dual challenge of psychosocial issues and an uncommon medical condition

**Mudit Kotwal[1], K. K. Gupta[1], Ahmad Ozair[2], Virendra Atam[1]**

*[1]Department of Medicine, [2]Faculty of Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India*

## Abstract

Patients with human immunodeficiency virus (HIV) have been reported to experience a spectrum of homeostatic dysregulation and resulting manifestations in their vascular system. This may be due to either disruption in the coagulation-anticoagulation pathways or due to damage to vessels from either HIV or other opportunistic infections. However, gangrene in an HIV-infected patient is an uncommon phenomenon. We herein report a case of a 30-year-old female, who had been taking antiretrovirals irregularly for 10 years, developing bilateral limb gangrene during her hospitalization for cryptococcal meningitis. Unfortunately, her condition continued to deteriorate and her attendants took her from the hospital against medical advice, with her death soon after. We illustrate how several biopsychosocial factors came together here to result in poor outcomes. To note, peripheral arterial disease (PAD) in HIV can rapidly lead to critical limb ischemia, resulting in limb gangrene. Aggravating risk factors for the same include smoking, poor glycemic control, and/or low CD4 T-cell count (<200 cells/mm$^3$). General practitioners should be aware that HIV patients are far more prone to PAD than the normal population. Early recognition of at-risk patients, both medically and psychosocially, by family physicians is thus critical.

**Keywords:** HIV/AIDS, infectious disease, gangrene, peripheral arterial disease, vasculopathy

## Introduction

Peripheral arterial disease is more prevalent in populations affected with human immunodeficiency virus (HIV), with prior studies reporting up to a six-fold higher risk, despite adjusting for other factors.[1] HIV-positive patients in developing countries, including India, are particularly prone to contracting complications considering the poor access to healthcare and delayed reporting to healthcare facilities.[2] This is a greater concern among women in developing nations, as occurred in the following case.

**Address for correspondence:** Mr. Ahmad Ozair, Faculty of Medicine, King George's Medical University, Chowk, Lucknow, Uttar Pradesh - 226 003, India.
E-mail: ahmadozair@kgmcindia.edu

**Received:** 11-04-2020 **Revised:** 10-06-2020
**Accepted:** 01-07-2020 **Published:** 30-09-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_605_20

## Case Report

A 30-year-old female of poor financial condition was brought to the apex public referral hospital of a province in India with a history of 2 months of fever, followed by blurring of vision and altered behavior for the past 2 days. She was a previously diagnosed case of HIV for 10 years but had been taking antiretroviral therapy irregularly. Despite being married, she had a history of hazardous sexual behavior, which was extremely atypical for her cultural background and low socioeconomic status. Prior medical records indicated a CD4-positive T-cell count of 386 cells/mm$^3$. She had been a known case of pulmonary tuberculosis for which a documented course of antitubercular therapy had been completed. She was a nonsmoker and nondiabetic.



**How to cite this article:** Kotwal M, Gupta KK, Ozair A, Atam V. Bilateral limb gangrene in an HIV patient due to vasculopathy: Managing the dual challenge of psychosocial issues and an uncommon medical condition. J Family Med Prim Care 2020;9:5049-51.

A clinical examination revealed Glasgow Coma Scale (GCS) score of $E_3V_4M_4$, neck rigidity, and bilateral extensor plantar response. Vital signs, hemodynamic status, and review of other systems were all unremarkable. We diagnosed her with meningitis, admitted her and started her on broad-spectrum antimicrobials, with fixed-dose combination of tenofovir, lamivudine, and efavirenz, the current mandated regimen by the National AIDS Control Program of the Government of India.

Due to her poor finances, our laboratory testing was selective. Routine workup indicated mild normocytic, normochromic anemia with anisopoikilocytosis. Serum iron was 57 μg/dL and ferritin was 108.9 ng/mL. Tests for syphilis and Hepatitis B and C were negative, these tests especially relevant considering her sexual history. No abnormality was detected on noncontrast CT head, done on account of meningitis.

Testing of cerebrospinal fluid (CSF) revealed glucose 58.0 mg/dL (corresponding blood glucose 154 mg/dL), protein 59 mg/dL, leukocyte count <5 cells/mm$^3$ with all lymphocytes, negative for gram stained organisms, negative for acid-fast bacilli. She was also negative for anti-Japanese Encephalitis IgM antibodies in CSF and real-time PCR for herpes simplex virus. Keeping in mind a tuberculous etiology for her meningitis, her adenosine deaminase levels in CSF had been sent, which were 6.9 IU/L (normal <10 IU/L).

Post-admission, patient's general condition, and GCS improved for 2 days. However, her fever started spiking thereafter. Meropenem and teicoplanin were then added to the ceftriaxone she had already been on. The same day, CSF was found positive for cryptococcal antigen. She was then switched to meropenem with amphotericin-B, accompanied by electrolyte monitoring and intravenous hydration. Still, acute-onset worsening of her kidney function tests occurred, indicating nontolerance of amphotericin-B. She had to be finally put on fluconazole.

However, after 3 days of hospital stay, we noticed her toes turning black. She had started developing acute-onset dry gangrene of both feet. It progressed to involve up till her medial malleoli within a few days, accompanied by progressive loss of distal pulses, indicating an ischemic vasculopathy. Later, bullae started developing over gangrenous areas [Figure 1]. Questioning of attendants found no history of consumption of any ergot-related compound or any claudication-like pain.

Further workup was sent, including autoimmune, viral markers, and coagulation factor assays. Notably, her protein C levels were 22 IU/dL (normal: 70–140 IU/dL) and protein S levels were 40 IU/dL (normal: 65–140 IU/dL). Her INR was 1.41. Her lipid profile was unremarkable except for total cholesterol being 74.6 mg/dL. Antinuclear antibody was positive using indirect immunofluorescence with titers 1:100 in a fine speckled pattern, which was nonspecific. Ultrasonography of legs revealed no vessel wall lesions or thrombi, and no anomaly on color flow. However, loss of normal tri-phasic pattern was present bilaterally on spectral pattern. Thus, she was diagnosed with peripheral arterial disease, of yet unclear etiology. Aspirin and cilostazole were started.

However, soon after, she developed hypotension with lactate 10 mmol/L and required aggressive resuscitation. After 8 days of hospital stay, her condition had deteriorated enough to require ventilatory support, with GCS dropping to $E_1V_TM_1$. Throughout her stay, antiretroviral medications had been continued.

Considering her low CD4 T-cell count and her current condition, it was clear that she had a poor prognosis. Her family had been kept informed of her condition. But when told of her current prognosis, they decided to leave against medical advice, despite counseling.

On the day the patient left, after 12 days of hospital stay, her C-reactive protein was 68.0 mg/L. Additional workup had

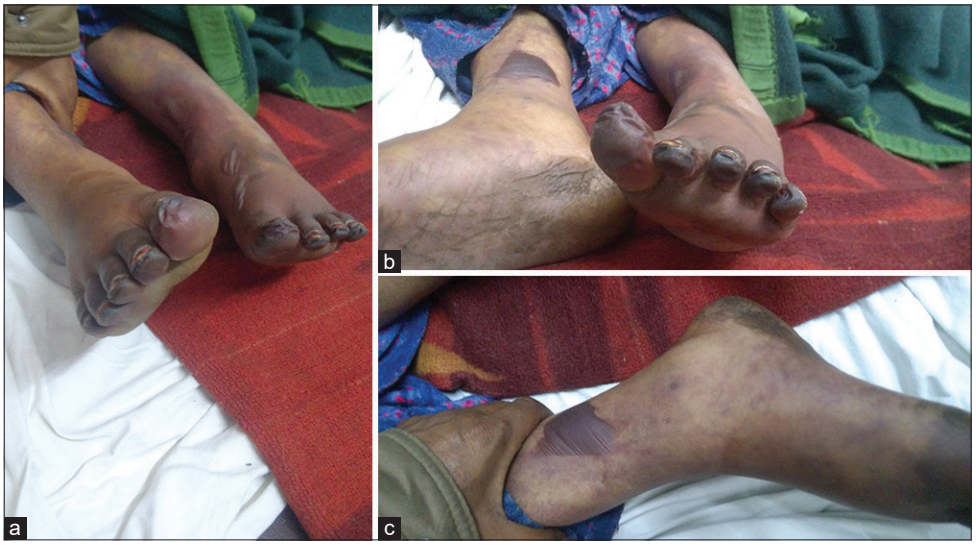


**Figure 1:** (a-c) Gangrene and bullae seen bilaterally on feet of HIV-infected patient, with loss of distal pulses and cold extremities

been ordered for magnetic resonance imaging head, HIV viral load, antitoxoplasma antibody, cytomegalovirus, autoimmune antibodies, adenovirus, and parvovirus, which could not be performed. The family did not return for follow-up due to large expenses and distance. When contacted, they informed that the patient had expired soon after reaching their village.

## Discussion

This case of an HIV-positive patient who had developed bilateral limb gangrene illustrates the unique challenges in managing both psychosocial issues and an uncommon medical condition. A number of factors came together to cause a poor patient outcome: (i) illicit and hazardous sexual history; (ii) a dearth of regular medical care that could have tackled her problems early; (iii) non-adherence to anti-retroviral medications; and (iv) the decision of the family to leave against medical advice despite counselling.

HIV-positive patients are prone to developing a wide spectrum of vascular diseases, including aneurysms and occlusive disorders. Still, limb gangrene in an HIV patient is uncommon. HIV-associated vasculopathy is a term used in the literature to include any abnormality of intracranial or extracranial blood vessels associated with HIV other than neoplastic vessel involvement.[3] Olubaniyi *et al.* describe a 53-year-old HIV patient who developed digital gangrene secondary to thrombosis in distal leg vessels, later resulting in digital autoamputation.[4] However, here, all leg vessels were patent.

Several mechanisms have been proposed for PAD in HIV. These include direct invasion of arterial smooth muscles by HIV, damage to vascular endothelium, accentuated atherosclerosis, endothelial dysfunction, and/or leukocytoclastic vasculitis.[5,6] Sviridov and colleagues in a recent review suggest that dysregulation of cellular cholesterol metabolism may be the driving factor of HIV-associated comorbidities including cardiovascular disease.[7] The strategies for management of antiretroviral therapy (SMART) study group investigators have also suggested a possible role of dyslipidemia secondary to chronic HIV infection and/or antiretroviral therapy interruptions.[8] While medication interruptions were indeed present here, the lipid profile was normal. However, protein C and S were deranged, possibly contributing to a hypercoagulable state, to which opportunistic infections have been found to contribute.[4]

Early on do the general practitioners need to recognize the at-risk HIV patients, both medically and psychosocially.[2] Predictors of peripheral arterial disease in HIV-positive patients include age, smoking, diabetes, and low CD4 T-cell count, risk factors which family physicians must be cognizant of.[1] Here, due to poor financial condition, this HIV patient had not been regularly going to any physician for years. The family also was unaware of the gravity of poor medication compliance and had taken the patient away from the hospital against medical advice. Thus, much work needs to be done to create awareness in this patient population.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

## Acknowledgments

Nil

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Periard D, Cavassini M, Taffé P, Chevalley M, Senn L, Chapuis-Taillard C, *et al.* High prevalence of peripheral arterial disease in HIV-infected persons. Clin Infect Dis 2008;46:761-7.
2. Dlamini-Simelane TTT, Moyer E. 'Lost to follow up': Rethinking delayed and interrupted HIV treatment among married Swazi women. Health Policy Plan 2017;32:24856.
3. Benjamin LA, Bryer A, Emsley HC, Khoo S, Solomon T, Connor MD. HIV infection and stroke: Current perspectives and future directions. Lancet Neurol 2012;11:878-90.
4. Eugenin EA, Morgello S, Klotman ME, Mosoian A, Lento PA, Berman JW, *et al.* Human immunodeficiency virus (HIV) infects human arterial smooth muscle cells *in vivo* and in vitro: Implications for the pathogenesis of HIV-mediated vascular disease. Am J Pathol 2008;172:1100-11.
5. Duffy P, Wang X, Lin PH, Yao Q, Chen C. HIV Nef protein causes endothelial dysfunction in porcine pulmonary arteries and human pulmonary artery endothelial cells. J Surg Res 2009;156:257-64.
6. Olubaniyi AO, Short CE, Remedios D, Kapembwa M. An unexpected cause of digital gangrene: HIV associated peripheral arterial thrombosis. Br J Gen Pract 2013;63:162-3.
7. Sviridov D, Mukhamedova N, Makarov AA, Adzhubei A, Bukrinsky M. Comorbidities of HIV infection: Role of Nef-induced impairment of cholesterol metabolism and lipid raft functionality. AIDS 2020;34:1-13.
8. Strategies for Management of Antiretroviral Therapy (SMART) Study Group, El-Sadr WM, Lundgren J, Neaton JD, *et al.* CD4+ count-guided interruption of antiretroviral treatment. N Engl J Med 2006;335:2283-96.