A 15-year-old boy diagnosed with human immunodeficiency virus (HIV) infection and on Highly Active Anti-Retroviral Therapy (HAART) (zidovudine 300 mg bd, lamivudine 150 mg bd, and nevirapine 200 mg bd) for 1 year was admitted with history of fever, myalgia, pain, and discoloration of hands of 9 days duration. He is not a known diabetic and had no evidence of tuberculosis.

On examination, he was sick looking, with a pulse rate of 100/min and a blood pressure of 100/70 mm Hg. There was a dusky black discoloration of the right middle finger with superficial ulceration and early gangrenous changes on the fourth and fifth fingers of the left hand. There were multiple ecchymotic patches on the legs and feet and dorsum of hands as shown in Figure 1. All peripheral pulses were palpable. Cardiovascular, respiratory, and digestive systems were within the normal limits.

Investigations revealed hemoglobin of 10.3 g%, total leukocyte count of 47,000/mm³ with polymorphs 90% and lymphocytes 10%. Blood sugar was normal (random blood sugar 100 mg%). Erythrocyte sedimentation rate by Westergren method was 70 mm in the 1st h. Serum creatinine was 0.7 mg%. Urine microscopy was normal. Serum aspartate transaminase 135 IU, serum alanine transaminase 136 IU, alkaline phosphatase 355 IU, creatinine phosphokinase (CPK) 1497, antinuclear antibody (ANA) negative, serum lactate 60 mg% (normal value 4.5-20 mg%). Hepatitis B surface antigen and hepatitis C virus were negative. His CD⁴ count was 854 cells/mL. Peripheral smear showed mild anisocytosis, normocytosis, elevated white blood cell count, with predominant neutrophils, and toxic granulation. Neutrophils were hyper-segmented and there was adequate amount of platelets. Doppler study of both upper limbs showed normal triphasic flow pattern in radial and ulnar arteries. Ultrasound scan of abdomen showed hepatomegaly with coarse hepatic parenchyma and bilateral hyper-echoic kidneys. Echocardiogram was normal. Chest X-ray was within the normal limits. A diagnosis of HIV infection with associated vasculitis of the upper extremities was made.

DISCUSSION

The common etiologies of gangrene of the extremities...
are atherosclerosis and diabetes mellitus.\(^{[1]}\) Other diseases which can cause gangrene of extremities include systemic lupus erythematosus, progressive systemic sclerosis, Henoch-Schonlein purpura, anti-neutrophil cytoplasmic antibody associated vasculitis, Takayasu arteritis, infective endocarditis, gangrene associated with procoagulant states due to malignancy, anticardiolipin antibody syndrome, and disseminated intravascular coagulation.\(^{[1]}\) Rare causes of gangrene include heparin-induced thrombocytopenia, hemolytic uremic syndrome and HIV infection.\(^{[1]}\) Widespread digital ischemic changes and gangrene of the hands and feet are uncommon presentation in the patients with HIV infection.\(^{[2]}\) Infections such as tuberculosis and cytomegalovirus, occlusive disease due to a hypercoagulable state, vasculitis are some of the mechanisms suggested for gangrene of the extremities in HIV.\(^{[1]}\) HIV-associated gangrene may be associated with a known pathogen or trigger, or may occur in the absence of an obvious identifiable agent.\(^{[1]}\) To establish an opportunistic infection associated with the vascular pathology either a serological test, staining of smears on light microscopy, cultures, immunohistochemistry testing, and in situ hybridization tests or viral markers may be done as are relevant based on the clinical presentation. In this patient, there was no evidence of tuberculosis, diabetes mellitus or hepatitis (B and C) infection. His CD\(_4\) count was above 800. HIV vasculitis has been associated with a much lower CD4 count,\(^{[3]}\) unlike in this patient. Work up for autoimmune diseases and procoagulant states-ANAs, antiphospholipid antibodies, protein C, protein S, and anti-thrombin III need to be planned in HIV patients with gangrene, because there have been reported findings of antiphospholipid antibody syndrome, deficiencies of free protein S, protein C, and anti-thrombin.\(^{[1,4]}\)

This patient had negative ANA screening possibly eliminating an autoimmune cause of vasculitis. Patients with peripheral arterial disease can be easily and reliably identified by ankle brachial index testing. Doppler study of arterial and venous system is essential in all patients with ischemic changes. There is a pathognomonic sign with hypoechoic spotting within the arterial wall best described as a string of pearls sign.\(^{[4]}\) In this patient, Doppler study did not show any evidence of large vessel occlusion. Vasculitis is one of the less common but important consequences of HIV infection. Incidence of vasculitis in HIV positive patients are low and in the order of 1%.\(^{[3]}\) The organs that are usually involved include: Skin, peripheral nerve and skeletal muscle, and the central nervous system; in addition, the lung, gastrointestinal tract, oropharynx, and kidney can also be affected, although less commonly. Skin and skeletal muscles were affected in this patient. The raised CPK could be taken as evidence of muscle damage as raised CPK is a known indicator of muscle damage.\(^{[6]}\)

Almost every pattern and type of vasculitis of small, medium, and large vessels has been encountered in the HIV setting.\(^{[7]}\) The various types of vasculitis seen in HIV infection include:

- **Infective causes including tuberculosis, cytomegalovirus Epstein-Barr virus, varicella zoster virus, and herpes simplex virus toxoplasmosis, pneumocystis, salmonella.**\(^{[7]}\) It can also be the result of direct infection by HIV.\(^{[2]}\)

The two major mechanisms by which infection is thought to induce a vasculitis are direct microbial invasion, with resultant damage of the vessel wall, and immune mediated injury (both humoral and cellular).\(^{[7]}\)

- **Polyarteritis nodosa (PAN)-like vasculitis.** The target organs that are usually involved are muscles and nerves, although skin and the gastrointestinal tract can also be involved.\(^{[8]}\) In general, there are two modes of presentation: Either as a peripheral neuropathy or with digital ischemia. There are several important differences between PAN-like vasculitis seen in the HIV setting and so called classic or idiopathic PAN.\(^{[7]}\) First, the waxing and waning clinical course of classic PAN is not seen in patients with HIV infection. Second, it is well-recognized that classic PAN can be associated with viral infections, especially hepatitis B virus (HBV), but in HIV associated cases serology for HBV is invariably negative,\(^{[8,9]}\) as was the case in this patient.
Third, multisystem organ involvement, particularly renal involvement, is not seen in HIV associated cases. Gherardi et al.\textsuperscript{[10]} observed that the affected arteries in HIV associated PAN tend to be smaller than that seen in classic PAN. In their series, there was a consistent and pronounced involvement of the microcirculation.\textsuperscript{[10]} Immune complex depositions have been implicated in pathogenesis.

- Hypersensitivity vasculitis: Henoch-Schonlein purpura, drug induced hypersensitivity vasculitis, and cryoglobulinaemia have all been encountered in the HIV setting.
- Angiocentric immunoproliferative vasculitis.
- Primary angitis of the central nervous system.
- Large vessel (aorta, femorals, and carotids) vasculopathy.
- Non-specific vasculitides not fitting into any of the characteristic patterns. These include non-specific or mononuclear inflammatory vascular disease. In this case, the non-specific vasculitis associated with HIV infection could be held responsible for the digital gangrene and raised CPK.

The treatment in patients with acute thrombosis type of occlusive disease depends on the clinical presentation. In those patients where the limb cannot be salvaged, primary amputation is done. Where the limb is salvageable, treatment options include endovascular procedures such as thrombectomy and thrombolytic or bypass procedures.

Patients with HIV infection with widespread ischemic necrosis and gangrene may require treatment with corticosteroids (in the event of possible vasculitis), thrombolytic agents (for the thrombotic component).

**CONCLUSION**

Widespread digital ischemic changes and gangrene of the hands and feet is an uncommon presentation in patients with HIV infection. Even though rare, vasculitis can lead on to devastating consequences. HIV associated vasculitis should be one of the differential diagnosis for patients presenting with gangrene of the extremities.

**REFERENCES**