

Kaposi's sarcoma, lymphoedema and gangrene in AIDS – a therapeutic challenge

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The manifestations of the HIV pandemic are manifold, affecting all organ systems. With respect to the vascular system, it is recognised that vasculitides constitute one of the less common but none the less challenging consequences of HIV infection.¹ The HIV pandemic has also seen a dramatic increase in the prevalence of Kaposi's sarcoma² and its frequently associated complication of chronic lymphoedema.³ When these three manifestations of HIV (Kaposi's sarcoma, lymphoedema and vasculopathy) coexist in the same limb, as in this report, unique clinical and management challenges are presented.

Case report

A 34-year-old man who had been confirmed HIV positive a year earlier presented to the surgical services at King Edward VIII Hospital, Durban, with a 1-month history of rest pain in the right leg with associated gangrene of the little toe.

In addition to generalised lymphadenopathy, the patient was noted to have right femoro-popliteal arterial disease with dry gangrene of the right fifth toe and skin changes suggestive of ischaemic changes along the second, third and fourth toes. Purple nodular lesions were noted on both lower limbs, suggestive of Kaposi's sarcoma. Non-pitting oedema up to the level of the right knee was also evident, less so on the opposite limb. The clinical assessment was critical ischaemia of the right lower limb with associated chronic lymphoedema secondary to Kaposi's sarcoma.

The haemoglobin level was 12.6 g/dl, the white cell count $8.2 \times 10^9/l$, and the platelet count $479 \times 10^9/l$. The urea and electrolyte levels and the results of liver function tests were normal. The international normalised ratio (INR) measured 1.08 and the CD4 count was 110 cells/ μ l.

The thrombophilia screen (antithrombin III, protein C, protein S levels) was normal. A skin biopsy of the nodular lesions confirmed Kaposi's sarcoma. The chest radiograph was normal. A venous Doppler study excluded a deep-vein thrombosis.

The right common and superficial femoral arteries appeared normal on arterial duplex Doppler examination. However, extensive 'beading' was noted in the right popliteal artery, which appeared patent at the knee. A thrombus was noted in the distal popliteal artery with a 'knocking' pulse. No flow was detected in the distal popliteal or tibial arteries at the ankle.

A computed tomography angiogram of the lower limbs revealed a sharp cut-off of vessels below the right knee, suggestive of thrombus formation. Poor distal flow was noted, and the rest of the vessels were normal.

The patient was commenced on highly active antiretroviral therapy (HAART) and anticoagulation. A distal limb ablation was undertaken after demarcation of the gangrenous segments. The patient is currently receiving oncotherapy for management of the Kaposi's sarcoma.

Discussion

Understanding the pathogenesis and formulating the effective management of HIV-associated vasculopathy and Kaposi's sarcoma-associated lymphoedema remains a challenge to the attendant practitioner. When these manifestations of HIV occur together (and on the same limb) this challenge is increased, since the treatment of one may compromise the treatment of the other.

Kaposi's sarcoma is caused by Kaposi's sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus 8 (HHV8). In the early 1980s the increasingly frequent diagnosis of Kaposi's sarcoma in AIDS patients led to the inference that AIDS weakened the immune system.⁴

The incidence of Kaposi's sarcoma has declined sharply since HAART became widely available, and HAART is indispensable in the treatment of epidemic Kaposi's sarcoma. In 40% or more of patients with AIDS-related Kaposi's sarcoma, the lesions will regress upon commencement of HAART.^{5,6} In some patients, however, Kaposi's sarcoma may recur after years of HAART, especially if HIV is not com-

pletely suppressed. Patients with a few local lesions can often be treated with local measures such as radiation therapy or cryotherapy. Surgery is generally not recommended, as Kaposi's sarcoma can appear in wound edges. More widespread disease, or disease affecting internal organs, is generally treated with systemic therapy with interferon alpha and liposomal anthracyclines.⁷

Obstructive lymphoedema caused by AIDS-related Kaposi's sarcoma, although previously rare, is now being seen with increasing frequency.² It is suggested that lymphatic and venous obstruction, protein-rich interstitial fluid, tissue haemosiderin and subcutaneous infection contribute to the evolution and perpetuation of chronic lymphoedema.³

Morbidity and mortality in patients with Kaposi's sarcoma-associated lymphoedema is influenced by coexistent sepsis because of stasis and trauma; the recognition of infection may therefore be limb- or life-saving.²

Many types of vasculitis have been reported in HIV-positive patients, affecting mainly small and medium-sized vessels. Large vessels can also be involved, usually as part of a leucocytoclastic vasculitis of the vasa vasora or periadventitial vessels.¹ Large-vessel vasculopathy consists of either aneurysms or occlusive disease. Arteries affected include the common carotid, abdominal aorta, common iliac, femoral and popliteal.⁷

Primary arterial thrombosis associated with HIV infection, as in the case reported here, is a distinct clinicopathological entity. Young patients particularly are at increased risk. Involvement of both upper and lower limbs is documented, presenting with varying degrees of ischaemia ranging from claudication to frank tissue necrosis.⁸

Vascular occlusion is on the basis of an organising localised thrombus within the vessel lumen, with no evidence of atherosclerosis in the intima. The major changes involve the adventitia and the peri-adventitial area, with leucoclastic vasculitis of the vasa vasora.⁸ Significant features include the normality of the arterial tree proximal to the thrombosed arteries, and thrombosis of the distal vessels with no demonstrable run-off. Typically, Duplex ultrasonography shows hyperechoic 'spotting' in the arterial wall with the 'string of pearls' sign, found to be a sensitive indicator of HIV thrombosis.⁹

While several causes of primary HIV-associated thrombosis have been documented, its pathophysiology is not well understood. In general, HIV infection is associated with aberrations of coagulation that include thrombocytopenia and hypercoagulable states. Hypercoagulable states are predisposed to by acquired protein C and protein S deficiency, as well as by elevated levels of antiphospholipid antibodies and von Willebrand factor.

Thrombectomy usually results in thrombus recurrence within 48 hours, and whether it impacts on level of ablation is not known at present. The anecdotal use of steroids after thrombectomy has not been found to prevent re-thrombosis. Vascular grafts have been used with satisfactory outcome being reported.⁹ However, this option may be contraindicated in patients with associated Kaposi's sarcoma.

The occurrence together of Kaposi's sarcoma (with or without associated lymphoedema) and vascular manifestations of HIV may be considered an uncommon presentation in the HIV patient; however, the sheer scale of the pandemic will see an increase of this problem that will prompt innovative clinical decisions to facilitate appropriate therapy.

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