

Mixed Arterial and Venous Thromboembolism in a Person with HIV Infection

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People with human immunodeficiency virus (HIV) infection are more susceptible to thromboembolic events. Venous thromboembolism (VTE) occurs frequently in HIV infected persons but arterial thrombosis has only rarely been reported. We describe a case of a person with HIV infection who developed an arterial thrombosis and 3 months later an extensive VTE. Several non-HIV and HIV related thrombogenic factors were identified.

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INTRODUCTION

Venous thromboembolism (VTE) is 10 times more likely to occur in persons with HIV infection when compared to the general population(1). The reported incidence of VTE in persons with HIV infection ranges from 0.25 to 3.31% per y in clinical studies, but up to 17% in post mortem studies (2). On the other hand, only a few cases of isolated arterial embolism have been reported in persons with HIV infection (3, 4). To our knowledge, only 1 case report of a concomitant arterial and venous thrombosis in an HIV infected person has been published (5). We report a case of an HIV positive female who first developed an arterial thrombosis and a VTE 3 months later.

CASE REPORT

A 58-y-old Caucasian female with HIV infection was admitted in January 2003 because of sudden onset of pain, pallor and pulselessness of the right lower limb.

The HIV infection had been diagnosed in 1997. Highly active antiretroviral therapy (HAART) was started in 1999, consisting of zidovudine (300 mg twice daily), zalcitabine (300 mg twice daily) and didanosine (200 mg twice daily). One year later, because of treatment failure, lipodystrophy and polyneuritis, this regimen was replaced by zidovudine (300 mg twice daily), zalcitabine (300 mg twice daily) and didanosine (200 mg twice daily). On admission, she was still treated with the same HAART regimen together with lorazepam (2 mg once daily), clonazepam (5 mg PRN), diltiazem (300 mg once daily) and fenofibrate (200 mg once daily). Her medical history revealed arterial hypertension and Frederickson type IIa dyslipidemia. 20 y earlier a hysterectomy was performed, followed by chemo- and radiotherapy because of a uterine carcinoma. She did not take any hormonal substitution therapy and has never smoked. On admission the HIV viral load was undetectable and the CD4+ lymphocyte count 551/µl. The serum cholesterol level was 346 mg/dl (reference value: < 190 mg/dl) and triglyceride level was 275 mg/dl (reference value: < 200 mg/dl). Fibrinogen and d-dimer levels, prothrombin and activated partial thromboplastin time were within normal limits.

A digital subtraction angiography of the aorta and lower limbs showed an extensive thrombus originating from the right lateral distal aorta, extending beyond the bifurcation into the iliacal arteries

and resulting in a complete obliteration of the right and a partial obstruction of the left iliacal artery. An abdominal computed tomography (CT) scan showed calcified aorto-iliacal atherosclerotic plaques without signs of inflammation. An aorto-bi-iliacal vascular prosthesis was inserted, with complete restoration of the blood flow to the lower limbs. Aspirin (160 mg once daily) was added to the therapy. Three weeks postoperatively, another thrombus occurred resulting in the occlusion of the aorto-bi-iliacal vascular prosthesis. A thrombectomy was performed and the aspirin was replaced by clopidogrel (75 mg once daily). Three months postoperatively, there was a sudden onset of dyspnoea and thoracic pain. A spiral CT scan of the thorax showed a massive thrombus in the right arteria pulmonalis and in the upper and lower branch of the left arteria pulmonalis. Doppler examination showed a deep venous thrombosis in the right deep femoral vein. Coagulation tests were performed before low molecular weight heparin and coumarine treatments were started (Table I). Folic acid (3 mg once daily) and a vitamin B complex were added to the therapy. The fenofibrate was switched to pravastatine (20 mg once daily). A CT scan of the thorax, an abdominal ultrasound and a gynaecological examination did not reveal any neoplastic disorder. She was discharged in good clinical condition on oral acenocoumarol therapy.

DISCUSSION

In persons with HIV infection, several factors resulting in hypercoagulability related to HIV and antiretroviral therapy

Table I. Coagulation factors determined before to start of anti-coagulation

	Value	Reference Interval
Fasting homocysteine	50 µmol/l	< 15 µmol/l
Factor II	151%	70–120%
Factor VIII Coagulans	298%	60–150%
Factor X	160%	70–120%
Antithrombine III	127%	80–125%
Protein C activity	165%	60–150%
APC [§] resistance	Ratio 2.5	1.8–3%
Protein S activity	183%	60–125%
Lupus anticoagulans	Absent	Absent
Protrombine	No factor II mutation	

§ Activated Protein C

have been identified (6). Combined with inherited or acquired factors not related to HIV, these factors predispose people with HIV to thromboembolic events.

In our patient several non-HIV and HIV-related thrombogenic factors were probably responsible for causing an extensive thromboembolic disease. First, our patient was predisposed to arteriosclerosis due to the Frederickson type IIa dyslipidemia and hypertension. Secondly, a high level of factor VIII was measured. This has been associated with venous thromboembolism (7) and arterial thrombosis (8). Inflammation might have been partially responsible for the elevated levels of factor VIII since it is an acute phase reagent (7) and the C-reactive protein (CRP) level remained increased since the vascular surgery. However, other coagulation factors tested were uniformly less elevated, indicating that other unknown and independent factors were responsible for the elevated factor VIII (9). Thirdly, the inflammation parameter, CRP, itself is an independent risk factor for peripheral arterial disease, by inducing the expression of adhesion molecules in human endothelial cells (10). Fourthly, our patient presented with high homocystein levels, a risk factor for thromboembolism (11). Homocystein levels are known to increase during HIV infection (12) and treatment with fenofibrates (13).

HIV also induces endothelial dysfunction (14), thereby promoting platelet activation, inflammatory reactions, and progression of arteriosclerosis. This endothelial dysfunction correlates with viral activity, but abates once the HIV viral load is undetectable. The viral load in our patient was undetectable for 2 years, therefore it is unlikely that in her case endothelial dysfunction caused by the HIV infection played an aetiological role in inducing the thromboembolic events. Protein C deficiency, protein S deficiency and antiphospholipid antibodies, which have all been implicated in HIV infection and thrombosis (15), were absent in our patient.

Finally, protease inhibitors (PI) have been implicated in thrombotic events in HIV positive patients, and can also cause dyslipidemia (16). However, our patient had not taken any PI for two years.

Several of the thrombogenic factors that were identified in our patient were treated. Folate and vitamin B12 were given to lower the homocystein level. The fenofibrate was discontinued and the dyslipidemia treated with a statin. The arterial hypertension was treated with a calcium antagonist. Aspirin and clopidogrel was started to inhibit platelet aggregation and coumarines to inhibit vitamin K dependent clotting factors. This case report emphasizes the need to identify all correctable thrombogenic factors, whether acquired, inherited, HIV or HAART related in people with HIV infection presenting with a thromboembolic event. All

correctable factors need to be treated in order to prevent the recurrence of these events.

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