SHORT REPORT

Surgical Experience with Carotid Stenosis in Young HIV-1 Positive Patients Under Antiretroviral Therapy: An Emerging Problem?

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Introduction

The introduction of antiretroviral drugs has led to a substantial decrease in HIV patient morbidity and mortality.

We report two cases of HIV-1 positive patients with asymptomatic hemodynamically significant stenosis of the internal carotid arteries, being followed with serial echo color Doppler (ECD) as a part of the PREVALEAT (premature vascular lesions and antiretroviral therapy) study. This study aims to detect carotid lesions in HIV-positive patients and to evaluate various risk factors, including the role of antiretroviral treatments (Fig. 1). To our knowledge, our cases are the first to be reported and supported by histological and microbiological studies in the English language literature.

Report


1997: stavudine, lamivudine and indinavir. By 1998, stable suppression of viral load (<80 NASBA), CD4 count was 1214/mm³.

1999: enrolled in the PREVALEAT study and submitted to a first ECD examination of the carotid vessels showing an intimal media thickness of 1.25 mm at the right carotid bulbus and a 65% left internal carotid stenosis.

2002: right stenosis now 38% and left 80%. Considering these findings together with the patient’s immunodeficiency, angiography was rejected. Abdominal aorta and lower limb arteries investigated by duplex scan were normal.

Total cholesterolemia 208 mg/dl, HDL 33 mg/dl, triglyceridemia 391 mg/dl, glycemia 106 mg/dl.


1993: antiretroviral therapy with idodovine.

1997: saquinavir, didanosine, stavudine.


1998: enrolled in the PREVALEAT study and submitted to a first ECD of the carotid vessels revealing a 32% stenosis of the right ICA (internal carotid artery) and 70% of the left.

2002: left stenosis now 82%. A 30% stenosis of the left superficial femoral artery was detected.

CD4 count 153/mm³ and viral load 160.000. Total cholesterolemia 110 mg/dl, HDL 16 mg/dl, triglyceridemia 134 mg/dl, glycemia 80 mg/dl.
CT brain scanning and transesophageal echocardiography were negative in both patients. They also were smokers.

Surgical treatment

The surgical procedures were performed under local anesthesia. The carotid bifurcation was exposed through periarterial inflammatory adhesions. In the first patient, at palpation, a nodule was noted in the medial wall of the internal carotid artery. Thick, fibrotic tissue narrowing the lumen by at least 80% was found in both patients while no endarterectomy plane was evident.

Resection of about 1.5 cm of the ICA was performed in both cases and the remaining artery was re-implanted to the ECA. The patients were discharged 48 h after the operation.

Results

Histological examination of both samples showed intimal lesions with focal fragmentation of the elastic fibres of the media, fibrosis and scarring. There was mild fibrosis of the adventitia. The vasa vasora and periadventitial vessels had a mildly thickened media with occasional perivascular lymphocytes. The intima and media showed a moderate infiltrate characterized by small lymphocytes and occasional plasma cells. An intimal fibrofatty plaque was also noted in both cases (Fig. 2).

HIV-1 isolation was effected from plasma samples and from biopsies, PBMCs and plasma culture supernatants in both patients. Interestingly, plasma samples were positive for HIV p24 antigen detection in both, while the culture specimens yielded different results. In fact, in patient 1, HIV-1 p24 antigen detection was negative in all the cultures, while patient 2 yielded an HIV-1 isolate in all plasma, PBMCs and biopsy cultures; this last finding is considered an expression of resistance to the drugs taken since December 1997.

Microbiological cultures searching for bacteria, mycobacteria, Chlamydia spp. and fungi were negative. Clinical and ECD examination (AU 5 ESAOTE) performed at 30 days, 3 and 6 months showed no neurological deficits and patency of the ICA and ECA (external carotid artery) with no restenosis.

Discussion

Our experience concerns a distinct group of patients treated with antiretroviral therapy,1 presenting with a peculiar clinical and histopathological pattern of carotid arterial narrowing.

In these two patients, ultrasound showed a homogeneous lesion, while the endoluminal surface appeared smooth and regular. The narrowing of the
ICA and CCA (common carotid artery) was segmental and there was no involvement of the ECA.

HIV-positive patients may show a large range of vasculopathies mostly affecting small and medium-sized visceral arteries, namely polyarteritis-type necrotizing vasculitis, eosinophilic vasculitis, isolated granulomatous angiitis of the brain, leukocytoclastic vasculitis and lymphomatoid angiitis. Recently, the occurrence of large artery vasculopathy in HIV-positive patients has been reported, characterized by a proliferation of slit-like vascular channels in the adventitia and the presence of a leukocytoclastic vasculitis of the vasa vasora. In these cases, the intimal changes were very mild and no evidence of atherosclerotic lesions was reported. Our cases showed a bland adventitial inflammation without the features of leukocytoclastic vasculitis; the intimo-medial layers had prominent inflammation with no granulomatous pattern nor giant cell infiltration. These features are partly shared with the ‘scar stage’ of vascular Bechet’s disease, but neither aneurysm formation nor arterial and venous occlusion were identified. Moreover, destruction of the media was not severe but focal, predominantly at the intimo-medial junction, not far from the atherosclerotic plaque, whereas the involvement of the media was mild with no signs of active arteritis. All these features were suggestive of a concomitant mild small vessel vasculopathy of the vasa vasora and an intimo-medial arteritis of the great vessels not previously described. These could be directly attributed to viral fostering of a large array of opportunistic infections and immune-mediated events.

Protease inhibitors, an important component of HAART (highly active antiretroviral therapy), cause glucose and lipid metabolic alterations which could expose HIV-1 patients to a premature risk of atherosclerotic events. The real extent of this phenomenon is still unclear, but evidence suggests that, in a certain percentage of patients, the vascular damage could be due to the effect of the antiretroviral therapy as we showed in a previous study. Moreover, the young age of both patients, rapid onset and progression of the lesions together with the histological findings, raise the suspicion that we are facing a distinct clinical and pathological entity.

The ECD findings, absence of compensation at TCD, and the longer life expectancy of these patients were considered proper indications for surgery; carotid angioplasty and stenting might have been reasonable alternatives. Nevertheless, being unaware of the real nature of the arterial damage, we considered PTA premature. Resection of the ICA and reimplantation on the ECA requires only one anastomosis, avoiding a saphenous vein by-pass using a vein which might have been damaged by previous drug abuse, or the use of PTFE which poses a high risk of infection.

Lesions of the carotid vessels have a higher than expected incidence. A periodic ultrasonographic study of the supra aortic trunks must be included in the general follow-up of these cases and surgery or PTA considered in the presence of rapid and progressive worsening of the disease, taking into account the operative risk and life expectancy.

References


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