Large-vessel vasculitis in human immunodeficiency virus-infected patients

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ABSTRACT

Objective: The objective of this study was to describe large-vessel vasculitis (LVV) in patients with human immunodeficiency virus (HIV) infection. It is a retrospective single-center study conducted between 2000 and 2015 through a university hospital of 11 HIV-infected patients with LVV.

Methods: The characteristics and outcome of 11 HIV-infected patients with LVV (7 patients fulfilled international criteria for Takayasu arteritis, 5 patients had histologic findings of vasculitis, and 5 patients had imaging features of aortitis) were analyzed and compared with those of 82 patients with LVV but without HIV infection.

Results: Concerning the HIV-infected patients with LVV (n = 11), the mean age was 40 years (range, 36-56 years), and 55% of patients were female. At diagnosis of LLV, the mean initial CD4 cell count was 455 cells/mm^3 (range, 166-837 cells/mm^3), and the median HIV viral load was 9241 copies. Vascular lesions were located in the aorta (n = 7), in supra-aortic trunks (n = 7), and in digestive arteries (n = 3). Inflammatory aorta infiltrates showed a strong expression of interferon-γ and interleukin 6. In HIV-negative LVV patients (n = 82), the median age was 42 years, and 88% of the patients were women. Thirty patients had an inflammatory syndrome. Seventy patients had been treated with glucocorticosteroids and 57 with immunosuppressive treatments. Compared with their negative counterparts, HIV-positive patients with LVV were more frequently male (P = .014), had more vascular complications (ie, Ishikawa score; P = .017), and had more frequent revascularization (P = .047). After a mean follow-up of 96 months, four relapses of vasculitis were reported, and one patient died. Regardless of the HIV virologic response, antiretroviral therapy improved LVV in only one case.

Conclusions: LVV in HIV-infected patients is a rare and severe entity. (J Vasc Surg 2018;67:1501-11.)

Viral infections have been implicated in the pathogenesis of systemic vasculitis.[1] The relationship between vasculitis and infection is complex owing to the wide array of pathogens that may be involved and varied expressions of vascular inflammation in different tissues. Many viruses are associated with vasculitis, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV).[2] HBV, which was associated with polyarteritis nodosa, was the first viral pathogen to have a causal relation with vasculitis.[3] Different vessel sizes are affected according to the type of viral agent. HBV-associated polyarteritis nodosa usually affected medium-size vessels, whereas HCV-related cryoglobulinemia vasculitis mainly involved small and medium-size vessels.[4] The relation between HIV and vasculitis remains rarer. HIV is associated with a wide range of vasculitic phenotypes, affecting small or large vessels. The vasculitic patterns encountered in HIV-infected patients included infective vasculitides, systemic necrotizing and drug-induced vasculitis, primary angiitis of the central nervous system, and large-vessel vasculopathy.[5]

Large artery involvement in HIV infection is uncommon and not well documented.[6] However, several patients showed a leukocytoclastic vasculitis of the vasa vasorum and of periadventitial vessels and no evidence of atherosclerosis, and microbiologic cultures of blood, aneurysm wall, and thrombus were negative.[7,8] In addition, affected HIV-positive patients tend to be young and to present with multiple aneurysms or occlusions of the carotid, femoral, and popliteal arteries.[9] Patients had evidence of adventitial slitlike vessels, and T lymphocytes were noted in the adventitia in most HIV-positive patients. Taken together, these features overlap with those of Takayasu arteritis (TA).[10]

In this study, our aim was to describe the characteristics and outcome of large-vessel vasculitis (LVV) in patients

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with HIV infection compared with a cohort of age-matched HIV-uninfected patients.

METHODS

Patients. We performed a retrospective study in the departments of internal medicine and infectious diseases of Pitié-Salpêtrière hospital between 2000 and 2015. Inclusion criteria were HIV seropositivity and features of LVV, including imaging, histology, and Ishikawa or American College of Rheumatology (ACR) criteria of TA[11] (Figs 1 and 2). All patients had large-vessel vascular lesions, including aneurysmal and occlusive disease. Patients with positive syphilis titers, positive bacterial blood cultures, positive bacterial cultures of aneurysm wall, and positive bacterial cultures of thrombus were excluded from this study. Exclusion criteria were patients with evidence of atherosclerosis and infectious vascular disease. This study was approved by the local ethics committee. Because it is a retrospective study, informed consent of the patient was not required. Diagnosis of LVV was made by imaging (computed tomography [CT], positron emission tomography [PET], and magnetic resonance angiography [MRA]), biologic inflammation, and histologic evaluation when available. Patients should have fulfilled at least one of the following criteria to be considered as having LVV: evidence of aortitis on vascular imaging (CT angiography, MRA, or fluorodeoxyglucose [FDG]-PET/CT); histologic evidence of LVV (giant cell aortitis associated with lymphoplasmacytic infiltrate involving the media and the adventitia); and Ishikawa or ACR criteria of TA[11] (which are still effective in HIV-infected patients).

Information about demographic data (age, gender), HIV infection history (diagnosis date, HBV or HCV coinfection, immunovirologic features, treatment), and vasculitis history (diagnosis date, immunovirologic status at diagnosis, treatment, and outcome) was collected. Aortitis was defined on vascular imaging (CT angiography, MRA, or FDG-PET/CT) as lesions of the aorta and its branches, with parietal thickening or increased uptake of aorta on FDG-PET/CT.

The data of HIV-infected patients with LVV were compared with those of a control group of age-matched, HIV-negative patients with TA using the χ^2 test.

Disease activity and treatment response definitions. Disease activity was defined according to the National Institutes of Health (NIH) criteria (Fig 3) used in TA: new ischemic vascular sign (ie, claudication, bruit or asymmetry in pulses or blood pressure, carotidynia, pulse abolition); new arterial lesion or worsening of pre-existing lesions on imaging, visualized by CT angiography, magnetic resonance imaging, or MRA; systemic clinical features (ie, weight loss, fever, or myalgia); and biologic activity—increased erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) levels. Disease was considered active if the NIH score was 2 or more and inactive otherwise. Steroid dependence was defined as prednisone ≥20 mg/d during at least 1 month before each new therapeutic agent.

Treatment response with any regimen (disease-modifying antirheumatic drugs, biologic targeting treatment) was defined as improvement in the NIH score <2 and prednisone <10 mg/d or when steroid dosage decreased at least 50% compared with baseline and stabilization if no new vascular lesions appeared. Relapse was defined as the disease's becoming active after a remission period, requiring change of the treatment regimen.

Literature review. A comprehensive review of the literature was performed using PubMed (http://www.ncbi.nlm.nih.gov/pubmed) by entering the following keywords: large-vessel vasculitis, aortitis, arterial aneurysms, aortic aneurysms, vasculopathy, and HIV. There was no limit of the publication date. We added relevant articles that were not identified using this strategy but were present in the reference list of other studies.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective cohort study
- **Take Home Message:** Of 93 patients with large-vessel vasculitis (LVV) treated at a tertiary university center, 11 patients (12%) also had human immunodeficiency virus (HIV) infection. HIV-positive patients with LVV were more frequently male, developed more vascular complications, responded less to antiretroviral therapy, and had worse outcome than HIV-negative patients with LVV.
- **Recommendation:** These data suggest that HIV-positive patients with LVV have more vascular complications, respond less to treatment, and have worse prognosis than HIV-negative patients with LVV.

RESULTS

Main characteristics of HIV-infected patients with LVV. The main clinical and demographic characteristics of the 11 patients included are presented in Tables I and II. Mean age at vasculitis diagnosis was 40 years (36-56 years); 55% of the patients were women. Delay between HIV infection and vasculitis diagnosis ranged from 0 to 24 years; in three patients, both were diagnosed at the same time. Mean CD4 T-lymphocyte count and HIV viral load at vasculitis diagnosis were, respectively, 459.5 cells/mm^3 and 9241 copies (for one patient, data not available). Three patients had detectable viral load and one patient had CD4 T lymphocytes <200 cells/mm^3. Two patients had HCV coinfection and three had history of opportunistic infections (Castleman disease, n = 2; Kaposi sarcoma, n = 1). Six patients were receiving antiretroviral treatment at the time of vasculitis