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Short communication

Atherosclerosis risk in HIV-infected patients: The influence of hepatitis C virus co-infection

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ABSTRACT

Background: The influence of hepatitis C virus (HCV) infection on atherosclerosis risk in HIV-infected patients has not been adequately evaluated in real-life situations.
Objectives and methods: We compared indexes of early atherosclerosis evaluated by echo-Doppler ultrasound (presence of plaque in carotid or femoral arteries) in 18 HCV–HIV co-infected patients *versus* 22 HIV mono-infected patients.
Results: Prevalence of subclinical carotid plaque was significantly higher in HCV–HIV co-infected patients ($p = 0.04$), despite of the fact LDL-cholesterol and blood pressure (BP) were lower in the co-infected patients ($p = 0.003$). HCV chronic infection (OR = 10; IC: 1.5–72; $p = 0.02$) was an independent risk factor.
Conclusion: This cross sectional study suggests that HCV infection might be an independent cardiovascular risk factor in HCV–HIV co-infected patients. HCV infection might be considered as not only a liver infection but also as a metabolic disease in HIV patients, justifying regular cardiovascular surveillance.

1. Introduction

Since the onset of highly active antiretroviral therapy (HAART) use, morbidity and mortality of HIV-infected patients have significantly decreased due to a pronounced reduction of the complications related to immuno-suppression. Concomitantly, the significant increase in HIV patient survival has led to the expression of other complications, many of them cardiovascular. More recently, relationships between HCV chronic infection and CVD have been suggested but remain controversial [1]. The influence of HCV infection on atherosclerosis risk in HIV-infected patients has not been evaluated. Among early atherosclerosis markers, wall thickening (carotid intima–media thickness (cIMT) >0.9 mm) or subclinical plaque of carotid or femoral arteries measured by Doppler ultrasound have been reported to be reliable and predictive markers for CVD [2].

The aim of the present study was to compare an index of early atherosclerosis, cIMT and the presence of plaque in carotid or femoral site, in HCV–HIV co-infected patients and in HIV mono-infected patients.

2. Methods

2.1. Patients

From December 2006 to January 2008, we prospectively studied HIV–HCV co-infected patients hospitalised for either an indirect liver fibrosis evaluation in liver clinics or atherosclerosis evaluation in cardiovascular clinics. These evaluations were performed in the settings of the standardised care. All patients gave their oral consent.

Inclusion criteria were: age above 18 years and HIV infection and HCV infection proved by polymerase chain reaction (PCR) and present for over one year. The patient had imperatively been examined in CVD clinics within a year of the liver tests. Exclusion criteria were: patients treated or having failed to eradicate HCV, patients with Child C cirrhosis, positive hepatitis B serology, diabetes mellitus, known CVD, or discovery of vascular stenosis above 60%. For HIV mono-infected patients, inclusion criteria were the same, with the exception of HCV criteria (cross sectional study).

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The clinical parameters measured were: weight, height, body mass index (BMI), waist circumference, blood pressure (BP), smoking, drugs and alcohol habits, history of HIV and HCV infections. The definition of the metabolic syndrome (MS) retained was that of the 2005 International Diabetes Federation [3]. Blood parameters tested were: glycaemia, lipids, liver enzymes, complete blood count, CD4, C-reactive protein (CRP), prothrombin time, albumin, ferritin, HIV and HCV polymerase chain reaction and HCV genotype.

Fibrosis test and score index were the following: hyaluronic acid, APRI [4], Fibrometre® [5] and FIB-4 [6]. The Fibrometre score was computed from the Bioscale website. Liver stiffness was measured by Fibroscan® using usual modalities [7].

Vascular Doppler ultrasound was performed by only one operator (P.S.) using a HDI 5000 ultrasound system (ATL® Ultrasound, Bothell, WA, USA) and a L12-5 (5.0–12.0 MHz) 38 mm linear array transducer. The operator was blind with regard to the clinical and biological data of the patients. Carotid IMT measurements of the right and left common carotid arteries were performed over a distance of 10 mm on the far wall of the common carotid artery. Three measurements were performed in each patient and an average was calculated. A carotid plaque was defined as a focal enlargement over 1.5 mm and femoral plaque by a focal enlargement exceeding 2.0 mm.

2.2. Statistical analysis

Non-parametric Mann–Whitney and Fischer tests were used for comparison of quantitative data. Non-parametric Spearman test was used for correlation. Univariate analysis measured the association between plaques and explicative variables. Multivariate analysis was based upon a logistic regression model: factors found significant on univariate analysis ($p < 0.05$) were then included in the stepwise multiple logistic regression analysis in order to identify independent factors associated with atherosclerosis. All statistical analyses were performed with StatView 5.0 (SAS Institute Inc.©, Cary, NC, USA).

3. Results

3.1. Patient characteristics

From December 2006 to January 2008, 29 patients HIV–HCV co-infected and 30 HIV mono-infected were included but only 40 patients were studied throughout. Characteristics of the 18 HIV–HCV co-infected and 22 HIV mono-infected patients are presented in Table 1.

3.2. Vascular Doppler ultrasound characteristics

The prevalence of vascular plaque was significantly higher in the HIV–HCV co-infected patients (8/18, 44%) compared to mono-infected patients (3/22, 14%) ($p = 0.04$). In patients with plaque, 4 (36%) had only one plaque and the others had at least 2 plaques over the 4 Doppler studied zones, 4 had plaques only in femoral site. We found no significant differences of cIMT between the 2 groups of patients whatever the location studied: 0.70 mm (0.60–0.75) compared to 0.75 mm (0.6–0.9).

3.3. Factors associated with atherosclerosis

In univariate analysis, CRP was significantly higher in patients with vascular plaques: 4.9 mg/l (3.9–8.5) *vs.* 1.0 mg/L (0.9–4.9) in case of absence of plaque ($p = 0.05$), and in patients with MS: 5 mg/L (3.5–14.5) *vs.* 1.0 mg/L (0.9–4.9) in case of absence of MS ($p = 0.005$). In patients with MS, even though there were no significant differences concerning presence of plaque, cIMT was significantly higher (Fig. 1).

Table 1
Baseline characteristics.

Parameters	HCV–HIV co-infected ($n = 18$)	HIV mono-infected ($n = 22$)	p-Value
Age (years)	46 (36–50)	51 (43–58)	ns
Gender (male/female)	12/6 (66%/44%)	16/6 (72%/28%)	ns
HIV contamination duration (years)	14 (12–20)	12 (9–20)	ns
HAART duration (years)	10 (8–17)	10 (5–15)	ns
PI treatment duration (years)	5 (1–9)	5 (1–8)	ns
Body mass index (kg/m^2)	21 (18–22)	24 (22–26)	0.002
Waist circumference (cm)	87 (78–89)	88 (83–97)	ns
Systolic blood pressure (mm Hg)	111 (109–120)	130 (118–138)	0.003
Diastolic blood pressure (mm Hg)	70 (70–71)	77 (70–80)	0.02
Metabolic syndrome	4 (22%)	7 (32%)	ns
Current smoking	8 (44%)	7 (32%)	ns
Smoking consumption in active smokers (packs a year)	19 (15–25)	15 (11–21)	ns
Alcohol consumption >40 g a day in men, >20 g in women	3 (16%)	3(13%)	ns
Use of cannabis	1 (5%)	0 (0%)	ns
Use of cocaine	0 (0%)	0 (0%)	ns
Glycaemia (mmol/L)	4.84 (4.62–5.12)	5.23 (4.95–5.50)	0.05
Total cholesterol (mmol/L)	4.08 (3.07–5.06)	4.70 (4.33–5.6)	ns
HDL-cholesterol (mmol/L)	1.16 (1.01–1.94)	1.32 (1.06–1.94)	ns
LDL-cholesterol (mmol/L)	1.68 (1.16–2.45)	2.68 (2.19–3.33)	0.003
Triglycerides (mmol/L)	2.05 (1.12–2.86)	1.46 (1.06–2.00)	ns
CRP (mg/L)	4.9 (0.9–6.5)	2.0 (0.9–4.5)	ns
GOT (U/L) $N < 50$ U/L	52 (26–91)	24 (19–30)	0.0008
GPT (U/L) $N < 50$ U/L	45 (23–92)	28 (16–47)	0.02
GGT (U/L) $N < 60$ U/L	97 (59–309)	46 (24–98)	0.01
Ferritin (μg/L)	167 (84–476)	61 (33–139)	0.003
CD4 (/mm^3)	495 (339–797)	571 (417–855)	ns
No detectable HIV RNA	15 (83%)	21 (95%)	ns
Antihypertensive treatment	1 (5%)	5 (23%)	ns
Statin treatment	8 (44%)	11 (50%)	ns

Results are presented as median and (interquartiles) or n and (%). HAART = highly active antiretroviral therapy; PI = protease inhibitor; CRP = C-reactive protein; GOT = glutamic-oxalacetic transaminase; GPT = glutamic-pyruvic transaminase; GGT = gamma-glutamyl-transpeptidase.