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Carotid intima media thickness with no cardiovascular disease in HIV-infected patients correlates with a hyperactivated/pro-apoptotic T-cell phenotype

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Background

HIV-infected patients may be at increased risk of cardiovascular disease (CVD), and present higher carotid intima media thickness (IMT) compared with healthy controls. Besides clinical and metabolic factors, atherosclerosis in HIV is influenced by immune and inflammatory parameters. Given that T-cell activation correlates with CVD and HIV accounts for heightened T-cell hyperactivation, we hypothesized that early IMT increases associate to T-cell hyperactivation.

Methods

We performed a cross-sectional correlation between carotid IMT and immunological parameters on a cohort of 71 HIV patients: 17 subjects had a positive history for cardiovascular events (CE), 22 patients presented increased IMT measurements (>1 mm, IIMT), and 32 had normal IMT values (<1 mm, NIMT). No clinical signs of CVD were shown in the IIMT and NIMT groups. Parameters of T-cell homeostasis (CD127), activation (CD38+CD8+) and death (CD95/Fas) were assessed by flow cytometry. Plasma IL-6 and TNF-α levels were also measured.

Summary of results

The three groups were comparable in terms of CVD risk factors, and HIV-related viro-immunological parameters. Major results are shown in Table 1. Compared to NIMT subjects, CE patients presented higher activated CD38+CD8+ ($p = 0.01$), lower CD95+CD8+ and CD127+CD8+ cells ($p = 0.03$) and increased plasma IL-6 ($p = 0.02$) and TNF-α. Surprisingly, IIMT patients presented CD38+CD8+ proportions comparable to CE ($p = 0.18$), significantly higher than NIMT ($p = 0.01$), resulting in a significant positive correlation between IMT and T-cell activation ($p = 0.04$). Analogously, IIMT patients displayed CD95+CD8+ and CD127+CD8+ proportions comparable to CE ($p > 0.5$), and significantly lower than NIMT ($p = 0.08$ and $p = 0.03$, respectively).

Conclusion

Despite no overt sign of CVD, HIV-infected patients with pathologic IMT increases display a peripheral T-cell immune phenotype and activation similar to CVD patients characterised by a highly activated/senescent, pro-apoptotic T-cell pool. By showing specific T-cell patterns associated to IMT increases, our findings support a possible role of immunological parameters as early surrogate markers of CVD risk in HIV-infected patients.

Table 1:

	CE (n = 17)	IIMT (n = 22)	NIMT (n = 32)
Left carotid IMT (mm)	0,9 (0,6–1,26)	1,2 (0,6–1,86)	0,86 (0,6–0,9)
Right carotid IMT (mm)	0,92 (0,73–1,38)	1,24 (0,99–1,75)	0,89 (0,75–0,99)
CD38+CD8+ %	1,5 (1–8)	2 (1–6)	1 (0–6)
CD38+CD8+ n	20 (11–192)	28 (8–84)	16 (0–65)
CD95+CD8+ %	1 (1–9)	1 (1–9)	2 (1–3)
CD95+CD8+ n	22 (11–64)	24 (13–68)	26 (11–336)
CD127+CD8+ %	12 (8–21)	12 (5–23)	14 (8–23)
CD127+CD8+ n	173 (121–286)	202 (64–364)	247 (108–572)
IL-6 (pg/mL)	1,5 (0,2–2,2)	0,8 (0,4–7,4)	0,88 (0,24–8,3)
TNF-α (pg/mL)	3,2 (2,3–4,7)	1,6 (1,5–2,9)	1,5 (1,27–2,10)

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