ABSTRACT

HIV viraemic patients downregulate CD94/NKG2A inhibitory receptors on NK as well as CD8 T cells in comparison with aviraemic counterparts

M. Zeddou, S. Rahmouni, A. Vandamme, N. Schaaf-Lafontaine, M. Moutschen

Background: The CD94/NKG2 heterodimer is a C-type lectin receptor formed by the association of CD94 and one of the NKG2 molecules (namely NKG2A, -B, -C or –E). The interaction of CD94/NKG2A with non classical HLA-E molecules delivers inhibitory signals. CD94/NKG2A is normally expressed on most NK cells whereas less than 5% of peripheral resting CD8+ T cells are positive. Although several reports have clearly shown an upregulation of CD94 on CD8 T cells in HIV infection, the simultaneous expression of both subunits of the inhibitory receptor on NK and T cells and its relation with viral load is largely unknown.

Methods: PBLs from 30 HIV-infected patients (16 viraemic and 14 aviraemic under HAART) and 18 healthy volunteers were analysed by flow cytometry after staining with the following monoclonal antibodies (Percp-conjugated anti-CD8, FITC-conjugated anti-CD3, APC-conjugated anti-CD94, PE-conjugated anti-NKG2A).

Results: The proportion of CD8 T cells expressing the CD94/NKG2A inhibitory receptor was not significantly increased in HIV-infected patients (5.68 ± 3.72%) in comparison with non-infected controls (4.90±2.84%). Interestingly, patients with viral load < 50 copies/ml had a higher proportion of CD8 T cells expressing the inhibitory receptor (7.15 ± 3.63%) than patients with HIV viraemia (4.40 ± 3.40%), p= 0.041. The same pattern was observed for NK cells and was even more pronounced. In aviraemic individuals, 61.75 ± 20.39% of NK cells expressed the inhibitory receptor vs 42.88 ± 26.38% in viraemic patients. The proportion of CD94/NKG2A positive cells was correlated between NK and CD8 T cell subsets (p=0.0351) but there was no correlation with absolute or relative CD4 counts.

Conclusions: Our results suggest that chronic stimulation with HIV antigens in viraemic patients could lead to decreased rather than increased expression of inhibitory receptors on NK and CD8 T cells. This could contribute to the abnormal activation of the immune system associated with advanced HIV disease.

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