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Poster presentation

Cathepsin B and Cystatin A as Indicators of a Separate Apoptotic Pathway in HIV-1 Infection

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Apoptosis has been proposed to explain the dysfunction in HIV-1 infection and FAS has been given a pivotal role. However, apoptosis in lymphoid follicles has also been explained by a follicular dendritic cell (FDC) dependent pathway regulated by a cathepsin-dependent endonuclease activity in germinal centre (GC) cells. Cystatin A is present in FDCs and is a natural inhibitor of cysteine proteinase, as Cathepsin B. As yet, the Cystatin A and Cathepsin B interaction in HIV-1 infection has not been studied.

Methods

Tonsillar tissue was obtained from 20 patients at various stages of HIV-1 infection and 10 controls. Eleven of the patients received HAART for 48 weeks. Cathepsin B, Cystatin A, FAS(CD95) and HIV-1 p24 in the GC cells were analyzed by immunohistochemi-cal staining. Cathepsin B/Cystatin A ratios were calculated for controls and for patients before and after 48 weeks of therapy.

Results

Cathepsin B/Cystatin A ratio was 2-fold higher in patients as compared to controls; 1.03 and 0.43, respectively. After 48 weeks of therapy, this ratio was normalized (0.32). In patients, Cathepsin B correlated negatively with Cystatin A ($r = -0.686$, $p = 0.002$), and both markers correlated with the p24 antigen; $r = 0.777$ ($p = 0.001$) and $r = -0.622$ ($p = 0.013$), respectively. In multiple regression analysis presence of p24 antigen could not fully explain this relationship. There was no correlation with FAS(CD 95) for these parameters.

Conclusion

A 2-fold higher Cathepsin B/Cystatin A ratio was found in patients before HAART, suggesting a HIV-1 driven cathepsin-dependent pathway of apoptosis. Thus, Cathepsin B and Cystatin A possibly represent an apoptotic pathway distinguishable from the FAS-FAS Ligand pathway.