Markers of HIV-associated Cognitive Impairment Are Elevated in HIV-infected Patients with Neurosyphilis

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Introduction

- Despite combination antiretroviral therapy (cART), cognitive impairment is common in HIV-infected patients.
- Compared to those without cognitive impairment, cerebrospinal fluid (CSF) concentrations of IP-10, MCP-1, neurofilament light chain (Nfl) are higher in cognitively impaired HIV-infected patients. Blood concentrations of activated monocytes are also higher in HIV-infected patients with dementia.
- Cognitive impairment may also be more common in HIV-infected patients with past syphilis.
- The goal of this study was to determine if markers of HIV-associated cognitive impairment were higher in HIV-infected patients with neurosyphilis.

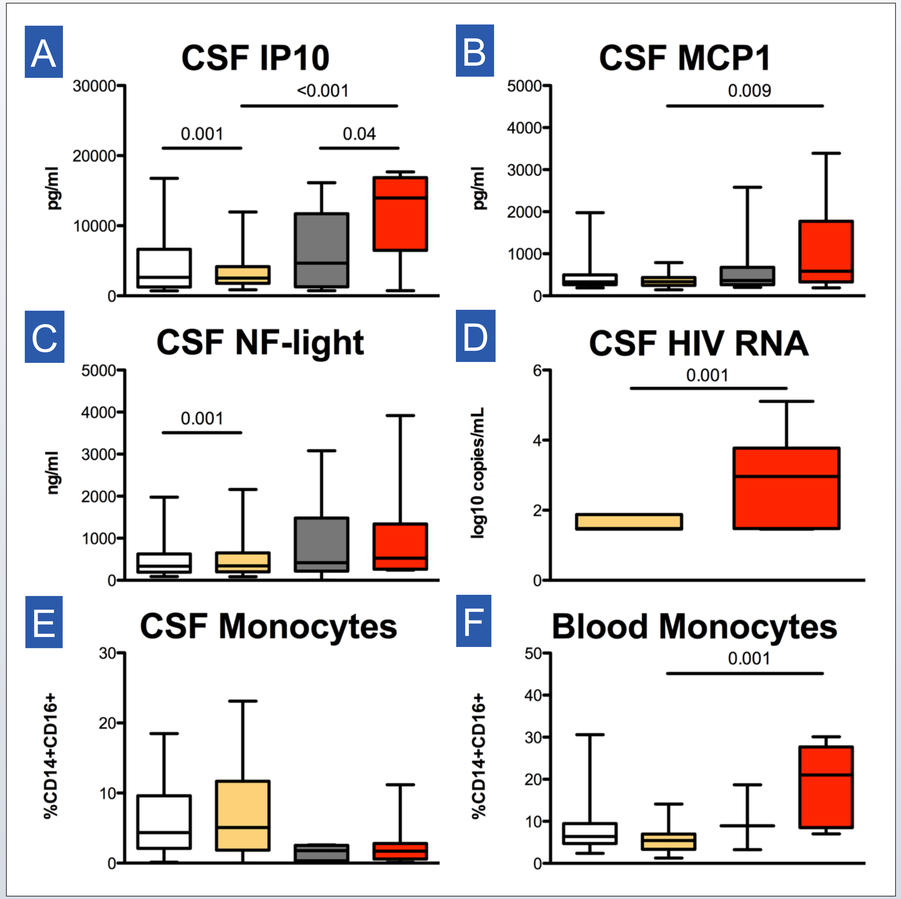
Materials and Methods

- Banked frozen CSF and cryopreserved CSF cells and peripheral blood mononuclear cells (PBMCs) were collected from 109 individuals: 48% HIV-infected (72% on cART), 95% men, 76% Caucasian; 64% early syphilis; 35 had neurosyphilis (reactive CSF-Venereal Disease Research Laboratory [VDRL]), 74 had uncomplicated syphilis (syphilis; CSF white blood cells [WBCs] ≤5/ul, nonreactive CSF-VDRL).
- CSF concentrations of HIV RNA were measured by RT-PCR; MCP-1, IP-10 were measured by multiplex assay (Mesoscale Discovery), Nfl by ELISA (Uman Diagnostics), % activated monocytes (coexpressing CD14 and CD16) by flow cytometry.
- Differences between groups was assessed by Mann-Whitney U test. The influence of covariates was assessed using linear regression.

Results

Table 1. Patient Characteristics

Median (IQR or %)	HIV negative (n=57)	HIV positive (n=52)
Age	37 years (28-46)	42 years (33-47)
Male	52 (91%)	51 (98%)
Race/ethnicity		
Caucasian	34 (60%)	40 (77%)
Black	10 (18%)	8 (15%)
Hispanic	7 (12%)	2 (4%)
Other	6 (10%)	2 (4%)
Syphilis stage		
Early	30 (53%)	40 (77%)
Late	27 (47%)	12 (23%)
Previous syphilis	13 (23%)	12 (23%)
Neurosyphilis	16 (28%)	19 (37%)
1/RPR titer		
Syphilis	64 (32-64)	32 (4-128)
Neurosyphilis	64 (64-256)	256 (128-512)
CSF tests (Neurosyphilis)		
WBC/mm^3	26 (8-93)	58 (19-102)
1/VDRL titer	2 (1-4)	2 (1-8)



Summary

- Among the groups with syphilis and with neurosyphilis, CSF IP-10 concentrations were higher in the HIV-infected patients than in the HIV-uninfected patients (A).
- Among patients with syphilis, CSF NFL was higher in the HIV-infected patients than the HIV-uninfected patients, but CSF NFL did not differ between the neurosyphilis patients (C).
- Among patients with HIV, CSF HIV RNA, IP-10 and MCP1; and blood % activated monocytes were higher in those with neurosyphilis than in those with syphilis (D, A, B).
- Taking into account CSF WBCs, CSF IP-10 but not MCP1, HIV RNA or blood activated monocytes remained significantly higher in HIV-infected patients with neurosyphilis than in HIV-infected patients with syphilis (P<0.001).

Conclusions

- Compared to HIV-infected patients with syphilis and patients with neurosyphilis alone, HIV-infected patients with neurosyphilis have higher concentrations of CSF and peripheral blood biomarkers that are associated with cognitive impairment.
- These studies suggest that patients with concomitant HIV and neurosyphilis may be at higher risk of cognitive impairment.

Acknowledgements: We thank the UW Virology Lab for assistance in measuring CSF HIV RNA and Dr. Sheila Lukehart for helpful discussions. This work was supported by NIH (P30 AI027757) and by NIH/NINDS NS34235 and NS082120. E.L.H. was a recipient of a Centers for AIDS Research New Investigator Award.

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