Poster # 479

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CSF Biomarker profile in HIV patients with and without CSF Viral Escape

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CHARTER
CNS HIV Anti-Retroviral Therapy Effects Research
CNS HIV ANTI-RETROVIRAL THERAPY EFFECTS RESEARCH

Objective

To explore the potential association between CSF Viral Escape and high levels of inflammatory biomarkers.

Background

- Persistent viral replication inside the CNS has been associated with local inflammation and neurocognitive impairment.
- In some aviremic patients on ART, CSF viral escape (CVE) has been reported as an uncommon and generally transient condition.
- During CSF viral escape episodes, it is possible that viral particles released may increase inflammation and produce subsequent neurocognitive decline in the long-term.

Methods

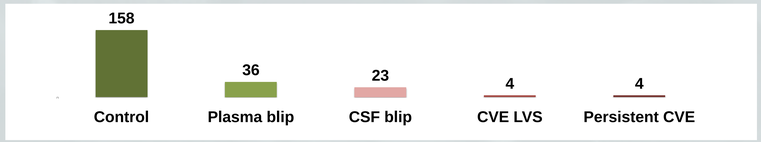
- Cross-sectional analysis performed to compare inflammatory biomarkers in patients with or without CSF viral escape (CSF HIV-RNA >50 cop/mL and plasma HIV RNA <50).
- For that purpose, we selected aviremic HIV individuals on ART from the CHARTER and HNRP cohorts, tested for CSF and plasma inflammatory biomarkers: (IL6, CXCL10, TNF-Alpha, MCP-1 and WBC).
- Our first objective was to compare, levels of plasma and CSF inflammatory biomarkers in patients with and without CSF viral, using a multivariable logistic regression model adjusted for demographics and HIV clinical data.
- As a secondary objective, we compared levels of plasma and CSF inflammatory biomarkers between these 5 categories, defined according to follow up characteristics: Control (always suppressed in plasma & CSF); Plasma blip (transient plasma detectability); CSF blip (transient CSF detectability); CVE LVS (CVE linked to previous plasma detectability); or Persistent CVE (CVE in $\geq$ 2 consecutive CSF evaluations).

Results

BASELINE CHARACTERISTICS

	ALL (N=296)	CSF Viral Escape (N=8)	CSF HIV RNA <50 cop/mL (N=288)	p Value
Age, mean (sd)	46.6 (7.9)	47 (4.3)	46.5 (8)	p = 0.89
Education, mean (sd)	13.4 (2.6)	14.1 (2.6)	13.4 (2.6)	p = 0.51
Gender: Male, N (%)	257 (86.8)	8 (100)	249 (86.5)	p = 0.26
Ethnicity: Caucasian, N (%)	172 (58.1)	7 (87.5)	165 (57.3)	p = 0.55
CD4 nadir, median (IQR)	110 (19-209)	12 (6-107)	115 (20.3-209)	p =0.04
HCV condition: HCV Ac+, N (%)	70 (24.9)	0 (0)	70 (25.5)	p = 0.12
Years being HIV+, median (IQR)	13 (6.6-17.3)	18.2 (13.3-23.8)	12.9 (6.6-17.1)	p = 0.03
ART				
Years of ART, median (IQR)	4.6 (1.6-7.9)	7.6 (2.8-11.6)	6.5 (3.2-10)	p = 0.63
PI+NRTIs, N (%)	156 (53.2)	7 (87.5)	149 (52.3)	
NNRTI+NRTIs, N (%)	96 (32.8)	1 (12.5)	95 (33.3)	p = 0.14
Other ART regiments, N (%)	41 (14.0)	0 (0)	41 (14.4)	
CPE score; median (IQR)	7 (6-9)	6.5 (6-9.3)	7 (6-9)	p = 0.49
Neurognitive impairment, N (%)	124 (42.3)	2 (25)	122 (42.8)	p = 0.31
Plasma				
WBC, median (IQR)	5500 (4410-6600)	4900 (4050-6075)	5500 (4410-6600)	p = 0.51
Current CD4, median (IQR)	474 (311-654)	370 (238-621)	480 (312-654)	p = 0.41
Protein level, median (IQR)	7.5 (6.9-8.5)	6.8 (6.7-8.2)	7.5 (6.9-8)	p = 0.61
MCP-1, median (IQR)	377 (288-503)	374 (310-398)	382 (287-504)	p = 0.67
TNF-α, median (IQR)	16.5 (10.3-24)	17.1 (10.6-23.9)	16.4 (10.3-24.1)	p = 0.98
CXCL10, median (IQR)	1049 (698-1737)	1118 (728-2099)	1040 (693-1731)	p = 0.71
IL-6, median (IQR)	3 (1.1-6.1)	1.6 (0.3-2)	3 (1.1-6.2)	p = 0.05
CSF				
WBC pleocytosis, N (%)	39 (13.3)	4 (50)	35 (12.3)	p < 0.01
Protein level, median (IQR)	42 (33-53)	38.5 (33-54.5)	42 (33-52.8)	p = 0.88
MCP-1, median (IQR)	1151 (879-1744)	1330 (719-2153)	1151 (878-1747)	p = 0.99
TNF-α, median (IQR)	4.1 (2.7-5.6)	7.1 (2.6-10.9)	4.1 (2.7-5.5)	p = 0.19
CXCL10, median (IQR)	2815 (1542-4800)	6417 (4468-14551)	2771 (1516-4585)	p = 0.01
IL-6, median (IQR)	15 (9.8-23.6)	13.7 (0.9-16.3)	15.1 (9.8-23.8)	p = 0.22

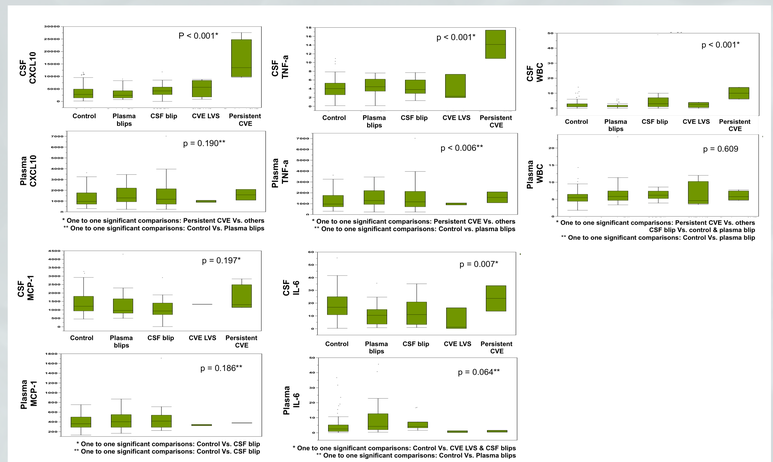
TYPE OF PATIENTS (Defined by prospective evolution)



PRIMARY ANALYSIS: Multivariable model

	CSF Viral Escape (N=8)	CSF HIV RNA <50 cop/mL (N=288)	p Value
CSF CXCL10, median (IQR)	6417 (4468-14551)	2771 (1516-4585)	p = 0.03
CSF WBC pleocytosis, N (%)	4 (50)	35 (12.3)	p = 0.38
Years being HIV+, median (IQR)	18.2 (13.3-23.8)	12.9 (6.6-17.1)	p = 0.30
CD4 nadir, median (IQR)	12 (6-107)	115 (20.3-209)	p = 0.36

SECONDARY ANALYSIS: (Biomarkers by patient's type)



Conclusions

- **CSF CXCL10 is elevated during CSF viral escape, implying higher inflammation.**
- **Persistent CVE was associated with higher inflammatory markers in CSF (CXCL10, TNF-α and WBC), CSF blips with higher levels of MCP-1 in plasma & CSF and plasma blips with higher inflammatory markers in plasma (IL-6, CXCL10, TNF-α and WBC).**
- **Further research is needed to explore the effects of the different profiles of inflammation observed in patients with CVE over cognition.**

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