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#371

CSF Escape in Treated HIV Infection Shows X4 Tropism and Defective Viral Sequences

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BACKGROUND

There is often clinical concern when HIV is detectable in cerebrospinal fluid despite plasma virologic suppression in plasma in patients with HIV infection. We describe such "asymptomatic" CSF escape in participants enrolled in a neurologic cohort study at the National Institutes of Health (NIH).

OBJECTIVE

In this study we describe “asymptomatic” CSF escape and compare results of MRI, neurocognitive, and psychiatric outcomes in those with and without escape.

METHODS

Neurocognitive Testing

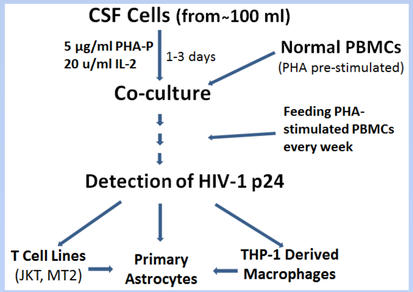
- Seven cognitive domains with a battery of tests lasting 3-4 hours for each participant.
- Raw scores were transformed to T-scores using widely available neuropsychological normative software, and scores were corrected for demographic variables (age, gender, race, and education level) when available.
- Along with an assessment of daily living activities, participants’ T-scores were used for GDS and HAND categorization.

Lumbar Puncture:

- CSF HIV determined using Roche COBAS Taqman HIV-1 v2.0 with limit of detection of 20 copies/ml.

Viral Isolation and outgrowth assay:

- 100-150 ml of CSF was collected via lumbar drain from 6 patients with plasma viral suppression; 5 had normal cognitive performance and one had HIV-associated neurocognitive disorder (HAND). The cells from CSF were collected for HIV isolation



Viral PCR:

- Full length HIV-env PCR and 5’LTR to 3’LTR PCR was performed on cells from 20 mls of CSF from each of four patients

Brain MRI:

- T1- & T2-weighted MRI on 3T scanners (GE Medical Systems) within 4 weeks of LP.
- Freesurfer was used to determine brain volumes.

PARTICIPANTS

	Age, years (range)	Female, no. (%)	African-American, no. (%)	Time since HIV diagnosis, years (range)	Time since ART initiation, years (range)	Nadir CD4, cells/mm3 (range)	Current CD4, cells/mm3 (range)	Current Plasma HIV RNA
N=62	53 (30-63)	24 (39%)	40 (65%)	19.9 (2.4-34.8)	12.6 (2.1-29.9)	114.8(1-650)	653 (124-1492)	<40 copies/ml

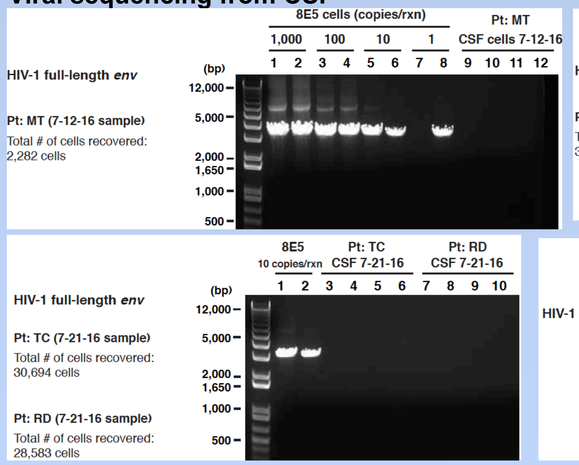
RESULTS

Clinical Comparisons	CSF > Plasma HIV (n=9)	CSF ≤ Plasma HIV (n=53)	P-value
Age, mean years	54	53	0.94
Female, %	44%	37%	0.67
African-American, %	60%	100%	0.02
CSF HIV RNA, copies/ml	74 (41-289)	-	-
Time since HIV diagnosis, mean years	20	18	0.09
Time since ART initiation, mean years	13	9	0.56
Nadir CD4, mean cells/mm^3	117	110	0.97
Current CD4, mean cells/mm^3	624	675	0.27
Beck Depression Inventory, mean	6	9	0.38

MRI Comparisons	CSF > Plasma HIV	CSF < Plasma HIV	P-value
Total Gray Matter Volume, mm^3	518,359	573,429	0.09
Total White Matter Volume, mm^3	427,812	451,964	0.42

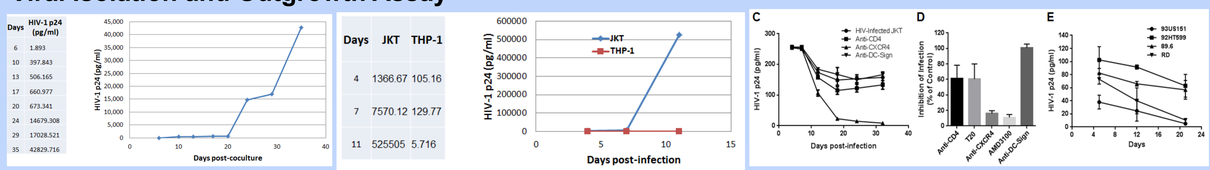
Neuropsychiatric Comparisons	CSF > Plasma HIV	CSF < Plasma HIV	P-value
% HAND	22.2	27.8	0.8
Average GDS	0.32	0.22	0.22
Average T-score	47.3	50.8	0.10

Viral sequencing from CSF



Of four patients in whom the HIV-env was amplified by PCR we found that one patient (GC) had full length env and another (RD) had defective viral sequences. 8E5 cells were used as a control

Viral Isolation and Outgrowth Assay



In one of six patients, HIV could be detected by viral outgrowth assay in CSF. The virus was T-cell tropic and could also infect astrpcytes but not monocytic cells

CONCLUSION

X4 tropic viral sequences predominate in the CSF in asymptomatic CSF escape, the clinical significance of which needs to be determined by longitudinal monitoring of changes in neurologic, cognitive, and psychiatric outcomes.