QUANTITATION OF CEREBROSPINAL FLUID PLEOCYTOSIS AND HIV-1 RNA DURING ACUTE INFECTION

Poster 0432

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BACKGROUND

- HIV-1 RNA can be detected in cerebrospinal fluid (CSF) within days after viral transmission. CSF leukocyte level (clinically determined as white blood cell count, or WBC) is linked with levels of systemic and CSF HIV-1 RNA in untreated chronic HIV infection.
- We quantitated CSF WBC and investigated its associations with HIV-1 in blood and CSF during untreated acute HIV infection (AHI).

METHODS

- Individuals with AHI were enrolled in the RV254 cohort in Bangkok, Thailand. From March 2016 to March 2019, CSF WBC was measured using standard clinical laboratory methods in a subset (61/246) of participants who underwent optional lumbar puncture.
- We measured WBC, protein and glucose in whole CSF in Chulalongkorn University Hospital, Bangkok, Thailand. HIV-1 RNA was tested in CSF supernatant by Roche COBAS TaqMan HIV-1 V2.0 with a lower limit of quantification (LLQ) of 80 copies/mL. A level of 79 copies/mL was assigned to samples with levels below LLQ (**Table 1**).
- Logistic regression was used to determine factors predicting CSF pleocytosis (WBC>5 cells/mm^3).

Table 1. Demographic and Clinical Parameters of Lumbar Puncture Participants

Male, n (%)	60 (98)
Fiebig, n (%)	
1	9 (15)
2	13 (21)
3	35 (57)
4	3 (5)
5	1 (2)
Acute retroviral syndrome, n (%)	36 (59)
Log_{10} Plasma HIV-1 RNA	6.10 (5.15-6.78)
Log_{10} CSF HIV-1 RNA	3.15 (1.90-4.11)
PCratio	2.78 (1.93.-3.29)
CD4+ T-cell	332 (IQR 242-545)
CD8+ T-cell	539 (IQR 361-799)
CD4/CD8	0.72 (IQR 0.46-1.03)
Untreated (Active) syphilis, n (%)	7 (12)
CSF WCC	2 (IQR 1-8) (range 0-105)
CSF Glucose	62 (IQR 57-69)
CSF Protein	27 (IQR 23.2-31.9)
CSF Wcc > 5, n (%)	20 (33)
CSF Wcc ≥ 10, n (%)	14 (23)
CSF Wcc ≥ 20, n (%)	6 (10)
CSF Wcc ≥ 30, n (%)	4 (7)
CSF Wcc ≥ 50, n (%)	3 (5)
Overt Meningitis Symptoms, n (%)	0(0)

SUMMARY OF FINDINGS

- None of the acute HIV participants presented with overt neurologic signs or symptoms.
- 2/3 of individuals during acute infection had CSF WBC within normal range (≤ 5 cells/mm^3).
- In the multivariate analysis, CSF pleocytosis (CSF WBC > 5 cells/mm^3 was independently associated with CSF HIV-1 levels and blood CD8 T-cells (**Table 2**).
- Emergence CSF pleocytosis lagged behind the rise in CSF HIV-1 RNA during acute infection, suggesting that marked CSF lymphocytosis is not necessary to early CNS viral transmigration. (**Figure 1**).
- Four outliers had CSF WBC > 40 cells/mm^3 of whom 2 were later diagnosed with neurosyphilis (**Table 3**).

RESULTS

Table 2. Logistic Regression Model for Factors Associated with CSF WBC > 5 cells/mm^3

	Univariate		Multivariate*	
	OR (95%CI)	p-value	aOR (95%CI)	p-value
Age	1.00 (0.94 – 1.07)	0.89		
Log_{10} Plasma HIV-1 RNA	1.75 (1.02 – 2.99)	0.04		
Log_{10} CSF HIV-1 RNA	2.93 (1.61 – 5.35)	<0.001	2.69 (1.44 – 5.04)	0.002
PC ratio	0.54 (0.30 – 0.98)	0.04		
CD4+ T-cells, per 100 cells/ul	0.87 (0.67 – 1.13)	0.29		
CD8+ T-cells , per 100 cells/ul	1.29 (1.07 – 1.56)	0.008	1.24 (1.00 – 1.54)	0.046
CD4/CD8	0.18 (0.04 – 0.87)	0.03		NS
Fiebig				
I-II	0.20 (0.05 – 0.81)	0.02		NS
III-V	**Ref.**			
HCV infection				
No	**Ref.**			
Yes	0.744 (0.13 – 35.5)	0.606		
Untreated syphilis				
No	**Ref.**			
Yes	1.63 (0.33 – 8.11)	0.55		
ARS				
No	**Ref.**			
Yes	2.86 (0.88 – 9.33)	0.08		NS

NS = Not Significant

Figure 1. CSF WBC, CSF & Plasma HIV-1 RNA Levels by Fiebig Stage

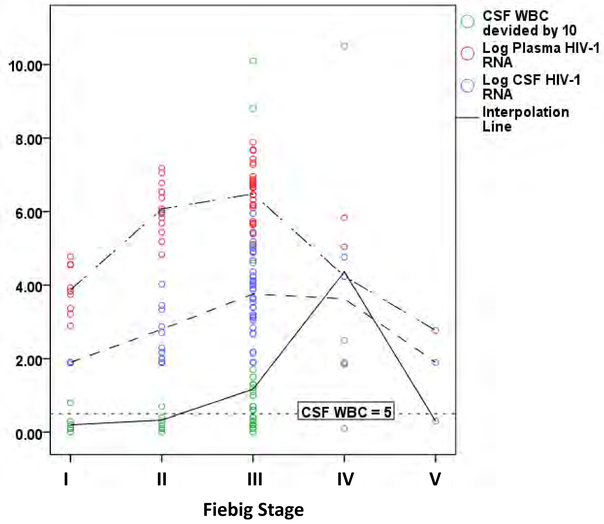


Table 3. Clinical Parameters of Extreme CSF WBC Outliners (>40 cells/mm3)

PID	Fiebig	CSF WBC	CD4/CD8	Log_{10} Plasma VL	Log_{10} CSF VL	HCV	Untreated syphilis	Neuro-syphilis	CSF VDRL/TPHA	Plasma VDRL/TPHA
465	3	101	0.09 (195/2198)	6.66	5.08	-	-	-	-/ND	-/-
494	4	105	0.60 (101/169)	5.04	4.23	+	+	+	-/+	+/+
539	3	46	0.44 (262/593)	6.84	4.92	-	-	-	-/ND	+/+
553	3	88	0.23 (217/960)	7.89	5.95	-	+	+	-/+	+/+

Abbreviations: VL = viral load

LIMITATIONS

- Samples sizes of Fiebig IV and V are small (n= 3 & 1 respectively).
- Potential effect of HIV-1 subtype was not analyzed due to limitation of sample size.
- All participants initiated antiretroviral therapy within days after the acute HIV infection diagnosis, and thus natural history and long term CNS consequence of untreated CSF pleocytosis starting in AHI remains undetermined.

CONCLUSIONS

- Despite the overt elevation of immune activation markers in CSF [1], CSF pleocytosis is relatively uncommon during acute HIV infection in comparison to primary and chronic HIV infection.
- CSF pleocytosis appears to emerge temporally after CSF viremia, suggesting that marked CSF lymphocytosis is not necessary to early CNS viral transmigration.
- Future studies should examine the functionality of the excessive T-cells among those with CSF pleocytosis and whether the presence of pleocytosis may impact central nervous system outcomes in long term follow up after ART.

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Disclaimers

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