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Acute HIV plasma/CSF HIV RNA ratios are variable and greater than in chronic HIV

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Background

Clarifying the early dynamics of HIV invasion into the central nervous system (CNS) will inform understanding of the neurologic complications of HIV, and may facilitate cure interventions that rely on preventing establishment of viral reservoirs.

Methods

Forty-two Thai subjects identified in the acute phase of HIV infection (Fiebig I-V) had plasma and cerebrospinal fluid (CSF) samples for viral load and cytokine analysis, and magnetic resonance spectroscopy (MRS) an average of 16 days after self-reported estimated date of infection and all with measurable HIV RNA in plasma. We examined factors associated with ultra-low CSF HIV RNA (unquantifiable or undetected) compared to those with measurable CSF HIV RNA and examined the mean difference between log10 plasma and CSF HIV RNA during acute HIV infection (AHI). Pre-cART plasma and CSF viral loads were compared to that of 42 Thai cases evaluated just prior to cART initiation during chronic HIV.

Results

AHI subjects (n=42) were mean age of 29.8 (+/-7.8) and 9.5% female, whereas the 42 chronic cases were mean age of 34 (+/-6.6) and 54.8% female. 50% of chronic cases had a diagnosis of HIV-associated neurocognitive disorder (HAND). The mean difference between log10 plasma and CSF HIV RNA was 2.7 +/-1.4 for AHI compared to 0.8 +/-1.0 for chronic cases (p<0.0001). Ten of 42 AHI subjects had unquantifiable CSF HIV RNA and these cases tended towards the earliest stages of infection: Fiebig I (n=8); II (n=1); III (n=1). Individuals with undetectable CNS HIV RNA were then one-to-one matched by Fiebig stage to a random selection of cases with quantifiable CSF HIV RNA. Cases with unquantifiable CNS HIV RNA showed lower serum neopterin (p<0.05) and trended toward lower log10 CSF IP-10 (p<0.08).

Conclusions

The difference between log10 plasma and CSF HIV RNA (ratio of plasma/CSF) is significantly higher in acute compared to chronic HIV infection, with some individuals in the earliest stages of AHI manifesting ultra-low levels of HIV RNA in CSF. Subjects with initially ultra-low CSF HIV RNA trend towards lower markers of monocyte activation.

Acute vs. chronic HIV infection

	Acute HIV	Chronic HIV
Subjects	42	42
Percent male	91	45.4
Mean age	30	34
Infection duration, est. days (range)	15.7 (4-28)	-

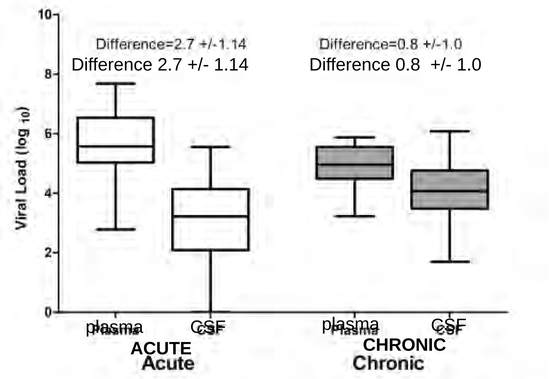

Figure 1. Mean HIV RNA in plasma and CSF for acute and chronically infected HIV subjects

Acute HIV infection (AHI)

	Ultra-low CSF HIV RNA (n=10)	Quantifiable CSF HIV RNA (n=32)
Percent male	90	91
Age (range)	35 (21-48)	28 (19-46)
Infection duration, est. days (range)	14 (4-25)	16 (5-28)
% Fiebig I (n)	80 (8)	12.5 (4)
% Fiebig II (n)	10 (1)	9.4 (3)
% Fiebig III (n)	10 (1)	62.5 (20)
% Fiebig IV (n)	0 (0)	6.3 (2)
% Fiebig V (n)	0 (0)	9.4 (3)

Table 2. Demographics for acutely infected HIV subjects with or without quantifiable CSF HIV RNA

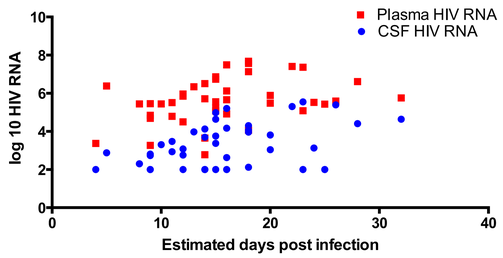

Figure 2. HIV RNA in plasma and CSF at diagnosis for acutely infected HIV subjects compared to estimated days of infection

Immune activation biomarkers in AHI participants with undetectable vs. detected CSF HIV RNA, matched by Fiebig stage

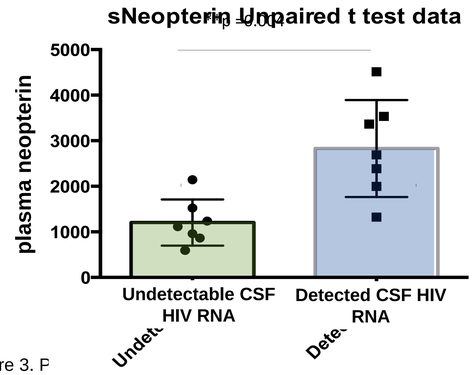

Figure 3. P
undetectable vs. detected CSF HIV RNA

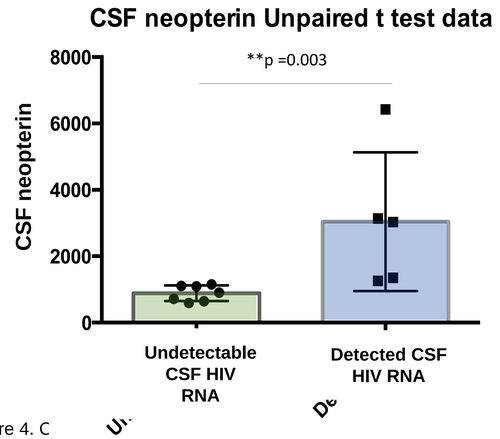

Figure 4. C
undetectable vs. detected CSF HIV RNA

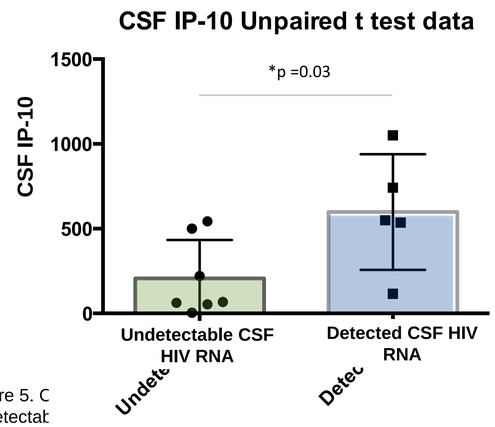

Figure 5. C
undetectab

Conclusions

- The plasma/CSF ratio (log10 plasma HIV RNA/log 10 CSF HIV RNA) was significantly greater in acute HIV infection (AHI) compared to chronic HIV infection.
- **Ten of 42 AHI individuals manifested ultra-low levels of HIV RNA in CSF.**
- Subjects with AHI with ultra-low CSF HIV RNA levels **trended towards the earliest Fiebig stages.**
- In AHI, ultra-low CSF HIV RNA was **not associated with estimated infection duration or plasma HIV RNA level.**
- **AHI subjects with undetectable CSF HIV RNA** had **lower markers of immune activation** in the plasma and CSF, specifically:
  - **plasma neopterin** (macrophage activation)
  - **CSF neopterin** (macrophage activation)
  - **CSF IP-10** (lymphocyte chemokine)
- A magnetic resonance spectroscopy (MRS) measure of neuronal inflammation, choline/creatinine, did not correlate with CSF HIV RNA in acute HIV infection

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