CD8 T-Cells in HIV related neurocognitive impairment (NCI)

T Rawson[1], T J Barber[2], W P Kelleher[1], S Mandalia[1, 2], B Gazzard[2], A Pozniak[2]

[1]Imperial College London, London UK

[2]St Stephen's Centre, Chelsea and Westminster Hospital NHS Foundation Trust, London UK

Background

There is much evidence in the literature associating factors such as plasma viral load (pVL) and CD4 lymphocytes to the pathogenesis of HIV related NCI[1, 2]. There is still, however, little evidence in the literature regarding CD8 lymphocytes in this process. Multiple studies have suggested CD8 lymphocytes may be a possible marker for inflammation a contributing factor to NCI[3, 4].

This preliminary analysis aimed to investigate any associations of HAND with CD8 lymphocytes.

Methods

We retrospectively audited data from our HIV related NCI screening clinic, open for referral to all HIV infected patients between 18-50 years of age (there is a separate service for patients over 50 years). All patients seen in this clinic are screened for depression (PHQ9) and anxiety (GAD7) prior to neurocognitive testing. Patients at risk of NCI were identified using the International HIV Dementia Scale (IHDS≤10) and Brief NeuroCognitive Screen (BNCS). This included Trailmaking A&B (TMA/TMB) and Digital Symbol Testing (DST). The Everyday Memory Questionnaire (EMQ) was used as a subjective assessment of memory.

Electronic patient records were used to collect HIV associated laboratory parameters from the time these tests were performed. Statistical analysis to look for significance between results was done using Mann Whitney testing.

Characteristic	Description	Entire Cohort
Age	Mean (Range)	46 (30 – 73)
Sex	M:F	33 : 1
CD4	Median (Range)	545 (114 – 1065)
Nadir CD4	Median (Range)	178 (0 – 826)
CD3	Median (Range)	1456 (580 – 2949)
CD8	Median (Range)	901 (443 – 2170)
Nadir CD8	Median (Range)	443 (0 – 1270)
Peak CD8	Median (Range)	1290 (563 – 2803)
Ratio	Median (Range)	0.5 (0.1 – 1.1)
pVL	Detectable : Undetectable	11 : 23
	Median (Range) of Detectable	283 (51 – 82100)
On ART	Yes : No	28 : 6

Table 1: Cohort (n=34) demographics and neurocognitive testing results.

Abbreviations: pVL = HIV plasma viral load; ART = antiretroviral therapy;

Results

- We excluded subjects with confirmed anxiety or depression
- This left 34 patients for analysis
- 5 had an abnormal total EMQ score (average >2.07), with 3 patients scoring abnormally in the retrieval (R>2.68) and 3 in accrual (A>1.89) components.
- 10 patients scored ≤10 in IHDS
- We are currently defining the normal range for composite BNCS scores in our cohort [5] with an aim of using the NPZ3 method which Ellis et al (2005) showed to be more sensitive and specific than using impairment points to evaluate NCI[6]
- For this pilot study, however, we took being >1s.d. away from the mean in at least 1/3 tests to be abnormal
- Using this criteria 4/34 subjects were abnormal on BNCS
- In total 12/34 patients had an abnormal IHDS and/or BNCS

	Abnormal Score (N=12)	Normal Score (N=22)	P - Value
Median CD8 (Range)	969 (461 – 2170)	886 (448 – 1428)	0.632
Median Peak CD8 (Range)	1479 (563 – 2803)	1234 (853 – 2759)	0.607
Median Nadir CD8 (Range)	422 (101 -912)	531 (0 – 1270)	0.234
Median Ratio (Range)	0.5 (0.2 – 1.0)	0.5 (0.1 – 1.1)	0.957

Table 2: Table comparing median CD8, peak CD8, nadir CD8 and CD4:CD8 ratios between patients who scored abnormally on the International HIV Dementia Scale (IHDS ≤10) and/or Brief NeuroCognitive Screen (BNCS) testing (n=12) against the rest of our cohort (n=22), who all scored normally in these tests (n=22). P-Values between groups were calculated using Mann-Whitney statistical testing.

Conclusion

In this small group we have shown no correlation between HIV related NCI and current, peak or nadir CD8 counts, or CD4:CD8 ratio.

BNCS scores were not used to construct composite neuropsychometric z (NPZ) scores for this early analysis, nor were they compared to standardised population norms. This may have slightly overcalled NCI in this small group, although it is unlikely to have affected outcomes in terms of our CD8 analysis.

It may be worth further considering the role of inflammation and CD8 T cells in larger neurocognitive studies to more clearly determine the role of CD8 T cell levels in the pathogenesis, or for the diagnosis and monitoring, of HIV related NCI, whilst also considering the role of other CSF or plasma inflammatory biomarkers.

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