Cerebrospinal fluid HIV RNA and viral nucleic acid detection in persons with HIV

Manraj Bawa[1*], Merle Henderson[1,2*], Nuala Pepper[1*], David Muir[3], Alex Everitt[4], Nicola E. Mackie[2], Alan Winston[1,2]

[1] Department of Infectious Disease, St Mary's Campus, Imperial College London, London. [2] Department of HIV and GU Medicine, St Mary's Hospital, London.
[3] North West London Pathology, Charing Cross Hospital, London. [4] Department of Neurology, St. Mary's Hospital, London.

Background

- AIDS-related central nervous system (CNS) conditions have declined in incidence since the introduction of antiretroviral therapy (ART), but neurological symptoms remain commonly reported in people with HIV.
- Cerebrospinal fluid (CSF) analysis is hence used to assess for CNS conditions, including CSF HIV RNA escape and opportunistic viral CNS infections.
- However, literature on the frequency of CSF escape and non-HIV viral nucleic acid detection in the modern ART era is limited.

Aims

- In people with HIV undergoing CSF examination for clinical indications, we aimed to:
  1. **Determine the recent frequency of CSF escape and non-HIV viral nucleic acid detection.**
  2. **Evaluate the clinical factors associated with positive findings.**

Methods

- Data were collected from Imperial College Healthcare NHS Trust, a large London HIV centre responsible for the care of 3362 people with HIV.
- People with HIV with CSF virology results from 2017-2022 were identified from pathology records, and their electronic clinical notes were retrospectively reviewed for demographic, clinical and laboratory data.
- CSF HIV RNA escape was defined as CSF HIV RNA concentrations greater than in the plasma. HIV RNA <20 copies/mL were considered undetectable.
- CSF viral panel included herpes simplex virus type 1 (HSV-1) and 2 (HSV-2), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus 6 (HHV-6) and JC virus (JCV).
- For case detection in ≥5 individuals, associated factors were assessed using linear regression modelling.

Results

- **114 patients with CSF virology results identified**
  - **Baseline demographics:**

81 (71%) male | 49 (43%) white, 30 (27%) black | Median age 48.8 years | Median CD4 546 cells/μL (range 12-2390)

  - **Indication for CSF examination:**
    - New-onset neurological symptoms, n=84 (74%)
    - New-onset psychiatric symptoms, n=6 (5%)
    - Investigation for neurosyphilis, n=24 (21%)

2) Positive non-HIV CSF virology in 16 of 98 patients (16%)

- **One virus detected in CSF of 13 patients**
- **Multiple viruses detected in CSF of 3 patients**
- EBV was the most frequent CSF virus, detected in 10 patients
- Only VZV and JCV in the CSF were clinically significant

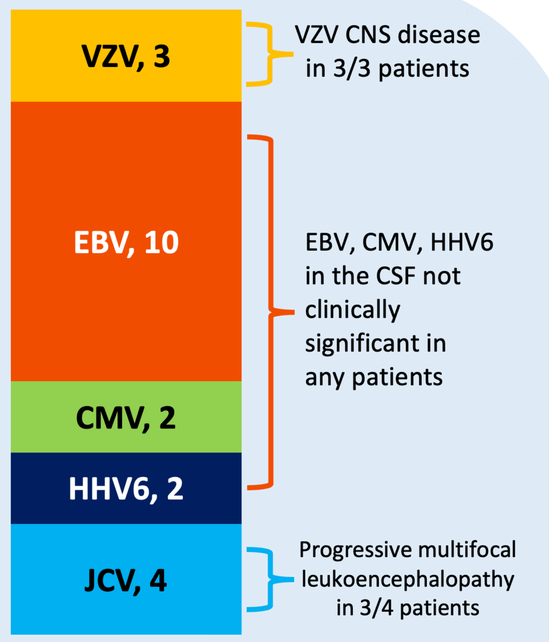

Fig. 1: Number of patients with positive CSF virology for each virus, and the associated diagnoses

1) CSF HIV RNA escape present in 19 of 114 patients (17%); CSF escape patients were:

- **More likely to have CSF HIV drug-resistance mutations**
- **Less likely to be on ART regimens containing an INSTI**
- No other statistically significant associations were observed

Parameter	No CSF Escape (N=95)	CSF Escape (N=19)	p-value
Previous AIDS†	21 (22)	6 (32)	0.384
On ART	N=75	N=18	
INSTI-containing†	36 (48)	3 (17)	**0.017***
PI-containing†	27 (36)	10 (55)	0.180
Current CD4 count§ *(cells/μL)*	510 (12-2390)	698 (42-1311)	0.223
Nadir CD4 count§ *(cells/μL)*	250 (3-968)	190 (10-600)	0.410
Low-level plasma HIV viraemia† *(20-200 HIV RNA copies/mL)*	19 (20)	8 (42)	0.071
Plasma HIV drug mutation†	4 (4)	1 (5)	>0.999
CSF HIV drug mutation†	2 (2)	3 (16)	**0.032***

Table 1: Clinical and laboratory parameters associated with CSF HIV RNA escape
*† - n (%); § - median (range); * - p < 0.05 statistically significant*

3) Detectable EBV in the CSF was statistically significantly associated (p<0.05) with:

- **Previous AIDS, and lower current and nadir CD4 counts**
- **CSF pleocytosis and concomitant CNS infections**
- But did not correlate with the presenting symptoms and was not deemed to be clinically relevant in any patients

Conclusions

- **CSF escape was detected in 1 in 6 people with HIV with neurological symptoms**, a frequency unchanged from historical data.
- Clinicians should thus remain vigilant for CSF escape as a potential cause of neurological symptoms, and should also consider HIV drug resistance testing in individuals with confirmed CSF escape.
- **EBV DNA was detected in 1 in 10 individuals in our study**, but was not itself considered to be clinically relevant.
- Based on associations with CSF pleocytosis and concomitant CNS infections, EBV DNA in the CSF may have been caused by viral trafficking into the CSF compartment.

References: 1. European Aids Clinical Society (EACS) Guidelines V11.1. PART IV p104. 2022. 2. Eden et al. J Infect Dis 2010;202:1819 25. 3. Cinque et al. AIDS 1996; 10(9):951-958.

Presenting author: Manraj Bawa, manraj.bawa@nhs.net