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

Manraj Bawa1, Merle Henderson1,2, Nuala Pepper1, David Muir3, Alex Everitt4, Nicola E. Mackie2, Alan Winston1,2

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, Median age 48.8 years, Median CD4 546 cells/μL (range 12-2396)
  ▪ Indication for CSF examination:
    • New-onset neurological symptoms, n=84 (74%)
    • New-onset psychiatric symptoms, n=6 (5%)
    • Investigation for neurosyphilis, n=24 (21%)

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No CSF Escape (N=95)</th>
<th>CSF Escape (N=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous AIDS†</td>
<td>21 (22)</td>
<td>6 (32)</td>
<td>0.384</td>
</tr>
<tr>
<td>On ART</td>
<td>N=75</td>
<td>N=18</td>
<td></td>
</tr>
<tr>
<td>INSTI-containing‡</td>
<td>36 (48)</td>
<td>3 (17)</td>
<td>0.017†</td>
</tr>
<tr>
<td>PI-containing‡</td>
<td>27 (36)</td>
<td>10 (55)</td>
<td>0.18</td>
</tr>
<tr>
<td>Current CD4 count§ (cells/μL)</td>
<td>510 (12-2390)</td>
<td>696 (42-1311)</td>
<td>0.223</td>
</tr>
<tr>
<td>Nadir CD4 count§ (cells/μL)</td>
<td>250 (3-968)</td>
<td>190 (10-600)</td>
<td>0.410</td>
</tr>
<tr>
<td>Low-level plasma HIV viraemia¶ (20-200 HIV RNA copies/mL)</td>
<td>19 (20)</td>
<td>8 (42)</td>
<td>0.071</td>
</tr>
<tr>
<td>Plasma HIV drug mutation¶</td>
<td>4 (4)</td>
<td>1 (5)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>CSF HIV drug mutation¶</td>
<td>2 (2)</td>
<td>3 (16)</td>
<td>0.032†</td>
</tr>
</tbody>
</table>

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

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

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.