Neuroretinal Degeneration in HIV

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KEY POINTS

• Patients with well-suppressed HIV-infection show minimal signs of neuroretinal loss.
• The slight increase in retinal thickness detected in these patients might reflect chronic low-grade inflammatory activity.

BACKGROUND

Loss of neuroretinal structure and function, ascribed to a ‘HIV-associated Neuroretinal Disorder’ (HIV-NRD), in the absence of ocular opportunistic infections, has been reported in HIV-infected individuals treated with combination antiretroviral therapy (cART). Whether HIV-infected individuals with prolonged well-suppressed infection remain at risk for HIV-NRD, is unknown.

METHODS

Study Participants

<table>
<thead>
<tr>
<th>Data are presented as median (range) or %</th>
<th>HIV+ men (n=92)</th>
<th>HIV- men (n=63)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.5 (45-76)</td>
<td>52 (45-80)</td>
<td>0.940</td>
</tr>
<tr>
<td>Prior clinical AIDS</td>
<td>32.6%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Known duration HIV, years</td>
<td>14.5 (1-27)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nadir CD4 cell count, cells/µl</td>
<td>180 (0-620)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Current CD4 cell count, cells/µl</td>
<td>595 (320-1110)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cumulative duration CD4 &lt;200 cells/µl, months</td>
<td>0.78 (0 - 96.8)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Undetectable viral load, year before enrollment</td>
<td>98.9%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cumulative duration undetectability, years</td>
<td>10.2 (0-15.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CD4/8 ratio</td>
<td>0.75 (0.29-4.13)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Years since start of first ART</td>
<td>12 (1-21)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ever-smokers</td>
<td>76.1%</td>
<td>56.7%</td>
<td>0.012</td>
</tr>
<tr>
<td>Hypertension; using medication</td>
<td>29.3% (63%)</td>
<td>29.5% (44.4%)</td>
<td>0.983</td>
</tr>
</tbody>
</table>

Optical Coherence Tomography (OCT)

Spectral-Domain OCT images (Topcon 3D OCT-1000) were used to obtain thickness measurements of total retina & individual retinal layers (Figure 1), as well as peripapillary retinal nerve fiber layer (Figure 2), following automated segmentation with the Iowa Reference Algorithm².

RESULTS

OCT

Peripheral RT significantly increased in the HIV+ group (279.8 ± 12.5 µm vs 274.4 ± 12.0 µm, P=0.029), predominantly due to an increase in INL+ OPL thickness (57.2 ± 3.0 µm vs 55.2 ± 3.6 µm, P<0.001)

CS

Pelli Robson CS significantly lower in HIV+ (1.89 vs 1.93 logCS; P=0.001)

No difference in TCS values between HIV+ and HIV- (2.17 vs 2.17 logCS; P=0.888).

DISCUSSION

• Pelli Robson CS: only 1 letter loss in HIV+ not clinically relevant
• No difference in TCS values: discrepancy PR and TCS outcomes PR outcome influenced by optical aberrations, TCS purely retinal function
• Instead of expected neuroretinal thinning increase of retinal thickness in HIV= unexpected finding low grade inflammatory activity?
• Different results compared to most previous studies: likely due to better immunological status AgeHIV cohort & inclusion of highly similar control group

FUTURE

• Retinal vascular caliber measurements: subclinical vasculopathy?
• Comparison OCT and retinal vessel calibers with MRI examinations and neuropsychological assessment: similar underlying pathophysiology retina & brain?
• Follow-up measurements complete at end of 2015: changes over time?
• Additional tests visit 2: color vision, FDT perimetry (central 20° visual field), Rarebit perimetry (central 4° visual field)

REFERENCES

1. Demirkaya et al. Neuroretinal degeneration in HIV patients without opportunistic ocular infections in the cART era. AIDS Patient Care STDS. 2015 Jun; 29(6):299-311

FIGURE 1. Spectral-Domain OCT scan with segmented retinal layers

A. RNFL= Retinal Nerve Fiber Layer
B. GCL= Ganglion Cell Layer
C. IPL= Inner Plexiform Layer
D. INL= Inner Nuclear Layer
E. OPL= Outer Plexiform Layer
F. ONL+IS= Outer Nuclear Layer+ Inner Segments
G. OS= Outer Segments
H. RPE = Retinal Pigment Epithelium

FIGURE 2. Left: Example of peripapillary ring (blue) centered around the optic disc for measurement of the RNFL thickness, averaged and in quadrants: S: superior, N: nasal, I: inferior, T: temporal. Right: Analysis of RNFL thickness in quadrants shows a characteristic ‘double hump’ pattern with RNFL peaks in the superior and inferior quadrants and troughs in the nasal and temporal quadrants.

Contrast Sensitivity (CS)

FIGURE 3. Left: Pelli Robson chart (‘gold’ standard). Right: C-Quant device (new method)³. Measuring TCS: The stimulus consists of a circular test area, radius 1.6º, divided in two halves (A/B), surrounded by an area of constant luminance (C). Average luminance of the stimulus and the surround is 25 cd m². Randomly in one half, 8 Hz square wave flicker is applied. The subject has to choose which half (A or B) is flickering. Of note, the Pelli Robson outcome is influenced by both optical and retinal components, while TCS assesses purely retinal function.

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