Introduction

- Retinal vein occlusion (RVO)
  - Vascular damage by complex cellular & inflammatory reactions.
  - Disturbed balance of cytokines in ocular fluid of RVO.

- Concentration of aqueous or vitreous cytokines
  - Cytokine levels in aqueous humor are supposed to reflect levels in the vitreous.
  - VEGF, IL-6, IL-8, MCP-1, PIGF, and TNF-alpha in aqueous and vitreous humor.

- Measurement of angiogenic & inflammatory cytokines
  - Quantification of UWF FA images with best corrected visual acuity (BCVA) and central macular thickness (CMT).

Methods

- Study design
  - Prospective cross-sectional study.
  - To investigate the extent and location of nonperfusion area (NP) associated with changes of aqueous cytokines in patients with macular edema secondary to retinal vein occlusion (RVO) to analyze their association with best corrected visual acuity (BCVA) and central macular thickness (CMT).

- Exclusion criteria
  - Any previous treatment, other evidence of maculopathy.
  - Age-matched control subjects (n=9).

- Equipment and techniques
  - Using stereographic projection technique from the early (45 sec), middle (2 min 30 sec), and late (5 min) phases UWF FA.
  - Area and length of the lesions to be automatically calculated in mm² by correcting the non-linear distortion.

- Analysis
  - Areas of peripheral retinal nonperfusion and treatment response in branch and central retinal vein occlusion.
  - Relationships between retinal thickness and cytokines & VA.

Results

Table 1. Baseline demographics

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Age (years)</th>
<th>Sex (M:F)</th>
<th>BCVA (logMAR)</th>
<th>SubCFT (µm)</th>
<th>Total area of retina (µm²)</th>
<th>Isometric area of retina (µm²)</th>
<th>Isometric index</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVO (n=31)</td>
<td>63.75 ± 12.72</td>
<td>10:21</td>
<td>0.38 ± 0.46</td>
<td>370.29 ± 47.36</td>
<td>337.44 ± 133.82</td>
<td>9.34 ± 0.32</td>
<td>0.0041</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Distribution of ischemic area according to retinal zones

<table>
<thead>
<tr>
<th>Partial ischemia</th>
<th>Nonperfusion area (µm²)</th>
<th>P-value</th>
<th>Isometric index</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perimacular (µm²)</td>
<td>6.74 ± 7.55 (3.56%)</td>
<td>&lt;0.001</td>
<td>0.01 ± 0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Near periphery (µm²)</td>
<td>85.62 ± 41.05 (23.96%)</td>
<td>0.11 ± 0.10</td>
<td>0.10 ± 0.10</td>
<td>0.06 ± 0.04</td>
</tr>
<tr>
<td>Far periphery (µm²)</td>
<td>20.43 ± 24.00 (15.60%)</td>
<td>0.06 ± 0.04</td>
<td>0.06 ± 0.04</td>
<td>0.06 ± 0.04</td>
</tr>
<tr>
<td>Complete ischemia</td>
<td>22.00 ± 88.47</td>
<td>0.10 ± 0.09</td>
<td>0.10 ± 0.09</td>
<td>0.10 ± 0.09</td>
</tr>
<tr>
<td>Perimacular (µm²)</td>
<td>2.25 ± 3.72 (3.56%)</td>
<td>&lt;0.001</td>
<td>0.00 ± 0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Near periphery (µm²)</td>
<td>74.03 ± 27.24 (23.96%)</td>
<td>0.05 ± 0.05</td>
<td>0.05 ± 0.05</td>
<td>0.05 ± 0.05</td>
</tr>
<tr>
<td>Far periphery (µm²)</td>
<td>30.43 ± 16.98 (26.24%)</td>
<td>0.05 ± 0.02</td>
<td>0.05 ± 0.02</td>
<td>0.05 ± 0.02</td>
</tr>
</tbody>
</table>

Table 3. Correlation of ischemic and cytokines, VA & CMT

- Total and partial ischemia showed significant correlation with CMT, Ang-1, Ang-2, MCP-1, IL-8, IL-6, PIGF, and VEGF-A.
- Complete ischemia may be the results of increased cytokines.
- Partial ischemia was mainly distributed in posterior retina & mid-periphery.
- Complete ischemia was predominantly involved with partial ischemia reperfusion during acute phase.

Conclusion

- Antiangiogenic and inflammatory cytokines in aqueous were overexpressed in RVO patients and showed a distinct differences according to the location and extent of NP.
- In acute phase of RVO, mid-periphery, which is predominantly involved with partial ischemia reperfusion and the blood oxygenation deficiency, contributed to the production of angiogenic cytokines.
- Complete ischemia may be the results of increased cytokines.
- Clinically, anti-VEGF with targeted retinal photocoagulation for complete ischemia may not reduce treatment burden for the patients with ME related to RVO.

References

- Association of inflammatory factors with macular edema in branch retinal vein occlusion. Orshansky Y et al. Ophthal. 2011