Vitreoretinal Lymphoma: Changing Trends in Diagnosis and Local Treatment Modalities

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Abstract# 3074

Background

- Primary intraocular/vitreoretinal lymphoma (PIOL/PVRL), a rare eye malignancy, accounts for <1% of all non-Hodgkin’s lymphoma (NHL).
- Secondary IOL is usually associated with central nervous system (CNS) NHL and represents metastasis to uvea, and is considered as low-grade, extranodal, marginal zone, B-cell type.
- PVRL involves vitreous, retina, subretinal space and rarely optic nerve and usually of diffuse large B-cell lymphoma.
- PVRL mimics chronic uveitis and vitritis with many relapses and resistance to steroids and is associated with poor visual and clinical outcomes.
- Delay in diagnosis is common and diagnosis can be made by vitreous aspiration/biopsy cytology.
- Newer methods for definite diagnosis of lymphoma are:
  - Immunochemistry (CD3, CD19, CD20, CD22 with kappa or lambda chain restriction)
  - Biochemical (IL-6, IL-10 levels)
  - Molecular markers (Ig H & T cell receptor gene rearrangement)
- Treatment options:
  - Enucleation
  - External beam radiation therapy (EBRT)
  - Systemic chemotherapy-combination therapy, intrathecal chemotherapy-methotrexate, cytarabine, intravitreal chemotherapy-methotrexate & rituximab
  - Autologous stem cell transplantation

Purpose

- To report changing trends in treatment EBRT & intravitreal chemotherapy from a single institution and report clinical & ocular imaging findings of patients with VRL.

Material and Methods

- Retrospective chart review of 8 patients with non-responsive uveitis & vitritis was performed
- Data recorded included:
  - Demographics
  - Systemic lymphoma status & treatment
  - Ocular symptoms & clinical findings
  - Optical coherence tomography (OCT)
  - Fluorescein angiography (FA)
  - Immunophenotyping, biochemical and molecular markers
- Treatment methods:
  - Intravitreal methotrexate (MTX): 300 μg/0.05 ml biweekly for 1 month, weekly for 1 month and monthly maintenance injections.
  - Intravitreal rituximab: 1000 μg in 0.1 cc, once a month till corneal epitheliopathy stabilized and then switched back to methotrexate
  - EBRT: 3600-4500 cGy
  - Response to treatment
- Ocular & systemic lymphoma outcomes at last follow-up visit.

Results

- Mean age 64.5 years (range: 50-83).
- CNS-NHL was present in 7 of 8 pts (87.5%).
- Iritis and uveitis were seen in 6 eyes (50%) and vitritis in 11 eyes (91.7%).
- Retinal infiltrates were present in 8 eyes (66.7%).
- Two eyes had choroidal lesions (16.7%).
- On OCT, mean central foveal thickness was 270 μ (range 215-371) with presence of CME in 2 eyes, SRF in 1 and RPE irregularities in 3 eyes.
- Most common FA findings were macular edema in 6 eyes (60%), perivascular leakage in 2 (20%) and no leakage in 2 eyes (20%).
- Vitreous biopsy revealed B cell lymphoma in all patients (100%).
- Immunocytologic analysis in 2 pts showed elevated levels of IL-6 (26.7 pg/ml), IL-10 (12783.5 pg/ml) and IgH gene rearrangement.
- Three pts were treated with EBRT (36-45 Gy)
- Six eyes were treated w/ intravitreal MTX (2-15 injections, mean 9.7).
- Two pts developed marked keratitis secondary to MTX toxicity (33.3%), 1 received intravitreal rituximab injections for persistent vitritis.
- None developed rituximab related side effects.
- The mean duration of follow-up was 37.8 months (range 4-96).
- One pt died due to advanced CNS NHL 6 months after completion of treatment for VRL.

Table: Demographics and treatment outcomes

<table>
<thead>
<tr>
<th>No</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Laterality</th>
<th>Ocular symptoms</th>
<th>Prior local Rx</th>
<th>Current local Rx</th>
<th>VRL status</th>
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<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>F</td>
<td>Bilateral</td>
<td>Blurry VA</td>
<td>Topical steroids</td>
<td>Intravitreal MTX</td>
<td>Persistent</td>
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<tr>
<td>2</td>
<td>61</td>
<td>M</td>
<td>Bilateral</td>
<td>Blurry VA + Floaters</td>
<td>-</td>
<td>Intravitreal MTX, rituximab</td>
<td>Resolved</td>
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<tr>
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<td>57</td>
<td>M</td>
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<td>Blurry VA</td>
<td>Topical steroids</td>
<td>EBRT</td>
<td>Resolved</td>
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<tr>
<td>4</td>
<td>50</td>
<td>F</td>
<td>Unilateral</td>
<td>Floaters</td>
<td>-</td>
<td>Topical steroids + systemic CTx</td>
<td>Resolved</td>
</tr>
<tr>
<td>5</td>
<td>83</td>
<td>F</td>
<td>Unilateral</td>
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<td>EBRT</td>
<td>Persistent</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>M</td>
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<td>Blurry VA</td>
<td>-</td>
<td>EBRT</td>
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<td>Topical steroids</td>
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<td>Blurry VA + Floaters</td>
<td>Topical steroids</td>
<td>Intravitreal MTX</td>
<td>Persistent</td>
</tr>
</tbody>
</table>

Conclusions

- EBRT was effective in the treatment of VRL with no apparent evidence of radiation retinopathy
- Intravitreal chemotherapy provided good control rates for VRL in our limited series
- Immunophenotyping and molecular markers are additional newer modalities for definitive diagnosis of VRL
- Patients with associated CNS NHL had poorer outcomes