Vitreoretinal Lymphoma

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Overview

- Definition
  - Intraocular lymphoma mimicking intermediate, posterior, or panuveitis in older patients not responsive to steroid therapy; typical subtype is diffuse, large B-cell, non-Hodgkin's
  - Primary intraocular lymphoma (PIOL) denotes absence of central nervous system (CNS) involvement
- Symptoms
  - Blurry vision
  - Floaters
  - Scotoma
  - Frank inflammatory symptoms such as redness, pain, and photophobia are rare unless there is significant anterior segment infiltration
- Laterality
  - 80% bilateral
- Course
  - Insidious and progressive
- Age of onset
  - 50–60 years (range 15–85)
- Gender/race
  - Slight female and Caucasian predilection
- Systemic association: CNS lymphoma
  - 20% of CNS lymphoma patients have ocular disease at the time of diagnosis; however
  - If intraocular lymphoma is diagnosed first, 60–80% develop CNS disease after 2–3 years

C. S. Foster et al. (eds.), *Uveitis*, https://doi.org/10.1007/978-3-030-52974-1_62

- Overall, intraocular-CNS lymphoma makes up only 1% of all non-Hodgkin's lymphoma in immunocompetent patients (200 cases diagnosed a year in the United States)
- Higher incidence of intraocular-CNS lymphoma in acquired immunodeficiency syndrome (AIDS), post-organ transplant, and congenital immunodeficiencies

Exam: Ocular

Anterior Segment

- No or very mild external sign of inflammation
- Conjunctival hyperemia
- Keratic precipitates
- Mild Anterior Chamber reaction

Posterior Segment

- Large clumps or sheets of cells in vitreous
- Mild to very dense vitritis
- Multifocal, large, yellow sub-RPE or subretinal infiltrates

Exam: Systemic

- Headache
- Personality change
- Alertness alteration
- Memory loss
- Nausea/vomiting
- Gait imbalance
- Weakness
- Seizure

Imaging

- OCT: Sub-RPE hyper-reflective material; no CME
- FA: RPE granularity and possible blockage corresponding to sub-RPE infiltrates, but no vasculitis, papillitis, or macular leakage that would be expected in inflammatory syndromes

Laboratory and Radiographic Testing

- Gold standard for ocular diagnosis is either
  - Vitreous biopsy or sub-RPE aspirate via pars plana vitrectomy; not uncommon to need repeat biopsy if first one negative; ALL following analyses are recommended to have best yield
    Undiluted sample for cytopathology
    Diluted sample for molecular genetics to look for monoclonality
    - IgH gene rearrangement: B-cell lymphoma
    - T-cell receptor gene rearrangement: T-cell lymphoma

    Diluted sample for interleukin (IL)-6 and -10 levels
    - High IL-10/6 consistent with lymphoma
  - Chorioretinal biopsy
    Used when there is obvious, focal chorioretinal lesion but little vitreous cellularity
    Significantly higher ocular morbidity than vitreous biopsy alone (retinal detachment, vitreous hemorrhage, proliferative vitreoretinopathy, etc.)
- MRI brain to assess extent of any CNS involvement
  - Deep brain structures, especially front lobe, are more often involved than cerebral cortex compared to other brain tumors (thus change in personality and alertness).
  - Supratentorial and multicentric in half the cases; characteristically dense and diffuse enhancement with distinct borders.
- Positron emission tomography (PET) (may not detect Primary intraocular lymphoma [PIOL])
- Lumbar puncture: Required in all patients suspected of CNS lymphoma

Differential Diagnosis

- Sarcoidosis
- Tuberculosis
- White dot syndromes, especially Birdshot
  - White dot syndrome in an older patient ➔ think lymphoma
- Viral retinitis
- Lymphoid hyperplasia of the uvea (usually unilateral and responds well to steroids)
- Amelanotic uveal melanoma
- Uveal metastasis

Treatment

- Local therapies

  - Intravitreal methotrexate (MTX) 400 mcg/0.1 cc or rituximab (RTX) 1 mg/0.1 cc weekly for 6 weeks, extended as needed if cellularity or lesion persists; repeat cycles as needed
  - If subretinal lymphoma is threatening macula and there is little suspicion for infectious uveitis, then empiric intravitreal MTX may be appropriate before biopsy result is available
  - External beam radiation
- Given the high rate of eventual CNS involvement, we recommend systemic chemotherapy as prophylaxis even if there is no CNS involvement at the time of diagnosis

Referral/Co-management

- Neuro-oncology
- Radiation oncology
- Neurology