Case Study

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8/23/13
Case

- 65 year old male with recent onset decreased vision OD diagnosed as multifocal choroiditis with pan uveitis. A month prior to presenting to MERSI he developed blurred vision OD with a black veil in center with a hole with “shimmering of lights”.

- Ocular Meds:
  - Omnipred 6x/day OD
  - finished Valtrex 1gm QID for 10 days (questionable herpes iritis)
  - Avelox for 14 days
  - Prednisone 30mg daily for 15 days.

- Ocular Hx:
  - CE/IOL OD 3/08
  - Diagnostic PPV 11/08
    - Unable to perform IL 6 studies. IL 10 was elevated
  - CE/IOL OS 12/08
Case

- He tested positive for CMV antibodies and he was started on Valcyte.
- PMHx:
  - Lyme disease
  - Seasonal allergies
  - Sinus disease
  - Fungal rashes
  - Recent joint and lower back pain.
- FHx:
  - Father has a history of Histoplasmosis, Mother with Crohn's disease, Brother with diverticulitis.
Case

- Exam: OD OS
  - Vision: 20/50 20/20
  - IOP: 20 16
  - Anterior exam: normal deep quiet chambers OU
  - Posterior exam: Vitreous haze OD
    Vitreous debris OD
    Scattered punctate choroidal lesions OD
Photos 3/09
FAF
Case 4/09

- Patient feels his vision is worsening despite being on valcyte.
- On follow-up his vision OD is 20/30
- Exam unchanged otherwise
- What next?
Vitreous Sample

- Diagnostic PPV done
- Insufficient samples for IL10/IL6
- Cytology showed no malignant cells
- HSV, VZV and CMV PCRs are all negative
- Clonal pattern of IgH rearrangement by PCR.
- Lumbar puncture done - no clonal pattern of IgH rearrangement in CSF noted.
Treatment

- Treatment started with IV methotrexate and rituxan
- Intravitreal MTX commenced
Follow-up 3/10

- 20/20 OU
Follow-up 9/10

- 2 weeks of floaters OS
- Vision: 20/20 OU
- 2+ vitreous cell and 2+ vitreous haze OS
- PPV OS scheduled with intravitreal MTX
Vitreous Sample OS

- Cytopathology - atypical cells with apoptotic bodies
- IL-10: IL-6 ratio of 40.6:11.0 (3.69)
- Immunoglobulin heavy gene rearrangement PCR studies showing monoclonality.
- PIOL confirmed OS and Intravitreal rituxan started OU.
Case

- MRI thus far has been normal.
- MRI in 5/12 showed widespread CNS lymphoma and IV MTX started by neuro-oncologist for 10 months.
- He has since been doing well with no CNS or ocular recurrence.
Primary Vitreoretinal Lymphoma (PVRL)

- Intraocular lymphoma represent < 1% of non-Hodgkin’s lymphomas
- Mean age 50-60 years but occur in children
- No sexual predilection
- Most are of diffuse large cell lymphomas of B cell origin.
  - T cell lymphomas are rare
- Immune suppression is a risk factor
  - AIDS
  - Transplant patients
  - Congenital immunodeficiencies
Clinical Presentation

• Symptoms:
  – Blurred vision and floaters most commonly
  – Redness and pain rarely
  – Bilateral disease but may start out unilaterally
  – Patient usually lack constitutional symptoms present in systemic lymphoma

• Signs:
  – Mild anterior segment inflammation with KPs
  – Vitreous with large clumps of sheets of cells
• Fundus can show multifocal yellow sub RPE lesions with overlying PED
• Lesions have feathery or distinct borders
• Vision is better than expected

OCT shows hyper reflective lesion at level of RPE
Diagnosis

- Many patients are referred after a trial of steroid which can shrink lesions because it is cytolytic to lymphocytes.
- Cytology of vitreous is gold standard
  - Reactive lymphocytes are mixed in with B cells
- Immunohistochemistry or flow cytometry for markers for leukocytes CD45 and B cells such as CD10, CD20 and others and monoclonal kappa and gamma light chains
Large nuclei, prominent nucleoli, and scanty basophilic cytoplasm

CD 20+ cells on immunohistochemistry
Diagnosis

• Cytokine studies
  – IL 6 – present in aqueous and vitreous in non-neoplastic uveitis
  – IL10 – potent growth factors for B cells and induce release of IgG, IgA, and IgM.
  – Elevated IL10 is suggestive of lymphoma but not diagnostic
  – IL10:IL6 ratio > 1 is an adjunct test
Relation to CNS lymphoma

- 80% of PVRL patients develop CNS lymphoma
- 20% of PCNSL present as PVRL
- Frontal lobe is most commonly involved
  - Changes in cognitive level, personality and alertness
  - Seizures and motor deficits are less common than other CNS cancers.
  - Must obtain MRI
    - Lesions show diffuse enhancement with distinct borders
  - Lumbar puncture
    - Can be normal since CNS disease lags ocular involvement
CNS Lymphoma
Treatment

- Only eyes – local therapy
  - Intravitreal MTX 400 mcg or Intravitreal Rituximab or both in alternating fashion
  - External beam radiation 30-35 Gy
  - If both eyes are involved local therapy is still preferred but systemic chemo is also an option

- CNS + Eyes
  - Systemic MTX with or without radiation.
    - Combined chemo + radiation can cause delayed neurotoxicity especially in older patients
  - Thiotepa, busulfan, and cyclophosphamide, combined with hematopoietic stem cell rescue have been tried for refractory or recurrent cases
  - Autologous stem cell transplant can also be offered
Other thoughts

- Must have a high clinical suspicion in order to diagnosis PVRL
- Management must involve a team consisting of neuro-oncologist, ophthalmologist, and pathologist experienced in examining tissue for lymphoma
References


- H. Nida Sen, MD, MHSc, Bahram Bodaghi, MD, PhD, Phuc Le Hoang, MD, PhD, and Robert Nussenblatt, MD, MPH. *Primary Intraocular Lymphoma: Diagnosis and Differential Diagnosis*. Ocul Immunol Inflamm. 2009 May–Jun; 17(3): 133–141.