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

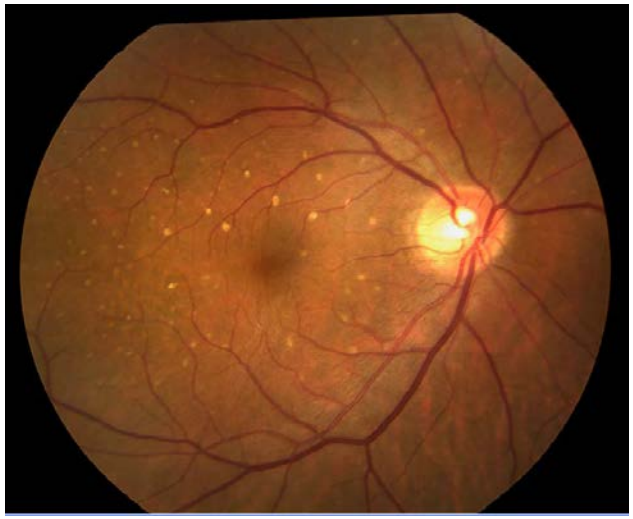
Case

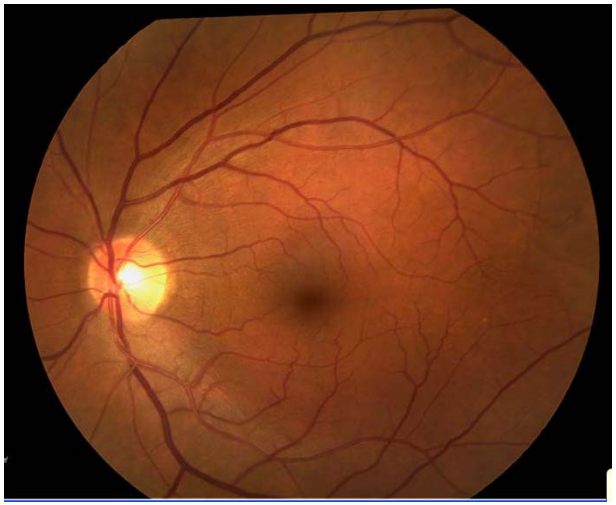
- He tested positive for CMV antibodies and he was started on Valcyte.
- PMHx:
  - Lyme disease
  - Seasonal allergies
  - Sinus disease
  - Fungal rashes
  - Recent joint and lower back pain.
- FHx:
  - Father has a history of Histoplasmosis, Mother with Crohn's disease, Brother with diverticulitis.

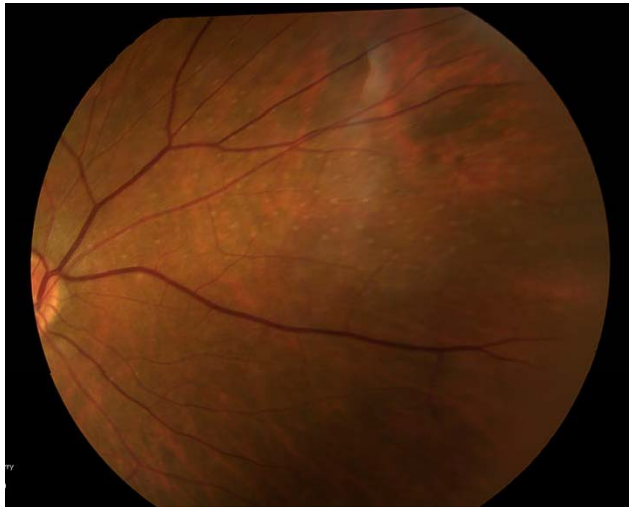
Case

- 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







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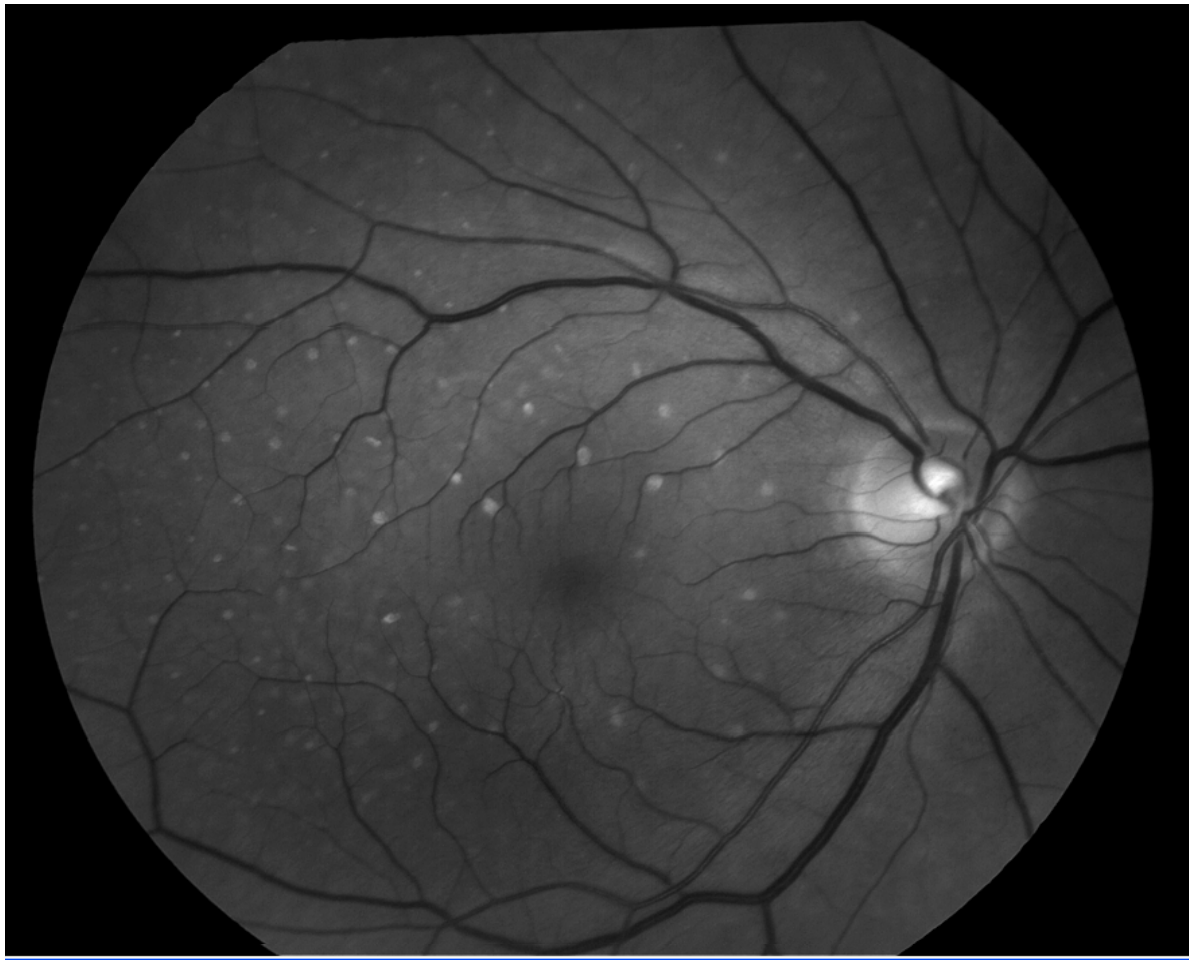

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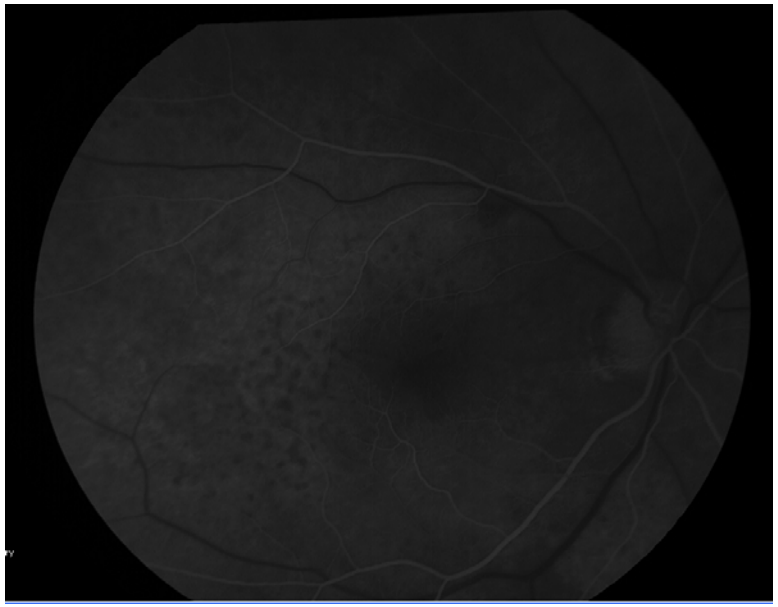
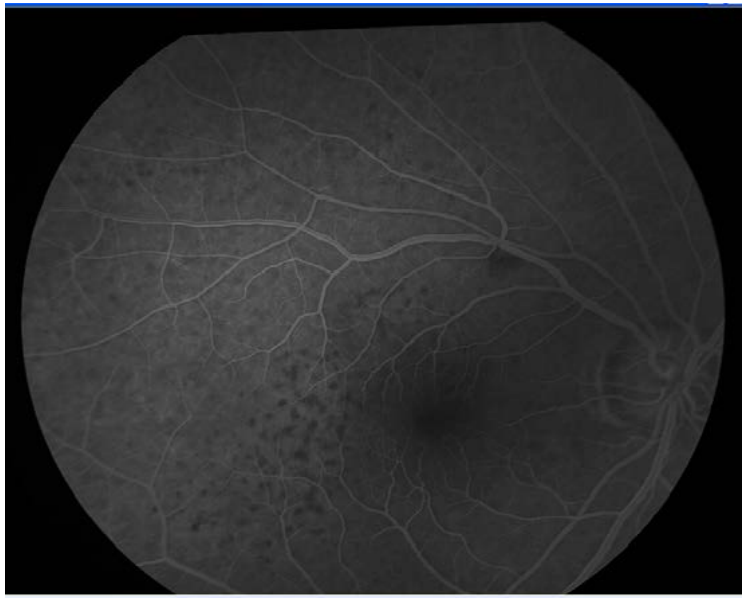
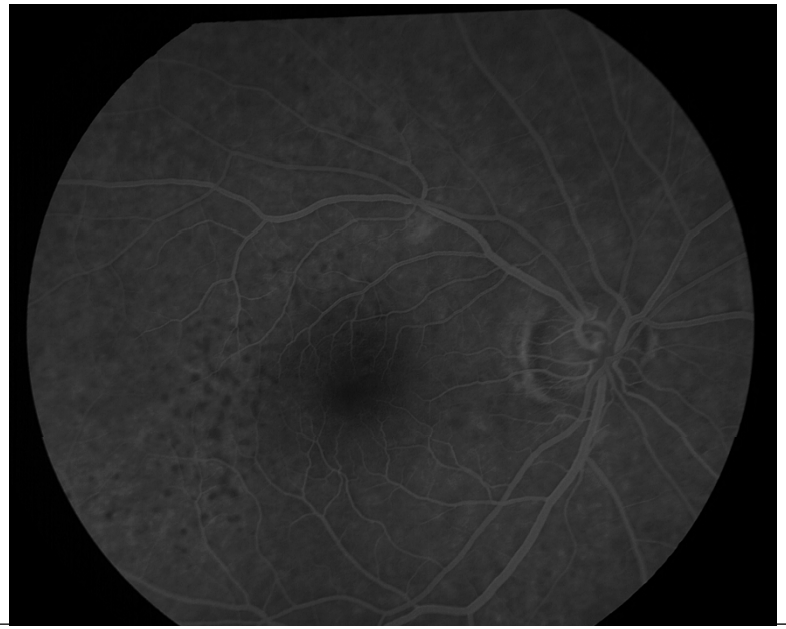
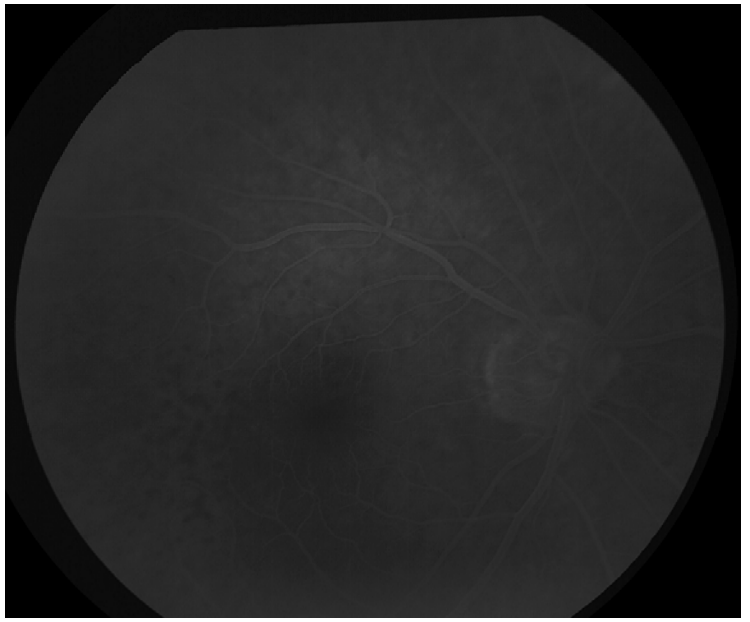








Case 4/09

- 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

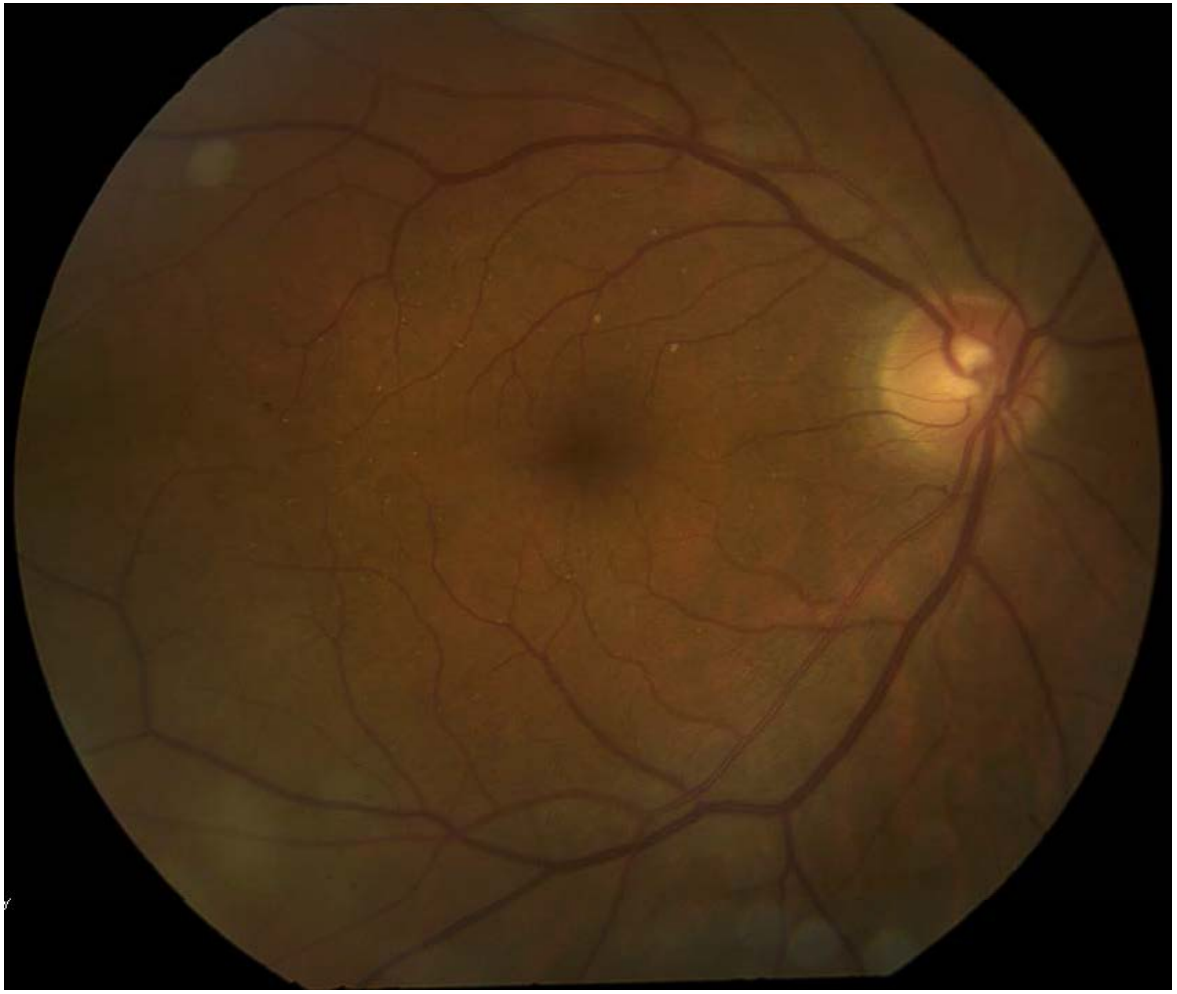
- Diagnostic PPV done
- Insufficient samples for IL10/IL6
- Cytology showed no malignant cells
- HSV,VZV and CMV PCRs are all negative
- Clonal pattern of IgH rearrangement by PCR.
- Lumbar puncture done - no clonal pattern of IgH rearrangement in CSF noted.

Treatment

- Treatment started with IV methotrexate and rituxan
- Intravitreal MTX commenced

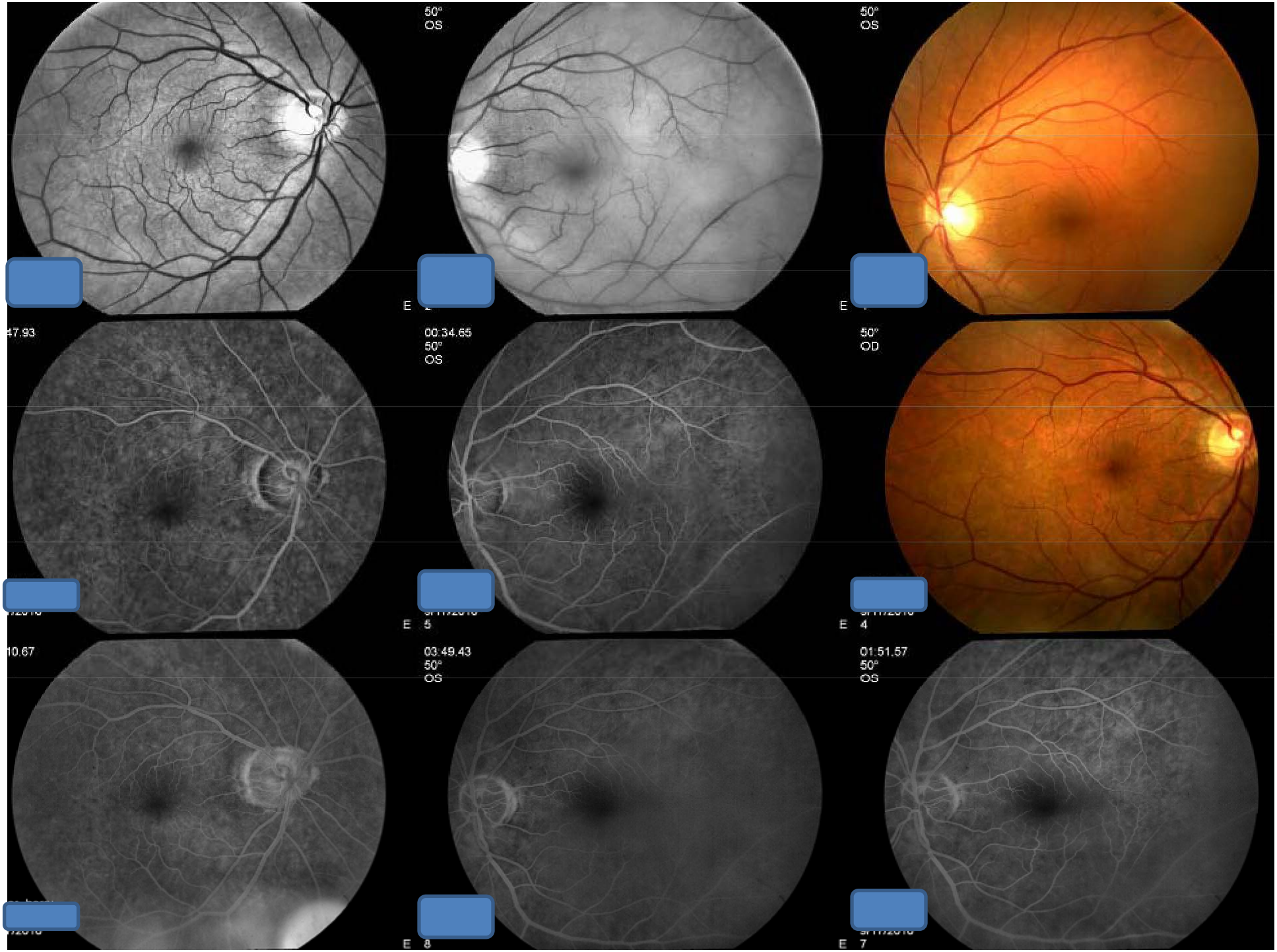
Follow-up 3/10

- 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


50°
OS
50°
OS
47.93
00:34.65
50°
OS
50°
OD
E 5
E 4
10.67
03:49.43
50°
OS
01:51.57
50°
OS
E 8
E 7

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

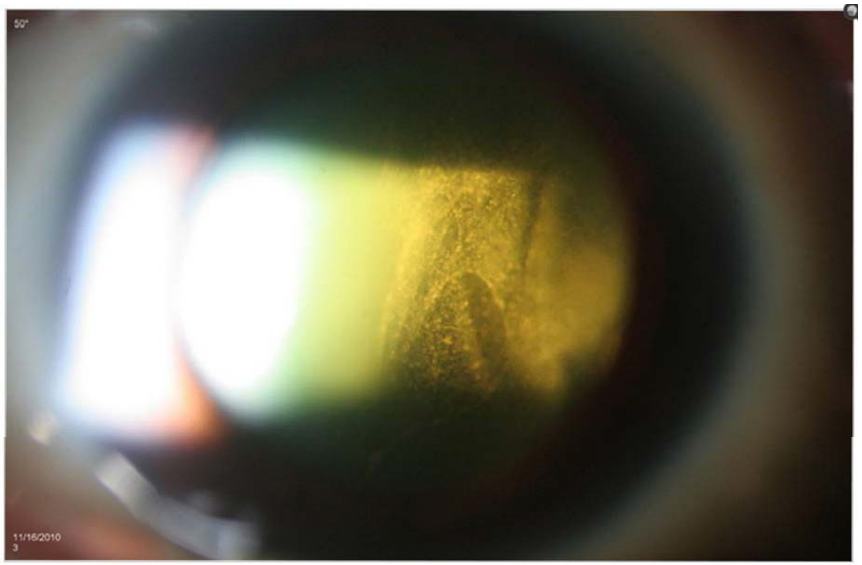
- MRI thus far has been normal.
- MRI in 5/12 showed widespread CNS lymphoma and IV MTX started by neuro-oncologist for 10 months.
- He has since been doing well with no CNS or ocular recurrence.

Primary Vitreoretinal Lymphoma (PVRL)

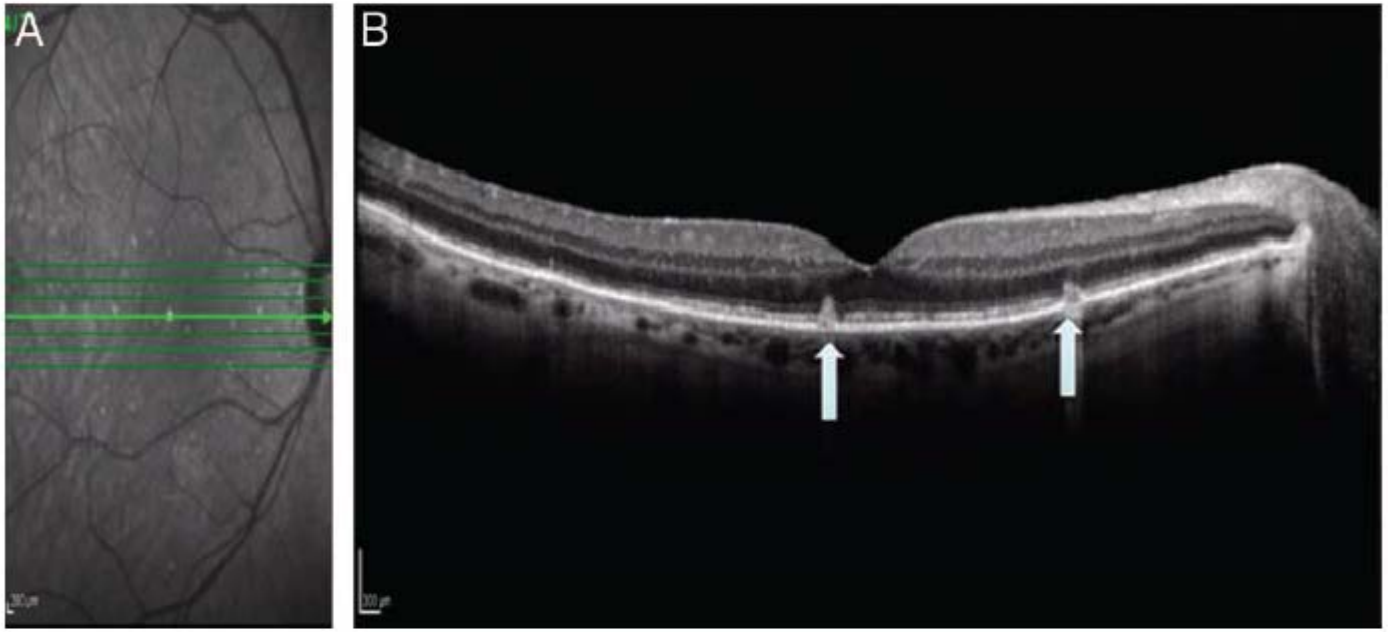
- Intraocular lymphoma represent < 1% of non-Hodgkin's lymphomas
- Mean age 50-60 years but occur in children
- No sexual predilection
- Most are of diffuse large cell lymphomas of B cell origin.
  - T cell lymphomas are rare
- Immune suppression is a risk factor
  - AIDS
  - Transplant patients
  -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



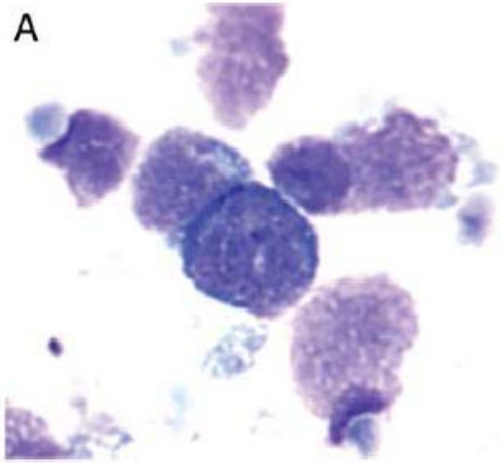
•Fundus can show multifocal yellow sub RPE lesions with overlying PED
•Lesions have feathery or distinct borders
•Vision is better than expected



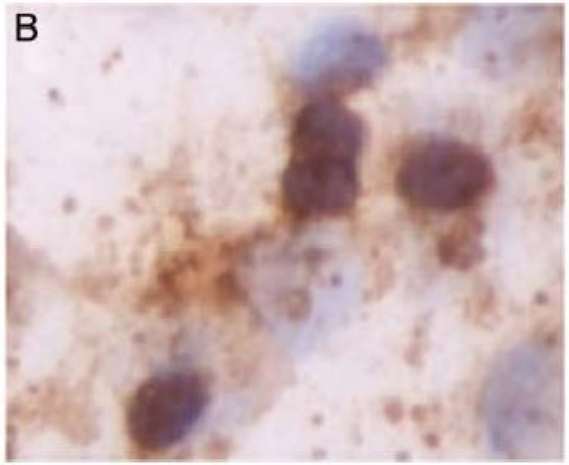
OCT shows hyper reflective lesion at level of RPE

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 immunohistochemisty

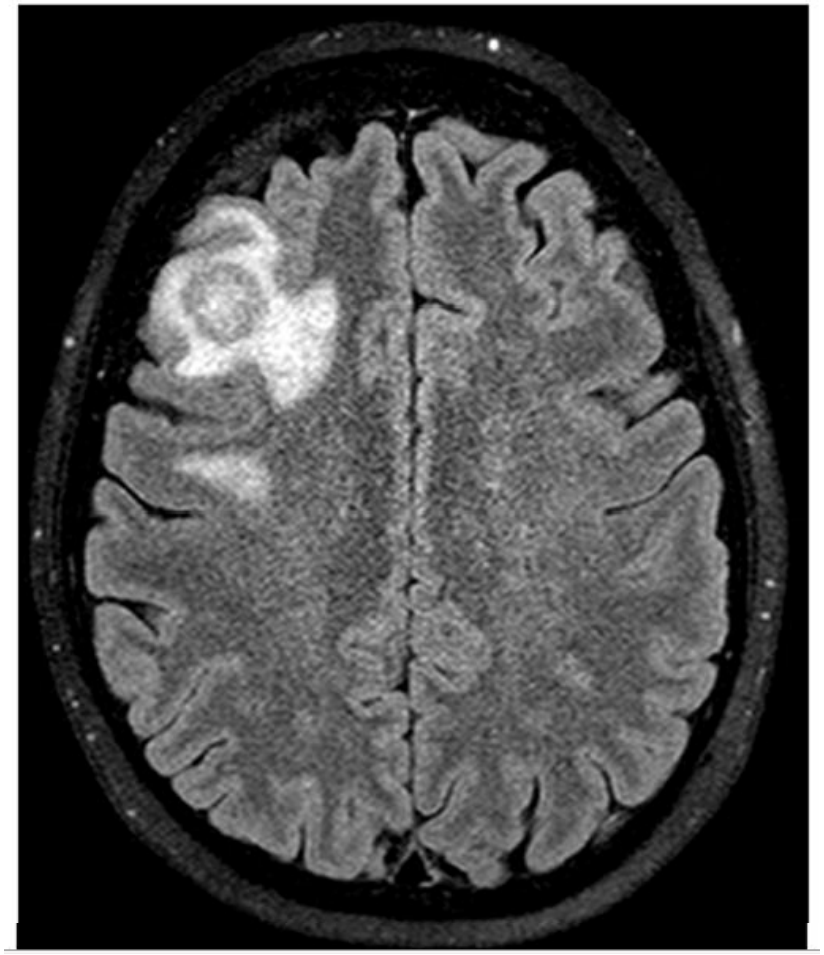
Diagnosis

- 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

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