1. New England Medical Center Grand Rounds - Primary CNS Lymphoma

New England Medical Center Grand Rounds

Primary CNS Lymphoma

My Hanh T. Nguyen, M.D.
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2. Case Presentation

Case Presentation

- 57 year old female
- CC: “blurry vision OU”
- HPI:
  - Referred for chronic vitritis OU
  - Initially: shadows and floaters OD x 1 month
    - BCVA 20/30 OD, 20/20 OS
    - 2+ vitreous cells & few snowball opacities OD
    - Subtenons Kenolog x once OD
  - One month later
    - 3+ vitritis OD
    - Prednisone 40mg QD with self taper
  - Six weeks later
    - BCVA 20/25 OD, 20/20 OS
    - 3+ vitritis OD, 2+ vitritis OS

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3. Case Presentation

Case Presentation

- **POHx:** No surgeries, trauma, or infections OU
- **PMHx:** borderline HTN
- **Medications:** Prednisone 20mg QD
- **Allergies:** NKDA
- **Fam Hx:**
  - ARMD
  - DM II
  - HTN
- **Soc Hx:**
  - Retired
  - Denies tobacco & ETOH use
- **ROS:** trouble sleeping and weight gain since prednisone use

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4. Office Examination

Office Examination

- **BCVA:** 20/30 OD, 20/20 OS
- **T:** 18 OU
- **Pupils:** 6 mm → 3 mm OU, no RAPD OU
- **EOM:** full OU
- **VF (conf):** full OU

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5. Office Examination

Office Examination

SLE:
LLL: wnI OU
C/S: white & quiet OU
K: clear OU, no KP OU
A/C: deep & quiet OU
I: no synechiae OU, no nodules OU
L: trace NS OU
V: 3+ cells OD, 2+ cells OS

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6. Fundus Examination

Fundus Examination

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7. Differential Diagnosis?

8. Differential Diagnosis

- Inflammatory
  - Sarcoidosis
  - Pars planitis
  - Systemic lupus erythematosus

- Infectious
  - Syphilis
  - Tuberculosis
  - Toxoplasmosis
  - Lyme Disease

- Neoplastic
  - Primary CNS lymphoma
  - Systemic lymphoma
  - Leukemia

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9. What would you do next?

10. Imaging Studies

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11. Primary CNS Lymphoma: Slide 11

12. Laboratory Studies

- CBC with differential
- CXR
- PPD
- ACE
- Lysozyme
- ESR
- RPR
- Lyme titer
- Toxoplasmosis titer
- Rheumatoid factor (RF)
- ANA
- Bartonella

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### Laboratory Studies

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC with differential</td>
<td>WNL</td>
</tr>
<tr>
<td>CXR</td>
<td>WNL</td>
</tr>
<tr>
<td>PPD</td>
<td>WNL</td>
</tr>
<tr>
<td>ACE</td>
<td>WNL</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Nonreactive</td>
</tr>
<tr>
<td>ESR</td>
<td>WNL</td>
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<tr>
<td>RPR</td>
<td>16</td>
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<tr>
<td>Lyme titer</td>
<td>Nonreactive</td>
</tr>
<tr>
<td>Toxoplasmosis titer</td>
<td>Negative</td>
</tr>
<tr>
<td>Rheumatoid factor (RF)</td>
<td>Negative</td>
</tr>
<tr>
<td>ANA</td>
<td>WNL</td>
</tr>
<tr>
<td>Bartonella</td>
<td>WNL</td>
</tr>
</tbody>
</table>

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### Now what?

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15. Treatment Options

- Observation with continued prednisone taper
- High-dose pulsed prednisone
- Immunosuppressive therapy
- Diagnostic PPV

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16. 4 months later; Diagnostic PPV OD

4 months later...
Diagnostic PPV OD

- Examination in OR:
  - Vitritis worse
  - No evidence of optic disc or retinal involvement
  - Few areas of depigmentation inferiorly, considered WNL

- Cytology:
  “Polymorphous population of lymphoid cells, monocytes, histiocytes, and debris, consistent with vitritis, no evidence of malignancy”

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17. 2 months later; Diagnostic PPV OS

2 months later…
Diagnostic PPV OS

Examination in OR:

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18. Post-op Evaluation

Post-op Evaluation

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19. Imaging Studies

20. Primary CNS Lymphoma: Slide 20
21. Cytology

**ATYPICAL LYMPHOID CELLS PRESENT**

“mixed lymphoid population” ... “scattered intermediate to larger, atypical lymphoid cells with high N/C ratio, convoluted nuclear contour and dispersed chromatin, suspicious for lymphoma”

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22. Primary CNS Lymphoma

- Cooper and Riker, 1951
- Historically “reticulum cell sarcoma”
- Subtypes
  - 98% non-Hodgkin B cell lymphoma of CNS
  - 2% T cell lymphoma
- Age of onset
  - 6-7th decade of life (range 13 to 85)
  - Rarely children and adolescents
- Incidence
  - Higher in immunocompromised patients
  - 51 of 10 million immunocompetent patients
  - 200 people in US annually

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23. Primary CNS Lymphoma - Ocular Involvement

Primary CNS Lymphoma
Ocular Involvement

- Ocular features 25%
  - 15% ocular alone
  - 15% ocular and visceral
  - 60% ocular and CNS
  - 4% ocular, CNS, and visceral

- Laterality
  - 30% unilateral
  - 85% delayed involvement of second eye

- Most common ocular symptoms
  - Decreased vision
  - Floaters

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24. Primary CNS Lymphoma - Ocular Signs

Primary CNS Lymphoma
Ocular Signs

- Chronic uveitis
  - Anterior and / or intermediate
  - Often severe
  - Initially responsive to steroids
  - Subsequently unresponsive to steroids

- Subretinal infiltration
  - Multifocal, creamy, yellow
  - Overlying RPE detachments and / or clumping
  - 1-2 mm in thickness

- Other findings
  - Retinal vasculitis
  - Vascular occlusion
  - Exudative RD

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25. Primary CNS Lymphoma - Treatment Options

Primary CNS Lymphoma Treatment Options

- Optimal method of treatment undetermined
- Historically: radiation therapy
  - High sensitivity of lymphoma cells to radiation
  - Recurrence and complications rates high
  - Does not decrease mortality
- Recent trends
  - < 60 yrs old: combination of intravenous ± intrathecal chemotherapy followed by radiotherapy
  - ≥ 60 yrs old: chemotherapy alone using high dose methotrexate
- Small case reports: intravitreal methotrexate (400ug/0.1mL)
- Autologous bone marrow transplant

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26. Primary CNS Lymphoma - Prognosis

Primary CNS Lymphoma Prognosis

- Poor
- Median survival
  - With supportive care: 2 - 3 months
  - With treatment: within 2 years
  - Longest reported: 40 months with treatment
- Prognostic data limited
  - Small treatment series
  - Rarity of disease

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27. **Case Summary**

- Elderly patient
- Bilateral, idiopathic, chronic uveitis poorly responsive to steroids
- Primary CNS lymphoma
  Supported by diagnostic PPV
- Follow up with neuro-oncologist
  - Lumbar puncture
  - Neuroimaging

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28. **Sources**

- AAO. Basic and Clinical Science Course: Uveitis. 2003; 219-231.

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29. Any Questions?