Disclosures

• none
A 44 year-old man admitted to an OSH following a fall

• One year of progressive memory loss, malaise, intermittent confusion, headache, and visual loss

• Past medical history:
  – Hypertension
  – Posterior uveitis with retinal vasculitis and macular degeneration
    • Treated with numerous immunosuppressive drugs, intravitreal steroids, and bevacizumab
  – Chronic progressive kidney disease, Stage 4
    • s/p 2 biopsies 2 & 4 years previously (results unavailable)
A 44 year-old man admitted to an OSH following a fall

- Labs:
  - CSF MBP: 10.6
  - CSF IgG: Mildly elevated
  - JC Virus, flow cytometry, VDRL within normal limits
  - “immunologic and vasculitic workup negative”
A 44 year-old man admitted to an OSH following a fall
A 44 year-old man admitted to an OSH following a fall

• Clinical differential diagnosis:
  – Infectious, TB, syphilis, viral, toxoplasmosis, sarcoid, vasculitis, neoplastic, demyelination (PML), Behçet's disease.

• Brain biopsy of right parietal lesion:
  – 2 biopsies performed over the following two weeks
  – Second biopsy provided for DSS
Biopsy 2
First biopsy
Diagnosis?
40 μm (40x)
PAS
Biopsy 1
Additional stains

- P53: Negative
- IDH1 (R132H): Negative
- SV40: Negative
- Myelin, Bodian: both reduced
- Congo red: Negative
- Gram, AFB, GMS, CMV, HSV: Negative
Descriptive final diagnosis

1. Focal white matter necrosis with white matter calcification

2. Focal white matter necrosis and abnormal vessels in white matter
Final Diagnosis

These findings, in the setting of retinopathy and renal dysfunction, are suggestive of retinal vasculopathy with cerebral leukodystrophy (RVCL)

(Kolar et al., Brain Pathology 2014, DiFrancesco et al., Neurol. Sci. 2015)
Retinal vasculopathy with cerebral leukodystrophy (RVCL)

- Autosomal dominant, 100% penetrance
- Heterozygous frameshift mutations in TREX-1
- Presents in 30s-40s with visual changes, headache, +/- focal neurologic deficits
- Vasculopathy of white matter, retina and other organs (kidney, liver)
RVCL pathologic features

• White matter ischemia, necrosis, and dystrophic calcification
• Thickened hyalinized vessels
• Fibrinoid vascular necrosis
• Vascular telangiectasias
• Multi-laminated basement membranes on electron microscopy

(Kolar et al., Brain Pathology 2014)
Additional history was obtained

<table>
<thead>
<tr>
<th>Family History:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Father died at age 36 from Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>• Paternal uncle died in his early 40s from an unclear disease with renal dysfunction</td>
</tr>
</tbody>
</table>
## TREX1 sequencing

- Novel C-terminal frameshift mutation
- c.830-833dupAGGA
Followup

**RVCL disease course:**
- Poor prognosis
- Limited therapeutic options
  - Glucocorticoids
- Death within 5-10 years of symptom onset

**This patient:**
- Trial of experimental immunosuppressive therapies
- Discontinued due to opportunistic infections
- Progressive renal disease requiring hemodialysis
- Transitioned to hospice care 13 months after first presentation
- He died 1 month later at age 45
References:


