Retinal Hemangioblastomas in VHL: Options for Treatment

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Learning Objectives / Outline

- Retinal Hemangioblastoma – Definition
- Implications – risk of blindness
- Surveillance – screening recommendations
- Surveillance within eye – techniques for detection
  - Techniques for treatment
    - Laser
    - Ant-VEGF
    - Surgery
    - Excision
- Emerging therapies

Disclosures

No conflict of interest to material presented here. Off label use of bevacizumab (Avastin®), ranibizumab (Lucentis®), aflibercept (Eylea®), and verteporfin (Visudyne®) will be discussed.

Retinal Hemangioblastoma

VHL 1 in 36,000
Retinal capillary hemangioblastoma (RCH) occurs in 50% of VHL patients and marks debut of disease in 1/3
- Lesions often small and difficult to see
- Leakage (exudation) can occur leading to blurred vision (macular edema), exudative retinal detachment
- Regression often triggers fibrosis (traction), which can cause tractional retinal detachment
Clinical Characterization of Retinal Capillary Hemangioblastomas in a Large Population of Patients with von Hippel-Lindau Disease

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NEI cohort (335 patients)

Blindness is rare but still can occur

Often attributable to multifocal lesions, and RCH at optic nerve.

Persistent exudation (leakage) and failure to close vascular channels leads to recurrent retinal detachment.

Surveillance - Screening Recommendations

For those at risk for VHL:
- At birth: pediatrician screen for nystagmus, strabismus, white pupil (leukocoria)
- Ages 1+: annual dilated eye exam using indirect ophthalmoscope by ophthalmologist

What is a good “dilated eye exam”?
- Indirect ophthalmoscope (beaded)
- Maximum dilation
- Recline patient
- More around the patient to get good view of the periphery
Gross Anatomy

Impact of Vision Loss

Visual acuity:

Severe Vision Loss

5/200

Optos Screening – Photography vs Fluorescein Angiography (FA)
Surveillance – Screening Techniques

- Dilated Eye Examination
- Eye Photography
- Fluorescein Angiography

Angiography – Fluorescein and Indocyanine Green
Techniques for Treatment - laser

Laser is the mainstay of treatment to close retinal capillary hemangioblastomas.

Initial burns often injure tissue but do not achieve complete closure.

Repeat treatment usually necessary.

Watch for fibrosis with regression of lesions.
Techniques for Treatment – anti-VEGF agents

Intravitreal Ranibizumab Therapy for Retinal Capillary Hemangioblastoma Related to von Hippel-Lindau Disease

Inflammation and angiogenesis in the subretinal membranes of the Optic Disc. Abbreviation: VHL

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Injections control leakage (exudation)
Leakage is due to persistent vascular channels

Durable control of exudation occurs with closure of vascular channels - taper injections to every 12 week, eventual discontinuation

Techniques for Treatment - Surgery

Techniques for Treatment – Excision & Ligation
Emerging Therapies

Repurposing propranolol as a drug for the treatment of retinal haemangioblastomas in von Hippel-Lindau disease

Propranolol – synthetic beta blocker
- Used for hypertension, arrhythmias, migraines
- Accidentally discovered in 2008 to be effective against infantile haemangioma
- Potential mechanism: antiangiogenic, reduction of VEGF and bFGF, apoptosis of endothelial cells
- 7 patients, multiple treatment methods, 2 patients with improved exudation
  Systemic VEGF levels reduced

Case Report
Long-Term Effect of External Beam Radiotherapy of Optic Disc Hemangioma in a Patient with von Hippel-Lindau Disease

Single case report with long-term follow-up for RCH of optic nerve
- 20 Gy external beam radiotherapy
- Gradual reduction in size and leakage over 6 years
- Vision stabilized at 20/60
- No angiographic data

Systemic Sunitinib Monotherapy Treatment for Advanced Juxtapatellar Retinal Hemangioblastoma Associated with von Hippel-Lindau Disease

Three patients treated with sunitinib (Sutent)
- Idea started in patient treated for metastatic neuroendocrine tumor with some regression of RCH leakage
- Second and third patients treated in prospective trial for 9 months
- Some reduction in exudation
- Significant systemic side effects (thyroid toxicity, low platelets, nausea, fatigue, jaundice, muscle aches)
Summary

1. Detection of eye tumors is key
2. Treatment of small tumor is relatively straightforward with laser photocoagulation
3. Photodynamic therapy has marginal utility but minimal side effects
4. Definitive regression can be achieved in some tumors with use of radiotherapy, but side effects will limit vision
5. Tumor resection, advanced surgical techniques may be employed in cases of advanced tumors, which can accomplish globe and vision salvage
6. Anti-VEGF Injections (Avastin, Lucentis, Eylea) help to control exudation (leakage) and provide best visual outcomes. However, no long-term control without serial injections
7. Overall goal is complete closure of vascular channels, with cleanup of exudation and fibrosis as indicated