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Outline

• Historical pearl
• Ophthalmic Epidemiology
• Traditional Treatments
• Options for Recalcitrant Tumors
• Screening

Who were von Hippel and Lindau?

• Eugen von Hippel
• German Ophthalmologist
  – angiomatosis retinae 1904

Hugo Manus & Ernst Fuchs
VHL & Ophthalmologist

- Retinal Hemangioblastoma is the most frequent and earliest manifestation of the VHL disease
- Ophthalmologist are often involved in the care and initial diagnosis of these patients.

Clinical Epidemiology

- Wong et al
- Ophthalmology 2008
- Prospective case series
- Demographics of a patient population in a large tertiary referral center


Significant Visual Impairment in Some Patients

- 42% unilateral, 58% bilateral
- 1 of 18 patients have severe bilateral visual impairment
- 1 in 5 affected patients were enucleated or prephthsical
- 1 in 4 eyes with RCH have severe visual impairment
- Severe visual impairment associated with increased age, juxtapapillary lesions and increased number of peripheral lesions

Number of lesions per eye

[Graph showing the distribution of number of lesions per eye]

Ophthalmology. 2008 January; 115(1): 181–188. Published online 2007 June 1. doi: 10.1016/j.ophtha.2007.03.089
Diagnosis

- Diagnosis is primarily clinical.
- Dilated retinal exam
- Dilated tortuous vessels leading to and away of the vascular tumor.
- Ultra-widefield (optos) retinal imaging
- Fluorescein angiography
- Optical coherence tomography
- Retinal edema

Reasons for Visual Loss

- Exudation - leakage
- Traction
- Vitreous hemorrhage
- Neovascular glaucoma

Treatment

- Observation
  - Photos
  - Angiogram
  - Amsler Grid
- Very Small Tumors
- Not affecting or threatening vision
- Juxtapapillary hemangiomas – near the nerve
Traditional Treatment Options

- Laser
  - Photocoagulation
    - Argon
  - Photodynamic therapy PDT
    - Veredporfin (photosensitizer)
    - Near optic nerve
  - Transpupillary thermotherapy TTT
    - 810 nm diode laser


Traditional Treatment Options

- Cryotherapy
  - Focal tumors
  - Larger than 3 mm
  - Good for anterior tumors
  - Significant subretinal fluid

Radiation

- Larger or unresponsive tumors
- External Radiation to the eye ball
- Focal Radiation to the RGH
  - Plaques
  - Proton beam radiation
Challenges

- Tumors that don’t respond to traditional therapies
- Tumors near the optic nerve
- Very large tumors

Surgical Vitrectomy

- Gaudric et al. Ophthalmology 2011
  - The long-term success rate of vitreoretinal surgery for severe RCH
  - 23 eyes in 21 patients
  - Vitreoretinal surgery is an effective treatment for severe retinal hemangiomas
- Retinotomy 9 eyes – all legally blind
- Endolaser 9 of 14 patients - severe visual impairment

Blocking the Pathway

- Addressing the up regulation VEGF & PDGF
- Intravenous versus intravitreal drug administration
- Macular Degeneration
  - Bevacizumab
  - Ranibizumab
- Sunitinib

Multiple Case Reports

- Ziemssen et al. Eye 2007
  - Combined PDT/ Intravitreal bevacizumab
  - Decreased exudation & improved vision
  - Intravenous bevacizumab
  - Decreased exudation no improved vision
- Aiello et al. Ophthalmology 2002
  - Intravenous SU5416 Semaxanib
  - Improved vision- tumor did not decrease
Small case series

- Dahr et al. Retina 2007
  - Intravitreal pegaptanib (min 6 injections)
  - 2/5 patient completed treatment course
  - Both had decreased exudation
  - One had significantly improved vision
  - Transient post injection hypotony
- No apparent effect on the size of the retinal angioma, may decrease exudation

Intravitreal Ranibizumab

- Wong et al. Ophthalmology 2008
- Case series
  - 5 patients
  - Intravitreal ranibizumab
  - 7 injections
  - Minimal treatment effects on most VHL lesions
  - Possible efficacy on smallest lesions with least exudation


Limitations

- No large clinical trial to date examining the efficacy of anti-VEGF
- Small cohort study Ranibizumab
  - minimal success on most VHL-related hemangioblastomas.
- Conclusion that Ranibuzimab may aid in control of associated findings (i.e decrease in subretinal fluid) limited efficacy on the RCH itself

Screening

- As genetics gets better
- Screening young children
- Visual outcomes usually based on early diagnosis
- Dilated eye exam by a Board Certified Ophthalmologist (Eye MD)
- At least on an annual basis
Future Directions

• Targeting multiple angiogenic molecules
• Combined modalities
  – Some type of anti-VEGF therapy
    • Intraocular sustained release devise
  – Ablative therapy
    • Laser photocoagulation or PDT