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Grand Rounds Presentation
39 yo African American woman with c/o difficulty seeing at night. Pt reports feeling “clumsy” and “bumping into things” more often.
History

PMH: denies
POH: denies
Fam Hx: “father has problems seeing”
Soc Hx: denies x3
All: NKDA
Meds: no gtt’s, no meds
Physical Examination

DVaSC

OD 20/25-2
OS 20/30-

MRx:

OD +1.75 sph 20/20-
OS +0.50 -1.00 x15 20/20-

EOM: full OU

CVF: grossly constricted OU

Pupils: PERRL OU, no APD

Tapp: 13/11 @1:50pm

Professionalism/Patient Care/Interpersonal & Communication Skills
Professionalism/Patient Care/Interpersonal & Communication Skills

Slit Lamp Examination

LLA: few inspissated glands OU
C/S: c&w OU
K: clear OU
I/P: round OU
AC: d&q OU
L: TR NS OU
Dilated Fundus Examination

Vit: TR ant vit cell OD, clear OS
Disc: pink, sharp OU c/d: 0.25/0.3
Mac: see photos
Vessels: see photos
Periph: see photos
Differential Diagnosis

- Pigmentary retinopathy
  - Non-syndromic
  - Syndromic
- Traumatic retinopathy
- Syphilis
- TORCH
- CAR/MAR
- DUSN
- Retinal drug toxicity
- Prior vascular occlusion
- Diffuse posterior uveitis
What now?

- Automated Visual Field
- ERG
- Color plates
  - Full OU
- FTA-Abs/RPR
  - Negative
- Consider FA
  - No beneficial to dx RP, but may be beneficial to r/o other conditions
- ROS
  - Denies hearing loss, h/o orbital/ocular trauma, renal problems, etc
HVF 24-2
Retinitis Pigmentosa

- Misnomer, since the pathogenesis is not inflammatory in nature
- Also known as: pigmentary retinopathy, rod-cone dystrophy, tapetoretinal degeneration
- Worldwide prevalence 1 in 4000-5000
  - Highest frequency of occurrence reported in Navajo Indians at 1 in 1878
- About 70% of pts have a family history of RP
- Slow and progressive disease
Retinitis Pigmentosa

- Non-syndromic form comprises the majority of cases of RP
  - ~65% of RP cases are non-syndromic in the US
- Syndromic
  - Usher syndrome, Bardet-Biedl syndrome, Refsum disease, etc
Clinical Presentation

- Typically presents in young adulthood
  - Can present anytime from infancy to the mid-30’s to 50’s
- Nyctalopia
  - Often one of the earliest symptoms
  - Pts may c/o being “disoriented” in dim light, or c/o slow adaptation to dark conditions
- Visual field loss
  - Often not noticed by the pt
  - Pts may c/o being “clumsy”, bumping into things

Medical Knowledge/Practice Based learning and improvement
Clinical Presentation

- Visual acuity
  - Variably affected
  - Often affected by CME or cataract (classically PSC)
- Photopsias
  - Small, shimmering, blinking lights
Physical Findings

Triad of findings:

Waxy, pallor of optic nerve
Believed to be due to a combination of gliosis and atrophy

Attenuation of retinal vessels

Bone-spicule pattern of intraretinal pigmentation
Physical Findings

- Cystoid macular edema can develop
- Abnormalities in the vitreoretinal interface
  - Cellophane maculopathy
- Cataract formation affect ~50% of RP pts
  - Classically posterior subcapsular cataract
- Dust-like pigmented substance in vitreous
  - Composed of pigment granules rather than inflammatory cells, as is suggested in the name “retinitis”
Physical Findings

- **Myopia**
  - In one study from 1978, 75% of 268 eyes with RP were found to have myopia, compared with 12% in the general population

- **Classic visual field defect is a ring scotoma, with eventual central island of vision**
  - Progressive, gradual constriction of the field over time
Physical Findings

- Visual acuity is generally maintained, but there is significant loss of contrast sensitivity
  - Gives pts a perception of decreased vision while visual acuity actually remains very good
- Color vision general remains intact until the macula becomes significantly involved
  - Generally a blue cone deficiency
Diagnosis

- Visual field
- Electroretinography (ERG)
  - Measure of the total retinal response
  - RP patients demonstrate depressed ‘a’ and ‘b’ waves
  - Correlates with the size of the remaining visual field
- Multifocal ERG
  - Useful in monitoring patients with more advanced...
Fig. 13. ERG recordings in a normal patient and one with retinitis pigmentosa.
Over 84 different genetic types of RP have been discovered

### Inheritance pattern in the United States

<table>
<thead>
<tr>
<th>Inheritance Pattern</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant</td>
<td>30%</td>
</tr>
<tr>
<td>Autosomal recessive</td>
<td>20%</td>
</tr>
<tr>
<td>X-linked</td>
<td>15%</td>
</tr>
<tr>
<td>Recessive early-onset</td>
<td>5%</td>
</tr>
<tr>
<td>Sporadic</td>
<td>30%</td>
</tr>
</tbody>
</table>

Medical Knowledge/Practice Based learning and improvement
Gene Mutations

The following accounts for ~30% of all RP:

- **Autosomal dominant**
  - RHO – comprises ~25% of AD RP
- **Autosomal Recessive**
  - USH2A (Usherin) – 20% of AR RP
    - Both non-syndromic and syndromic (Usher Syndrome)
- **X-linked**
  - RPGR (GTPase regulator) – 70-80% of X-linked RP
Pathophysiology

- Genetic defects cause apoptosis
  - Predominantly, apoptosis of the rod photoreceptors
  - May also affect the RPE and cone photoreceptor, which leads to loss of rod photoreceptors
- Rod photoreceptors are most concentrated in the mid-periphery, hence the classic appearance of RP in this location
Pathophysiology

Medical Knowledge/Practice Based learning and improvement
Fig. 13. ERG recordings in a normal patient and one with retinitis pigmentosa.
Pathology

Medical Knowledge/Practice Based learning and improvement
Treatment

- No cure
- Nutritional supplementation or avoidance
  - Vitamin A supplementation controversial
  - Avoid vitamin E
  - Omega-3 fatty acid
    - Major structural lipid of photoreceptor outer segment membranes – possibly involved in rhodopsin regeneration
    - Systemic review of 6 studies demonstrated trends suggestive of improved outcomes with omega-3 fatty acid supplements

Medical Knowledge/Practice Based learning and improvement
Experimental Therapy

- Retinal prosthetic
- Retinal implantation of retina and retinal pigment epithelium
- Gene therapy
Retinal Prosthesis

- Implantable microelectrode arrays are implanted onto the epiretinal surface
- Data and energy are transmitted via an inductive link from the outside of the eye to the implant
- In the EPI-RET-3 project that included 6 legally blind pts with RP, visual sensations reported as dots, arcs, or lines of different colors and intensities
- Based on current studies, it is believed that ambulatory vision and limited character recognition is a reasonable goal.
Retinal Prosthesis

Implant – Fabrication

Fully assembled retinal implant

Encapsulated implant with folded microcoil
Retinal Implantation of Retina/RPE

- The retinal implantation of fetal RPE is based on the theory that this tissue might rescue abnormal photoreceptors in RP
  - Several animal models have been investigated, with the common difficulty of integrating the tissue into the host retina – difficulty encountered in the development of synaptic connections b/w host and implant
- In one study by Radtke et al, 7 of 10 pts (6 with RP, 4 with ARMD) showed improved visual acuity after implantation of neural progenitor cell layers with RPE
- Studies are under way exploring the possibility of utilizing embryonic stem cells
Gene Therapy

- Gene therapy strategies:
  - Corrective expression of the mutated gene, directly reversing the effect of the deficiency resulting from the mutation
  - Non-specific gene therapy, with therapeutic expression of factors that improve the underlying problem indirectly
- Several vectors have been investigated, with the recombinant adenovirus-associated vector (rAAV), found to be one of the optimal and most commonly used vectors
- The vector-gene is administered by subretinal injection

Medical Knowledge/Practice Based learning and improvement
Prognosis

From a multicenter population study, pts with RP who were at least 45 years old were found to have:

- 52% with 20/40 or better vision in one eye
- 25% with 20/200 or worse vision
- 0.5% with no light perception
Pt plans to return to next visit with more information concerning her father’s vision problems.
Pt was referred for low vision evaluation.
Plan for referral for ERG.
Pt encouraged to follow-up for genetic counseling.

BCSC Retina and Vitreous 2007-2008, Section 12.


Koch C. EPI-RET-3: A wireless retina implant in human trial. Aachen University, Aachen, Germany.


Thank You!

Dr. Eric Shrier
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Dr. Marcus Edelstein