Grand Rounds
Department of Ophthalmology

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Case Presentation

- **HPI**: 35 yo male with a history of glaucoma presents for initial evaluation in the retina clinic. The patient denies change in vision, difficulty seeing at night, floaters/photopsia as well as denies photophobia.
- **PMHx**: hearing impaired since birth; “heart problem” as a child for which he had surgery
- **POHx**: glaucoma s/p trabeculectomy OD at age 20
- **Medications**: none
- **Eye gtt**: xalatan 1/1, cosopt 2/2, alphagan 3/3
- **NKDA**
- **Family history**: no blindness/glaucoma

Core competencies: Patient care/interpersonal and communication skills/professionalism
Case Presentation (cont)

- Exam:
  - BCVA:
    - OD: 20/25 +1
    - OS: 20/25 +1
  - EOM: full OU
  - CVF: full OU
  - Pupils: 4→2 OU, no APD
  - Tapp: 13/10 @ 10 AM
Case Presentation (cont)

- **SLE:**
  - LLA: WNL OU
  - C/S: elevated superior nasal bleb OD; white and quiet OS
  - K: clear OU
  - A/C: deep and quiet OU
  - I/P: round and reactive OU
  - L: clear OU

Core competencies: Patient care/interpersonal and communication skills/professionalism
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Case Presentation (cont)

- **DFE:**
  - **V:** clear OU
  - **C/D**
    - 0.85 sharp/pink OU
  - **M**
    - drusen with salt and pepper appearance OU
  - **V/P:** no tears/hemorrhage/detachment OU
Differential Diagnosis

- **Salt and pepper retinopathy**
  - Congenital Rubella
  - Leber’s congenital amaurosis
  - Congenital Syphilis
  - Cystinosis
  - Albinism (carrier state)
  - Retinitis pigmentosa (carrier state)
  - Choroideremia (carrier state)
  - Phenothiazine toxicity

- **Salt and pepper retinopathy and hearing impairment**
  - Congenital rubella syndrome
  - Congenital syphilis
  - Usher’s syndrome

Core competencies: Medical Knowledge/ Systems Based Knowledge
What would you do next?

- Thorough Birth History
  - Congenital infections?
  - Medical problems as a child? Cardiac? Musculoskeletal? Hepatic?
- Thorough family history
  - History of any ocular problems (retinitis pigmentosa/Usher syndrome/cystinosis)
  - Pedigree to determine mode of inheritance (Usher syndrome-x linked; cystinosis-AR; albinism-AR/x-linked)
- Medication use?
  - phenothiazine
- Labs
  - RPR
  - Rubella titers
  - Gene testing (retinitis pigmentosa, choroideremia, cystinosis, albinism)
- Electroretinogram
  - (cystinosis, RP/Usher syndrome, Leber’s, choroideremia, phenothiazine toxicity)
Differential Diagnosis

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  - Phenothiazine toxicity
  - Congenital Rubella

- **Salt and pepper retinopathy and hearing impairment**
  - Congenital syphilis
  - Usher’s syndrome
  - Congenital rubella syndrome

Core competencies: Medical Knowledge/ Systems Based Knowledge
Congenital Rubella Syndrome

- First described in 1941
- Triad of anomalies: congenital heart disease, cataracts, deafness
- Greatest risk during primary infection of the mother
- In pregnant women, the virus infects and replicates in the placenta → placental damage → virus crosses to fetus
- The earlier the infection occurs in the pregnancy, the higher the rate of transmission and the consequences are more profound
  - Immature fetal immune system
  - Majority of maternal antibodies reach fetus after 32 weeks of gestation

Core competencies: Medical Knowledge/ Systems Based Knowledge
Congenital Rubella Syndrome

- If infection occurs during
  - First 11 weeks of gestation $\rightarrow$ 100% infants will be affected
  - 12 to 20 weeks of gestation $\rightarrow$ 30% infants will be affected
  - After 20 weeks of gestation $\rightarrow$ 0% infants will be affected
- Virus can persist in the infected infant for an unknown period of time

Core competencies: Medical Knowledge
Rubella Virus

- Originally known as German measles
- Member of the togavirus family
- Enveloped, single-stranded RNA virus
- Droplet transmission
- Infection occurs 14-21 days after exposure
- Rubella infections are usually mild
- Vaccine released in 1969 after which new cases of congenital rubella have sharply decreased
Systemic Manifestations

- Deafness (44%)
- Mental retardation
- Cardiovascular defects
- Ocular defects
- Thrombocytopenia
- Hepatitis
- Myocarditis
- Bone lesions
- Dental defects
- Hypospadias

- Cryptorchidism
- Inguinal hernia
- Interstitial pneumonitis
- Meningo-encephalitis
- Cerebral calcification
- Splenic fibrosis
- Nephrosclerosis
- Nephrocalcinosis

Late onset manifestations
- Insulin dependent diabetes
- Thyroid dysfunction
- panencephalitis

Core competencies: Medical Knowledge
Ocular Manifestations

- Can affect every part of the eye due to the extensive capillary network
- Usually occur in combination with other non-ocular defects
- Most common: Pigmentary retinopathy, Cataract, microphthalmia, glaucoma
- Progressive disease - may develop ocular manifestations later in life

Core competencies: Medical Knowledge

**Table IV: Ocular Defects in Congenital Rubella Syndrome**

<table>
<thead>
<tr>
<th>Prenatal Onset*</th>
<th>Prenatal or Postnatal Onset†</th>
<th>Delayed Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iritis</td>
<td>Microphthalmia</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Iridocyclitis</td>
<td>Cataract</td>
<td>Cataract</td>
</tr>
<tr>
<td>Corneal clouding</td>
<td>Glaucoma</td>
<td>Optic neuritis</td>
</tr>
<tr>
<td>Intraocular pressure elevation</td>
<td>Corneal opacification</td>
<td>Optic atrophy</td>
</tr>
<tr>
<td>Virus presence in conjuctiva, aqueous and lens</td>
<td>Retinopathy</td>
<td>Strabismus</td>
</tr>
<tr>
<td></td>
<td>Iris hypoplasia</td>
<td>Nystagmus</td>
</tr>
<tr>
<td></td>
<td>Strabismus</td>
<td>Subretinal neovascularization</td>
</tr>
<tr>
<td></td>
<td>Nystagmus</td>
<td>Keratoconus</td>
</tr>
<tr>
<td></td>
<td>Staphyloma formation*</td>
<td>Lens absorption</td>
</tr>
<tr>
<td></td>
<td>Phthisus bulbi‡</td>
<td>Corneal hydrops</td>
</tr>
<tr>
<td></td>
<td>Visual impairment</td>
<td></td>
</tr>
</tbody>
</table>

* Core competencies: Medical Knowledge/ Systems Based Knowledge
Rubella Cataract

- Unilateral or bilateral
- Infection usually has to occur prior to development of the lens capsule
- Infects the embryonic lens causing lens fibers to degenerate and also a failure to dehydrate \(\rightarrow\) lens opacity
- Transparent secondary lens fibers cover the opaque embryonic lens
- Lamellar, nuclear, or membranous
- Lens can be a reservoir for the virus causing the cataract to progress over time

Core competencies: Medical Knowledge
Rubella Cataract

- Cataract surgery may have poor outcomes
  - Poor pupillary dilation
  - Can result in post-operative inflammation due to release of retained virus particles in the lens
  - Can cause the initiation or worsening of secondary glaucoma
Microphthalmos

- Occurs in 10% of children with CRS
- Eye is less than 16.6 mm in axial length
- Occurs as a result of generalized slowing of replication due to the rubella virus → ocular “failure to thrive”
- Often have co-existing ocular anomalies (glaucoma and/or cataract)
Rubella Retinopathy

- Occurs in 22% of children with CRS
- Unilateral or bilateral
- Diffuse mottling of the RPE with focal areas of decreased and increased pigmentation → ”salt and pepper fundus”
  - Most commonly occur in the posterior pole
- Neural retina and choroid are unaffected

Core competencies: Medical Knowledge

Lorenz B & Moore T.
Rubella Retinopathy

- Vision and ERG usually are normal
- Usually nonprogressive
- Subretinal neovascularization can be a rare complication due to progressive atrophy of the RPE

Core competencies: Medical Knowledge
Glaucoma

- Occurs in 10% of children with CRS
- Congenital
  - Result of failure of absorption of the mesoderm of the angle or failure of Schlemm’s canal to differentiate
  - Can be an isolated anomaly
- Secondary
  - Result of trabeculodysgenesis or persistent viral damage to the trabecular meshwork
  - Can also occur as a result of chronic uveitis
  - Usually occurs in eyes with microphthalmos or cataracts
  - Develops in the second decade of life
  - Poor visual prognosis

Core competencies: Medical Knowledge
Diagnosis

- Serology
  - Can be difficult to interpret due to transplacental passage of antibodies
- Amniocentesis with PCR of amniotic fluid
- Viral isolation
  - Preferred method
  - Nasopharyngeal swab, CSF, urine
- Placental biopsy

Core competencies: Medical Knowledge/ Systems Based Knowledge
Our Patient

- We explained the retinal findings to the patient and the need for routine follow-up due to the chance of developing subretinal neovascularization.
- The patient was continued on all of his glaucoma medications and referred back to the general ophthalmology clinic for continued management of his glaucoma.

Core competencies: Professionalism/Patient Care
Reflective Practice

- This was an interesting case especially because congenital rubella syndrome has become very rare since the advent of the rubella vaccine.
- It involved good communication with the patient to impress upon him the chronic nature of his disease and the need for close follow-up, especially with a glaucoma specialist.

Core competencies: Professionalism/Patient Care
Core Competencies

• Patient Care-our patient received the appropriate treatment and education for his condition as per evidence based medicine.

• Medical Knowledge-we used this case as a learning opportunity to increase our knowledge about congenital rubella syndrome

• Practice Based Learning and Improvement-this case helped us to focus our learning on the current treatment modalities for the complications associated with congenital rubella syndrome
Core Competencies

- Interpersonal and Communication Skills- We were able to communicate with the patient regarding his condition and to impress upon him the chronic nature of his syndrome
- Professionalism-we discussed the clinical findings with the patient in a manner that he understood all of the his ocular findings and the possibility for future complications
- Systems Based Practice-we demonstrated an awareness of the health care system so that we could effectively call upon our resources and provide the best treatment for our patient.
References

Thank You

- Dr. Gutman
- Dr. Glatman