Learning Objectives
Today, we will explore the varied causes and consequences of cherry red spots on the macula:
1. To cover some congenital and systemic causes behind central retinal artery occlusion (CRAO)
2. To review prevention and treatment of CRAO
3. To explore the varied presentation of the genetically-inherited lysosomal storage diseases, including Tay-Sachs, Niemann-Pick, Gaucher, and Sandhoff diseases
4. To differentially diagnose traumatic causes of cherry red macular spots, like commotio retinae

One Cherry Red Spot We Won’t Cover Today: Bullseye (Plaquenil) Retinopathy
https://diagnosticpathology.biomedcentral.com/articles/10.1186/1746-1596-5-20

Other Causes of Cherry Red Spots
1. Central Retinal Artery Occlusion
2. Tay-Sachs disease
3. Niemann-Pick disease
4. Other Causes (Gaucher, Commotio Retinae, Sandhoff disease)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864975/

1. CRAO: Diagnosis and Treatment
Cyanopsia in CRAO
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4764311/

CRAO: Objective “Cattle Trucking”
CRAO: Fluorescein Angiography

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4764311/

CRAO: Cilioretinal Artery Sparing OCT after 3, 7, 30, and 90 days

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3822202/

CRAO RNFL Improvement and Fluorescein Angiography: OCT after 3, 7, 30, and 90 days

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3822202/

CRAO Triggers: Cataract Surgery Retrobulbar Injection in a 65 YOF

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5433131/

CRAO Triggers: 49 YOM After Chiropractic Manipulation

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3325618/
CRAO Triggers: Chiropractic Manipulation Treated with Ginkgo?

CRAO Triggers: 58 YOM with Chung-Strauss Syndrome

CRAO Triggers: 58 YOM with Chung-Strauss Syndrome

CRAO Triggers: 8 YOM with Pediatric Pneumonia

CRAO Triggers: 8 YOM with Pediatric Pneumonia

CRAO Triggers: Congenital Single Heart Atrium in 23 YOAF

Chest X-ray showed that two lung markings were increased, the high density lower right lung patchy shadows and a small right-sided pleural effusion at the initial presentation.

b Chest X-ray showed that two lung textures were increased, the right lower lung had a high patchy density, and its edge was smooth.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3325618/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3714957/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3714957/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5148912/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5148912/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4612404/
Preventing and Treating CRAO in 23 YOAF with PTA (Patent or Persistent Truncus Arteriosus)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4612404/

CRAO DDx: 25 YOM with Sickle Cell Anemia and Hyperbaric O₂

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4244145/

CRAO DDx: 18 YOF with Pseudo-Cherry Red Spot in Dermatomyositis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3724690/

2. Tay-Sachs Disease

- One of the gangliosides, diseases of sialic acid-containing material found in neural tissue like gray matter
- If lysosomes don’t break these down efficiently, they accumulate in the brain and produce a spectrum of disorders, including a cherry-red spot in the macula
- Tay-Sachs disease is the most famous of the gangliosidoses

http://en.wikipedia.org/wiki/Tay-Sachs

Tay-Sachs and the Gangliosidoses

- Tay-Sachs Disease (TSD), or acute infantile GM₂, is often fatal by age 5
- It is named for British ophthalmologist Waren Tay and American neurologist Bernard Sachs first described the cellular appearance of the disease in the 1880’s
- It has a classic cherry-red macular spot that is a telling sign in patients, many of whom are children


Tay-Sachs Cherry-Red Macula

- The red spot is essentially a nerve fiber layer window at the fovea compared to the fatty accumulation elsewhere on the retina, seen in early-onset Tay-Sachs only
- The spot causes poor vision, that leads in turn to poor fixation
- Poor fixation commonly results in nystagmus because of larger-than-normal tremors of the eye
- Strabismus and poor binocularity are common in Tay-Sachs disease

Classic Cherry Red Spot

Wright, Figure 7-5A, page 374
Other Clinical Signs of Tay-Sachs

- Demyelination of optic nerve, chiasm and tracts
- Optic atrophy
- Progressive loss of vision
- Blindness, often by age 2
- Flatline VEP early, with normal ERG late
- Oculomotor ataxia

Degenerated Cherry Red Spot

Wright, Figure 7-38, page 374

Stalling Saccades in Tay-Sachs Disease

https://pn.bmj.com/content/15/3/164

Leigh & Zee, 4th ed. Tay-Sachs.mp4

Ethnic Predilection and Late-Onset Tay-Sachs

- Recessive carriers of Tay-Sachs are found in at least 1 in 30 in each of the following ethnic groups:
  - Eastern European (Ashkenazi) Jews (1:3600) – widespread genetic testing has led to early intervention
  - French Canadians
  - Louisiana Cajuns
  - Irish Americans have a 1 in 50 chance of being a carrier
  - In the general population, the incidence of carriers is 1 in 300


Early Detection of Tay-Sachs

- Most cases of Tay-Sachs disease are fatal early in life, others are not and often misdiagnosed
- All are autosomal recessive, meaning both the children of carrier parents are carriers themselves
- The full disease in this family of conditions penetrates as often as about 1 in 4 of certain populations
- Tear enzyme assay someday?

http://www.slideshare.net/aggabriel1/tay-sachs-disease-32430703

Future Treatment of Tay-Sachs: Enzyme Replacement?

http://beaconhillchildrensfarm.ca

https://en.wikipedia.org/wiki/Jacob_sheep

3. Niemann-Pick Disease

- This loosely-knit group of metabolic diseases are characterized by abnormal accumulation of fats and cholesterol in visceral and neural tissue
- This autosomal recessive disease happens due to missing enzymes to break down body fats which accumulate in the spleen, liver, and eyes
- There are three identified types:
  - Types A and B are caused by lipid buildup in myelin sheaths of nerve cells
  - Type C is caused by cholesterol accumulation
Diagnosing Niemann-Pick Disease (NPD – VIDEO)

- Preschool children with NPD Type A first show “failure to thrive”
- Next comes progressive vision loss and neurological deterioration
- As in Tay-Sachs disease, NPD is characterized by cherry-red macular spots and eye movement disorders (shown here)

Niemann-Pick Saccades video from Leigh & Zee, 4th edition

http://bcove.me/oe9bo26

The Five Known Types of Niemann-Pick Disease

- The ophthalmic hallmark of NPD Type C is progressive supranuclear vertical gaze palsy
- Look for hard blinks and head thrusts with vertical eye movements especially
- Oculomotor and other striated muscle ataxia is common, as are learning disabilities

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Niemann-Pick Disease: Type B vs. Type C

- Type B is mostly respiratory, has less neurological involvement, and survival into adulthood
- Expect orbital congestion due to increased orbital fat
- A macular halo may be seen instead of a cherry red spot in Type B
- Not usually associated with vision loss (normal BCVA)

In Type C, cholesterol-laden “foam cells” accumulate, classically leading to:
- Hepatosplenomegaly, all starting in late childhood
- Progressive dementia or intellectual disability
- Ataxia
- Dystonia
- Vertical gaze paresis

Other Ocular Manifestations of Niemann-Pick Disease, Type A

- Mild corneal haze
- Fine lenticular deposits
- Cherry-red spot (50%)
- Retinal “haze” that extends far beyond the fovea
- Central vision loss, occurring later in the disease (age 2)

http://imagebank.asrs.org/file/8649/niemann-pick-disease-type-b

CNS Effects of Types B and C Niemann-Pick Disease

- In type B, patients can develop psychosis due to accumulation of myelin in the central nervous system
- Since Type B patients survive well into adulthood, when these mental health disorders emerge, they have to be managed, sometimes surgically
- Seen here is the loss of gray matter in the brain of a Niemann-Pick Type C patient

https://neurowiki2012.wikispaces.com/Niemann-Pick+Disease

Signs and Symptoms of Niemann-Pick Disease, Type C

- In terms of eye effects, you can expect at least 4 out of 5 Niemann-Pick patients to exhibit:
- Oculomotor ataxia
- Vertical gaze palsy
- Learning disabilities and visual-perceptual problems
- Some have mental health concerns

https://neurowiki2012.wikispaces.com/Niemann-Pick+Disease
Oculography for Niemann-Pick

Treatments for Niemann-Pick Disease

- “No specific treatment is known for type A, but symptoms are treated.
- In adult patients with type B, physicians try to keep cholesterol levels down to normal levels.
- In 2010, the drug miglustat (Zavesca) had been approved in Canada for the treatment of progressive neurological manifestations in adult patients and pediatric patients with NPC.”

Other Lysosomal Storage Diseases

Other Causes of Macular Cherry Red Spots

- Gaucher disease
- Trauma (Commotio Retinae)
- Sandhoff disease
- Others: Sialidosis

Gaucher Disease: Systemic Manifestations

Gaucher Disease Progression Over Five Years in 7 YOF: Fundus Photos of French Canadian
Gaucher Disease Progression Over Five Years in 7 YOF: OCT “Crumpled Silk” Appearance

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3831135/

Other Cherry Red Spots: Commotio Retinae in 68 YOM 1 day after blunt trauma OS

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4185168/

Other Cherry Red Spots: Commotio Retinae in 68 YOM 20/25 OS 30 days later

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4185168/

Other Causes of Cherry Red Spots: Sandhoff Disease

https://i.pinimg.com/736x/b1/4a/39/b14a3978c36c66149aadea080a79e0a.jpg

Other Cherry Red Spots: Sandhoff Disease in 4 YOAF

“Sandhoff disease symptoms are clinically indeterminable from Tay-Sachs
There are three types of Sandhoff disease: classic infantile, juvenile, and adult late onset”


Other Cherry Red Spots: Sandhoff Disease in 4 YOAF

“Ophthalmologic findings showed that she could not fixate her eyes on objects and could not follow moving targets. Moreover, the oculocephalic reflex and optokinetic nystagmus did not exist. Anterior segments of both eyes showed normal findings but there was a weak and sluggish pupillary response to light in both eyes. A pale optic disc and a cherry red spot in the macula were seen in both eyes by ophthalmoscope.”

Other Causes of Cherry Red Spots: Sialidosis (Mucolipidosis)

https://youtu.be/JBodE9Sgzd8

A 53-year-old man, with non-consanguineous parents, presented to our hospital with a history of progressive decrease of visual acuity since the age of 26.

At 36, he developed generalized myoclonus and ataxic gait.

He showed low visual acuity, ataxic gait, dysarthria and difficulty in writing.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4202095/

Summary: Cherry Red Spots

http://epomedicine.com/medical-students/lysosomal-storage-disorders-made-easy/

Questions?

Thank You!
Readings and References

- For more information on Niemann-Pick and Tay-Sachs diseases, see chapter 7 of Wright’s Handbook of Pediatric Eye and Systemic Disease.