Iris…..The Forgotten Part of the Eye
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Heterochromia

• Congenital (AD)
• Acquired

• Melanocytes contain melanosomes which produce melanin.
  • Lot: brown
  • Moderate: green/hazel
  • Low: blue

Etiologies

• Waardenburg syndrome
  Usually autosomal dominant
  Improper melanocyte differentiation
  Hearing loss (Melanocytes needed for normal cochlear function)
  Heterochromia (Can also have bilateral bright blue eyes)
  Hair hypopigmentation (Patch of white hair)
  Premature gray hair
  Broad nasal root

Etiologies

• Glaucoma meds
  Prostaglandins
  Worse in blue-gray/brown, green-brown, and yellow-brown eyes.
  Increase melanin in stromal melanocytes only.

Etiologies

• Inflammation (Such as Fuch’s, Posner-Schlossmann)
  Brown eyes
  Blue eyes
Etiologies

- Trauma
- Look for iridiodenesis and dilated pupil

Etiologies

- Congenital Horner's Syndrome
  Disruption of sympathetic stimulation
  Iris melanocytes derived from neural crest cells

- Hirschsprung's Disease (Neural crest disorder)
  Intestine does not develop properly

Etiologies

- Siderosis (iron deposits from foreign body)
  Hemosiderosis (iron deposits from hyphema)
  Heterochromia
  Toxic to sphincter

Etiologies

- Glaucoma such as Sturge-Weber (Abnormal migration of melanocytes), ICE, Pigment Dispersion syndrome

Sturge-Weber: Increase in melanocyte activity
ICE

Age related iris atrophy
- Usually more so around the pupillary ruff
- Iris pigment epithelium more resistant to damage
- Pigment can go on endo, anterior lens, and TM
- Miosis, Decrease in light response

Iridioschisis
- Usually in elderly
- Split between anterior and posterior stroma
- Usually inferior
- Shredded wheat
- 50% of the time associated with glaucoma
  (Ischemia?)

Atrophy from cataract surgery

Iridiodialysis
- Separation of iris from CBB

Iridology
- Patterns in iris can determine systemic issues
- Iris is divided in zones that correlate to different body areas (Kidney correlates to lower part of iris)
- Predicts later health problems
- Studies have shown.....
Study
• Dark colored iris = more anxiety, increase in sleep disturbances, experience more pain, less tolerant to heat, more depressed

Benign

Iris Freckles
- Increase in pigmentation of the anterior border layer melanocytes (No increase in number of cells or mass)
- No stromal involvement
- Multiple
- Bilateral
- Never distort the iris architecture
- No associated thickening
- Always flat
- "Splotch"
- No malignant potential (Should never change or grow in size)
- Occurs in about 60% of the population!
- More commonly seen in a lighter iris
- Management: None

Iris Nevus
- Benign proliferation of stromal melanocytes (Composed of spindle cells)
- Blend with stroma
- On the superficial aspect of the iris
- More often solitary but can be multiple
- Can also be diffuse (Associated with ocular melanocystosis)
- Rarely can have a tapioca appearance
- More often unilateral but can be bilateral
- Rough/smooth surface
- Can be pigmented or amelanotic
- Usually flat but can be slightly elevated
- Usually less than 3mm
- 80% are along the inferior iris
- Benign...but does have malignant potential
- Affects 5% of the population

Iris Nevus
- Can change iris architecture (Can cause pupil distortion or sectoral cataract by infiltrating the iris)... Must differentiate from a melanoma
- Also associated with primary epithelial cysts

Iris Nevus
- On ultrasound, iris nevus will have higher reflectively than an iris melanoma.
- Is the iris pigment epithelium intact?
Iris melanocytoma

• Iris melanocytoma is a variant of an iris nevus but just more deeply pigmented and has a cobblestone appearance.
• High chance of leading to pigment dispersion (Pigment can break off)
• 5% risk of malignancy
• Rarely can have a necrotic center

Management of a Iris Nevus

• Typical iris nevus (Looks benign)...
  1. Take Anterior Seg photo
  2. Recheck in 6 months

Management of Iris Nevus

• Suspicious iris nevus (Not sure whether malignent or benign)
  1. Anterior seg photo, gonio
  2. Recheck in 3-6 months
  3. Recheck in 6-9 months
  4. Recheck in 1 year

Management of Iris Nevus

• Bad looking iris nevus (Looks malignant)
  1. Refer!!

Adenoma of the Iris Pigment Epithelium

• Benign (Very rarely can it become an adenocarcinoma which is malignant)
• Rare
• Dark/grey/black (Very heavily pigmented) nodule
• Typically solitary
• Typically small
• Smooth for the most part but can be multi-nodular
• Can enlarge but usually does not
• Does not involve the iris stroma (like seen in iris nevi, iris melanocytoma, and iris melanoma)
• Typically no feeder vessels
• No dilated episcleral blood vessels
• Usually at the peripheral iris (Because in the peripheral can affect the TM which can lead to pigment dispersion/glaucoma)
• Anteriorly displaces the iris stroma which leads to iris atrophy (This allows better view of the adenoma). First noticed when young vs. old??
• Under-diagnosed
• Treatment: Monitor as you would with a suspicious nevus
**Leiomyoma**

- Rare
- Benign
- Usually noted in females
- Originates from smooth muscle (can originate from the sphincter or dilator muscle)
- Solitary
- Typically amelanotic
- Can be vascular
- Hormones play a role in formation due to similar appearance of uterine leiomyoma
- Difficult to distinguish from an amelanotic melanoma (transillumination may help as it transmits more light...appears brighter)
- Treatment: Monitor

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**Juvenile Xanthogranuloma**

- Typically seen in infants/children (usually seen <3 years old)
- Dermatologic condition (inflammatory etiology)
- Benign
- Lesions typically seen on head/face (firm, well demarcated, multiple raised papulonodules that are tan, red, yellow, orange are noted)
- Almost always unilateral when involving the iris
- On the iris, multiple yellowish nodules are noted (can actually lead to heterochromia)
- Can be vascular (**most frequent cause of spontaneous hyphema in children as these lesions are fragile/weak**)
- Can have an uveitis
- Link with NF-1, Epilepsy, Niemann-Pick disease (lipid metabolism issue), and Juvenile myelomonocytic leukemia
- Nodules can be seen in other areas in the eye (second most common area is the eyelid)
- Treatment: topical/systemic/intra-vitreal steroid may help

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**Lisch Nodules**

- Melanocytic iris hamartomas (overgrowth of tissue)
- Benign
- Multiple
- Small (<2mm)
- Sharply defined
- Dome shaped
- Smooth masses on stromal surface
- Tan/brown
- Bilateral
- Seen in almost all NF-I patients (Café-au-lait spots, prominent corneal nerves, S-shaped ptosis, optic nerve gliomas, multiple neurofibromas)

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**Koeppe/Busacca Nodules**

- Busacca nodules (iris peripheral iritis): whitish-yellow in color usually
- Koeppe nodules (iris pupilary iritis): brown, more common, typically more pigmented
- Accumulation of inflammatory cells
- If nodules are found in the angle...Berlin's
- As indicators of a granulomatous iritis; but Koeppe nodules can also be seen in non-granulomatous iritis
- "Mutton-fat"KP's
- They
- 1. sarcoidosis (most common)
- 2. Uveitides (uveitis/uveitis-related histiocytosis)
- 3. tuberculous
- 4. Toxoplasmosis
- 5. Sympathetic ophthalmia
- 6. Neoplasms
- 7. Kaposi's sarcoma
- 8. Lyme disease
- 9. Fat transfer keratoconjunctivitis

Treatment: once the underlying iritis is taken care of, the nodules should go away

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**Pigmented granules on iris due to pigment dispersion syndrome**

- Pigment granules on iris within furrows
- Bilateral
- Brown (even if light iris)
- Posterior pigment layer of the iris rubs up against the lens zonules due to backward bowing of the peripheral iris (reverse pupillary block)
- Krukenberg spindle (the more dense this is, the more likely pigmented granules will be on the iris)
- Pigment in anterior chamber
- Radial slit defects in the mid peripheral iris which will eventually lead to iris atrophy. An irregular/larger pupil will develop over time.
- Pigment on posterior capsule (Zentmeyer’s line)
- Pigment on zonules
- Gonio shows wide open angles with heavily pigmented TM

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**Iris nodules secondary to Iris Nevus Syndrome /Cogan-Reese Syndrome**

- Cogan-Reese syndrome
- Corneal endothelium grows over the anterior chamber angle and iris
- Abnormal endothelium will eventually contact the cornea
- Can lead to secondary angle closure glaucoma
- Fine, beaten-metal appearance to endothelium
- Usually unilateral
- Females
- Iris is flattened
- Loss of iris crypts
- Matted or smudged appearance to the iris
- Cogan-Reese Syndrome: iris nodules represent buds of normal stroma ("Mushroom patch")
- Iris Nevus Syndrome: Thought to be an actual nevus

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Iris Mammillations

- If the only finding, this is an incomplete expression of ocular melanocytosis. This has not been found to be associated with uveal melanomas
- Can also be associated with NF-1, Axenfeld-Rieger’s, and Peter’s anomaly

Iris Cyst (Primary)

- Pigment Epithelial Cyst
  - Unilateral
  - Usually solitary
  - Dark/Brown
  - Globular
  - Usually in the inferior temporal quadrant
  - Abnormal focalized lodge under iris (“ball under carpet”)
  - Transparent/Translucent (key!!)
  - Minimal to no growth
  - Pupil is able to dilate normally
  - Can be at the pupillary border, mid zone, or iris root
  - Overlying iris may atrophy
  - Cysts can collapse and reform into multiple irregular cysts (iris flocculi)
  - Can be dislodged and can float in the anterior chamber (Can get stuck to the angle or endo)
  - Treatment: Watch

- Stromal Cyst
  - Similar to a pigment epithelial cyst but is usually within the stroma.
  - Less common
  - Appears more translucent/liquid filled
  - Tends to enlarge more quickly when compared to a pigment epithelial cyst
  - More likely to lead to a secondary glaucoma or corneal decompensation
  - Most will need to be removed (Aspiration and alcohol irrigation)

Secondary Cyst

- Ingrowth of surface epithelium
- Etiologies
  1. Parasites
  2. Tumors
  3. Miotics (Will typically be bilateral and smaller, can prevent with phenyl 2.5%)
  4. Trauma/Surgery (Two most common reasons)

Brushfield spots

- Iris stromal hyperplasia surrounded by hypoplasia
- Usually noted in lighter irises
- Small white/grayish spots in mid-peripheral iris
- Slightly elevated
- Bilateral
- 90% of patients will have Down’s syndrome
- If similar lesions are found in a normal patient (Called Wolfflin nodules, 24%), these nodules are more in the peripheral iris (Connective fibers)
Malignant Iris melanomas

- Make up 5% of uveal melanomas
- Malignant melanocytic neoplasm (from iris stroma). Composed usually of spindle B cells (most common)
- More common in blue/grey eyes
- M:F
- Usually occur in 5th or 6th decade of life
- If melanoma happens when patient is young think...
  1. Nevus of Ota
  2. Dysplastic cutaneous nevi (Hereditary development of nevi...increased risk of melanomas)
  3. Familial melanoma
  4. NF-1
- Typically from a pre-existing iris lesion
- Very few are aggressive (Less than 5% metastasize)
- 80% involve the inferior iris (sun exposure)
- Prognosis is typically good especially if it is caught early

4 types of iris melanomas

- Solitary (pigmented vs. non-pigmented)
- Ipsilateral hyperchromic heterochromia (Diffuse growing intrastromal melanoma...type of ring melanoma)
- Tapioca (Presents with multiple surface nodules...Glisten)
- Trabecular meshwork melanoma (Confined to the TM as a ring melanoma)

Risk Factors

- Greater than 3mm in diameter
- Greater than 1 mm in thickness
- Lesion is not transparent
- Surface vascularity (Easier to see in non-pigmented lesions)
- Feathery margins
- Pupil distortion
- Localized cataract
- Increased IOP
- Pigment on endo (Pseudo-Kruckenberg spindle)
- Iris
- Band keratopathy
- Hyphema
- Feeder vessels
- Pupil does not dilate normally
- Pigment in sclera adjacent to melanoma
- Documented growth (1st sign of malignancy)

Iris melanomas

- Must make sure there is no involvement of the CBB
- CBB tumors typically start behind the iris
- Look for dilated episcleral vessels (Sentinel blood vessels)...Can see with iris melanomas but more so in CBB melanomas
- Can be superior/inferior
- Can be a ring melanoma as well

Iris Metastasis

- Usually patient already has a systemic malignancy
- Usually amelanotic(pink/yellow lesions)
- Multiple nodules
- Fast growing
- Presents with an iritis
- Can get a hyphema, NVI
- Pseudo-hypopyon (Consists of tumor cells)
- Prostate/lung cancer: males
- Breast cancer: females
Retinoblastoma

- Multifocal iris nodules with iritis is noted
- Most common primary intra-ocular malignancy
- Usually seen before age 3
- Leukocoria
- Strabismus
- Increase in IOP
- Orbital inflammation
- Retinal tumor

Leukemia

- Can get iris infiltration which presents as nodules
- Hyphema
- Heterochromia
- Pseudo-hypopyon
- Iritis
- Associated with most types of leukemia (Acute lymphoblastic the most common)
- Poor survival rate if iris nodules are noted (less than 3 months)