Advanced Anterior Segment Cases: timely Diagnosis and Treatment

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7yo F with a white OD

- History:
  - Mom noted OD whiter than OS a week ago and now sees a white spot on the pupil
  - Vision seems fine
  - No known medical problems or med or allergies
  - Normal birth hx and no trauma
  - Fam HX negative for eye disease
7yo F with a white OD

- Exam:
- Vasc OD = 20/25
- IOP = 30 mmHg
- SLE: white and quiet with 3-4+ cells and clumps circ without fibrin; no Cataract.
- Iris – SLE photos**>>
• Findings: multicentric creamy white mass lesions of iris without inflammation and with secondary obstructive hypertension

• Differential Diagnosis:
  – Hematopoietic cancer (leukemic or lymphomatous)
  – Medulloblastoma (diktyoma)
  – Retinoblastoma (rare diffuse multicentric)
  – Neuroblastoma (metastatic)
  – Juvenile xanthogranuloma (JXG)
  – Uveitis?
7yo F with a white OD

• Plan:
  – Urgent EUA for thorough Retinal exam for RB and poss AC washout and biopsy with vitrectomy probe IF no RB seen.
  – Pathology consultation> Lymphoma specialist on call for specimen handling
  – Rescheduled elective cases and took to surgery the next working day.
  – Procedure **

7yo F with a white OD

• Pathology results:
  – TTUHSC – small blue cells not cw lymphoma/leuk with epithelioid characteristics > consult
  – Mayo eye path > small blue cell tumor cw RB, MB, LL, NB
  – Houston Dr. Barrios > RB: cytology, (+)synaptophysin, though (-)RB protein; fam req add opin
  – Will’s Path Dr. Eagle confirmed RB

• Meanwhile seen at MDA then two more local opinions from uveitis and retina specialists
Will’s Eye Institute  
Dr. Ralph Eagle

• Both show clumps and cohesive aggregates of small basophilic cells with scant cytoplasm that have a high NC ratio and irregular nuclear contours. ... Characteristic background of necrotic and apoptotic cells and cellular debris as well as scattered macrophages. A few small aggregates of cells have an arrangement reminiscent of rosettes. The tumor cells show positive cytoplasmic immunoreactivity for synaptophysin consistent with retinoblastoma. The tumor cells are not immunoreactive for RB protein with appropriate positive and negative controls. This pattern of immunoreactivity is also consistent with retinoblastoma.

• Diagnosis: anterior chamber fluid, right eye, fine needle aspiration biopsy adequate cytologic preparation positive for malignancy. Cytologic features consistent with retinoblastoma. Iris nodule, right, fine needle aspiration biopsy adequate cytologic prep in preparation positive for malignancy. Cytologic features consistent with retinoblastoma.

• Comment: a small blue cell tumor in the anterior chamber and iris of a child is a retinoblastoma until proven otherwise. The clumps of cells seen in the cytologic preparations resemble the tumor seeds that commonly involve the vitreous in retinoblastoma. Retinoblastoma cells show positive immunoreactivity for synaptophysin, as this case does. This observation excludes leukemia or lymphoma. Neuroblastoma metastatic to the eye is quite rare, involves infants and usually occurs in patients who are known to have metastatic neuroblastoma.

• The diffuse infiltrative variant of retinoblastoma's typically occurs in older children with an average age of 6 to 7 years who often present with anterior chamber involvement as a pseudohypopyon and or clumps of tumor. Malignant Medulloepithelioma of the ciliary body may contain foci of poorly differentiated tumor that resemble retinoblastoma, but such tumors are exceedingly rare.

Bilateral corneal opacification and glaucoma

• 59yo MAF referred for corneal edema 10/2013
• Mult LPIs OU for CACG; TRAB OU 2008; IOP 14/17

- OD: 1+ DM folds, 3+ microcystic edema, no subep bullae
- OS: 2+ DM folds especially temporally, 3+ microcystic edema, no subep bullae
- Anterior Chamber:
- OU: 3+ deep
- Iris:
- OD: temporal steeply with history of LPIs
- OS: large superior supertemporal indentations s p trab

- Lens:
- OD: 2+ NUC
- OS: PC IOL with at least 1+ PCO
- Optic Disc:
- OD: <20 NWI area, appears pink
- OS: 20/100 views appear -5.1 and no clear pupil with 20D od
Bilateral corneal opacification and glaucoma

- 59yo MAF referred for corneal edema 10/2013
- PKP 2/2014 OS 6mm
- Lost to FU/ ran out of meds mult times> rejected, treated 20/100 persist edema; OD > HM
- PKP 8/2015 initially cleared but more compliance issues and edema w IOP 40 on MMT 20/400 >>
- JY for Ahmed
- DLM 9/16 VA HM/400 IOP27/26 OS AC fibrosis and forward contraction of iris

Bilateral corneal opacification and glaucoma

- 59yo MAF referred for corneal edema 10/2013
- 4/17 VA HM/HM, IOP 29/36 (ran out meds) 4+ edema OS and fibrous changes OD: compliance discussion > kept 4 monthly visits >
- 8/17 PKP OS and tube trim> cleared to 20/150 but cyclitic membrane pushing AC shallower w tube touch > edema
- 7/18 down to LP/CF > disc options
Bilateral corneal opacification and glaucoma

• 59yo MAF referred for corneal edema 10/2013

• Options:
  – 4th PKP OS
    • Immune suppression syst
    • Other surgery for cyclitic membrane
  – Boston Kpro 1 OS w Pedi size 8.0mm back plate?
  – What about OD?
    • SK, PKP, CE, IOL + ?
    • Vispot?
Ectopia Lentis
Case 1812

• 59yo WF referred for CE w bilat. Zon laxity
  – No FHx eye, No known syst Dz.

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Ectopia Lentis

- Non Surgical Treatments if lens clear
  - Refractive correction if good BCVA
  - Aphakic CL for luxation or if subluxed sufficient to make vis axis aphakic
  - Pupillary constriction for dysphotopsias from aphakic crescent
Ectopia Lentis
Case 1812
• 59yo WF referred for CE w bilat. Zon laxity
Ectopia Lentis
Case 1812

• 59yo WF referred for CE w bilat. Zon laxity

Ectopia Lentis

• Definition: Subluxed vs luxated
  – Onset
    • Congenital – may have overlay of Amblyopia
    • Developmental
    • Acquired
  – Diagnosis
    • SLE signs
      – HOAs by retinoscopic reflex with NL topo,
      – iridodonesis,
      – equator of crystalline lens visible
Ectopia Lentis

• Etiology
  – Simple Ectopia Lentis
  – Ectopia lentis et pupillae
  – Syndromic/Heritable/systemic associations
  – Secondary to other ocular disorders
  – Infectious
  – Traumatic
  – Mass mechanical

Isolated

– Simple Ectopia lentis – congenital or acquired – usually bilateral and up and temporal
– Vit prolapse and RD risk higher
– Inheritance: AD + AR
  » Mutations in the FBN1 (AD)(Chromosome 15) or ADAMTSL4 (AR) (Chromosome 1)gene impair protein function and lead to a decrease in microfibril formation or result in the formation of impaired microfibrils. Fibrillin 1 gene.
Ectopia Lentis

• Syndromic and heritable
  1. Marfan Syndrome – up and out like simple, Aortic Dissection
  2. Homocysteinuria - increased risk of thrombotic episodes. 60% inferior or nasal
  3. Weill-Marchesani syndrome

Ectopia Lentis

• Secondary to other ocular disorders
  – Aniridia
  – Congenital Glaucoma
  – Pseudoexfoliation
  – Retinitis Pigmentosa
• Infectious - lues
• Traumatic
• Mass
• Ectopia Lentis et Pupillae

- Systemic disease of Connective tissue
- Fibrillin-1 defect DT FBN1 gene AD (25% de novo mut)
- 75% bilat symmetric Ectopia lentis **UP & OUT**
- Unusually flexible joints, long fingers, Tall and thin, arm span > stature, long narrow face, high arched palate, crowded teeth, scoliosis, pectus excavatum, Mitral valve prolapse or aortic dissection, Axial myopia
Marfan Syndrome

- An autosomal DOMINANT MULTISYSTEM disorder characterized by abnormal manifestations in the skeletal, cardiovascular, and ocular systems.

Wrist Sign

Arachnodactyly

Thumb Sign
In the presence of family history:

1. Ectopia lentis AND Family History of Marfan syndrome (as defined above) – Marfan syndrome - The presence of ectopia lentis and a family history of Marfan syndrome (as defined in 1-4 above) is sufficient for a diagnosis of Marfan syndrome.

2. A systemic score ≥ 7 points AND Family History of Marfan syndrome (as defined above) – Marfan syndrome - A systemic score of greater than or equal to 7 points and a family history of Marfan syndrome (as defined in 1-4 above) is sufficient for a diagnosis of Marfan syndrome. However, features suggestive of Shprintzen Goldberg syndrome, Loes-Dietz syndrome, or vascular Ehlers Danlos syndrome must be excluded and appropriate alternative genetic testing (TGFBR1/2, collagen biochemistry, COL3A1 and other relevant genetic testing when indicated and available upon the discovery of other genes) should be performed.

3. Aortic Root Dilatation Z score ≥ 2 above 20 yrs. old, ≥ 3 below 20 yrs. old – Family History of Marfan syndrome defined above) – Marfan syndrome - The presence of aortic root dilatation (Z ≥ 2 above 20 yrs. old, ≥ 3 below 20 yrs. old) and a family history of Marfan syndrome (as defined in 1-4 above) is sufficient for a diagnosis of Marfan syndrome. However, features suggestive of Shprintzen Goldberg syndrome, Loes-Dietz syndrome, or vascular Ehlers Danlos syndrome must be excluded and appropriate alternative genetic testing (TGFBR1/2, collagen biochemistry, COL3A1 other relevant genetic testing when indicated and available upon the discovery of other genes) should be performed.

Caveat: Without discriminating features of Shprintzen Goldberg syndrome, Loes-Dietz syndrome, or vascular Ehlers Danlos syndrome – AND after TGFBR1/2, collagen biochemistry, COL3A1 testing if indicated – other conditions/genes will emerge over time.

Homocystinuria I, II, III

- AR metabolic disorders of Amino Acid metabolism with accumulated homocysteine; prev. 1/250,000 overall but Germany 1/17,800, Norway 1/6,400, Qatar 1/1,800
- Most common form: Ectopia lentis, myopia, osteoporosis, some with developmental delay, Thrombocclusive events
- Mutations in the CBS,>>> MTHFR, MTR, MTRR, and MMADHC genes
Homocystinuria I, II, III

- Marfanoid habitus; fair skin & course hair
- 90% bil symmetric Ectopia lentis: Down & IN
- Mental retardation/seizures in 50%
- Circulation problems with thromboembolic events >>CVA hx or signs
Homocystinuria I, II, III
Ectopia Lentis

- Weill-Marchesani Syndrome
  - Short stature and fingers
  - IQ reduced in 25% - most Normal
  - Microspherophakia – lenticular myopia
  - Pupillary block or luxation to AC (OAG +NAG)
  - Angle developmental abnormalities and Glaucoma
  - Occ heart defects
  - Inheritance: AR + AD form with same fibrillin gene abnormalities as isolated Ectopia lentis

Weill-Marchesani
Homocystinuria I, II, III

Symptoms & Signs of Homocystinuria

- Dislocation of the eye lens
- Nearsightedness
- Glaucoma
- Osteoporosis

Sulfite oxidase deficiency

- Metabolic defect of Sulfur metabolism
  - Ectopia lentis
  - Progressive CNS abnormalities in first yr.
Hyperlysinemia

- AR metabolic defect of lysine
  - Ectopia lentis
  - Mental retardation

Other syndromes assoc. with Ectopia Lentis

- Ehlers-Danlos Syndrome
- Crouzon Disease
- Refsum syndrome
- Kneist syndrome
- Mandibulofacial dysostosis
- Sturge-Weber syndrome
Capsular fixation options
Morcher CTRs

Capsular Fixation Options
Cionni CTRs
ACIOL Relocation

- 53 yo LAM w AVM> seizure disorder, depression and peptic ulcers
- RRDs OU
- CE 1998 Galveston > Sil oil and now HM at 4 ft
- OS pneumatic retinopexy then CE uncompl then 3yrs later IOL dislocation>> PPV and ACIOL > 2yrs later dislocation

ACIOL dislocation with corneal edema