

Retinal potpourri: It isn't rare if it's in your chair!

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Disclosures



Speaker/Advisory Board/Consultant:

- ❖ Optovue (Visionix)
- ❖ iCare
- ❖ Apellis
- ❖ Iveric Bio
- ❖ LKC technologies

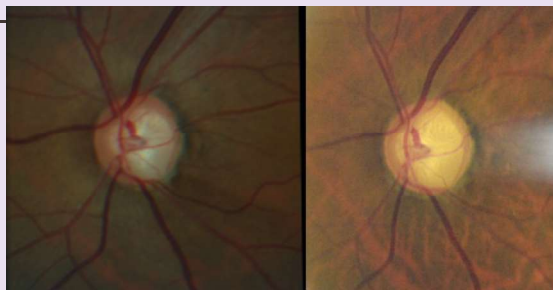
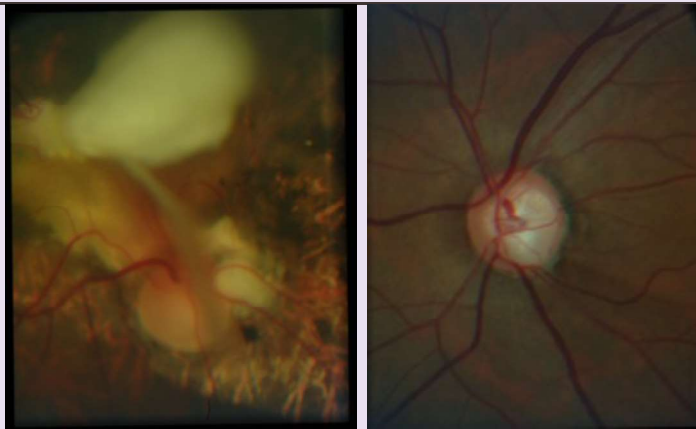
Case 1

Let's look at the case...

49-year-old African American Male

- PMH: Unremarkable
- BCVA: CF 1 FT OD, 20/20 OS
- (+)APD OD
- CF: Abnormal superior OS
- TAP: 14mmHg OD, OS
- Medications: Alphagan-P 0.1%

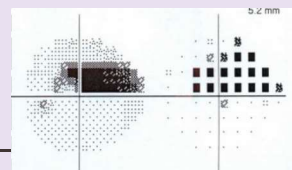
"I have been blind in my right eye since childhood...and I have glaucoma in my left eye."

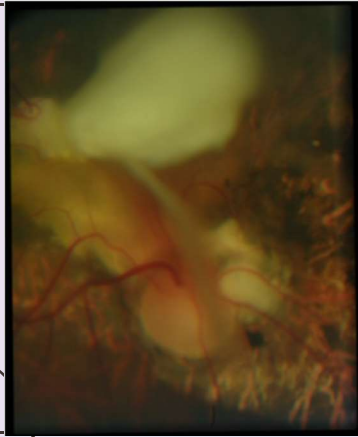


Then (2014) ...

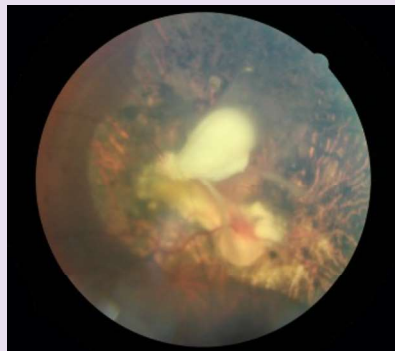
and now

OS:
Good Eye?



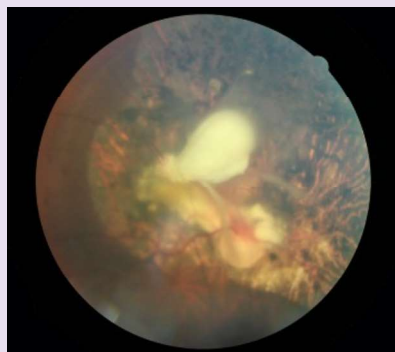


What about his
right eye???



1. Retinoblastoma
2. Persistent fetal vasculature
3. Toxoplasmic retinochoroiditis
4. Toxocariasis

So...What is the
clinical picture
most consistent
with?



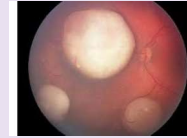
1. Retinoblastoma
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So...What is the
clinical picture
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with?

Retinoblastoma

Why?...*Leukocoria*....

- One of the primary signs of retinoblastoma.

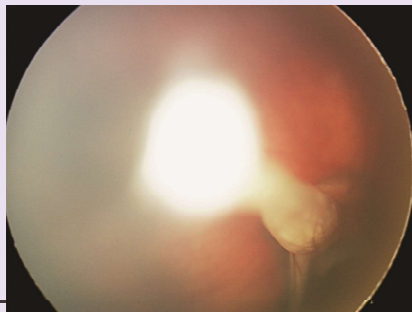


***However, a number of other conditions may also present with leukocoria, and it is critical to differentiate retinoblastoma from these so-called pseudoretinoblastomas for proper management.

<https://www.willbros.com/conditions/retinoblastoma/>

Persistent Fetal Vasculature

Persistent hyperplastic primary vitreous



- Developmental disorder
- Second most common cause of infantile leukocoria

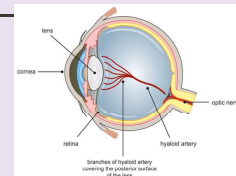
What is it???

Persistent Fetal Vasculature

Persistent hyperplastic primary vitreous

Vascular structures present during eye development fail to wither (regress)

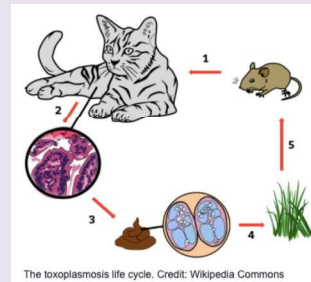
- Disease is non-progressive; but as the eye grows dangerous sequelae may ensue



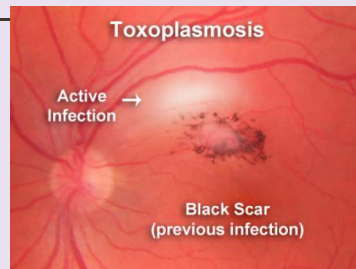
Toxoplasma Retinochoroiditis

Cats serve as a host for this parasite (*Toxoplasma gondii*) and can pass the oocysts in their feces. They acquire the pathogen by eating small infected rodents.

Also contracted through eating contaminated food.



Toxoplasma: A Cat-astrophe??



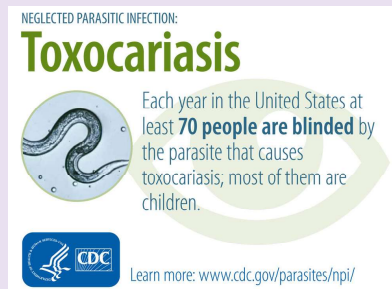
Toxoplasmosis is the most common cause of posterior uveitis.

Classic findings include a white fundus lesion with overlying, intense vitreous cells that frequently is described as "headlights in a fog."

What if you knew this...

- This patient liked to play in the sandbox as a child, and often put the dirty sand in his mouth
- The patient reported exposure to dogs and puppies as a young child
- The patient reports terrible vision in his right eye since childhood
- The patient grew up in Puerto Rico, in a socioeconomically disadvantaged area

And the final DDx?



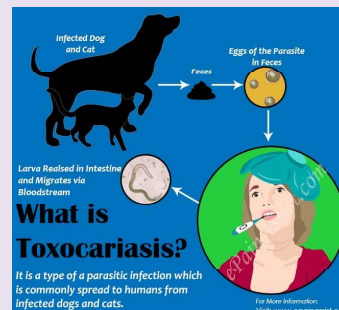
Toxocariasis is an infection transmitted from animals to humans (zoonosis)

Caused by the parasitic roundworms found in intestines of dogs (*T. canis*) and cats (*T. cati*)

How do we get it?

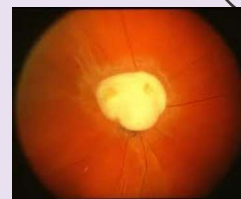
Adults and children can become infected by accidentally swallowing dirt that has been contaminated with dog or cat feces that contain infectious *Toxocara* eggs.

Although it is rare, people can also become infected from eating undercooked meat containing *Toxocara* larvae.



Ocular manifestations....

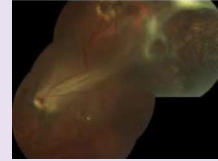
- Larva induces chronic inflammation
 - Anterior Uveitis
 - Posterior Uveitis (more common)
 - Vitritis
 - Chorioretinitis



Granuloma= Larva trapped in eye from inflammation: Large, white mass lesion

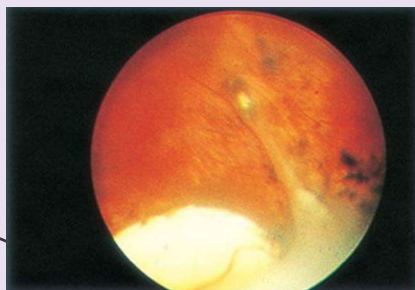
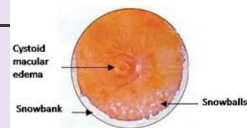
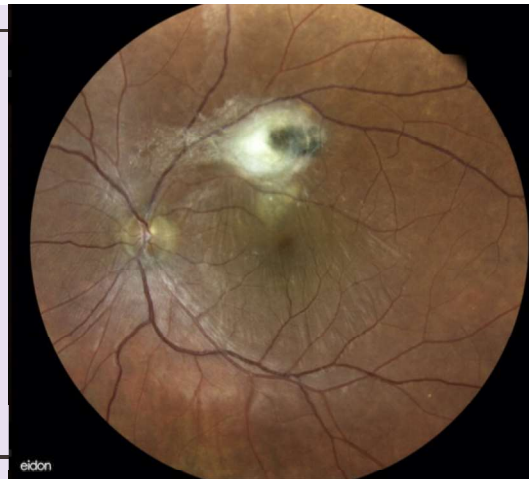
How does it get into the eye?

Larvae migrate to the eye through:
(1) the central retinal artery reaching the posterior pole,
(2) the long ciliary arteries, or
(3) the vitreous reaching the pars plana



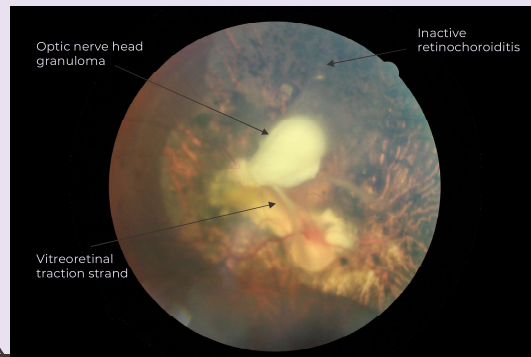
All produce inflammation and the formation of granuloma

Fibrous traction bands



Vitreous opacification can be accompanied by immune complexes in periphery "snowballs", "snowbanks" (Pars plana) and tractional bands leading to RD

Back to our patient.....



Review: *What are some ocular manifestations of ocular toxocariasis?*

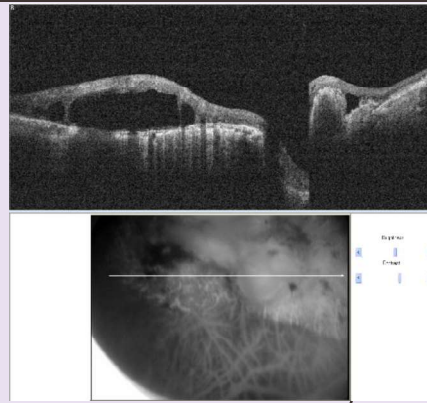
- A. Vitritis
- B. Tractional Retinal Detachment
- C. Retinochoroiditis
- D. Granuloma
- E. Strabismus
- F. All of the above

Review: *What are some ocular manifestations of ocular toxocariasis?*

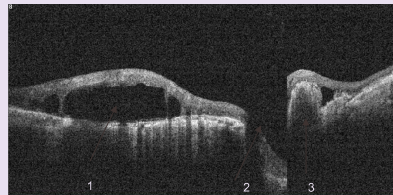
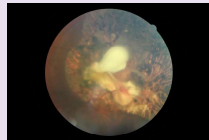
- A. Vitritis
- B. Tractional Retinal Detachment
- C. Retinochoroiditis
- D. Granuloma
- E. Strabismus
- **F. All of the above**

Ancillary Testing... SD-OCT!

Line scan through ONH and peripapillary tissue



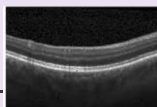
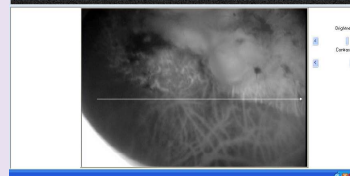
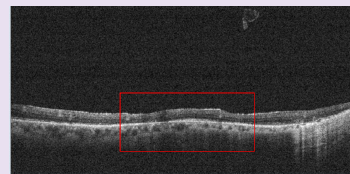
What is the OCT showing?



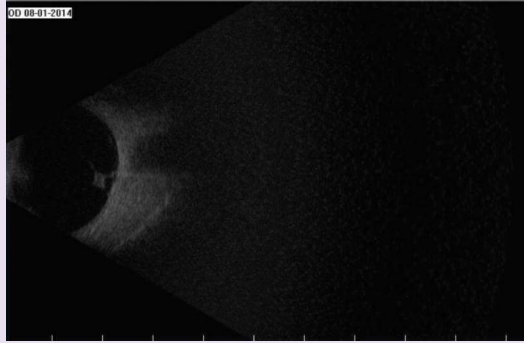
1. Neurosensory detachment
2. ONH
3. Hyper-reflective, dense lesion nasal to the optic nerve associated with granulomatous tissue on the nerve

What about the retinal scan?

- Attenuation of retina, RPE and choroid
- Thinning of inner and outer retina



Ultrasound



Presentation...

Patients (usually children) will present with decreased vision, strabismus, leukocoria... mimicking many other diseases!!

So.. How do we make the diagnosis???

Laboratory testing:

- Serum IgG (ELISA): 90% specificity and sensitivity
- Intraocular fluid

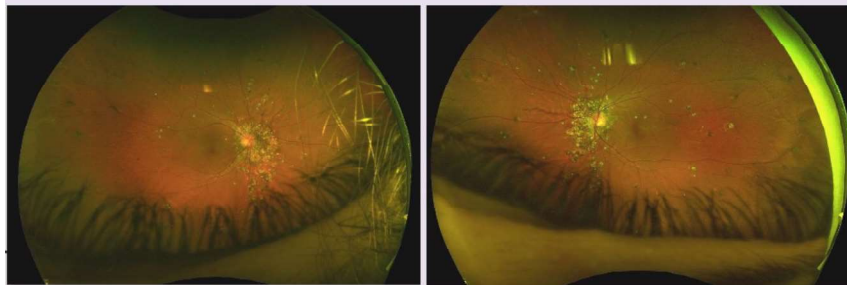
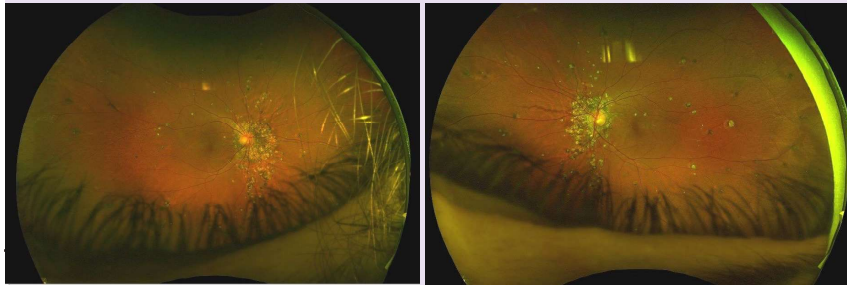
Case 2

39-year-old Hispanic female

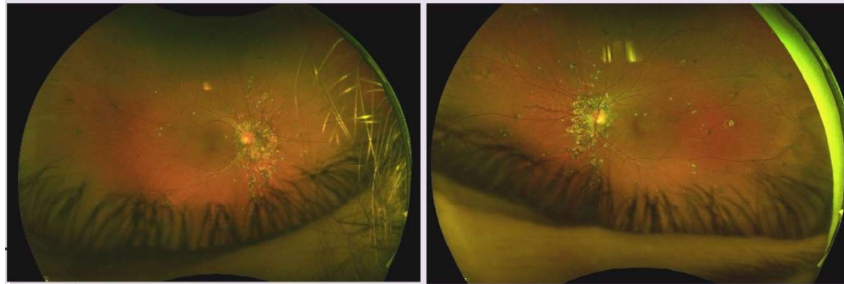
- Blurry vision OU without glasses
- BCVA 20/20 OD, 20/20 OS

Routine eye examination... I was told that I have "retinal scars".

Routine Eye Examination??



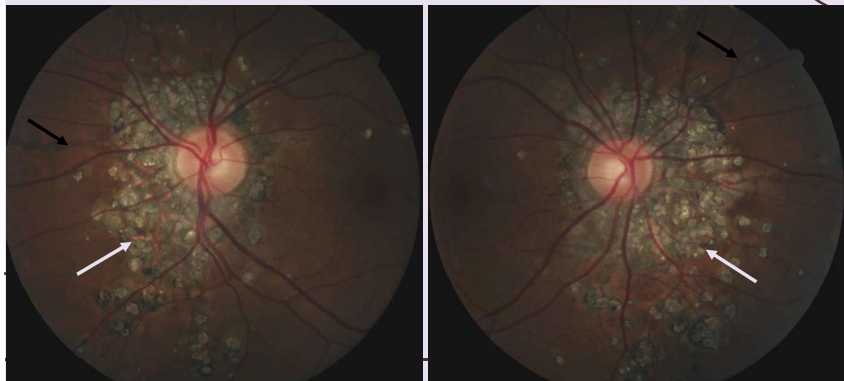
- What could this be?
1. Multifocal choroiditis
 2. Birdshot chorioretinopathy
 3. Traumatic chorioretinitis
 4. Serpiginous choroiditis?
 5. Something else???



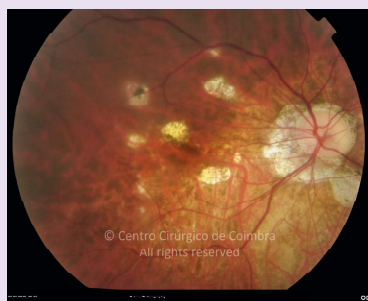
What could this be?

1. Multifocal chorioiditis
2. Birdshot chorioretinopathy
3. Traumatic chorioretinitis
4. Serpiginous chorioiditis?
- 5. Something else???**

Not sure..... Let's look a bit closer!



What is multifocal chorioiditis?

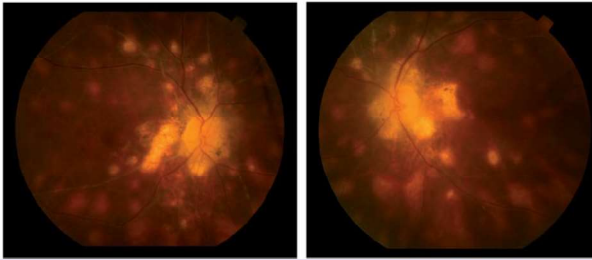


CELLS!!! ANTERIOR OR POSTERIOR



- o Spontaneous, inflammatory condition presenting with multiple lesions in the retina and choroid
- o Episodes of inflammation that can occur unilaterally or bilaterally

Birdshot Chorioretinopathy



Birdshot chorioretinopathy (BSCR) is a chronic posterior uveitis characterized by multiple cream-colored, hypopigmented choroidal lesions

- Bilateral
- HLA-A29 Association
- Blurred vision, floaters, photopsia, scotoma, nyctalopia

Serpiginous Choroiditis



Rare, bilateral, idiopathic inflammatory disorder that results in geographic destruction of the retinal pigment epithelium (RPE), retina, and choriocapillaris.

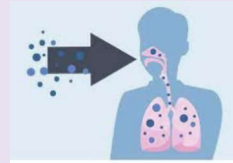
- Chronic
- Recurrent
- 30-60 y/o
- Asymptomatic unless macula involved
- Inflammatory etiology (HLA-B7)

Histoplasmosis??



Histoplasmosis

Histoplasmosis is a disease you can get when you breathe infected airborne spores from the fungus *Histoplasma capsulatum* into your lungs.



It enters the air when people disturb soil when plowing fields, sweeping chicken coops, or digging holes
Endemic in Ohio and Mississippi River Valleys.

Ocular Histoplasmosis: *How do we make the diagnosis?*

Inflammatory, multifocal chorioretinal disorder

POHS diagnosis is defined clinically by the following triad of signs:

- Peripapillary atrophy (PPA)
- Histo spots, which appear as “punched-out” lesions, along with similar macular scars
- CNV or subsequent disciform scarring

**At least two of these three criteria must be met

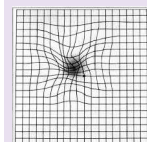
Ocular Histoplasmosis (POHS)

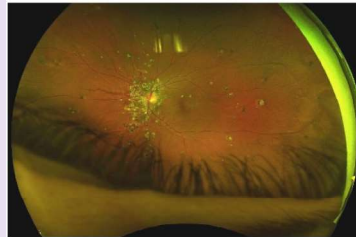
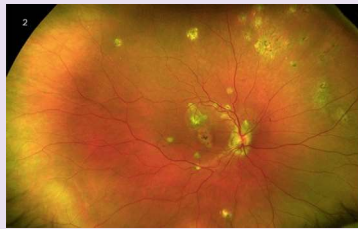
The infection can move from the lungs into the eyes, leading to vision loss.

What are the symptoms of OHS?

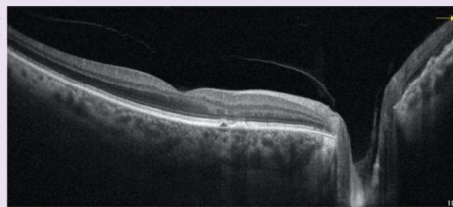
OHS usually doesn't cause any symptoms in the early stages. But over time, you may notice:

- Straight lines looking crooked or wavy
- Blind spots in your vision

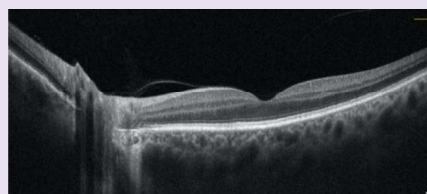
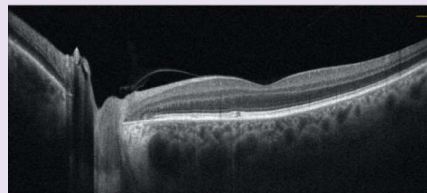




Back to our patient:

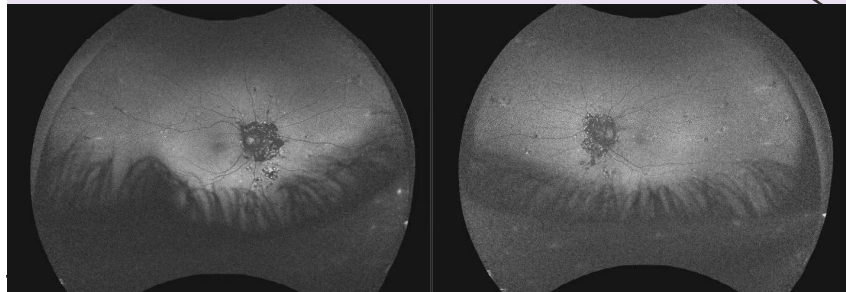


Back to our patient:



Fundus Autofluorescence

Hyper versus Hypo



Nonpigmented macular chorioretinal scars, which are distinguished by their round, hypoautofluorescent appearance

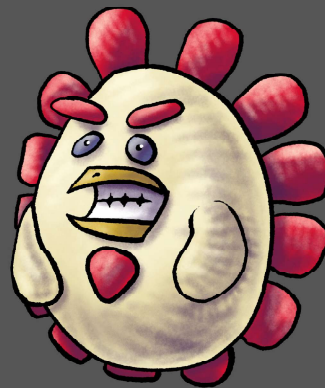
COME TO FIND.....

She grew up working
with chickens on a farm

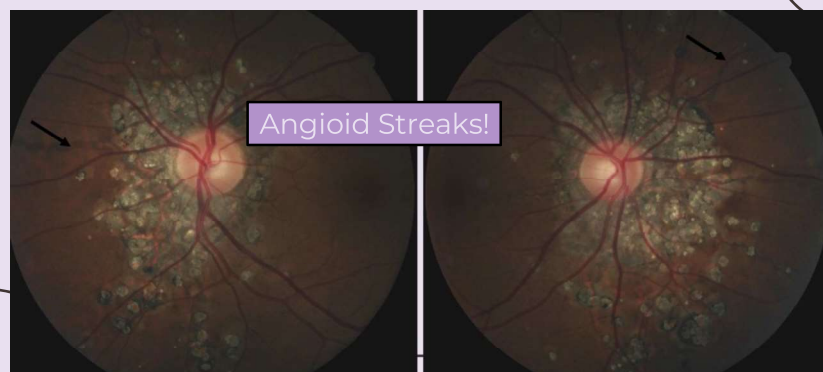
AND

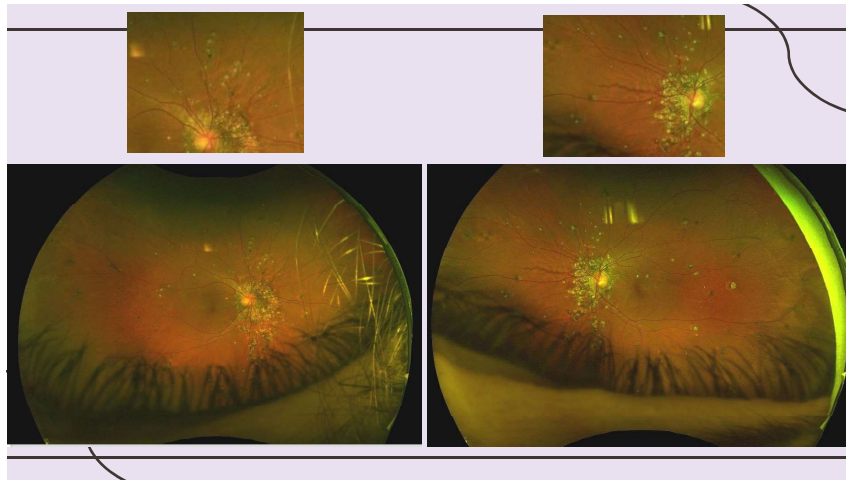
Her daughter has lung
disease from
Histoplasmosis!!

Histoplasma Capsulatum



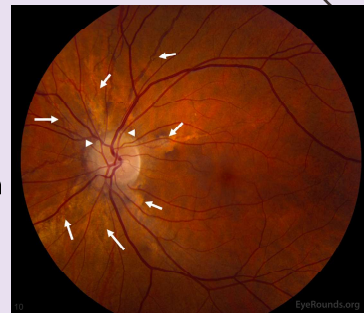
But what else?



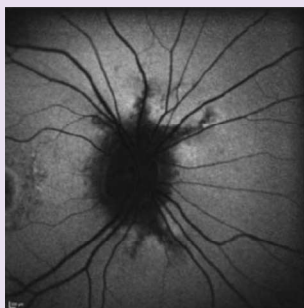


Angioid Streaks

P Paget's
E Ehler's Danlos
P Pseudoxanthoma Elasticum
S Sickle Cell
I Idiopathic

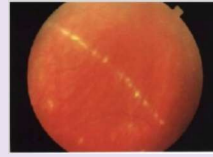
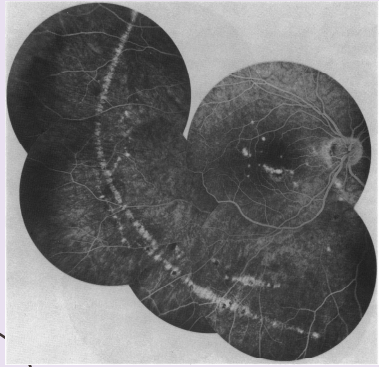


And others!!



Fundus Autofluorescence: Angioid Streaks

Angioid streaks appear as irregular lines of reduced autofluorescence running outwards from the optic disc



Linear streaks; 5% of
POHS... But, not
Angioid streaks??



"Patients can have as many diseases
as they damn well please."

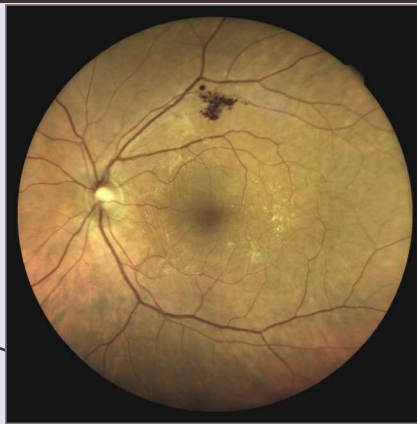
- Hickam's Dictum
Dr. John B Hickam

Case 3

67-year-old Hispanic female

Comprehensive eye examination; blurry vision OU; S/P Lasik 15 years;
h/o retinal lesion OS (40+ years)

❖ BCVA 20/20 OD; 20/25 OS



What could this be?

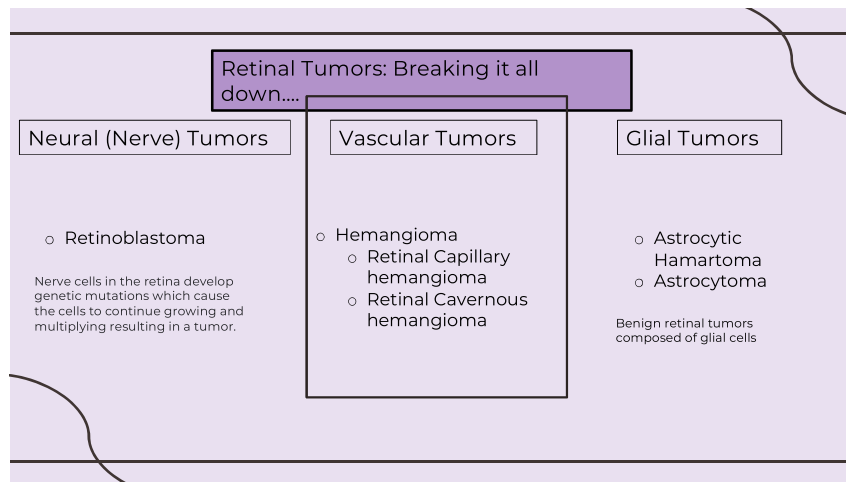
1. Retinal hemorrhages
2. Capillary Hemangioma
3. Retinal cavernous hemangioma

Retinal Hemorrhages



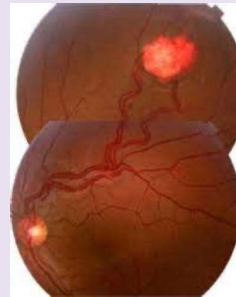
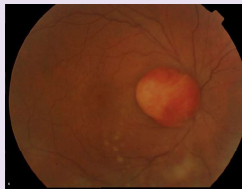
40+ years??





Retinal Capillary hemangioma (Retinal hemangioblastoma)

Hemangioma:
Benign vascular tumor derived from blood vessel; ONH or retinal



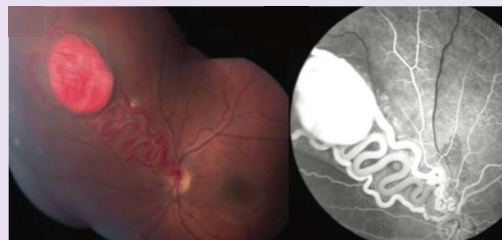
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11003528/>

Retinal Capillary hemangioma

- ❖ No sex predilection
- ❖ Average age at diagnosis= 25

- ❖ Reddish, orange mass

Dilated retinal vessels feeding and draining the tumor



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11003528/>

Von-Hippel Lindau: (Most common systemic association)

- ❖ Bilateral, multiple or solitary retinal hemangiomas

Characterized by the growth of various benign or malignant tumors of the retina and the brain, along with cysts of several visceral organs such as the kidneys, pancreas, and adrenal glands and reproductive organs



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11010100/figure/F1/>



Retinal Cavernous Hemangioma

Cavernous hemangioma of the retina (CHR) is a rare retinal vascular hamartoma

"Benign growth made up of cells that don't belong there"

"Cluster of grapes"

- Cluster of dark intraretinal venous aneurysms
- No feeding artery
- Typically located along retinal vein

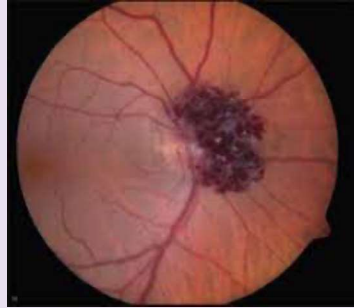


<https://imagebank.jans.org/files/10285/cavernous-hemangioma-of-the-retina>

....And more!

- ❖ >90% in Whites
- ❖ Primarily females
- ❖ Unilateral unifocal lesion

Can be associated with similar skin and central nervous system lesions (14% intracranial involvement)



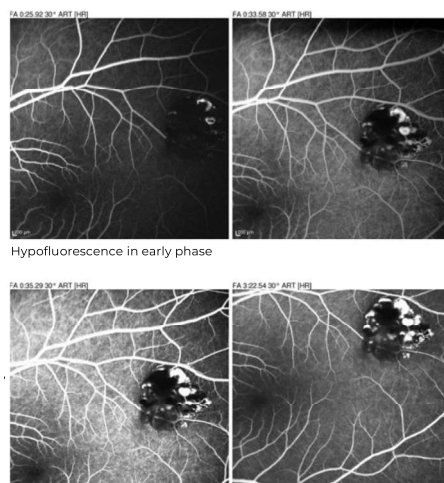
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2810101/>

Back to our patient:



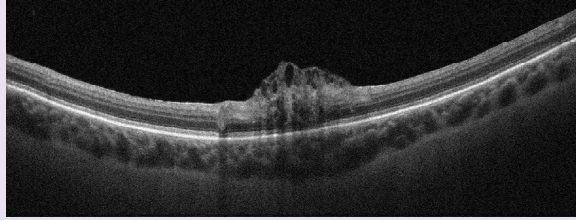
What could this be?

1. Retinal hemorrhages
2. Capillary Hemangioma
3. **Retinal cavernous hemangioma**

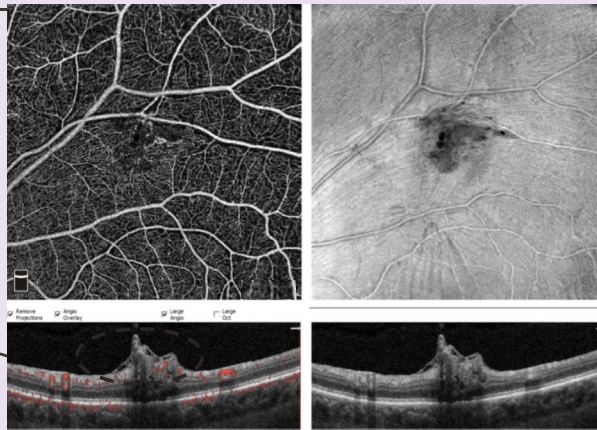


Fluorescein Angiography

Pooling of dye in upper half of saccule in late phase giving an appearance of “**fluorescein cap**”. No leakage!

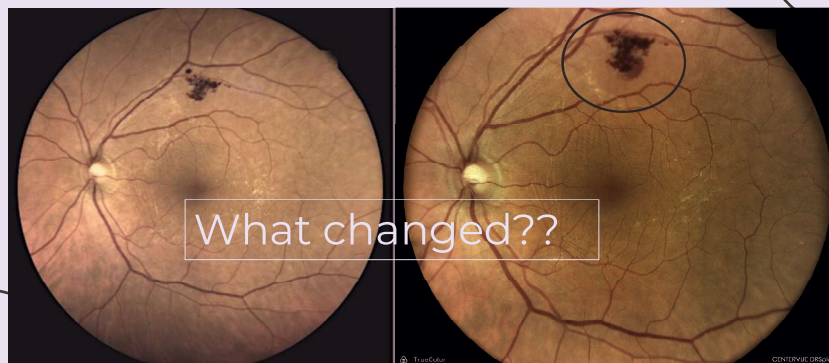


OCT shows 'grape bunch' multilobulated cavernous spaces located under the internal limiting membrane.



OCTA flow overlay demonstrated low-stagnant blood circulation inside retinal cavernous hemangioma

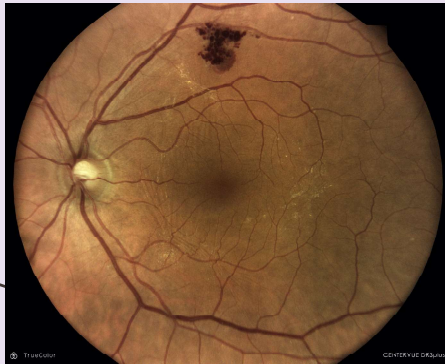
Our patient.....One year later???



2021

2022

Subretinal bleed....???



Complications of retinal cavernous hemangioma:

- Macular location
- Epiretinal membrane
- Vitreous hemorrhage

"...Retinal cavernous hemangiomas have rarely been reported to bleed..."

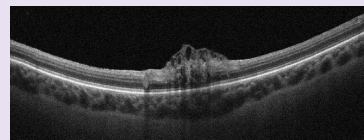


1. Colvard DM, Robertson DM, Traytmann JC. Cavernous hemangioma of the retina. Arch Ophthalmol 1978;96:2042-4
2. Gass JD, Braunste in R. Sessile and exophytic capillary angiomas of the juxtapapillary retina and optic nerve head. Arch Ophthalmol. 1980;98: 1790-1797.
3. Siegel AM. Familial cavernous angioma: an unknown, known disease. Acta Neurol Scand 1998;98:369-371

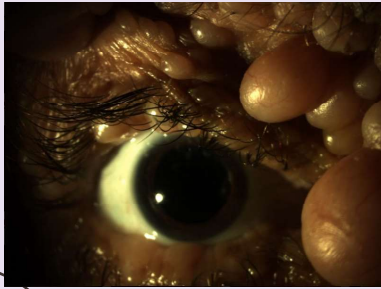
Subretinal bleed....Why?



The dilated vascular sacs are in the inner retinal layers



Sequelae of a rupture??



Case 4

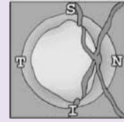
The Case:

- ❖ 14-year-old Hispanic male
- ❖ Blurry vision at distance in the right and left eye without glasses
- ❖ Patient reports blur improves while wearing his current SRx



History

- ❖ Systemic History: unremarkable
- ❖ Ocular History:
 - ❖ Glaucoma suspect vs Physiological large C/D
- ❖ Family History: Hypertension: Mother
- ❖ Medications: None
- ❖ Allergies: No known allergies



Entrance Examination

- ❖ Entering VA
 - ❖ 20/20 OD and 20/20 OS with current SRx at Distance and Near
- ❖ Entrance Examination
 - ❖ Pupils: Equal, round, reactive to light, no APD
 - ❖ Confrontation Fields: Full to finger counting OD, OS
 - ❖ Motility: FROM OU
 - ❖ Color Vision: HRR- pass OD & pass OS

All good.....

Refraction/BV

- ❖ Cover Test: Ortho @ Distance and 3Δ XP @ Near
- ❖ NPC: TTN
- ❖ Accommodative Amplitudes: 17D OD and 17D OS
- ❖ Current SRx
 - ❖ OD -2.50-0.25 x 150 20/20
 - ❖ OS -2.50-0.50 x 160 20/20
- ❖ Manifest Refraction
 - ❖ OD -2.25-0.25 x 170 20/15
 - ❖ OS -2.50-0.50 x 165 20/15

Unremarkable!!!

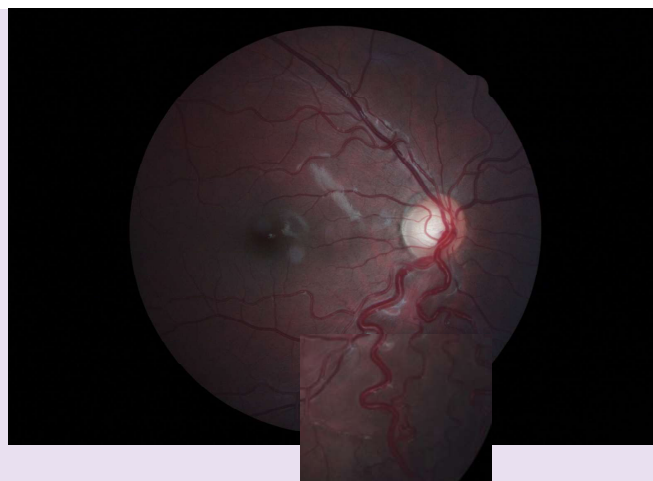
Slit Lamp Examination

OD		OS
Normal	Adnexae & Lids/Lashes	Normal
White & Quiet	Sclera/Conjunctiva	White & Quiet
Small temp epi defect (+) NaFl staining	Cornea	Normal
Deep & Quiet Van Herrick: 4+	Anterior Chamber	Deep & Quiet Van Herrick: 4+
Normal	Iris	Normal
Clear	Lens	Clear
14 mmHG	IOP	15 mmHG

Mother asks if we can defer dilation since everything looks good????

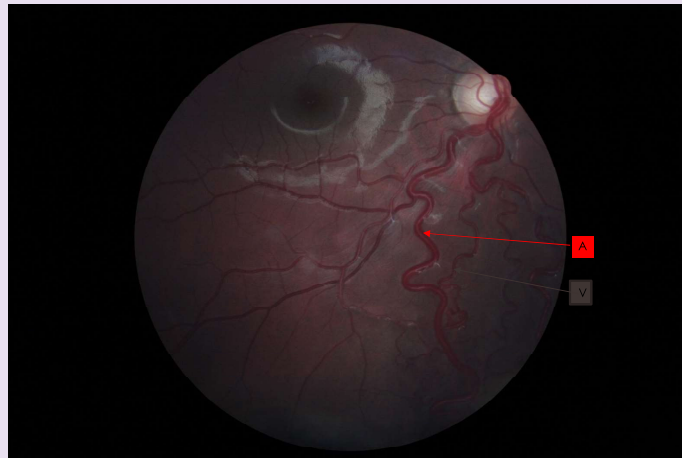
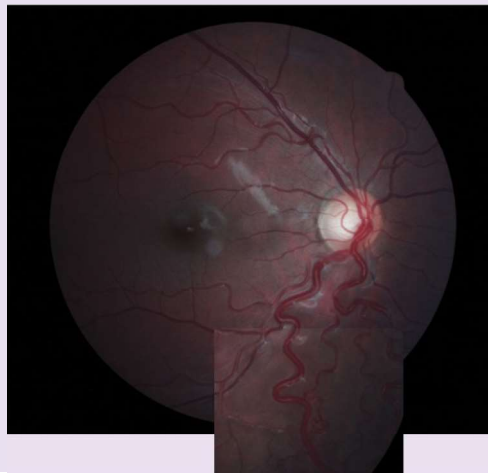


I WIN!

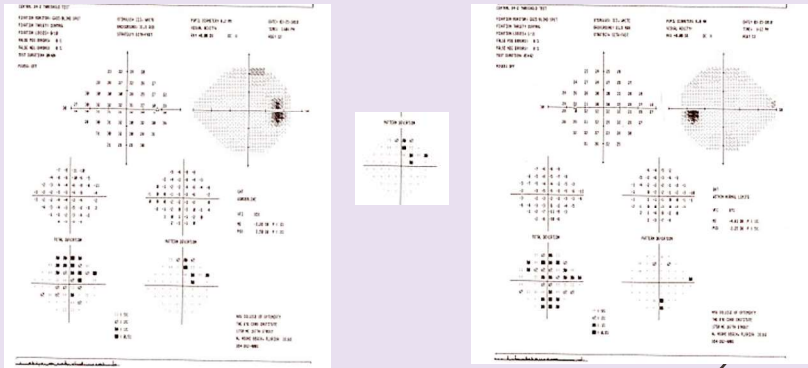


What do we see?

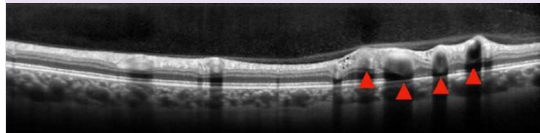
- ❖ Markedly dilated and tortuous vessels arising from the disc
- ❖ The arteries are connected with the veins directly, without the interposition of a capillary network



Visual fields



OCT

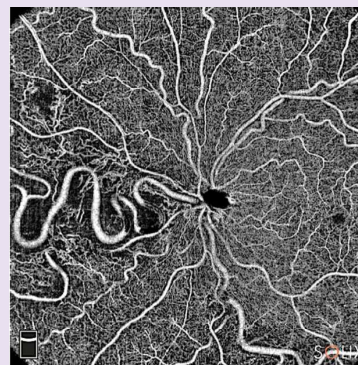


Hyporeflective intraretinal vascular lumens with shadow effect nasal to the fovea



OCT Angiography

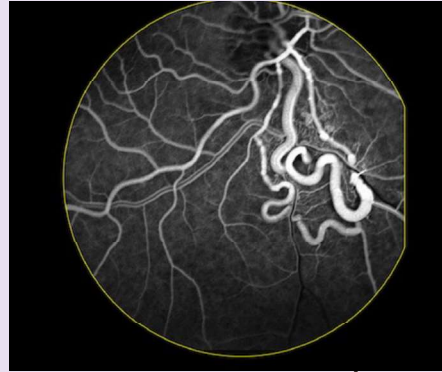
Superficial slab showing dilated and tortuous vessels without a neovascular network.



Fluorescein Angiography

Laminar Phase:

No leakage noted



Diagnosis/Management

Racemose Hemangioma OD

- ❖ Patient informed to see PCP/Neurology to evaluate for other AV malformations and/or organ involvement; including MRI

MRI of the Brain with Dye

- ❖ Unremarkable MRI examination of the brain

Reading Detail

MRI of the brain was obtained in 1.5 Tesla unit using regular standard sequences in technique including T1, T2 and flair axial images focal by coronal and sagittal T1-weighted images. T1 axial sagittal and coronal images of the after the intravenous administration of contrast material.

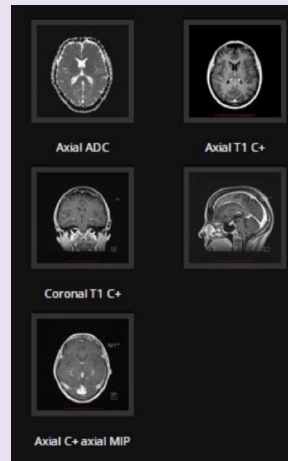
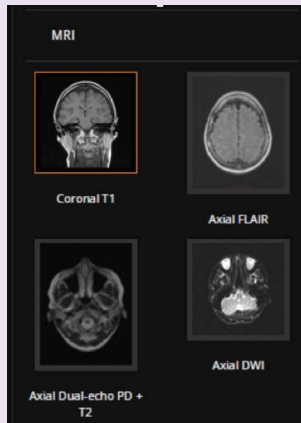
Findings: The brain appears normal in signal intensity and characteristics. There is no focal brain parenchymal lesions, no masses or mass effect. No intra- or extra-axial collections. The ventricles are normal in size, shape and configuration. No ventricular dilatation. There is no abnormal signal changes on the T1 or T2 weighted images of the supra- or infratentorial regions. The posterior fossa and the mid brain are normal in signal intensity and characteristics. No obvious ischemic changes of the midbrain or cerebellum. The seventh, eighth nerve complex, the optic chiasm and the pituitary infundibulum are normal. No evidence of CP angle masses.

Normal signal void of the internal carotid arteries and basilar arteries indicating patency. Visualized portions of the paranasal sinuses are grossly unremarkable for acute sinusitis. No abnormal enhancement after the intravenous administration of contrast material.

Conclusion:

Unremarkable MRI examination of the brain without evidence of abnormal signal changes, masses or mass effect along the supra- or infratentorial distributions. No abnormal enhancement after the intravenous administration of the contrast material.

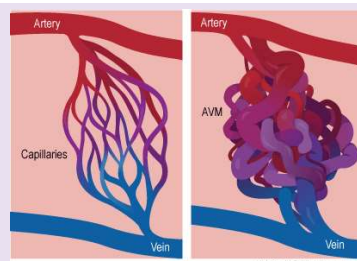
MRI results: Normal



What is Racemose Hemangioma?

A benign arteriovenous communication/AV malformation

- ❖ AV malformation: An abnormal tangle of blood vessels connecting arteries and veins
 - ❖ Disrupts normal blood flow and oxygen circulation
- ❖ Can occur in isolation or as part of Wyburn-Mason syndrome
 - ❖ Patients can have AV communications in retina, visual pathways, midbrain, and facial bones



- ❖ Arteries are responsible for taking oxygen-rich blood from the heart to the brain.
- ❖ Veins carry the oxygen-depleted blood back to the lungs and heart.
- ❖ When an AVM disrupts this critical process, the surrounding tissues may not get enough oxygen.
- ❖ Also, because the tangled blood vessels that form the AVM are abnormal, they can weaken and rupture. If the AVM is in the brain and ruptures, it can cause bleeding in the brain (hemorrhage), stroke or brain damage

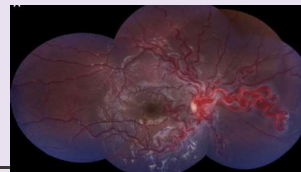
Cause of an A/V Malformation?

- ❖ Causes for A/V Malformations are UNKNOWN
- ❖ Tend to be congenital & sporadic, but do NOT follow a hereditary pattern
- ❖ Occurs in males and females of all racial or ethnic backgrounds at approximate equal rate



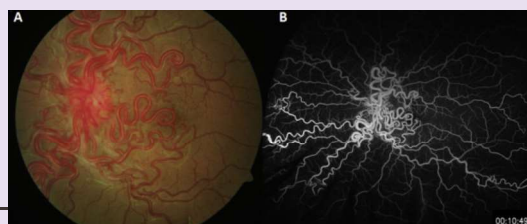
Racemose Hemangioma: AVM of retina!

- ❖ Typically, unilateral
- ❖ Large, dilated, tortuous artery
 - ❖ Passes from the optic disc for some distance into the fundus
 - ❖ Communicating directly with a dilated retinal vein and then back to the optic disc
- ❖ Not usually associated with exudate or hemorrhage
- ❖ Size and location assist in classification

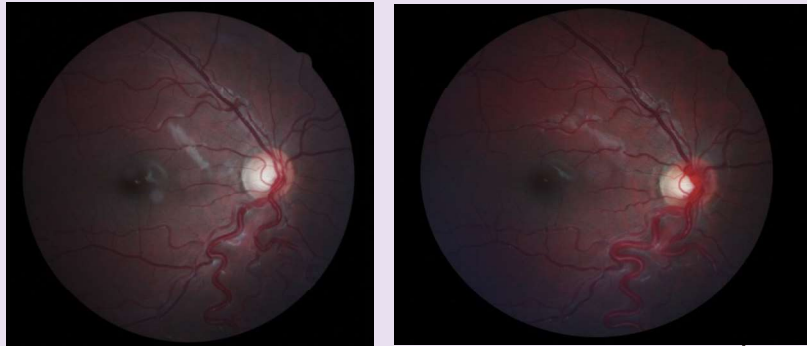


How do we make the diagnosis?

- ❖ Fluorescein Angiography
 - ❖ Shows rapid filling of the affected dilated artery and vein, usually with no intervening capillary channels and typically without leakage into surrounding tissues.
- ❖ MRI/MRA/MRV

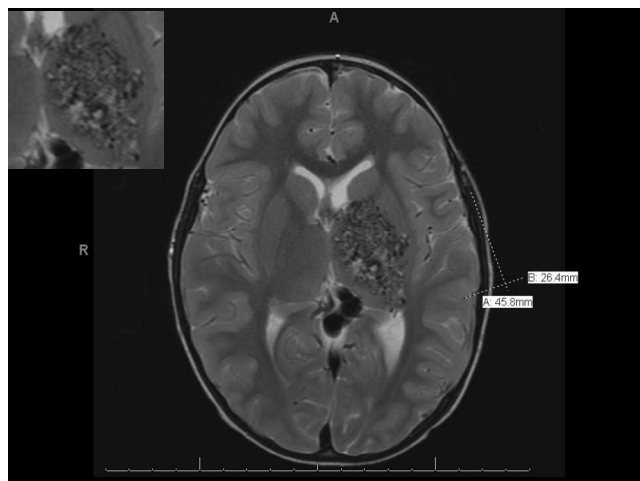


One year later...



Management and Course

- ❖ The management of a patient with this vascular tumor consists of systemic and ophthalmic monitoring.
- ❖ The patient should be evaluated for WMS with imaging studies for similar vascular abnormalities in the brain and facial bones.
- ❖ The retinal lesion usually remains stable, and treatment is rarely needed.

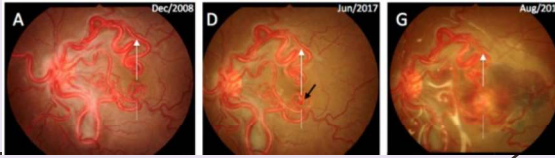


T2-weighted MRI of the brain with contrast displaying large left arteriovenous malformation in Wyburn Mason syndrome

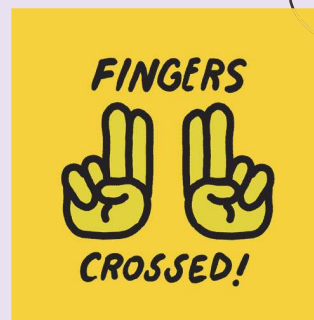
<https://www.ajronline.org/doi/full/10.1007/s10078-016-0204-1>

Ocular Risks & Complications

- ❖ Intraretinal or vitreous hemorrhage
- ❖ exudation and cystoid macular edema
- ❖ retinal vein occlusion
- ❖ mechanical compression of the optic nerve
- ❖ retinal detachment
- ❖ rubeosis, peripheral retinal neovascularization, and neovascular glaucoma



We are co-managing the patient
with retina and neurology....



Case 5

72-year-old Black Male

Presents with decreased vision bilaterally D and N

BCVA: 20/25+ OD, 20/25+ OS

PMH:

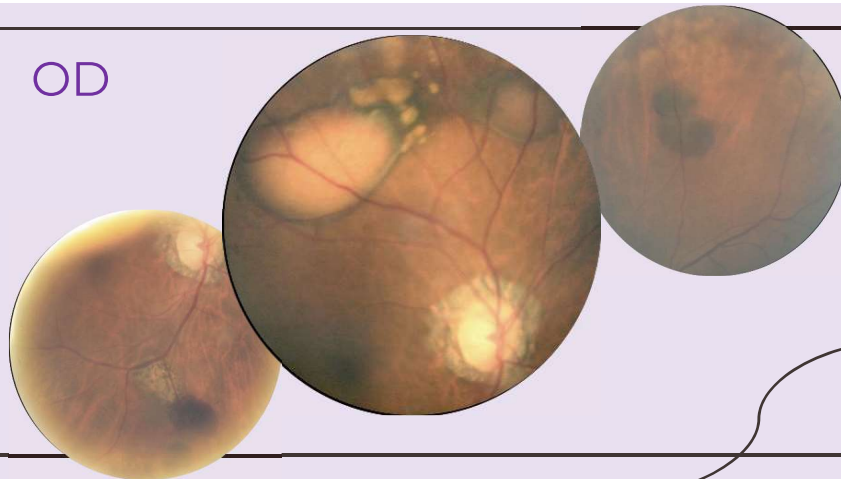
(+) HIV; CD4 Count 336; Viral load 46

(+)Hypercholesterolemia

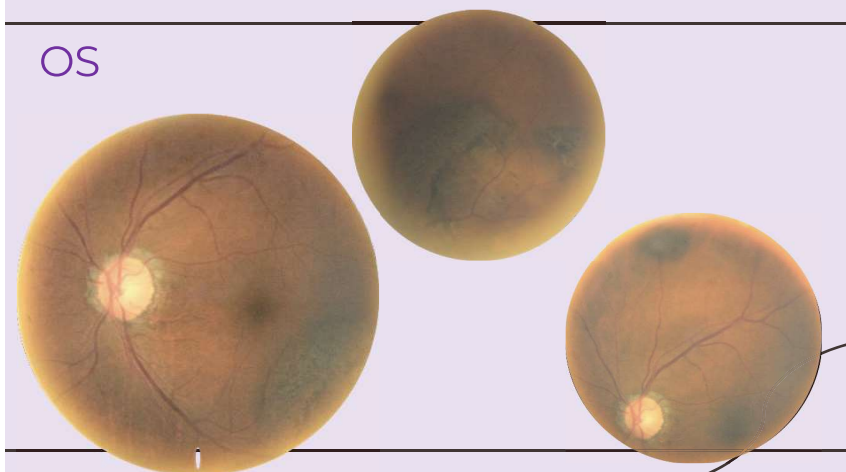
(+)Hypertension

(+)DM 2; poor BS control

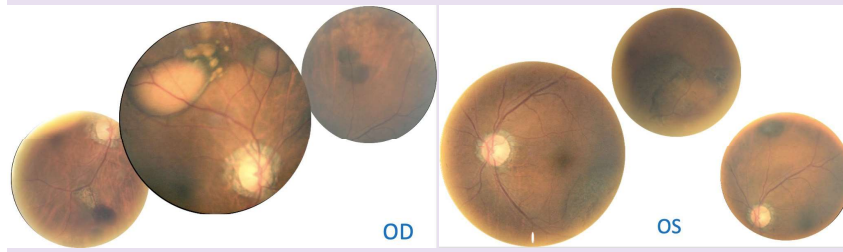
OD



OS

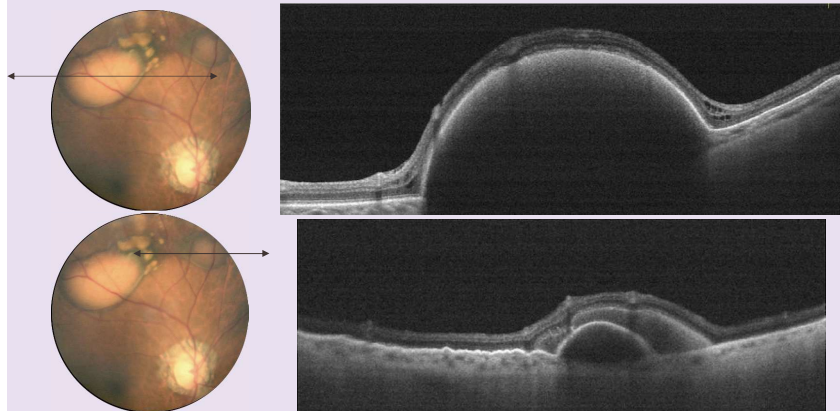


What could this be????

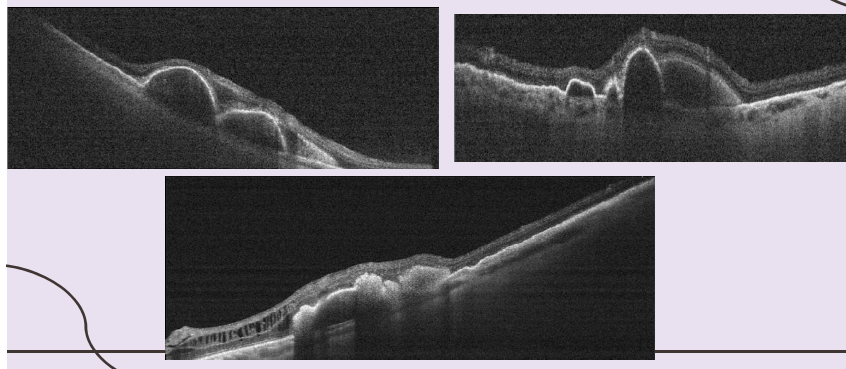


1. Choroidal melanoma?
2. Age Related Macular Degeneration?
3. Chorioretinitis?
4. Pathological myopia with neovascularization?
5. Something else?

Let's look at the OCTs!



And more cuts....



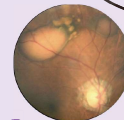
Polypoidal Choroidal Vasculopathy

- Clinical Subtype with features of Neovascular AMD

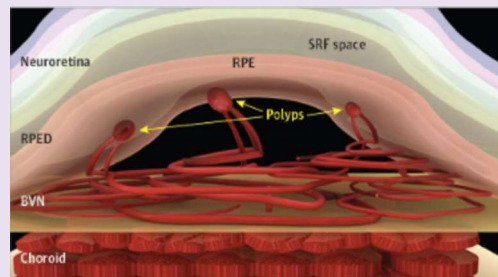
“Peculiar Hemorrhagic detachment of the RPE and choroid”

Polypoidal Choroidal Vasculopathy

- Suspected in patient with:
 - sub-retinal orange polyp-like lesions
 - Can be macular or peripapillary
 - Rarely in arcades as well
 - Especially African or Asian descent (F>M)

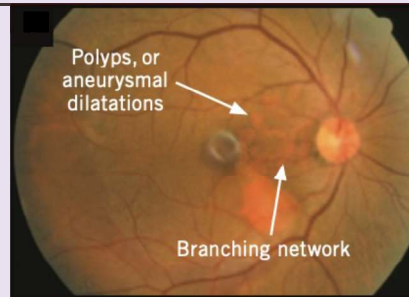


Pathophysiology

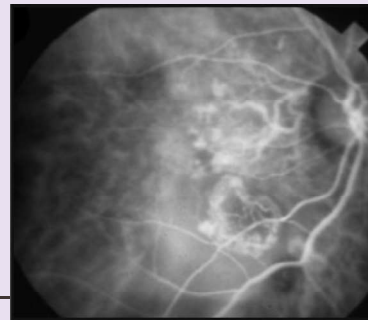


- Branching vascular network (BVN): originates in the choroid
- BVN may develop terminal, polyp-like aneurysmal dilations

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6000000/



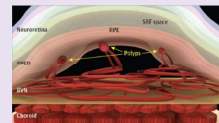
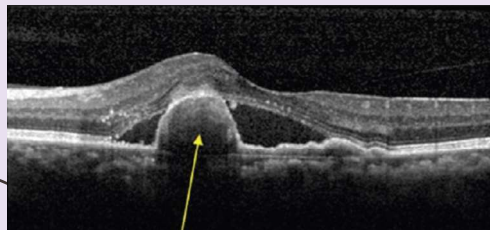
What does this look like clinically?



Serosanguinous RPE detachments

Serous Fluid

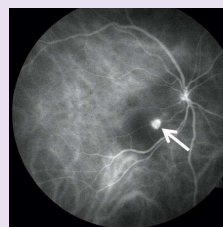
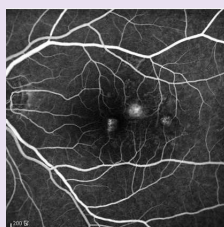
Blood



http://www.ku.washington.edu/~img/edu/cont/ret/ret_01_02_03_04_05_06_07_08_09_10_11_12_13_14_15_16_17_18_19_20_21_22_23_24_25_26_27_28_29_30_31_32_33_34_35_36_37_38_39_40_41_42_43_44_45_46_47_48_49_50_51_52_53_54_55_56_57_58_59_60_61_62_63_64_65_66_67_68_69_70_71_72_73_74_75_76_77_78_79_80_81_82_83_84_85_86_87_88_89_90_91_92_93_94_95_96_97_98_99_100_101_102_103_104_105_106_107_108_109_110_111_112_113_114_115_116_117_118_119_120_121_122_123_124_125_126_127_128_129_130_131_132_133_134_135_136_137_138_139_140_141_142_143_144_145_146_147_148_149_150_151_152_153_154_155_156_157_158_159_160_161_162_163_164_165_166_167_168_169_170_171_172_173_174_175_176_177_178_179_180_181_182_183_184_185_186_187_188_189_190_191_192_193_194_195_196_197_198_199_200_201_202_203_204_205_206_207_208_209_210_211_212_213_214_215_216_217_218_219_220_221_222_223_224_225_226_227_228_229_230_231_232_233_234_235_236_237_238_239_240_241_242_243_244_245_246_247_248_249_250_251_252_253_254_255_256_257_258_259_260_261_262_263_264_265_266_267_268_269_270_271_272_273_274_275_276_277_278_279_280_281_282_283_284_285_286_287_288_289_290_291_292_293_294_295_296_297_298_299_300_301_302_303_304_305_306_307_308_309_310_311_312_313_314_315_316_317_318_319_320_321_322_323_324_325_326_327_328_329_330_331_332_333_334_335_336_337_338_339_340_341_342_343_344_345_346_347_348_349_350_351_352_353_354_355_356_357_358_359_360_361_362_363_364_365_366_367_368_369_370_371_372_373_374_375_376_377_378_379_380_381_382_383_384_385_386_387_388_389_390_391_392_393_394_395_396_397_398_399_400_401_402_403_404_405_406_407_408_409_410_411_412_413_414_415_416_417_418_419_420_421_422_423_424_425_426_427_428_429_430_431_432_433_434_435_436_437_438_439_440_441_442_443_444_445_446_447_448_449_450_451_452_453_454_455_456_457_458_459_460_461_462_463_464_465_466_467_468_469_470_471_472_473_474_475_476_477_478_479_480_481_482_483_484_485_486_487_488_489_490_491_492_493_494_495_496_497_498_499_500_501_502_503_504_505_506_507_508_509_510_511_512_513_514_515_516_517_518_519_520_521_522_523_524_525_526_527_528_529_530_531_532_533_534_535_536_537_538_539_540_541_542_543_544_545_546_547_548_549_550_551_552_553_554_555_556_557_558_559_560_561_562_563_564_565_566_567_568_569_570_571_572_573_574_575_576_577_578_579_580_581_582_583_584_585_586_587_588_589_590_591_592_593_594_595_596_597_598_599_600_601_602_603_604_605_606_607_608_609_610_611_612_613_614_615_616_617_618_619_620_621_622_623_624_625_626_627_628_629_630_631_632_633_634_635_636_637_638_639_640_641_642_643_644_645_646_647_648_649_650_651_652_653_654_655_656_657_658_659_660_661_662_663_664_665_666_667_668_669_670_671_672_673_674_675_676_677_678_679_680_681_682_683_684_685_686_687_688_689_690_691_692_693_694_695_696_697_698_699_700_701_702_703_704_705_706_707_708_709_710_711_712_713_714_715_716_717_718_719_720_721_722_723_724_725_726_727_728_729_730_731_732_733_734_735_736_737_738_739_740_741_742_743_744_745_746_747_748_749_750_751_752_753_754_755_756_757_758_759_760_761_762_763_764_765_766_767_768_769_770_771_772_773_774_775_776_777_778_779_780_781_782_783_784_785_786_787_788_789_790_791_792_793_794_795_796_797_798_799_800_801_802_803_804_805_806_807_808_809_810_811_812_813_814_815_816_817_818_819_820_821_822_823_824_825_826_827_828_829_830_831_832_833_834_835_836_837_838_839_840_841_842_843_844_845_846_847_848_849_850_851_852_853_854_855_856_857_858_859_860_861_862_863_864_865_866_867_868_869_870_871_872_873_874_875_876_877_878_879_880_881_882_883_884_885_886_887_888_889_890_891_892_893_894_895_896_897_898_899_900_901_902_903_904_905_906_907_908_909_910_911_912_913_914_915_916_917_918_919_920_921_922_923_924_925_926_927_928_929_930_931_932_933_934_935_936_937_938_939_940_941_942_943_944_945_946_947_948_949_950_951_952_953_954_955_956_957_958_959_960_961_962_963_964_965_966_967_968_969_970_971_972_973_974_975_976_977_978_979_980_981_982_983_984_985_986_987_988_989_990_991_992_993_994_995_996_997_998_999_1000

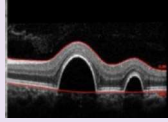
PCV and ICG

- Essential for detecting the choroidal network of polyps
 - Differentiation from AMD

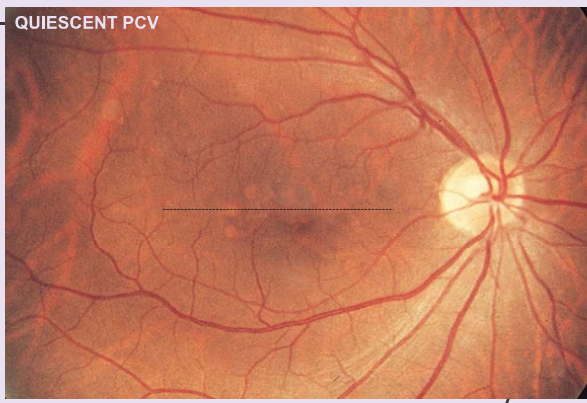


Pigment Epithelial Detachment

NO....hemorrhage
NO....exudate

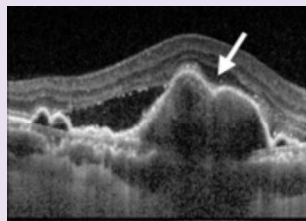


QUIESCENT PCV

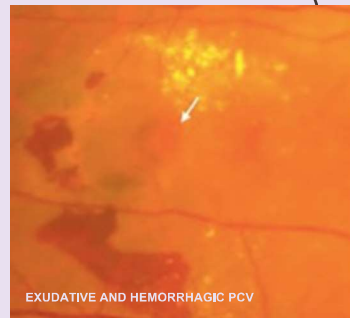


Polyps; sharp dome-like elevations

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4110145/>

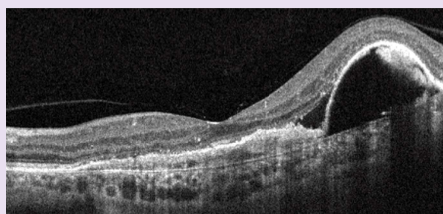


Serosanguinous
Pigment Epithelial
Detachments
(note turbid appearance)



EXUDATIVE AND HEMORRHAGIC PCV

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4110145/>

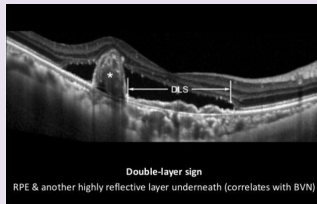


HEMORRHAGIC PCV



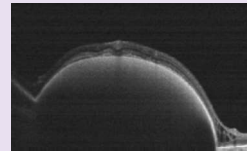
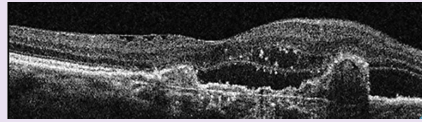
Double layer sign

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4110145/>

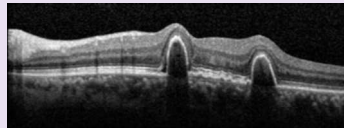


SO... how do we make the diagnosis??

Double Layer Sign



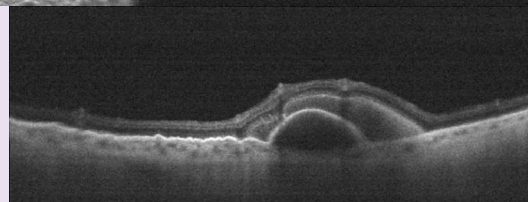
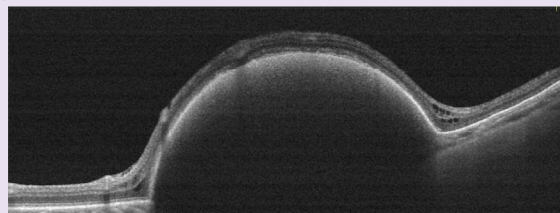
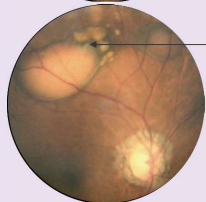
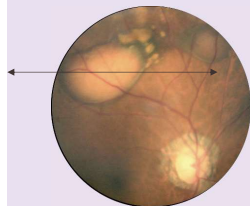
Large PEDs



Sharp PEDs

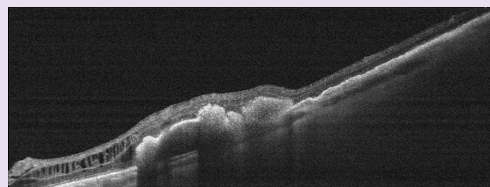
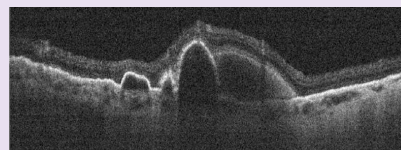
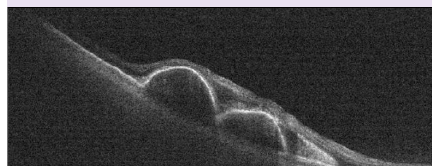
Back to our patient:

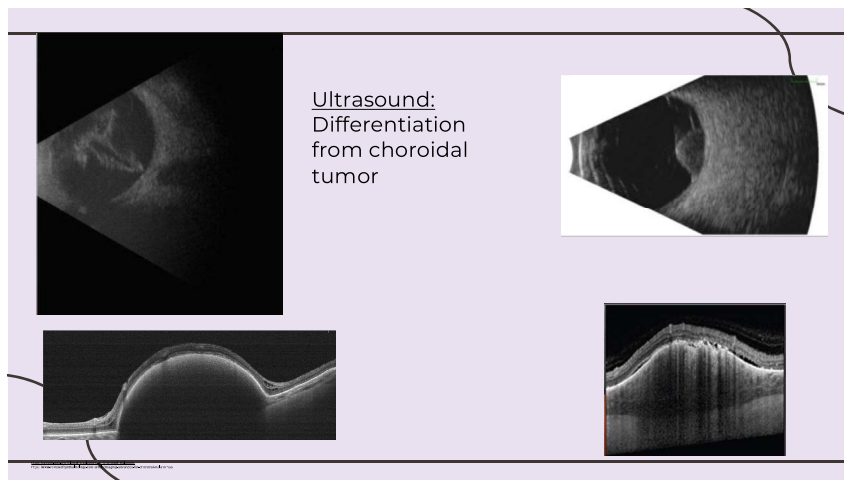
Serosanguinous PEDs



And more cuts....

Double layer sign; ?CNV





The clinical presentation of PCV is often like that of CSR or exudative AMD. The diagnosis of PCV can be challenging without ICG imaging. ICG should be considered in patients who have visible orange-red subretinal nodule(s), spontaneous massive subretinal hemorrhage, notched or hemorrhagic PED, or the lack of response to anti-VEGF therapy.

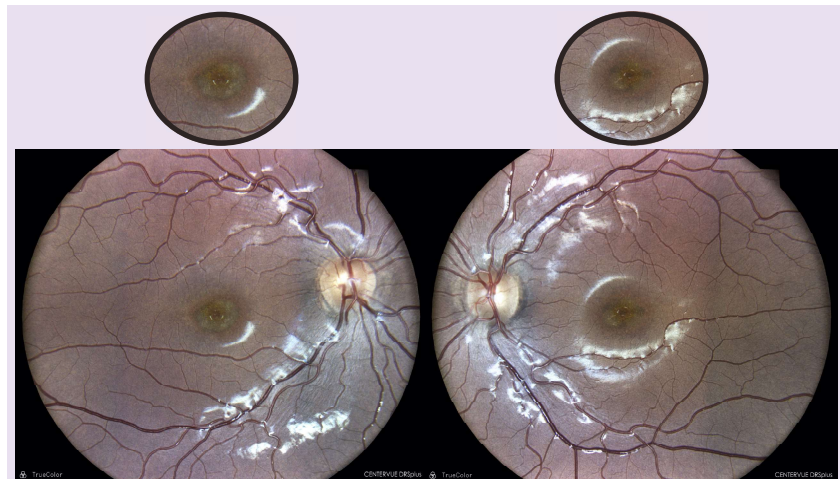
Case 6

13-year-old Black Female

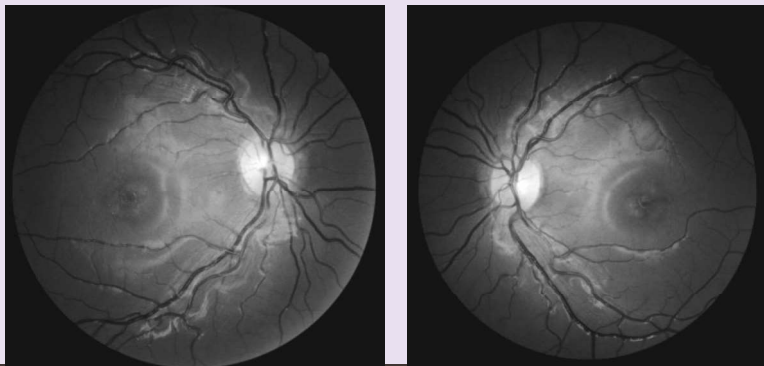
First eye exam ever!! Never had any visual problems
Mom reports that she is just NOT seeing right!

BCVA: 20/30 OD, 20/30 OS
Failed Color Vision OD and OS

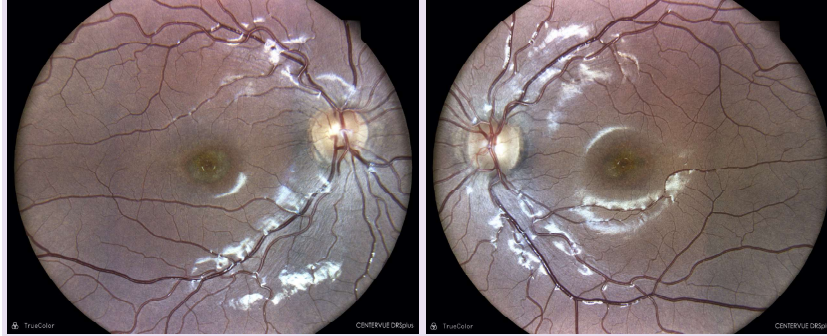
"I can't see the blackboard
at school and my grades
are sinking!!!"



Red-Free Photography



Bull's Eye Maculopathy???

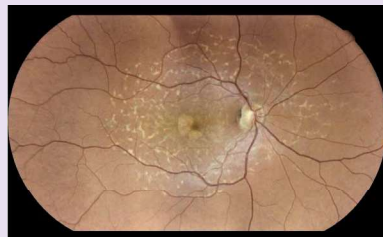


Differential Diagnosis:

1. Stargardt's Disease
2. Cone Dystrophy
3. Chloroquine Toxicity
4. Retinitis Pigmentosa?

Bull's Eye Maculopathy???

Stargardt's



- o Bilateral, decreased vision
 - o Manifests in childhood or young adulthood
 - o Vision loss precedes fundus findings
- o Pisciform, "fish-tail" deposits
- o Beaten-metal, bull's eye appearance at macula



Bull's Eye Maculopathy???

Cone Dystrophy

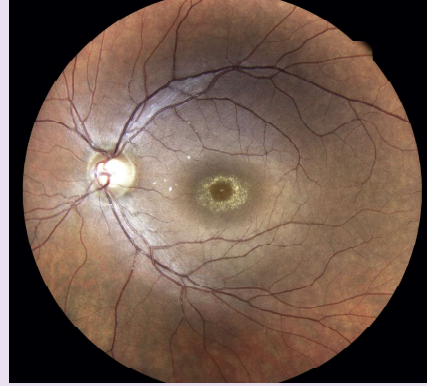
- o Slowly progressive bilateral visual loss
- o Poor color vision and DAY vision
- o Abnormal cone-function on ERG
- o Normal fundus early with poor VA
- o Bull's eye maculopathy (later)



Bull's Eye Maculopathy???

Chloroquine Toxicity

- Decreased vision
- Poor color vision
- Bull's eye macula
- H/O chloroquine use!



Images courtesy of Core

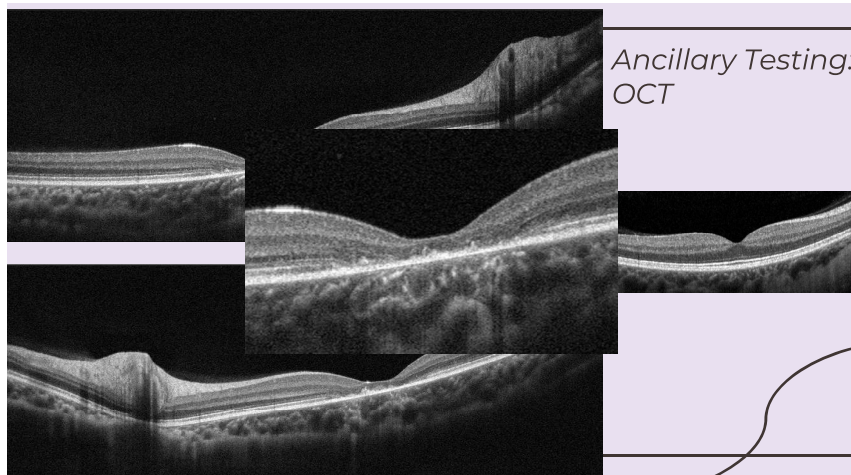
Bull's Eye Maculopathy???

Retinitis Pigmentosa

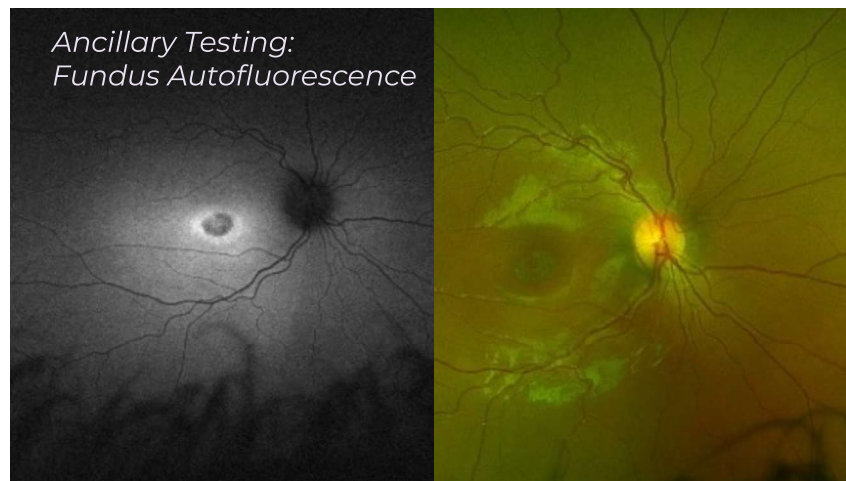
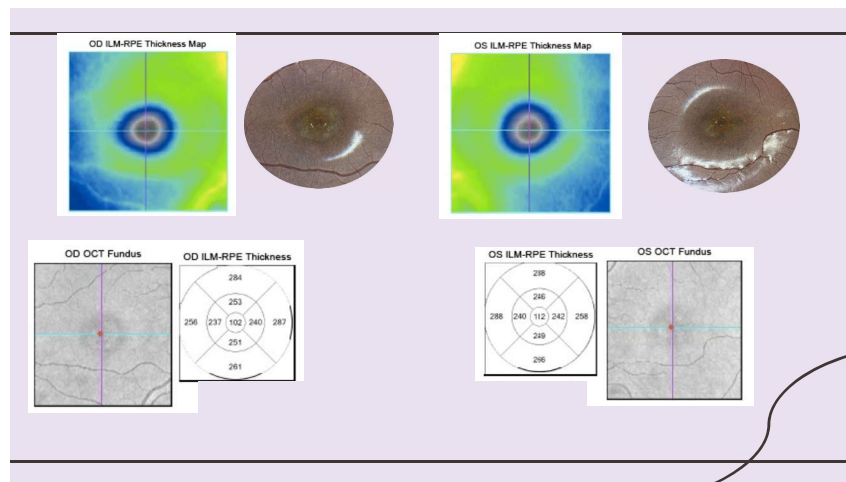
- Difficulty with night vision
- Loss of peripheral vision
- Poor central vision/CV late findings
- Waxy ONH pallor
- Arteriolar attenuation
- Bone spicules
- ERG reduced



Images courtesy of Core

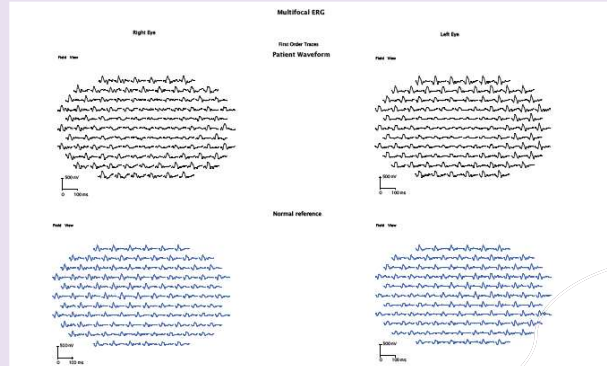


Ancillary Testing:
OCT



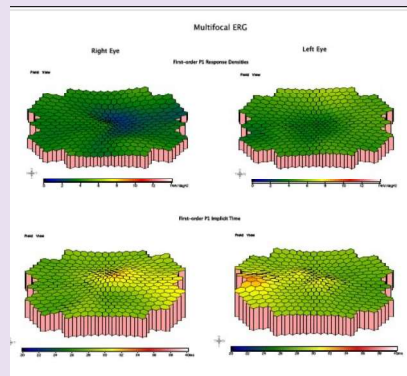
Electrodiagnostics: mfERG

The mfERG findings show moderate diffuse cone dysfunction in the macula area of the right and left eyes.



Electrodiagnostics: mfERG

The mfERG findings show moderate diffuse cone dysfunction in the macula area of the right and left eyes.



What is this??...13 y/o... we need help!!



Patient name:		Sample type:	Saliva	Report date:	11/08/2021
DOB:	09/29/2008	Sample collection date:	10/12/2021	Invitae #:	RQ2834631
Sex assigned at birth:	Female	Sample accession date:	10/23/2021	Clinical team:	Julie Rodman
Gender:		MRN:			

Reason for testing

Test performed

Sequence analysis and deletion/duplication testing of the 328 genes listed in the Genes Analyzed section.

- Invitae Inherited Retinal Disorders Panel

RESULT: CARRIER

One Pathogenic variant identified in EYS. EYS is associated with autosomal recessive retinitis pigmentosa.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
EYS	c.6794del (p.Pro2265Clnfs*46)	heterozygous	PATHOGENIC ←
ABCA4	c.2161-6T>C (Intronic)	heterozygous	Uncertain Significance
BBS1	c.1076C>A (p.Arg359His)	heterozygous	Uncertain Significance
COL11A2	c.2682G>A (Silent)	heterozygous	Uncertain Significance
PDE6A	c.916A>G (p.Arg306Gly)	heterozygous	Uncertain Significance
PDZD7	c.244C>A (p.Asp82Asn)	heterozygous	Uncertain Significance
PEX6	c.1081A>C (p.Thr361Ala)	heterozygous	Uncertain Significance
RP1	c.4397A>T (p.Glu1466Val)	heterozygous	Uncertain Significance

About this test
This diagnostic test evaluates 328 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Clinical summary

A Pathogenic variant, c.6794del (p.Pro2265Clnfs*46), was identified in EYS.

autosomal recessive retinitis pigmentosa (RP)

- The EYS gene is associated with autosomal recessive retinitis pigmentosa (RP) (MedGen UID: 350427).
- This individual is a carrier for autosomal recessive EYS-related conditions. This result is insufficient to cause autosomal recessive EYS-related conditions; however, carrier status does impact reproductive risk.
- Retinitis pigmentosa (RP) is a genetically heterogeneous group of inherited eye disorders characterized by progressive degeneration of the retina, typically beginning in the midperiphery and advancing toward the macula and fovea (PMID: 17296890). Abnormalities of the photoreceptors (rods and cones) or the retinal pigment epithelium (RPE) lead to progressive visual loss (PMID: 3883369, 30106463). Typical symptoms include night blindness followed by constriction of peripheral visual fields, which leads to tunnel vision and eventually loss of central vision (PMID: 17296890). RP is highly variable in regards to severity, clinical symptoms, and age of onset (PMID: 17296890).
- Biological relatives have a chance of being a carrier for or being at risk for autosomal recessive EYS-related conditions. Testing should be considered if clinically appropriate. The chance of having a child with autosomal recessive EYS-related conditions depends on the carrier state of this individual's partner.

A Variant of Uncertain Significance, c.2161-6T>C (Intronic), was identified in ABCA4.

autosomal recessive cone-rod dystrophy

- The ABCA4 gene is associated with autosomal recessive cone-rod dystrophy (CORD) (MedGen UID: 349030), Stargardt disease (STGD) (MedGen UID: 383891), and retinitis pigmentosa (RP) (MedGen UID: 400996). Additionally, there is preliminary evidence supporting a correlation with autosomal dominant age-related macular degeneration (AMD) (PMID: 10880298).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- Familial VUS testing is not offered. Testing family members for this variant will not contribute evidence to allow variant reclassification. Details on our VUS Resolution and Family Variant Testing Programs can be found at <https://www.invitae.com/family>.

A Variant of Uncertain Significance, c.1076C>A (p.Arg359His), was identified in BBS1.

autosomal recessive Bardet-Biedl syndrome

- The BBS1 gene is associated with autosomal recessive Bardet-Biedl syndrome (MedGen UID: 423432) and non-syndromic retinitis pigmentosa (PMID: 23143442, 27032803, 21303335).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- Familial VUS testing is not offered. Testing family members for this variant will not contribute evidence to allow variant reclassification. Details on our VUS Resolution and Family Variant Testing Programs can be found at <https://www.invitae.com/family>.

A Variant of Uncertain Significance, c.2682G>A (Silent), was identified in COL11A2.

autosomal recessive Bardet-Biedl syndrome

- The COL11A2 gene is associated with a spectrum of related autosomal recessive conditions including nonsyndromic deafness (MedGen UID: 400602), osteochondromatous dysplasia (OSMED) (MedGen UID: 1617409), and fibrochondrogenesis (MedGen UID: 479768). COL11A2 is also associated with a spectrum of related autosomal dominant conditions including Stickler syndrome II (MedGen UID: 345293 and 120503), OSMED (also known as Weissenbacher-Zwengmüller syndrome; MedGen UID: 341234) and nonsyndromic deafness (MedGen UID: 400917).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
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A Variant of Uncertain Significance, c.916A>G (p.Arg306Gly), was identified in PDE6A.

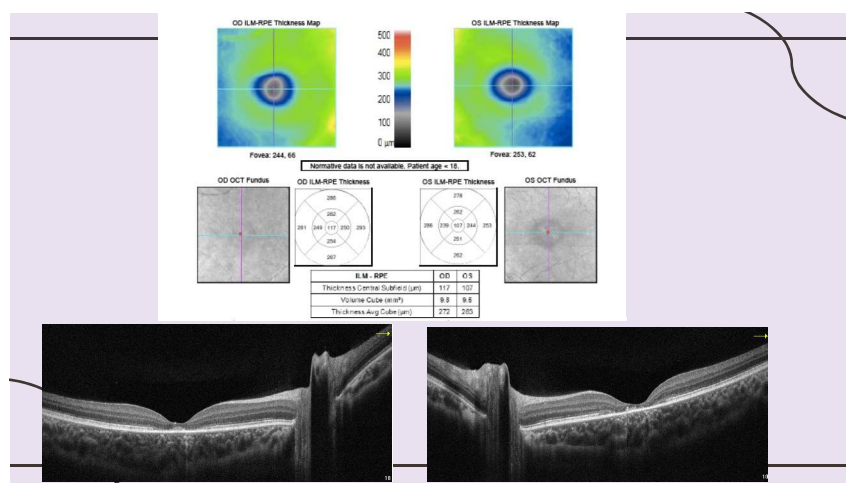
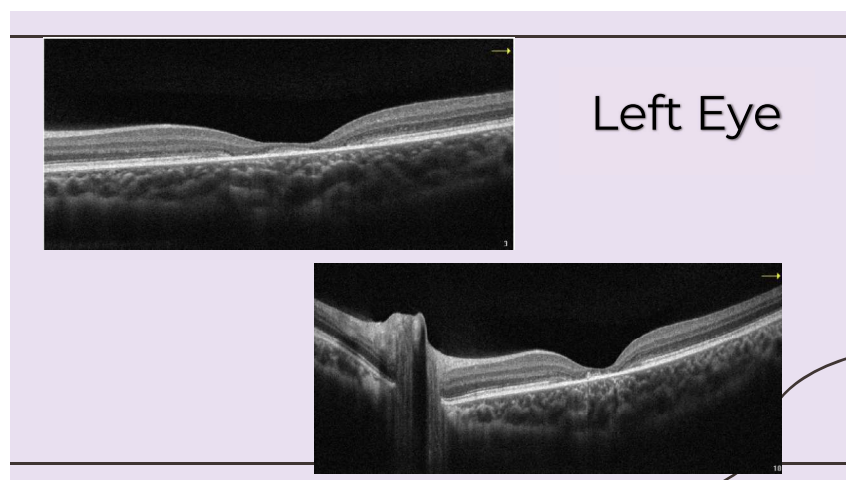
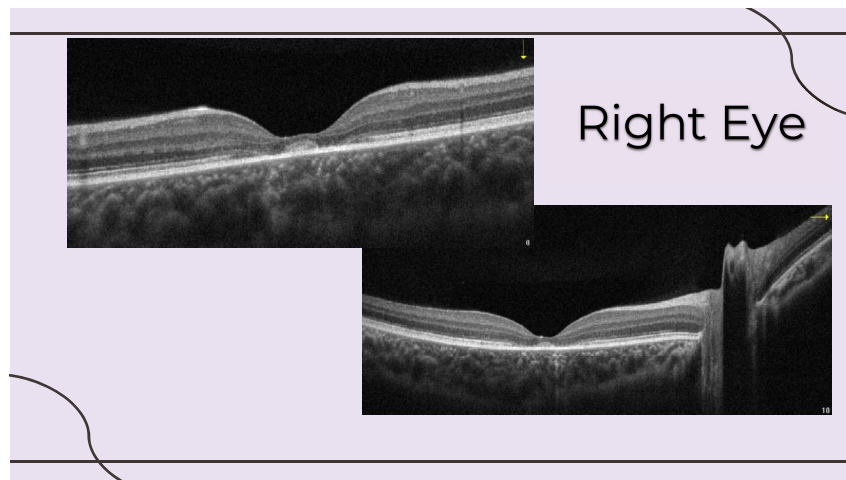
autosomal recessive Bardet-Biedl syndrome

- The PDE6A gene is associated with autosomal recessive retinitis pigmentosa (MedGen UID: 462488). Additionally, the PDE6A gene has preliminary evidence supporting a correlation with autosomal dominant periventricular nodular heterotopia (PMID: 29738322).

But that's not all!!!!

13-year-old twin sister with NORMAL vision came in for an exam also







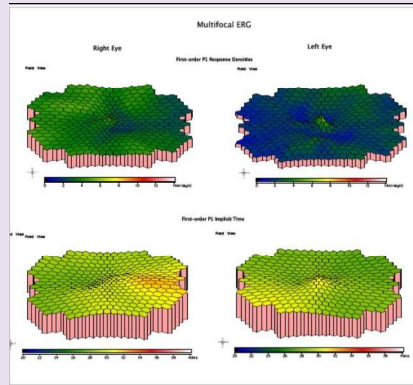
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RESULT: CARRIER

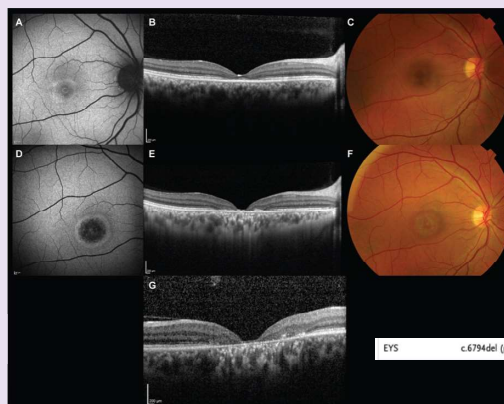
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PDZD7	c.244C>A (p.Asp82Asn)	heterozygous	Uncertain Significance
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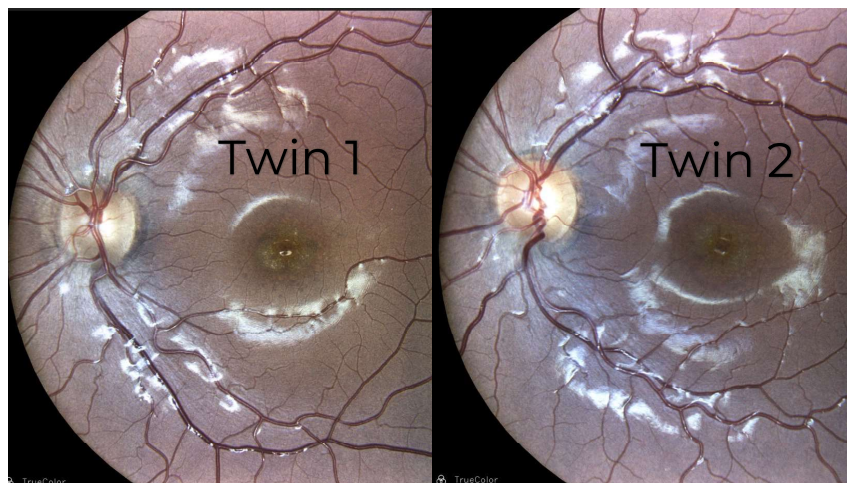
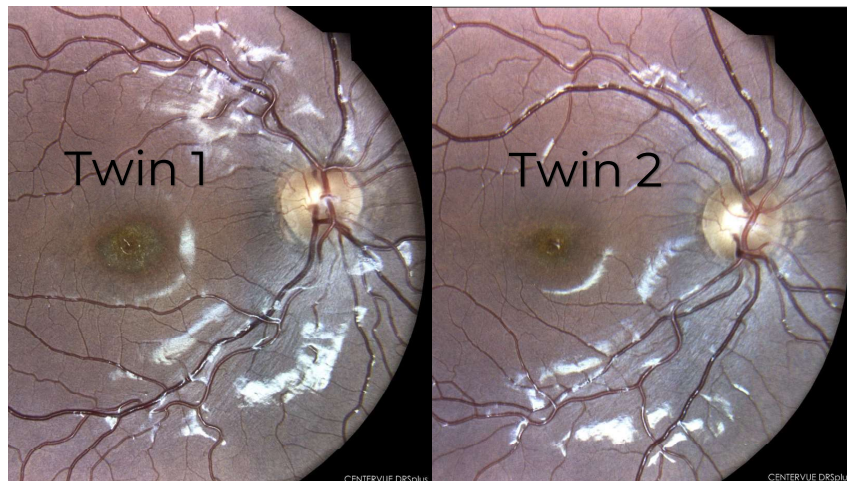


EYS mutations are one of the most common causes of autosomal recessive retinitis pigmentosa in Asia and Europe.

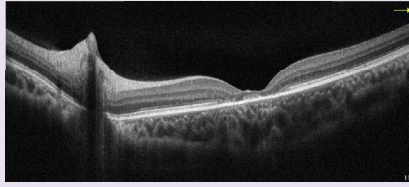
Novel findings include the presence of homozygous EYS mutations in Cone Rod Dystrophy patients and compound heterozygous EYS mutations in patients with macular dystrophy.

EYS c.6794del (p.Pro2265Glnfs*46) heterozygous PATHOGENIC

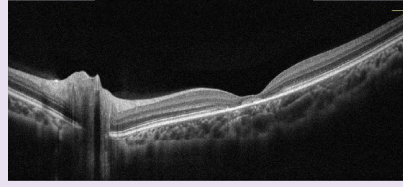
Comparison Between Twins



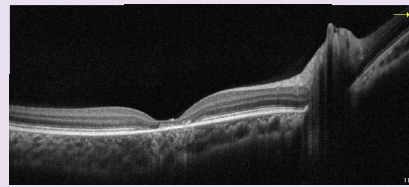
Twin 1



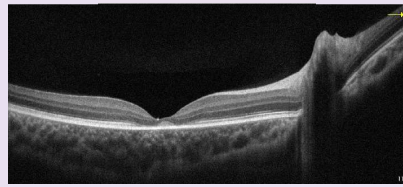
Twin 2



Twin 1



Twin 2



Thank you!

rjulie@nova.edu