HARADA

Mohamed Abdel Azim
FRCOphth

Vogt-Koyanagi-Harada disease

- Severe bilateral granulomatous intraocular inflammation associated with serous retinal detachments, disk edema, and vitritis, with eventual development of a sunset glow fundus.
- Autoimmune disease mediated by T cells that target melanocytes in individuals susceptible to the disease.

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Vogt-Koyanagi-Harada disease

- 4 different phases: prodromal, uveitic, convalescent, and recurrent,
- extraocular manifestations including headache, meningismus, hearing loss, poliosis, and vitiligo, to varying degrees.
- Vogt-Koyanagi-Harada disease can have good final outcomes if treated promptly.

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VKH Phases

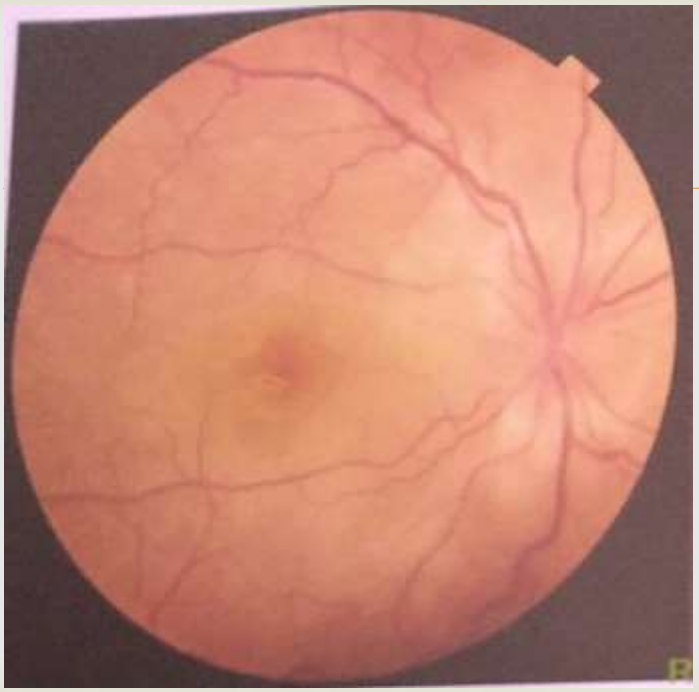
1-The prodromal phase

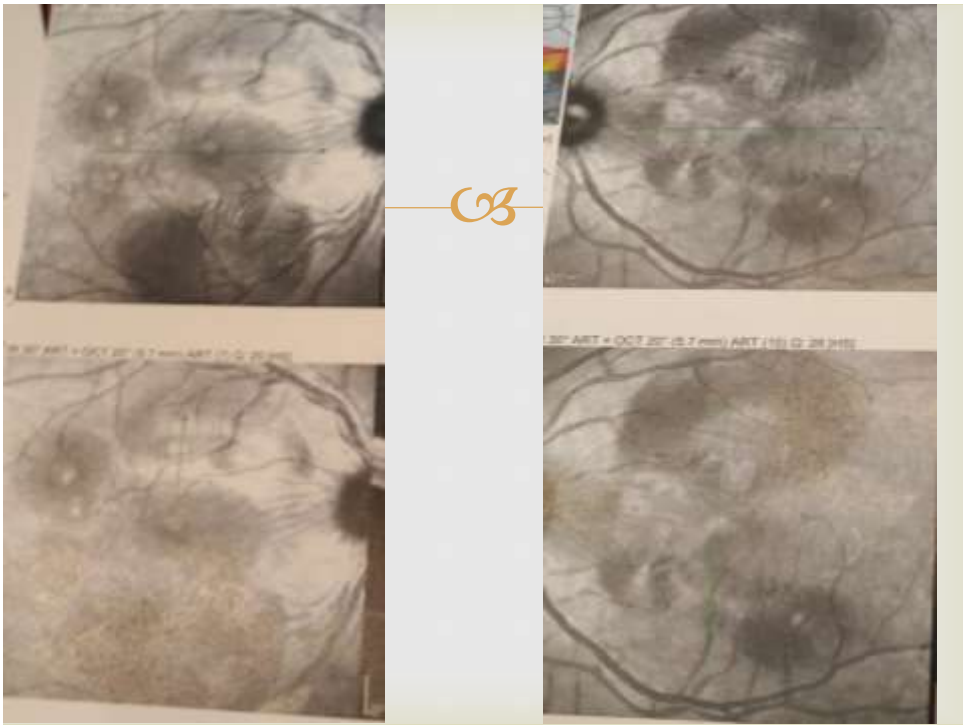
- may present as a viral infection (few days - few weeks).
- Include headache (82%), meningismus (55%), fever (18%), nausea (9%), vertigo (9%), orbital pain, and auditory disturbances.

VKH Phases

2- *Acute uveitic phase*

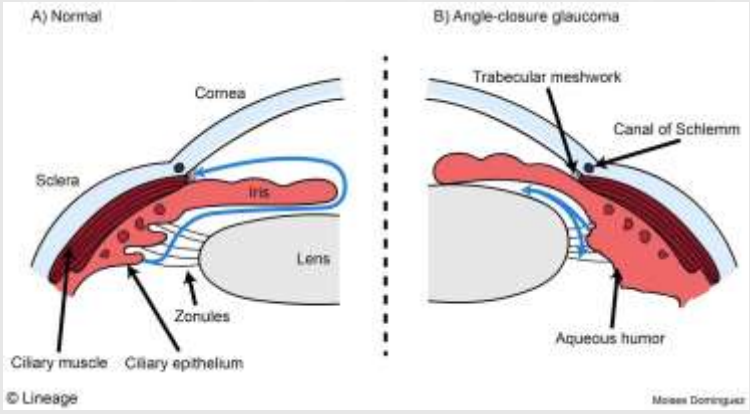
- Sudden onset, bilateral granulomatous uveitis in up to 70% of patients, with pockets of sub-retinal fluid and choroidal thickening, blurring of vision, and conjunctival injection.
- Signs also include swelling and hyperemia of the optic disc and retinal edema.
- *Vitritis and anterior uveitis* are not necessary for the diagnosis!

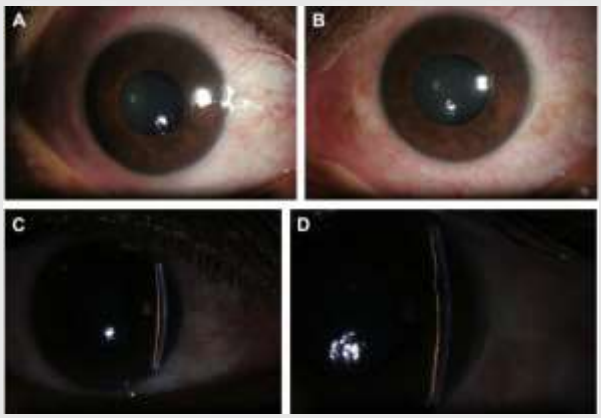




Intra Ocular Pressure

- Initialy there is <u>increase</u> in intraocular pressure in up to 54%.
- Transient swelling of the ciliary body → forward displacement of the lens-iris diaphragm→ <u>shallow AC.</u>
- The ++IOP responds better <u>to steroids</u> than to anti-glaucoma medications.
- However; hypotony can also be present.





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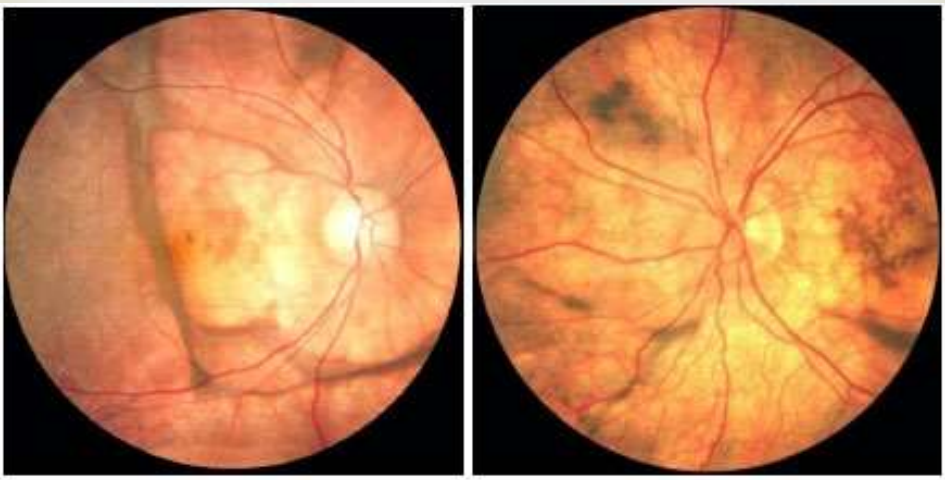
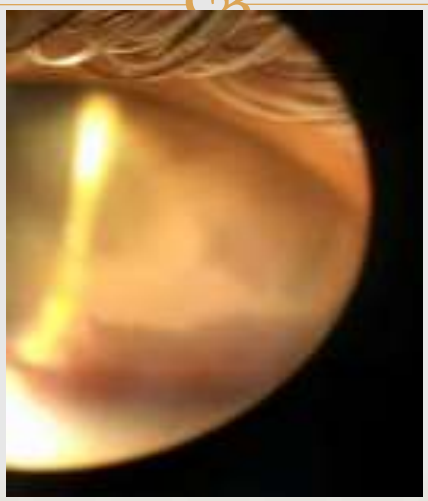
3- *Convalescent phase*

- Several weeks to months after the acute uveitic phase.
- Depigmentation of the choroid, vitiligo, and poliosis occurs.
- Depigmentation of the choroid usually takes 2 to 3 months → "sunset glow"



4- Chronic recurrent phase

- Chronic recurrent intraocular inflammation develops in some of the patients; usually resistant to systemic steroid therapy.
- This chronic recurrent phase usually 6 to 9 months after initial presentation
- Marked by complications such as retinal pigment epithelium (RPE) proliferation, subretinal fibrosis, CNV…



Extraocular manifestations

1- Neurologic findings

- headache, meningismus, or cerebrospinal fluid pleocytosis.
- Patients may also present with focal neurologic signs including cranial neuropathies, transverse myelitis, hemiparesis, and aphasia.

2- *Auditory findings*

- 18 - 50 % have some form of sensory hearing loss, (at higher frequencies).
- Tinnitus is present in 42%.
- Auditory symptoms often responds well to steroids.

3- *Integumentary findings*

- During the convalescent phase, with depigmentation of the choroid, the eyebrows, eyelashes, hair, and skin also lose pigment, resulting in poliosis and vitiligo.
- In 30 % of patients.

Revised diagnostic criteria for Vogt-Koyanagi-Harada disease

Complete Vogt-Koyanagi-Harada syndrome

1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis
2. No clinical or laboratory evidence suggestive of other ocular disease entities
3. Bilateral ocular involvement [(a) or (b) must be met, depending on stage of disease]
   a. Early manifestations
      1. Diffuse choroiditis, focal areas of subretinal fluid, bullous serous retinal detachments
      2. If equivocal fundus findings, then the following must be present:
         a. Focal areas of delays in choroidal perfusion, multifocal areas of pinpoint leakage, large placoid areas of hyperfluorescence, pooling within subretinal fluid, and optic nerve staining
         b. Diffuse choroidal thickening without evidence of posterior scleritis by ultrasonography
   b. Late manifestations
      1. History suggestive of prior disease based on findings in the following
      2. Ocular depigmentation: sunset glow fundus or Siguira's sign
      3. Other signs: nummular chorioretinal depigmented scars, RPE clumping or migration, or recurrent or chronic anterior uveitis
4. Neurological findings (may have resolved): meningismus, tinnitus, or CSF pleocytosis (Note: headache alone is not sufficient.)
5. Integumentary findings (not preceding the onset of uveitis): alopecia, poliosis, or vitiligo

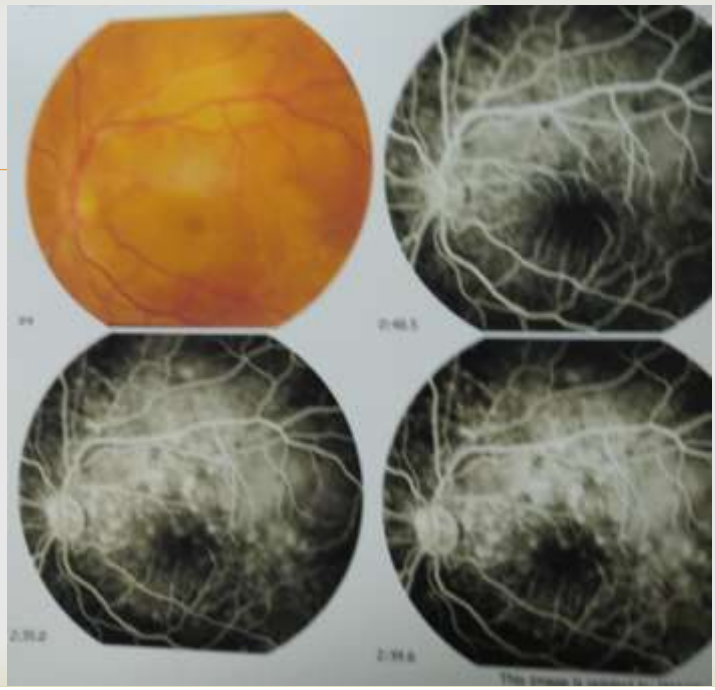
Incomplete Vogt-Koyanagi-Harada syndrome

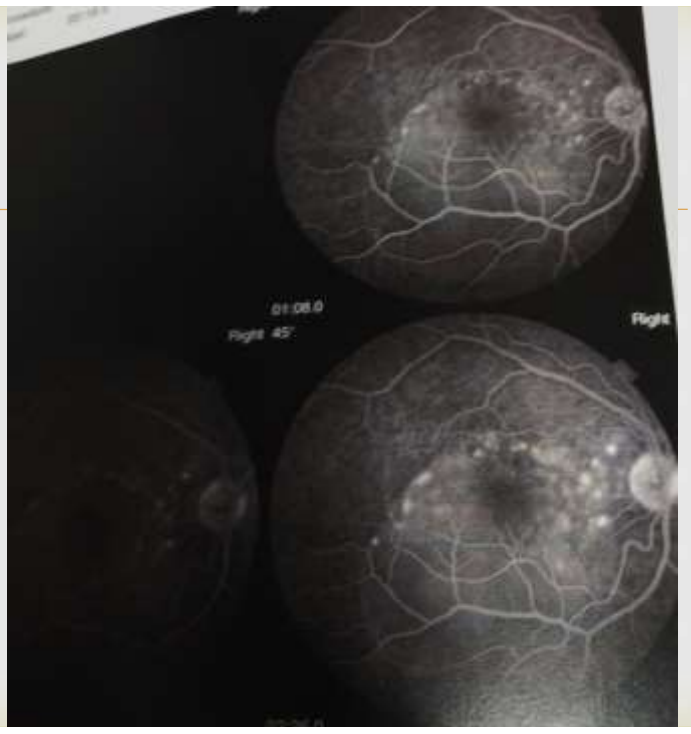
Criteria 1–3 and either 4 or 5 must be present

Probable Vogt-Koyanagi-Harada syndrome

Criteria 1–3 must be present

Am J Ophthalmol Vol 131. 2001:647–652.

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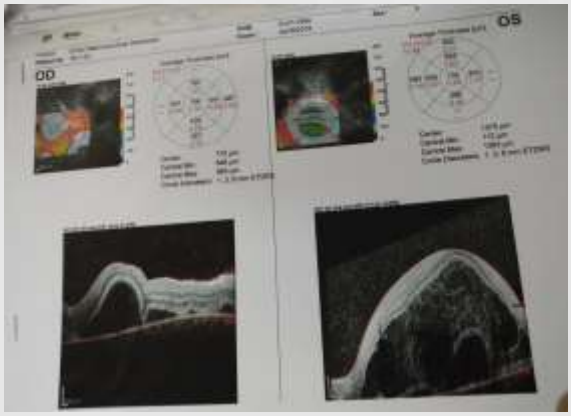
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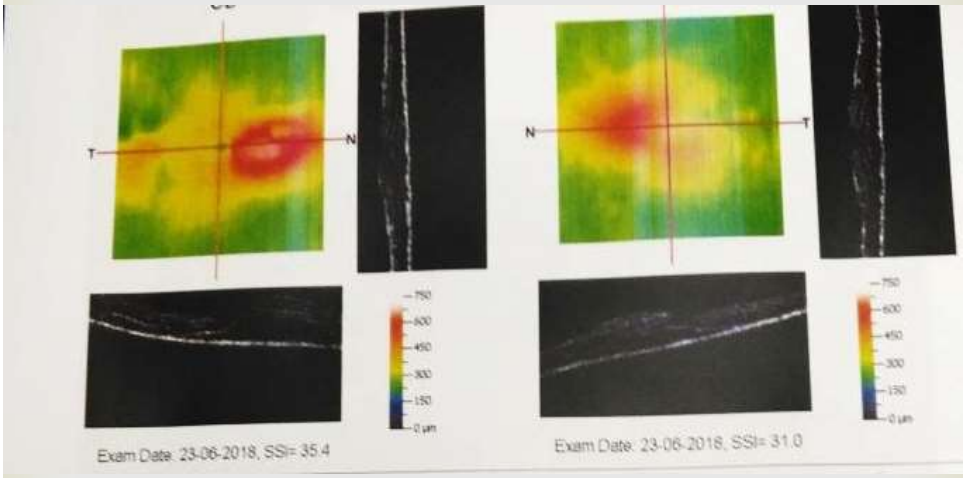
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Exam Date: 23-06-2018, SSI= 35.4
Exam Date: 23-06-2018, SSI= 31.0

Diffrential Diagnosis

Table 5 – Differential diagnosis of Vogt-Koyanagi-Harada syndrome

Prior trauma	Infectious etiologies	Malignancies	Inflammatory diseases
Sympathetic ophthalmia	Bacterial infection	Intraocular lymphoma	Bilateral posterior scleritis
	Fungal infection	Diffuse uveal lymphoid hyperplasia	Sarcoidosis
	Tuberculosis	Bilateral diffuse uveal melanocytic hyperplasia	Acute posterior multifocal placoid pigment epitheliopathy
	Syphilis	Monoclonal gammopathies	Multiple evanescent white dot syndrome
		Systemic lymphoma or leukemia	Lupus choroidopathy

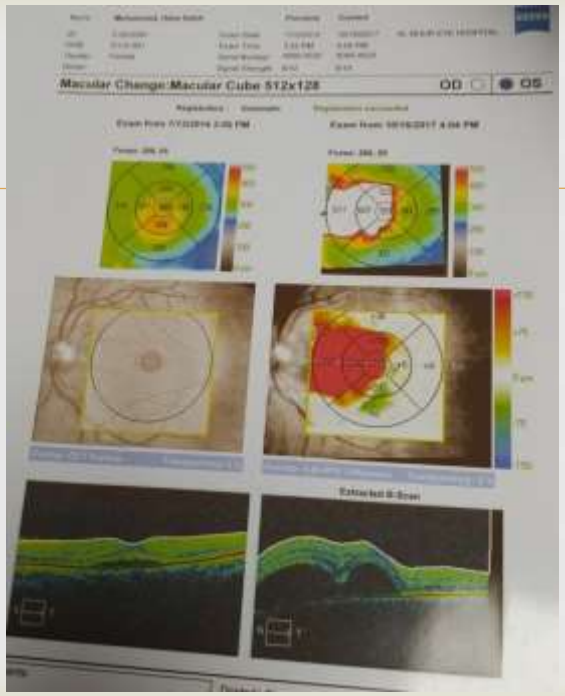
case # 1

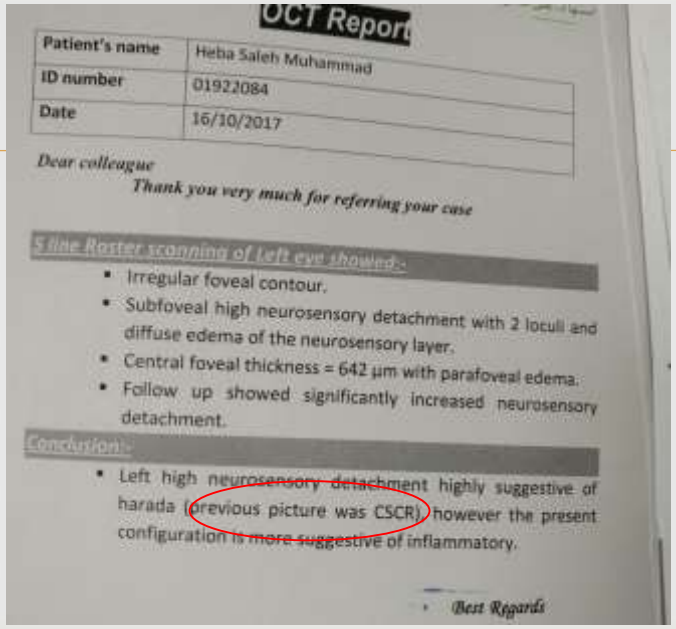
6/2014

- 22 y old female.
- Acute blurring of vision Left eye
- L CSR managed conservatively until spontaneous recovery with LVA 20/20-
- R eye normal.

10/2017

- Recurrence of L blurring of vision.
- Recurrence of L CSR.
- R eye normal.
- Ordered new FA and OCT.





OCT Report

Patient's name	Heba Saleh Muhammad
ID number	01922084
Date	16/10/2017

Dear colleague

Thank you very much for referring your case

5 line Raster scanning of left eye showed:-

- Irregular foveal contour.
- Subfoveal high neurosensory detachment with 2 loculi and diffuse edema of the neurosensory layer.
- Central foveal thickness = 642 µm with parafoveal edema.
- Follow up showed significantly increased neurosensory detachment.

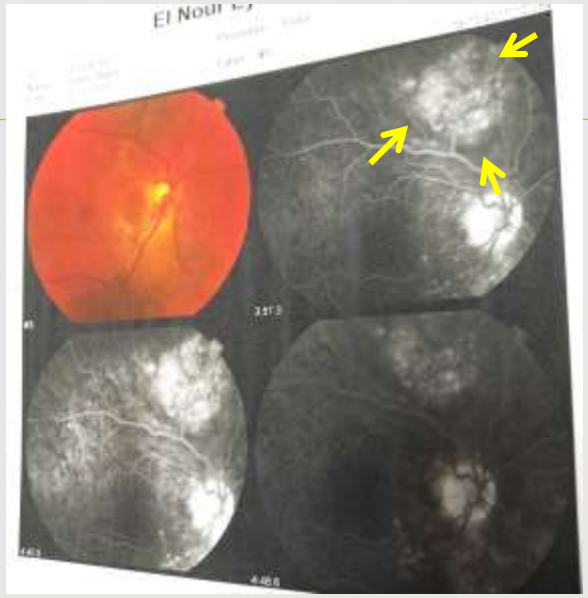
Conclusion:-

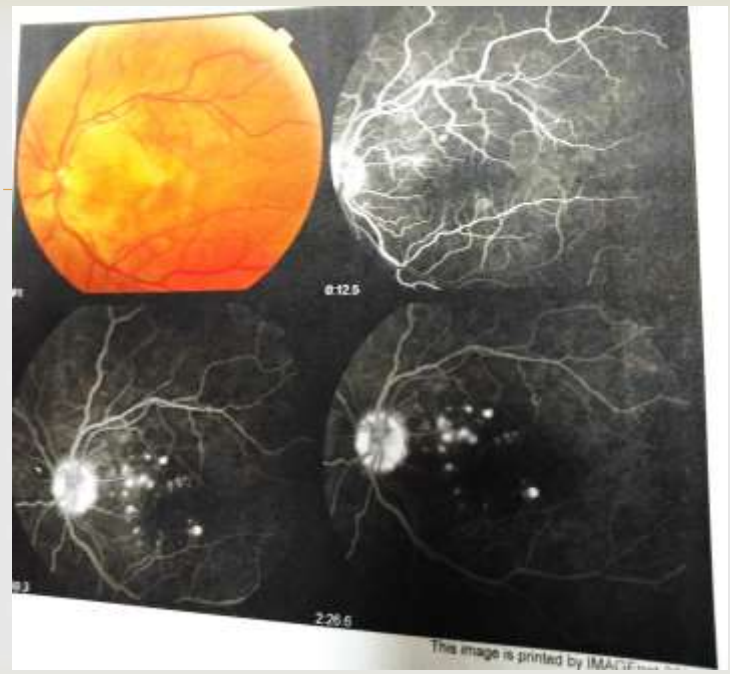
- Left high neurosensory detachment highly suggestive of harada (previous picture was CSCR), however the present configuration is more suggestive of inflammatory.

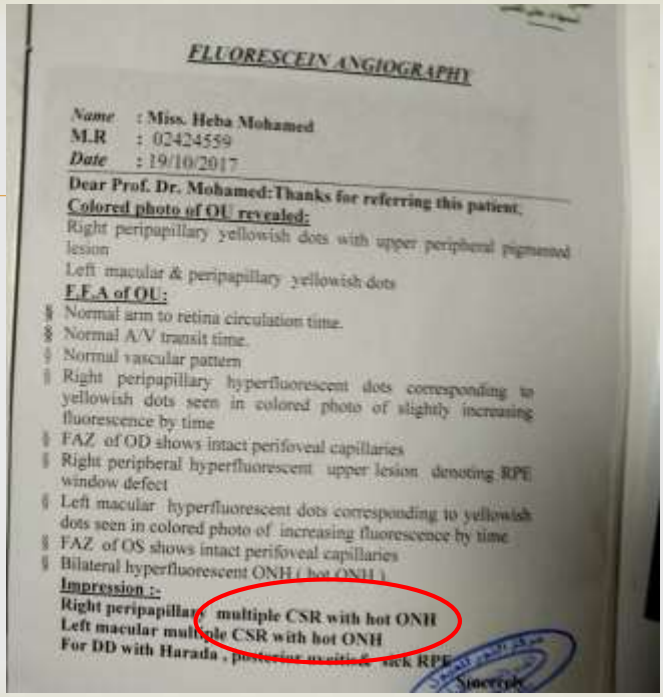
Best Regards

Revise diagnosis

- Noticed the presence of small exudative detachment in the right eye as well.
- Few vitreous cells and few small fresh KPs
- Diagnostic criteria for Harada is now present!
- Change in pathology? Atypical Harada at the beginning?
- Treatment is the opposite to that of CSR!







FLUORESCEIN ANGIOGRAPHY

Name : Miss. Heba Mohamed
M.R : 02424559
Date : 19/10/2017

Dear Prof. Dr. Mohamed: Thanks for referring this patient.

Colored photo of OU revealed:

Right peripapillary yellowish dots with upper peripheral pigmented lesion

Left macular & peripapillary yellowish dots

F.F.A of OU:

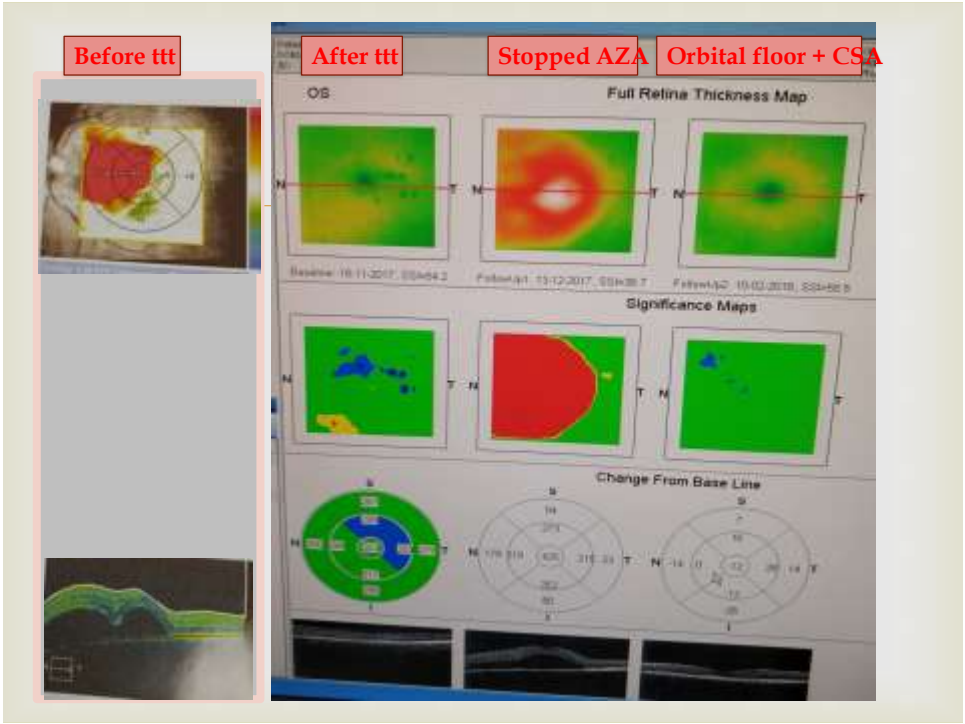
- Normal arm to retina circulation time.
- Normal A/V transit time.
- Normal vascular pattern
- Right peripapillary hyperfluorescent dots corresponding to yellowish dots seen in colored photo of slightly increasing fluorescence by time
- FAZ of OD shows intact perifoveal capillaries
- Right peripheral hyperfluorescent upper lesion denoting RPE window defect
- Left macular hyperfluorescent dots corresponding to yellowish dots seen in colored photo of increasing fluorescence by time
- FAZ of OS shows intact perifoveal capillaries
- Bilateral hyperfluorescent ONH (hot ONH)

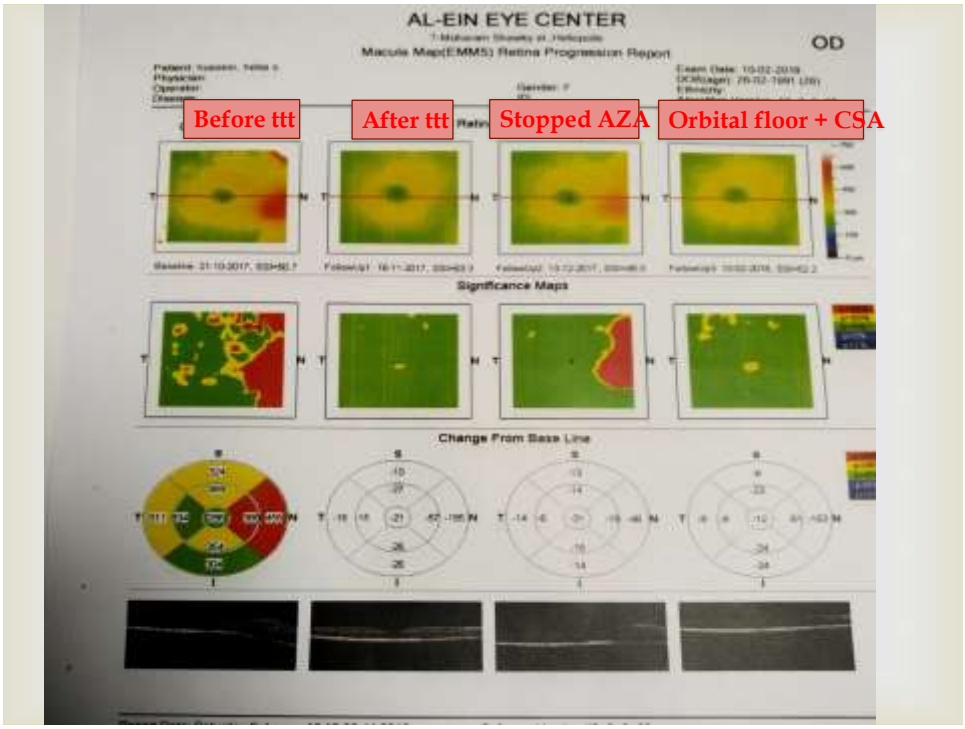
Impression :-

Right peripapillary multiple CSR with hot ONH
Left macular multiple CSR with hot ONH
For DD with Harada , posterior uveitis & sick RPE

Sincerely

- Started immunno-suppression Pred 20mg+ AZA 100 → Excellent recovery.
- Raised liver enzymes→ stopped AZA → relapse.
- L orbital floor deprofose + CSA 200mg +pred back to 20mg.
- Recovered and maintained remission on CSA 200 + pred 10mg.


Before ttt
After ttt
Stopped AZA
Orbital floor + CSA
OS
Full Retina Thickness Map
Significance Maps
Change From Base Line

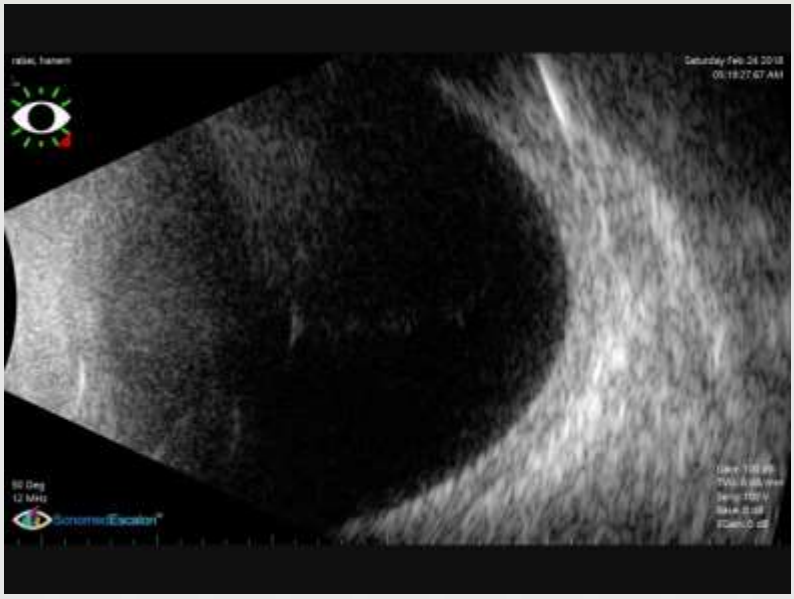

AL-EIN EYE CENTER
OD
Macula Map(EMM5) Retina Progression Report
Before ttt
After ttt
Stopped AZA
Orbital floor + CSA
Significance Maps
Change From Base Line

case # 2

15 year old girl.

- August 2017 headache and poor vision
  bilateral VA 0.3, shallow AC, CD 0.7 & 0.3 resp.
  IOP 30 & 26 resp. on Azarga & alphagan
  VEP & ERG sub-normal, FA choroidal atrophy?
- IOP steadily increased over the next months to 40s/50s despite adding Travatan.
- January 2018 Right trabeculectomy + MMC = releasable suture kept tight.

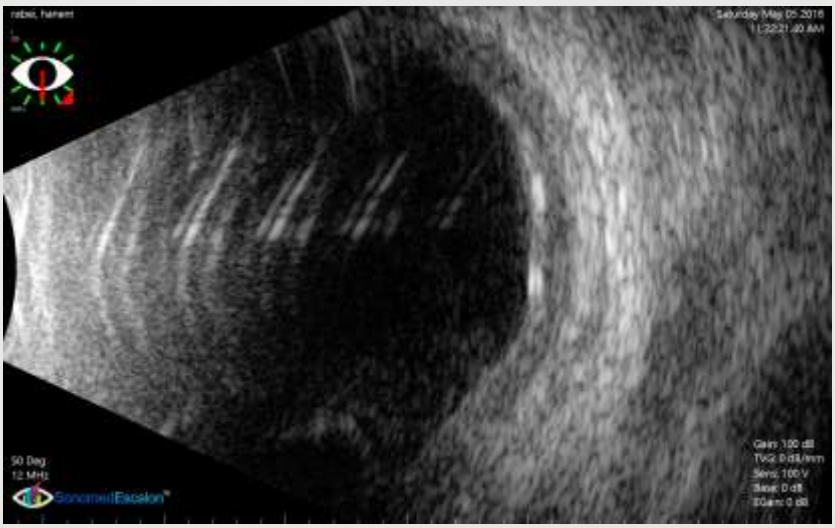
- R IOP 27 with very shallow AC (no touch).
- Suture released ---IOP 17 with formed bleb with shallow AC.

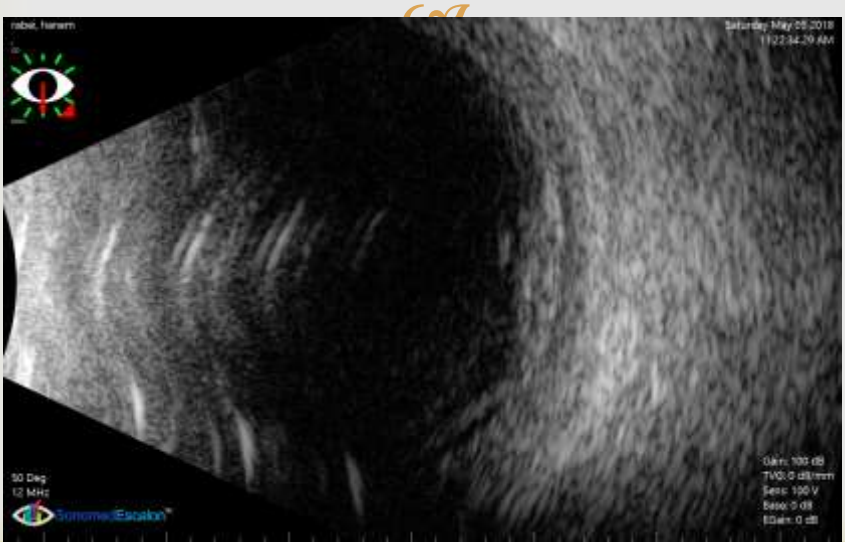


- March/2018 IOP 34 & 28 resp.
- April/2018 acute onset severe headache dizziness and loss of vision (HM) bilaterally .

  Bilateral+4 cells vitritis (BIO +++) inferior exudative RD, disc hyperaemia.

  B scan: vitritis, inferior exudative detachment, thickened choroid bilateraly.



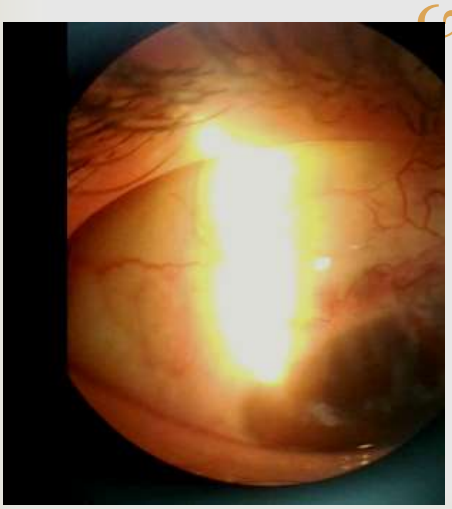


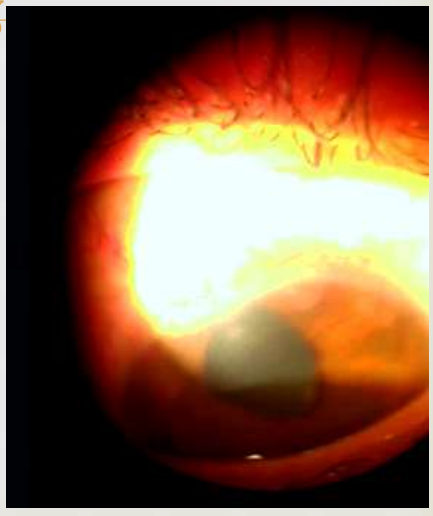
What is going on?

- Sympathetic ophthalmitis secondary to R trab?
- Harada presenting with chronic ACG due to CB swelling ?

VKH presenting as acute angle closure glaucoma at onset. Yang P, et al. Clin Exp Ophthalmol, 2011 Sep-Oct.

- April 2018: IV methyl pred X3 then oral pred 40mg and AZA 100mg
- June 2018: improved to CF 2m, AC deepened for the first time, IOP 16 bil.
- Shifted to Humira with excellent control.
- Stopped Humira due to unavailability → immediate severe relapse to only HM & CF.
- Started CSA 200 after IV methyl pred -→ controlled with 5/60 vision in one eye.





case # 3

Presented: in 2003

Age: 36 male military engineer

PC: Blurred vision waxing and waning since 2 months associated with tinnitus and hearing loss

POH: Attack of pan-uveitis 2 months ago improved on systemic steroids.

PMH: Sensory auditory loss

DH: was on systemic steroids tapered quickly

SH: Nil

RVA: 6/12 cells + Flare+/-	**A C**	**LVA:** 6/9 hazy BE cells + Flare+/-
Few ant vit cells BIO +	**fundus**	Few ant vit cells BIO +
16	**IOP**	16

- Systemic enquiry:

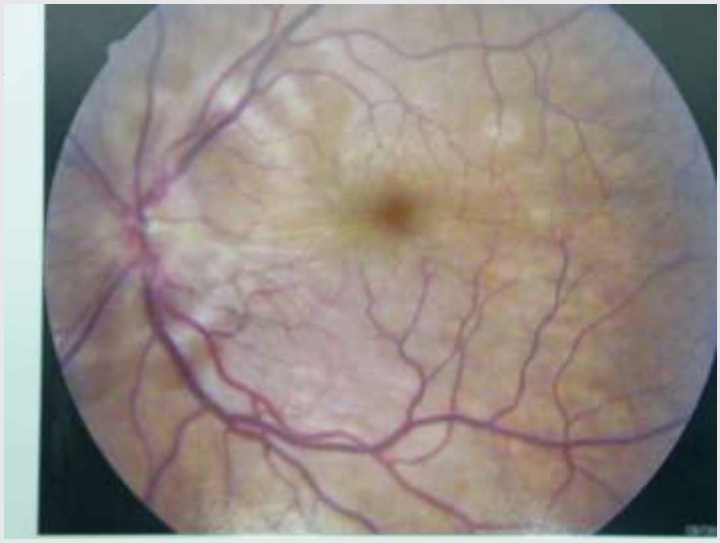
--Genito-urinary: rash on scrotum (nature?)

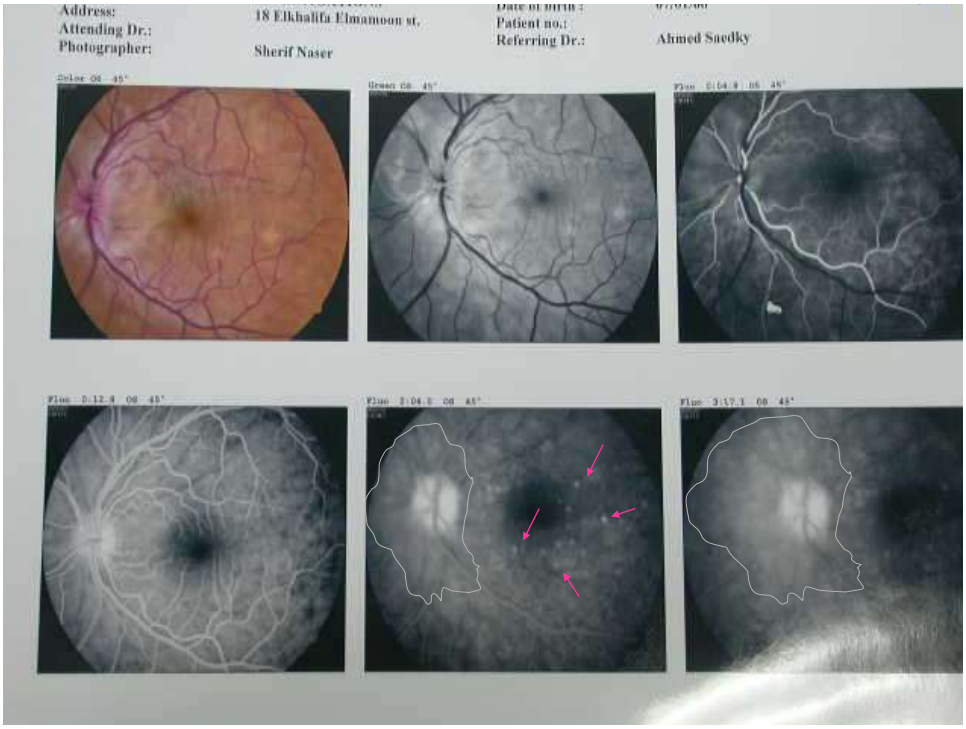
-Skin: recurrent abscesses

-CNS: headache, lack of concentration, tinnitus, some deafness

- Systemic examination:

-folliculitis in the axilla

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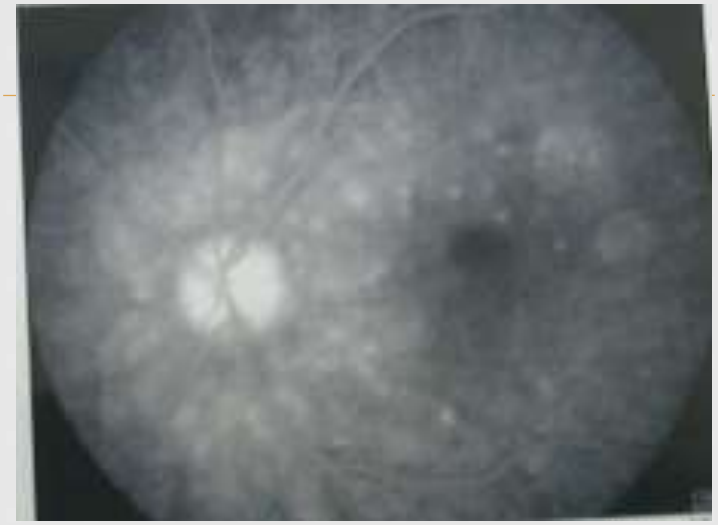
18 Elkhalifa Elmamoon st.
Attending Dr.:
Patient no.:
Photographer:
Sherif Naser
Referring Dr.:
Ahmed Saedky



- **Audiometry:** Sensory auditory loss
- **Head CT scan :** NAD
- **Blood chemistry:** Na, K, HCO3, urea, creatinine, liver function
- **CBC** ---- normal
- **Auto-antibodies** ---- normal
- **HLA B5** ----- negative
- **Radioactive GFR assessment**---- normal
- **Chest X-ray**---- normal
- **Behcetin test**----- positive

What is going on?

DD: -AMPPE (hearing loss, bilateral, male, AC reaction and vitritis)

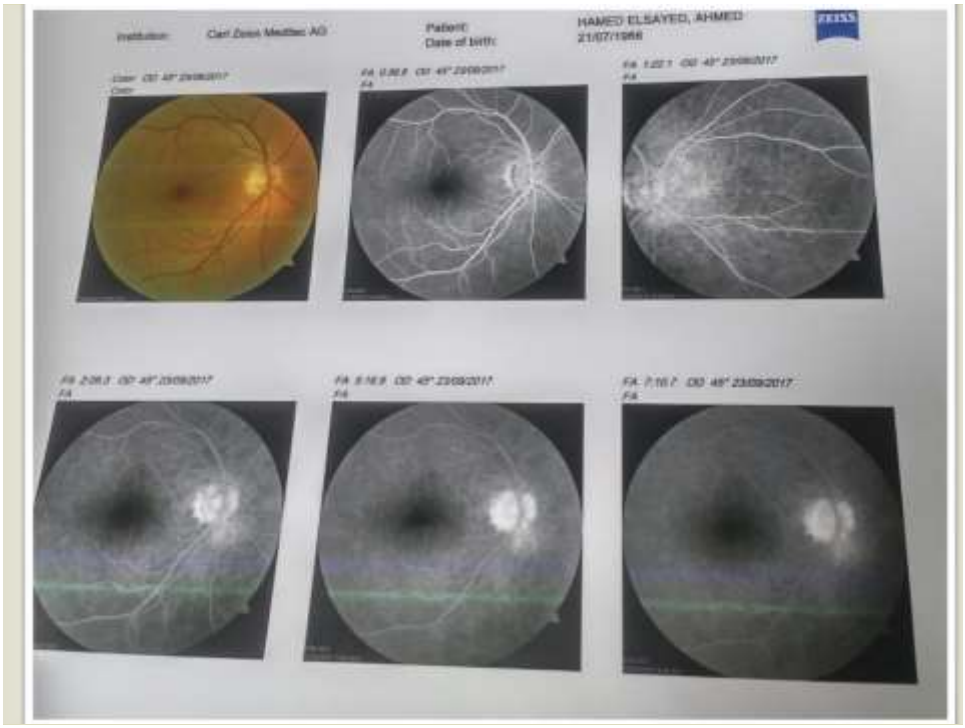
-MEWDS (Peripapillary serous detachment, small hyperflorescent spots)

-VKH syndrome (hearing loss, bilateral, male, AC reaction, headache, serous detachment, multifocal choroiditis).

Finding the diagnosis is often important but not crucial to the management.

	AMPPE	MEWDS	VKH
unilaterality	Bi /unilateral	unilateral	Bilateral
Gender	M=F	Mainly F	M< F
Serous detachment	Rare reports	few reports	Main feature
lesions	placoid	10-100um	larger
inflammation	common	uncommon	Main feature
Vision loss	Mild-moderate	mild	Moderate-severe
neurological (including auditory)	reported	Not reported?	common
extent	Post pole	Post pole	diffuse
FA	Early hypo	Early hyper	Hyper&hypo
course	Short (self-limiting)	Short (self-limiting)	long

Relentless APMPPE



In conclusion

- Harada's disease is probably the second most common uveitis in Egypt.
- Most of the time the diagnostic criteria is fulfilled and the diagnosis is straight forward.
- However; sometimes the lack of accompanying inflammation or atypical presentations can pose a challenge.

Thank you