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.

*survey of ophthalmology 62 (2017) 1-25*
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.

*survey of ophthalmology 62 (2017) 1-25*

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.
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

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

<table>
<thead>
<tr>
<th><strong>Complete Vogt-Koyanagi-Harada syndrome</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis</td>
</tr>
<tr>
<td>2. No clinical or laboratory evidence suggestive of other ocular disease entities</td>
</tr>
<tr>
<td>3. Bilateral ocular involvement ( bilateral visual field defects must be met, depending on stage of disease)</td>
</tr>
<tr>
<td>a. Early manifestations</td>
</tr>
<tr>
<td>i. Ocular findings, focal areas of subretinal fluid, bullous serous retinal detachments</td>
</tr>
<tr>
<td>ii. Hypoc contraceptive findings, then the following must be present:</td>
</tr>
<tr>
<td>a. Focal areas of delays in choroidal perfusion, multifocal areas of pinpoint leakage, small placoid areas of hyperfluorescence, pooling within subretinal fluid, and optic nerve staining</td>
</tr>
<tr>
<td>b. Diffuse choroidal thickening, without evidence of posterior scleritis by ultrasonography</td>
</tr>
<tr>
<td>b. Late manifestations</td>
</tr>
<tr>
<td>1. History suggestive of prior disease based on findings in the following</td>
</tr>
<tr>
<td>2. Ocular depigmentation: sunset glow fundus or Sugiura’s sign</td>
</tr>
<tr>
<td>3. Other signs, nummular choriretinal depigmented scars, RPE clumping or migration, or recurrent or chronic anterior uveitis</td>
</tr>
<tr>
<td>4. Neurological findings (may have resolved): meningismus, tinnitus, or CSF pleocytosis (Note: headache alone is not sufficient)</td>
</tr>
<tr>
<td>5. Intercurrent findings (just preceding the onset of uveitis): asepsia, polyuria, or vitiligo</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Incomplete Vogt-Koyanagi-Harada syndrome</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria 1–3 and either 4 or 5 must be present</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Probable Vogt-Koyanagi-Harada syndrome</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria 1–3 must be present</td>
</tr>
</tbody>
</table>

# Differential Diagnosis

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

<table>
<thead>
<tr>
<th>Prior trauma</th>
<th>Infectious etiologies</th>
<th>Malignancies</th>
<th>Inflammatory diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic ophthalmia</td>
<td>Bacterial infection</td>
<td>Intraocular lymphoma</td>
<td>Bilateral posterior scleritis</td>
</tr>
<tr>
<td></td>
<td>Fungal infection</td>
<td>Diffuse uveal lymphoid hyperplasia</td>
<td>Sarcoïdosis</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis</td>
<td>Bilateral diffuse uveal melanocytic</td>
<td>Acute posterior multifocal placoid,</td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
<td>hyperplasia</td>
<td>pigment epitheliopathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monoclonal gammopathies:</td>
<td>Multiple evanescent white dot syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic lymphoma or leukemia</td>
<td>Lupus choroidopathy</td>
</tr>
</tbody>
</table>
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.
<table>
<thead>
<tr>
<th>Patient's name</th>
<th>Heba Saleh Muhammad</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID number</td>
<td>01922084</td>
</tr>
<tr>
<td>Date</td>
<td>16/10/2017</td>
</tr>
</tbody>
</table>

Dear colleague,
Thank you very much for referring your case.

S line Rostro 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 CSR) however the present configuration is more suggestive of inflammatory.

Best Regards

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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!
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  Stopped AZA  Orbital floor + CSA

After ttt
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.
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 \(\rightarrow\) immediate severe relapse to only HM & CF.
Started CSA 200 after IV methyl pred \(\rightarrow\) 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+/-
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
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 hyperfloscent 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.
<table>
<thead>
<tr>
<th></th>
<th>AMPPE</th>
<th>MEWDS</th>
<th>VKH</th>
</tr>
</thead>
<tbody>
<tr>
<td>unilaterality</td>
<td>Bi /unilateral</td>
<td>unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Gender</td>
<td>M=F</td>
<td>Mainly F</td>
<td>M&lt; F</td>
</tr>
<tr>
<td>Serous detachment</td>
<td>Rare reports</td>
<td>few reports</td>
<td>Main feature</td>
</tr>
<tr>
<td>lesions</td>
<td>placoid</td>
<td>10-100um</td>
<td>larger</td>
</tr>
<tr>
<td>inflammation</td>
<td>common</td>
<td>uncommon</td>
<td>Main feature</td>
</tr>
<tr>
<td>Vision loss</td>
<td>Mild-moderate</td>
<td>mild</td>
<td>Moderate-severe</td>
</tr>
<tr>
<td>neurological (including auditory)</td>
<td>reported</td>
<td>Not reported?</td>
<td>common</td>
</tr>
<tr>
<td>extent</td>
<td>Post pole</td>
<td>Post pole</td>
<td>diffuse</td>
</tr>
<tr>
<td>FA</td>
<td>Early hypo</td>
<td>Early hyper</td>
<td>Hyper&amp;hypo</td>
</tr>
<tr>
<td>course</td>
<td>Short (self-limiting)</td>
<td>Short (self-limiting)</td>
<td>long</td>
</tr>
</tbody>
</table>

![Image of eye scans](image_url)
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 straightforward.

However; sometimes the lack of accompanying inflammation or atypical presentations can pose a challenge.

Thank you