VOGT KOYANAGI HARADA DISEASE

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TOPICS

1. background
2. clinical
3. diagnosis
4. treatment

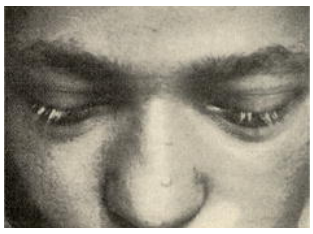
BACKGROUND

HISTORY

- earlier description by Arabic doctor in 12th century
- 1906 Alfred Vogt - anterior uveitis, poliosis, and vitiligo
- 1911 Jujiro Komoto reported in German.

1906

Prof. Alfred Vogt



XIX.

Aus der Universitäts-Augenklinik Basel.
(Prof. Dr. C. Mellinger.)

Frühzeitiges Ergrauen der Zilien und Bemerkungen über den sogenannten plötzlichen Eintritt dieser Veränderung.

Von **Dr. Alfred Vogt**, I. Assistenzarzt.

Mit 1 Abbildung.

Am 1. April vorigen Jahres wurde ein 18jähriger Bauernbursche wegen schwerer beiderseitiger Iridozyklitis, die angeblich seit 5 Wochen bestand, in unsere Behandlung aufgenommen. Die Anamnese zeigte nichts Besonderes. Patient war blass und von etwas gedunsenem skrofulösem Habitus. Die Augenlider waren ohne Besonderheiten. Die ziliar injizierten Bulbi zeigten das gewöhnliche Bild subakuter Iridozyklitis. Durch Exsudate und Hornhautpräzipitate war das früher angeblich gute Sehvermögen rechts auf $^{4}/_{200}$, links auf $^{2}/_{200}$ herabgesetzt.

XII.

Aus der Privat-Augenklinik von Prof. Dr. J. Komoto, Tokio.

Ueber Vitiligo und Auge.

Von Prof. Dr. J. Komoto.

1911

Prof J Komoto

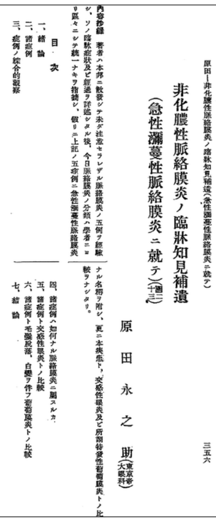
1914

Prof.Yoshizo Koyanagi
reported case in Japanese

1926

Harada's disease

uveitis with history of
headache CSF pleocytosis
and
skin involvement (vitiligo,
poliosis, alopecia)



原田―非化膿性脈絡膜炎ノ臨牀知見補遺（急性瀰蔓性脈絡膜炎ニ就テ） 三五六

非化膿性脈絡膜炎ノ臨牀知見補遺
（急性瀰蔓性脈絡膜炎ニ就テ）（圖二十三）

原田永之助（東京帝大眼科）

内容抄録 著者ハ本邦ニ散發シテ未ダ注意セラレザル脈絡膜炎ノ五例ヲ經驗シ、ソノ臨牀症狀及ビ經過ヲ詳述シタル後、今日脈絡膜炎ノ分類ハ學者ニヨリ區々ニシテ統一ナキヲ指摘シ、假リニ上記ノ五症例ニ急性瀰蔓性脈絡膜炎ナル名稱ヲ附シ、更ニ本疾患ト、交感性眼炎及ビ所謂特發性葡萄膜炎トノ比較ヲナシタリ。

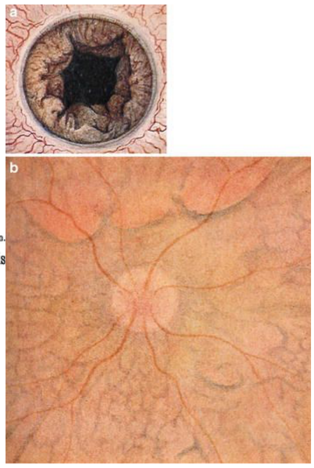
目次

一、緒論
二、諸症例
三、症例ノ綜合的觀察
四、諸症例ハ如何ナル脈絡膜炎ニ屬スルカ
五、諸症例ト交感性眼炎トノ比較
六、諸症例ト毛髮脱落、白髮ヲ伴フ葡萄膜炎トノ比較
七、結論

1929

Prof.Yoshizo Koyanagi

XXII.
Aus der Augenklinik der Tohoku-Universität in Sendai, Japan.
Dysakusis, Alopecia und Poliosis bei schwerer Uveitis nicht traumatischen Ursprungs.
Von Prof. Dr. Y. Koyanagi.
Mit 5 Textabbildungen, darunter 2 farbige auf Tafel IV.



HISTORY

- Harada's disease (still use in Japan till today)
- 1939 Vogt- Koyanagi syndrome (less systemic than Harada's disease)
- 1955 Vogt- Koyanagi- Harada disease
- 2001 revise diagnostic criteria of VKH disease

Am J Ophthalmol. 2001 May;131(5):647-52 survey of ophthalmology 62 (2017) 1 e2 5

EPIDEMIOLOGY

- VKH relatively rare in US (3-4%) (most non white)
- South America - 1.2-2.5%
- More common in Asia (6-20%)
- Middle East - Behcet > VKH

survey of ophthalmology 62 (2017) 1 e2 5

EPIDEMIOLOGY

- India - VKH most common of panuveitis (21%)
- **Thailand - most common of non infectious panuveitis (16%)**
- Japan - VKH 6.7-11%
- Japan, Middle east - Behcet > VKH

survey of ophthalmology 62 (2017) 1 e2 5

EPIDEMIOLOGY

- US Female> Male, onset 30+
- less common in children, elderly
- Elderly is higher in Japan > UK, US

ETIOLOGY

1. autoimmune to melanocytes
2. genetics
3. virus

ETIOLOGY

- pathology found:
- inflammation
- loss of choroid melanocytes
- target **tyrosinase peptide** by T cells

AUTOIMMUNITY

- CD4 T cells
- inflammation targets melanocytes
- target tyrosinase peptide in melanocytes
- cytokines IL17, IL 23

GENETIC FACTORS

- HLA DRB1*0405 increase risk 45X in Korean
- susceptibility genes
- protective genes
- protective haplotypes

VIRAL HYPOTHESIS

- evidence of simultaneous onset VKH in coworkers
- evidence of viral genome in CSF
- molecular mimicry of CMV and tyrosinase peptide
- viral RNA stimulates Toll-like receptor3 in human melanocytes leads to cell death

CLINICAL

CLINICAL MANIFESTATIONS

1. prodromal
2. acute uveitis
3. chronic
4. recurrent

prodrome

PRODROMAL PHASE

- a viral like
- last a few days to weeks
- extra-ocular symptoms

prodrome

PRODROMAL PHASE

- fever
- headache, meningismus, nausea, vomit
- orbital pain
- auditory symptoms

acute

ACUTE UVEITIS PHASE

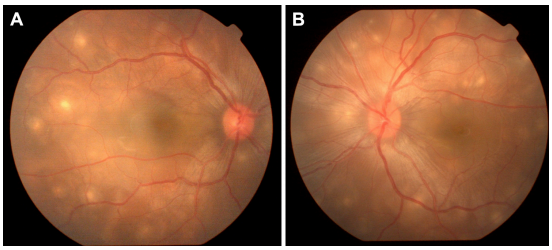
- 70% sudden bilateral granulomatous uveitis
- blurring of vision
- conjunctival injection
- visual field loss
- increase intraocular pressure

acute

ACUTE UVEITIS PHASE

- sub-retinal fluid
- choroidal thickening
- retinal edema
- optic nerve head swelling & hyperemia

acute

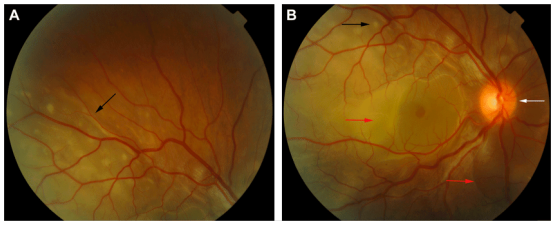


ACUTE VKH

Color fundus photos (A and B) of acute VKH

acute

subserous retinal detachment

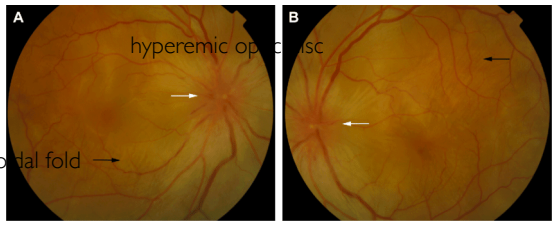


multifocal choroiditis hyperemic optic disc

Color retinal photographs of a patient during the acute phase of vKHD. Notes: (A) Multifocal choroiditis lesions of variable size representing along the superior arcade (black arrow). (B) The posterior pole depicting a hyperemic optic disc (white arrow), multifocal choroiditis (black arrow), and multiple areas of SRDs (red arrows).

Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt–Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

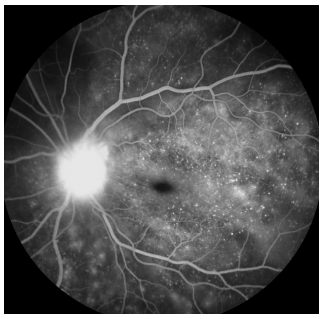
acute



Color retinal photographs of right (A) and left eye (B) showing **swollen and hyperemic optic discs (white arrows)**, with choroidal folds disc (black arrows), in the acute phase of vKHD.

Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt–Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

acute



FFA photograph of a patient in the acute phase of vKHD showing optic disc leakage and numerous hyperfluorescent pinpoint foci of leakage at the level of RPe leading to the classic " starry sky " appearance.
FFA, fundus fluorescein angiography; RPe, retinal pigment epithelium.

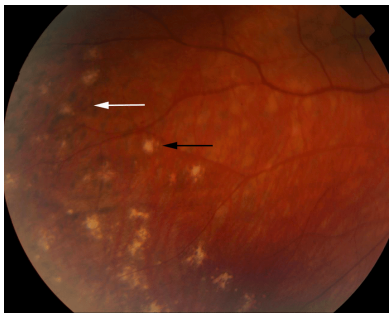
Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt–Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

chronic

CHRONIC PHASE

- weeks to months later
- depigmentation of **choroid, skin, eyelash**
- start at limbal area (Sugiura sign)
- sunset glow fundi

chronic



SUNSET GLOW FUNDI

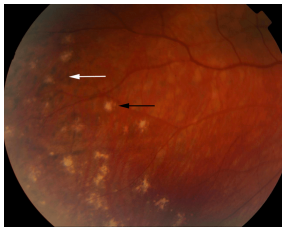
Color retinal photograph displaying sunset glow fundus with a numerous small choroidal depigmented atrophic lesions (black arrow) and hyperpigmented lesions (white arrow) in the retinal periphery during the convalescent phase of vKHD.

Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt–Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

chronic

SUNSET GLOW FUNDI

- bright orange red of fungus
- uveitis + sunset glow fundus
  - positive predictive 94.5
  - negative predictive value 89.2



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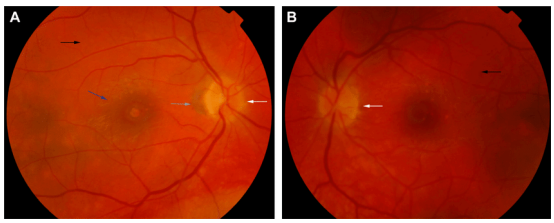


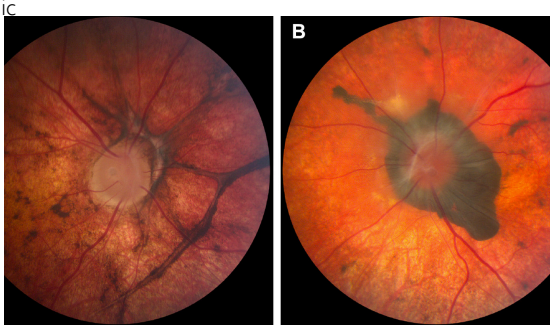
pale disc

CONVALESCENT PHASE

Color retinal photographs of right (A) and left eye (B) during the convalescent phase of vKHD, showing **sunset glow fundus with pale optic discs** (white arrows) and **bright-orange choroids** (black arrows). Note the peripapillary atrophy (gray arrow) and macular scaring (blue arrow) in (A).

Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt–Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

chronic

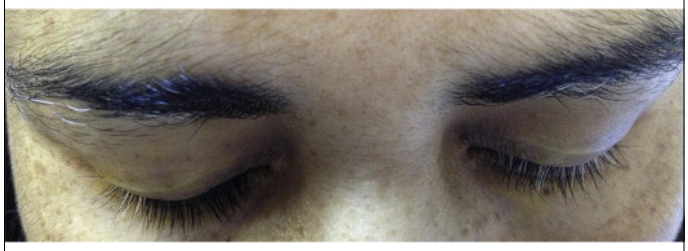


CHRONIC VKH

Color fundus photos (A and B) demonstrating fibrotic pigmentary changes in long-standing VKH.

survey of ophthalmology 62 (2017) 1 e2 5

chronic

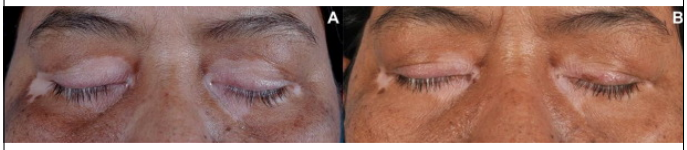


POLIOSIS

patch of white hair

Autoimmunity Reviews Volume 13, Issues 4–5, April–May 2014, Pages 550-555

chronic

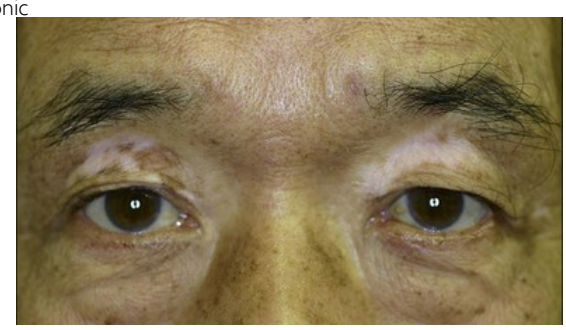


POLIOSIS

and vitiligo

Autoimmunity Reviews 15 (2016) 809–819

chronic



VITILIGO

eyelid

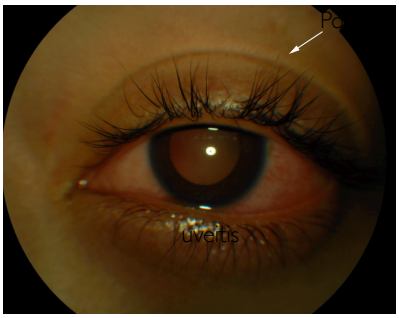
https://clinicalgate.com/vogt-koyanagi-harada-disease/

recurrent

RECURRENT

- exacerbation of granulomatous uveitis
- 6-9 months after acute
- sequele : cataract, glaucoma, retinal pigmentary change, sub retinal fibrosis, neovascularization, retinal detachment

recurrent

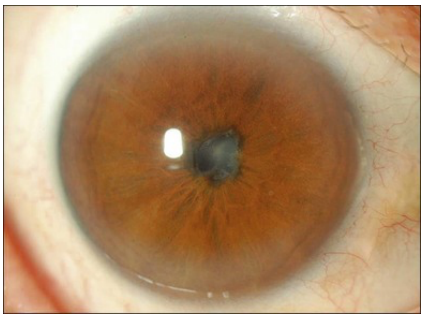


CHRONIC RECURRENT

Color photograph of a patient in the chronic recurrent phase of the vKHD showing acute anterior uveitis and mild poliosis (white arrow).

Baltmr, Abeir & Lightman, Sue & Tomkins-Netzer, Oren. (2016). Vogt-Koyanagi–Harada syndrome – current perspectives. Clinical Ophthalmology. Volume 10. 2345-2361.

recurrent



SIGUIRA'S SIGN

posterior synechiae and depigmentation at limbus

https://clinicalgate.com/vogt-koyanagi-harada-disease/

EXTRA-OCULAR MANIFESTATIONS

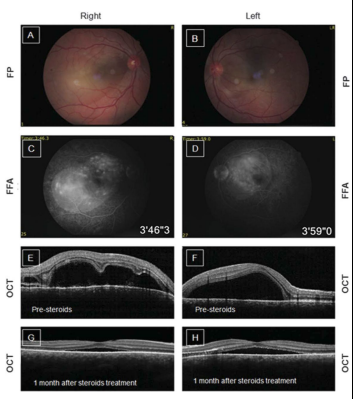
NERVOUS SYSTEM

1. nervous system
2. auditory system
3. dermatological

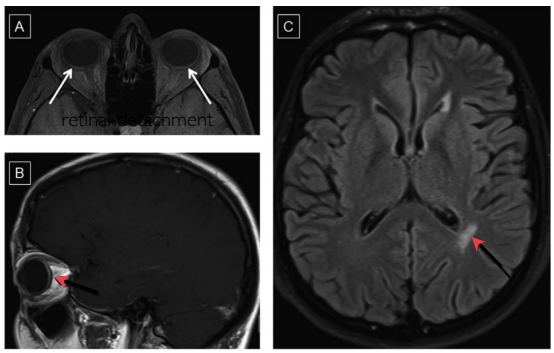
NERVOUS SYSTEM

- common during **prodromal phase**
- scalp sensitivity
- meningismus, cranial nerves, myelitis, focal signs
- CSF pleocytosis

- (A,B) Fundus photography reveals exudative retinal detachment of the macula in both eyes on presentation.
- (C,D) Fundus fluorescein angiography shows subretinal fluorescein pooling.
- (E,F) Optical coherence tomography displays exudative macular detachment in both eyes.
- (G, H) It also shows reduction of subretinal fluid after corticosteroid therapy in both eyes.



Cerebral white matter involvement in a patient with Vogt-Koyanagi-Harada syndrome.
Sadullah Keles, Hayri Ogul, Lokman Can Pinar, Mecit Kantarci. Neurology Sep 2013, 81 (11) e85-e86

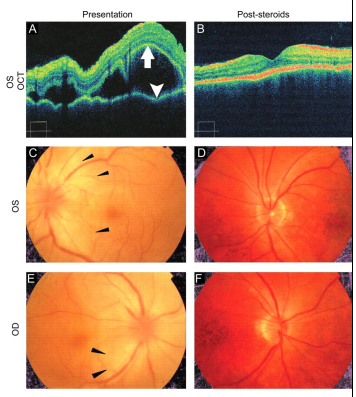


Axial T1-weighted MRI (A, B) demonstrates symmetric choroidal thickening with retinal detachment (arrows).
(C) Axial fluid-attenuated inversion recovery MRI shows hyperintense lesion in the periventricular left parietal deep white matter.

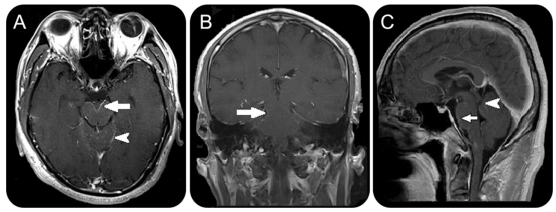
Cerebral white matter involvement in a patient with Vogt-Koyanagi-Harada syndrome.
Sadullah Keles, Hayri Ogul, Lokman Can Pinar, Mecit Kantarci. Neurology Sep 2013, 81 (11) e85-e86

35M FILIPINO

- acute visual loss,
- panuveitis
- retinal detachment
- tinnitus, dysacusis, vertigo
- gaze-evoked nystagmus



Basilar leptomeningitis in Vogt-Koyanagi-Harada disease. Yince Loh. Neurology Feb 2012, 78 (6) 438-439



Gadolinium-enhanced MRI of the brain (A) Axial, (B) coronal, and (C) sagittal gadolinium-enhanced magnetic resonance brain images demonstrate leptomeningeal enhancement of the midbrain (arrow), ventral pons (outline arrow), and cerebellum (arrowheads).

melanin-containing cell: locate predominantly at ventral medulla

Basilar leptomeningitis in Vogt-Koyanagi-Harada disease. Yince Loh. Neurology Feb 2012, 78 (6) 438-439

BILATERAL BELL'S PALSY

- male 54 with bilateral Bell's palsy
- history of uveitis, cataract, vitiligo and aseptic meningitis
- CSF: high protein 256 mg/dl. , others -normal

Bilateral Bell's Palsy Associated with Vogt-Koyanagi-Harada Disease ;A Case Report (P4.053) George Lai, DeWitt Pyburn. Neurology Apr 2017, 88 (16 Supplement) P4.053;

AUDITORY

- 18-50% has hearing loss esp. high frequency
- 42% tinnitus
- dysacusis

DERMATOLOGICAL

- 30% of VKH
- depigmentation of eyebrow, eye lashes (Poliosis)
- Vitiligo - after >> before uveitis
- alopecia

DIAGNOSIS

Table 2 – Revised diagnostic criteria for Vogt-Koyanagi-Harada syndrome

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 — probable = eye only

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

DIAGNOSIS

- fluorescein angiography of retina
- Optical coherence tomography (OCT)
- B scan ultrasonography

COMPLICATION

- **sunset glow fundi*****
- cataract
- glaucoma
- subretinal fibrosis
- choroidal neovascularization

TREATMENT

TREATMENT

- steroid
- immunosuppressive

VOGT-KOYANAGI-HARADA

- VKH - autoimmune disease
- involves 4 systems (Eye, Nervous, Ear, Skin)
- Nervous system มักช่วง prodromal phase
- meningism, CSF pleocytosis,
- myelitis, focal neuro deficit