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To Study the Clinical Profile of Patients with Vogt-Koyanagi-Harada Disease in a Tertiary Care Centre in Rural Western Maharashtra

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Abstract: ***To study the clinical profile of patients with Vogt Koyanagi Harada disease, Thereby Understanding the disease modality by appropriate diagnostic tools and investigative methods. Methods: A Cross sectional observational study was conducted in over 25 patients diagnosed with VKH in our tertiary care centre from July 2023-December 2023 .Results were analysed by a statistical test. Results: Mean age-Between 23-60 years of age= 40 (Approximate)Gender- 18 Females (72%),9 males (18%) Laterality- Bilateral- 98%, Unilateral - 2%Visual Acuity - <20/200- 27%,At 1 month – 8%, At 3 months- 35%, 20/200- or <20/40 – On presentation- 40%, At 1 month- 20%, At 3 months- 40%, 20/40 – On presentation- 33%,At 1 month -62%, At 3 months- 4% Stage of disease –Acute stage 24 eyes (48%), Chronic convalescent -18 eyes (36%),Chronic recurrent -8 eyes (16%)Clinical Presentation Panuveitis in 30 eyes (60%), Posterior uveitis in 18 eyes(36%) Slit lamp examination-Circumciliary congestion in 24 eyes (48%), Keratic precipitates 24 eyes (48%),Iris nodules in 2%. Fundus examination- Vitritis in 100%, optic disc involvement in 22 (44%), Sunset glow fundus in 6 eyes (12%), Exudative retinal detachment in 22 eyes (44%). Conclusion: In conclusion our study had more female patients compared to male, and presented more in the acute stage of the disease The rarity of VKH Syndrome makes its diagnosis a challenge, but speed in diagnosis and treatment are essential***

Keywords: VKH-Vogt koyanagi Harada disease, CSF-Cerebrospinal Fluid

1. Introduction

Vogt Koyanagi Harad Disease was first described by Alfred Vogt in 1906.VKH is defined as- "A rare granulomatous inflammatory disease that affects pigmented structures such as the eye, inner ear, meninges, skin and hair. Most commonly characterized by panuveitis. Most commonly occurring in Asians and Hispanics. It was Originally categorized as Vogt-Koyanagi Syndrome and Harada disease -Which stood for the integumentary and the Central nervous system involvement associated with pleocystosis in CSF respectively. Most of the patients known with VKH have association with HLA(Human Leucocyte antigen) DRB1*0405.The disease itself can be categorized based on the Age, Gender, Laterality, Visual Acuity, Slit lamp findings, The stage of clinical presentation and the Fundus findings.

Most commonly the VKH Disease manifests as panuveitis associated with Neurological signs such as headache, Pleocystosis of the cerebrospinal fluid. Integumentary signs such as vitiligo, Alopecia and poliosis along with ear disturbances, Phenotypically It can be divided into acute stage, Chronic convalescent and chronic recurrent stage. Most patients in the chronic stage have dermatological involvement. Patients present with Fundus findings of Vitritis, Exudative retinal detachment and Sunset-glow Fundus. The non-HLA genes related to the disease are IL-23A, IL-23R, IL-17F, IL-27. Recent studies in experimental autoimmune uveitis, in a classical animal model, point to a central role of Th 17 cells in the pathogenesis of uveitis. These results in the animal model were confirmed in a study of patients with VKH, according to which it is demonstrated that the production of IL-17, the main cytokine of Th17 cells, is an essential part of the mechanism involved in the development of uveitis in patients with VKH. This study demonstrates that the reduced expression of IL-27, which is an anti-inflammatory cytokine that regulates the activation of Th 17 lymphocytes, results in increased expression of Th 17 in patients with VKH and active uveitis. The importance of these findings lies in the fact that the manipulation of IL-27 can offer new treatments for VKH. So far it is known that treatment with corticosteroids, by inducing a positive regulation of IL-27 and a negative regulation of IL-17, contribute to the resolution of intraocular inflammation.

Several HLA genes that are related to VKH disease have also

been identified, but the strength of association between these genes and the disease is not the same in different ethnic groups. Thus, for example, the association of VKH with HDL-DR4/DRw53 was found in Asian, North American natives and Hispanic patients.

Conversely, the HLA-DRB1*0405 and HLA-DRB1*0410 alleles were strongly associated with VKH in Hindu patients.

In addition to autoimmune responses against melanocytes, VKH disease appears to be caused by autoimmune activity against melanocyte-associated antigens. It has been demonstrated that antigens of the tyrosinase protein family and GP100, a protein expressed in the basement membrane of the melanosome are antigenic targets recognized by T cells of VKH patients with positive HLA DRB1*0405 and have been related to the cause and the VKH disease.

KU-MEL-1 is another autoantigen that is widely expressed in most melanoma cell lines, samples of melanoma tissues and in cultured melanocytes.18 The antibody against KU-MEL-1 positive in serum showed a very significant association in VKH patients with positive HLA- DRB1*0405, compared with patients affected with other uveitis and with healthy controls.5,18 This association implies a primary function of KU-MEL-1 specific CD4 + T lymphocytes in the pathogenesis of VKH.

As for environmental and infectious factors, viral infections and autoimmune diseases have been correlated with VKH disease. Viruses such as Epstein-Barr and cytomegalovirus have been proposed as possible trigger factors of the disease. VKH has been reported after treatment with bacillus Calmette Guerin for melanoma, after surgery of metastatic melanoma and after traumatic skin wounds. Cases that associate VKH with hepatitis C therapy based on interferon alfa-2b combined or not with ribavirin are being reported. Prodromal phase

Patients who develop the prodromal phase simulate a systemic viral picture with clear neurological manifestations consisting of headache, orbital pain, nausea, hypoacusis or tinnitus, nuchal and back rigidity (meningism) and scalp hyperesthesia. These clinical manifestations range from 3 to 15 days before the acute uveitic phase.1 In this phase, cerebral focal signs such as confusion, aphasia and hemiparesis are rarely present.

Meningism is the most common extraocular clinical sign, present in Most of the patients presenting with VKH.

Lymphocytic pleocytosis in the CSF is found very commonly in patients diagnosed with VKH and it can persist for up to 8 weeks.

Other changes in the CSF include the presence of melanin-laden macrophages specific for VKH, increase in proteins and opening pressure.The CSF analysis is an important test for the early diagnosis of VKH, particularly in patients with headache, clear meningeal signs and few ocular signs;Lumbar Puncture along with fluorescein angiography and OCT, help as an adjuvant for the diagnosis of the same.

Sensorineural hearing loss, tinnitus, aural fullness and vertigo usually appear in the prodromal phase and can be concomitant with active uveitis]. The pattern of Sensorineural hearing loss is bilateral and mild, mainly in the high frequency range; however, cases of sudden and severe bilateral deafness are reported.

These audiological findings have allowed to recommend audiometry as part of the evaluation and control of the disease.

Acute uveitic phase

It is considered the distinctive phase of VKH disease and can last for several weeks, in the course of which the majority of patients consult ophthalmology for presenting bilateral visual loss, usually asymmetric, due to diffuse choroiditis.

In this acute uveitic phase the examiner can observe edema and hyperemia of the optic disc before observing cells in the vitreous and the classic bilateral exudative retinal detachment. The inflammatory involvement of the choroid alters the external hematoretinal barrier, formed by the Bruch's membrane and the RPE, and causes accumulation of subretinal fluid and multiple retinal detachments, which can converge and form large bullous detachments. The presence of choroidal thickening of peripapillary predominance can be clearly observed by OCT, findings that correlate with inflammatory diffuse mononuclear cell infiltration. In this phase, the inflammation can affect the anterior chamber. When ciliary body edema occurs, the intraocular pressure can rise and cause acute glaucoma by closure of the angle between the base of the iris insertion and the cornea.

Convalescent phase

The convalescent phase occurs several weeks after the acute uveitic phase, it can last several months and is characterized by the appearance of choroidal and cutaneous depigmentation areas. Sugiura's sign or perilimbal vitíligo is the earliest: it can appear in the first month of the disease.1,3 With the loss of RPE and choroidal melanocytes, the pale optic disc appears on a bright red-orange background, a color given by the depigmented choroid. This image evokes in the examiner the twilight, with its characteristic "brightness or glow of sunset", and constitutes the clinical sign known in the English literature as sunset glow fundus,3 which appears 2–3 months after the uveitic phase.1 In this phase, the ophthalmologist can also observe foci of hyperpigmentation due to migration of RPE cells, especially in Hispanic patients, and multiple small, rounded white-yellowish lesions that histologically correspond to Dalen-Fuchs nodules,6 which are aggregates of lymphocytes and pigment-laden macrophages that appear in the posterior pole between Bruch's membrane and the RPE.

The depigmentation of the skin (vitiligo),eyelashes, eyebrows and hair (poliosis) and alopecia are mainly observed during this phase as a characteristic finding. These cutaneous manifestations are more common in Asian patients. The vitiligo is usually distributed symmetrically and affects the facial region, eyelids, trunk and sacral skin area.

Chronic recurrent phase

Some patients may evolve into the chronic phase, which is characterized by the appearance of recurrent granulomatous anterior uveitis, which leads to the development of nodules in

the iris, focal atrophy of the iris and ocular hypotonia. During this phase, cases that have occurred with posterior choroidal inflammation, choroidal thickening and retinal detachments, demonstrated by idocyanine green angiography (ICGA)1 and OCT, have been reported. This chronic recurrent phase usually appears in the first 6 months of the disease, as a consequence of a rapid decrease or early suspension of corticotsteroid therapy.

Complications derived from the post inflammatory phase may result in cataracts and glaucoma, followed by subretinal neovascularization or fibrosis; less frequently, posterior synechiae, neovascularization of the optic disc, arteriovenous anastomoses and choroidal neovascularization may occur as well. These may Hamper the prognosis visually.

2. Literature Survey

The disease was initially described in 1906 by the Swiss ophthalmologist Alfred Vogt, who reported the case of a patient with iridocyclitis and poliosis. In a review article, published in 1929, Yoshizo Koyanagi described 16 cases illustrating the course of the disease. Einosuke Harada, internist and ophthalmologist, in addition to extraocular findings describes acute posterior choroiditis with exudative retinal detachments and pleocytosis in the CSF.1 Harada was the one who managed to make the full description of what is known today as VKH disease. The incidence of VKH is variable .It appears to be more common in Japan where it accounts for 6.7% of the uveitis referrals. Typically Features of VKH Include bilateral panuveitis associated with exudative retinal detachment, menigismus associated with pleocytosis of cerebrospinal fluid, Tinnitus and hearing loss and cutaneous changes such as poliosis and vitiligo. The clinical stage of presentation may vary from patient to patient. Prodromal stage, Acute stage ,The chronic convalescent and chronic recurrent stage.A series reported by National Institutes of health (NIH) showed that 50% of VKH patients were white,35% black, and 13% were Hispanic. Most studies have suggested that females are more commonly affected compared to males.

3. Methods/Approach

A Cross sectional observational study was conducted in over 25 patients diagnosed with VKH in our tertiary care centre from July 2023-December 2023. Results were analysed by a statistical test.

1) All patients presenting to the OPD who were already diagnosed with VKH were included in our study.
2) Appropriate informed consent was taken for the same from the patients who were included in the study.

4. Results/ Discussion

Vogt-Koyanagi-Harada (VKH) disease is a multisystem autoimmune disorder that primarily targets melanocytes, affects the eye, skin, inner ear, and meninges. In the eye, the disease affects the uveal tract, manifesting as granulomatous panuveitis. Acute presentation is characterized by the presence of exudative retinal detachment with preservation of the choriocapillaries. In the chronic stage, the disease is characterized by focal chorioretinal atrophy with loss of retinal pigment epithelium.

In chronic stage, patients develop extraocular manifestations. This cross-sectional hospital based observational study was carried out in Krishna Vishwavidya peeth karad, Maharshtra . The clinical profiles of 25 patients with Vogt-Koyanagi-Harada disease (VKH) were evaluated. Patients were more commonly presenting with Bilateral involvement with an age of 20-60 years, more common in women. Presenting more common in the acute stage. Patients were treated with IV Methyl prednisolone 1 gm/day followed by systemic steroids 1mg/kg/day for 6 month.

4.1 Results

Mean age
Between 23-60 years of age= 40 (Approximate) Gender- 18 Females (72%), 9 males (18%) Laterality- Bilateral- 98%, Unilateral -2%Visual Acuity- <20/200- 27%, At 1 month- 8%, At 3 months- 35% 20/200- or <20/40 – On presentation- 40%, At 1 month- 20%, At 3 months- 40% 20/40 – On presentation- 33%, At 1 month -62%, At 3 months- 4%

Stage of disease
Acute stage 24 eyes (48%), Chronic convalescent-18 eyes (36%), Chronic recurrent -8 eyes (16%) Clinical Presentation Panuveitis in 30 eyes (60%), Posterior uveitis in 18 eyes(36%)

Slit lamp examination
Circumciliary congestion in 24 eyes (48%), Keratic precipitates 24 eyes (48%), Iris nodules in 2%Fundus examination- Vitritis in 100%,optic disc involvement in 22 (44%),Sunset glow fundus in 6 eyes (12%), Exudative retinal detachment in 22 eyes (44%).

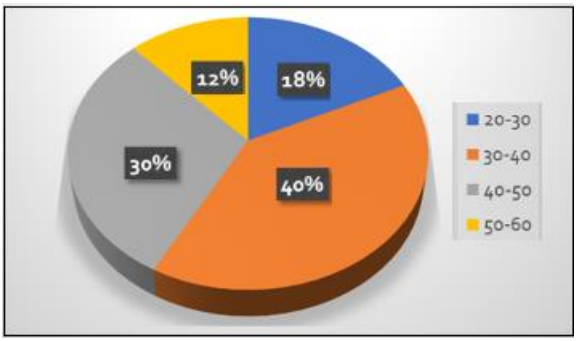


Figure 1: Mean age of presentation

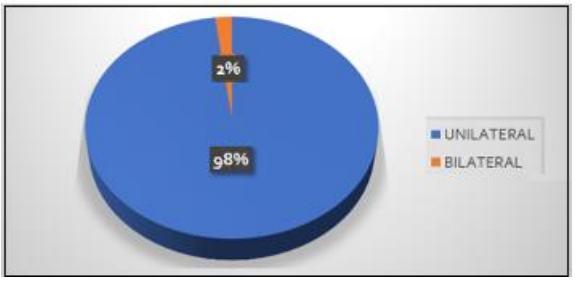


Figure 2: Laterality

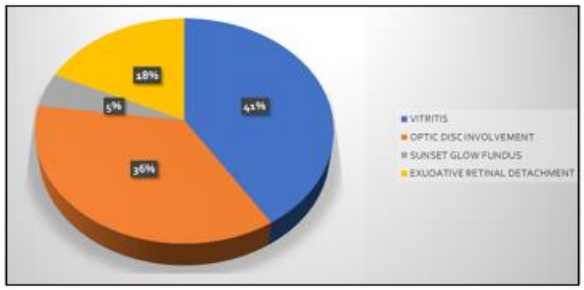


Figure 3: Fundus Examination

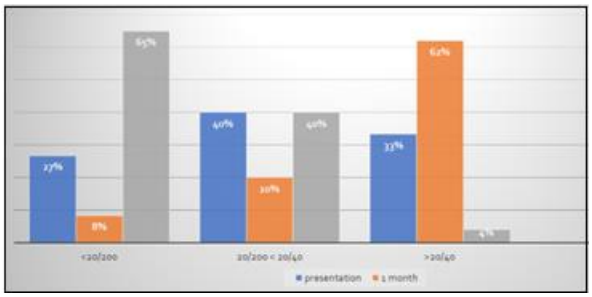
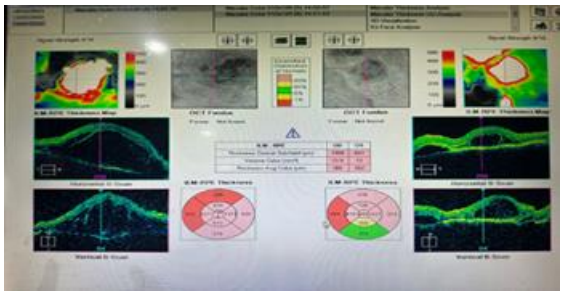
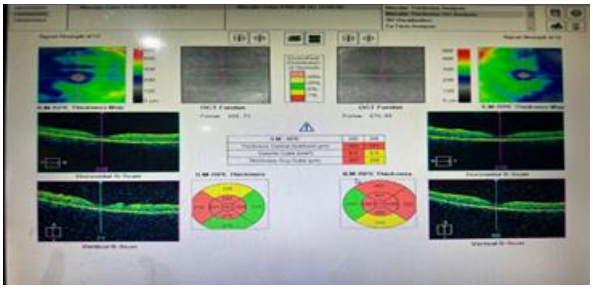


Figure 4: Visual Acuity

OCT Images

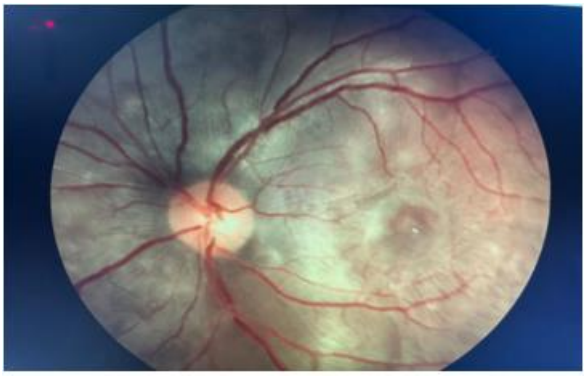


Case 1: On presentation

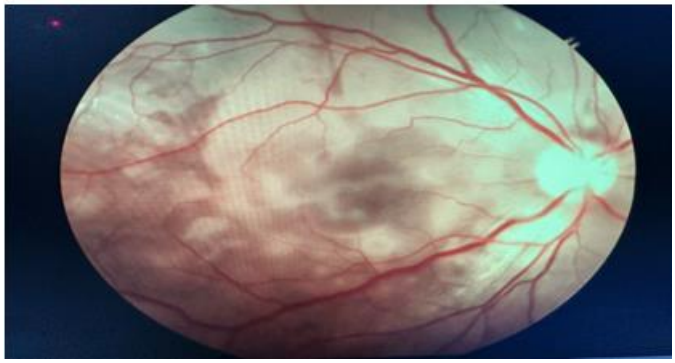


Case 1: On follow up

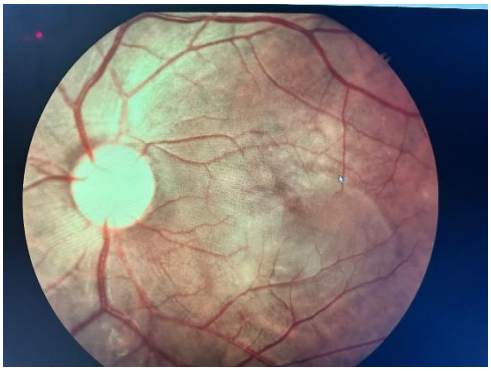
Fundus Images



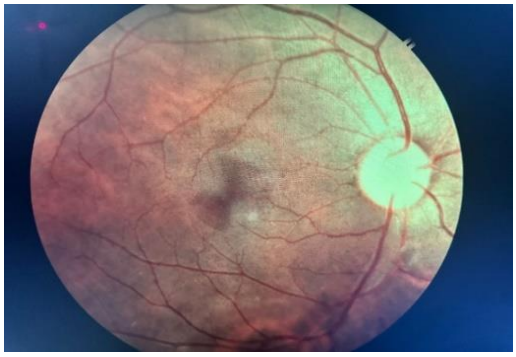
Case 1: Left eye Fundus photo- VKH



Case 1: Right eye fundus photo -VKH



Case 2: Left eye -VKH



Case 2: Right eye-Within Normal limits

Fundus Fluoroscein Angiography

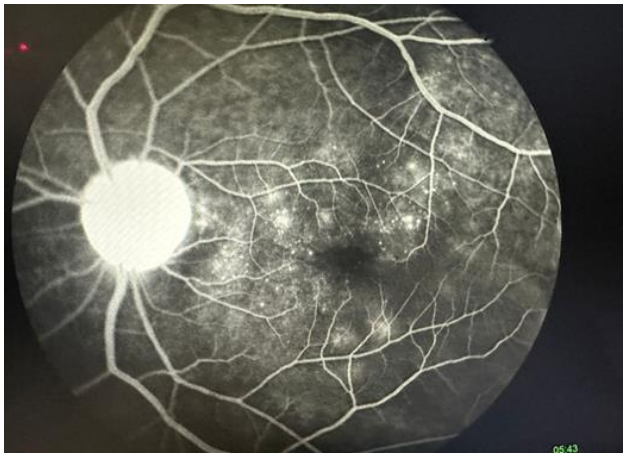


Figure A: Early Phase

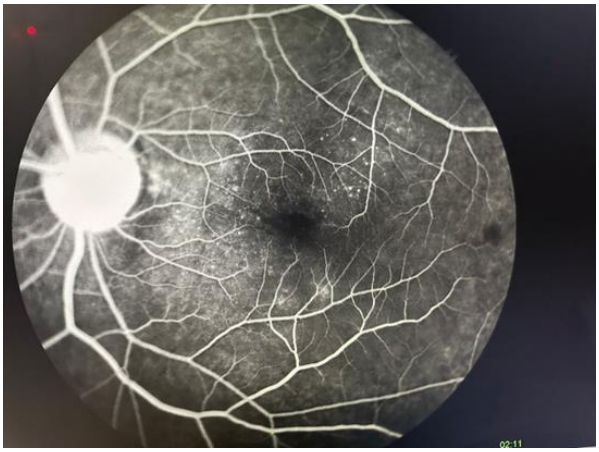


Figure B: Intermediate Phase

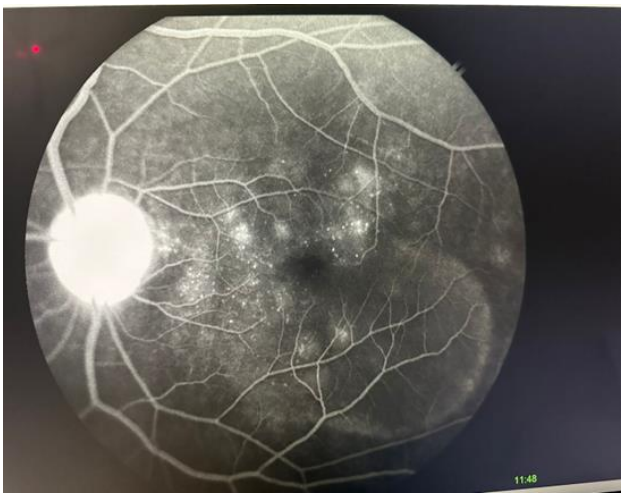


Figure C: Late phase

Fundus Flurooscein Images are suggestive of Hyperfluoroscent areas initially followed by dilatation of the capillaries and leaking.

5. Conclusion

The rarity of VKH Syndrome makes its diagnosis a challenge, but speed in diagnosis and treatment are essential.

Although the clinical criteria for the syndrome are well established, there is often great difficulty in diagnosing it due to the fact that patients present at different stages of development of the disease at the time of their consultation and its manifestations are often not perceived in their proper chronological order of appearance.

To avoid underdiagnosis and increase therapeutic precocity, it is worth mentioning that patients with deafness, tinnitus and dizziness should always be considered as having VKH. Patients can present with retinal detachment with signs of meningeal irritation and with or without extraocular manifestations during the chronic phase of the disease.

In addition, multidisciplinary assessment optimizes adequate systemic assessment and follow-up, since early diagnosis and a multidisciplinary approach are key components of the management of this complex syndrome.
Compliance with ethical standards

6. Future Scope

The extensive study of this rare disease will help in evaluation and appropriate treatment of the same.

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Declaration
The article is under consideration for publication elsewehere.

This article is the first to be published in accordance with rural western Maharashtra, The statistical analysis and data published is analysed and authentic. It's submission to IJSR publication has been approved by all authors.

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References

[1] https://fortuneonline.org/articles/clinical-profile-of-patients-with-.pdf
[2] https://joii-journal.springeropen.com/articles/10.1186/s12348-022-00293-3
[3] Vogt A (1906) Frühzeitiges ergrauen der Zilien und Bemerkungen über den sogenannten plötzichen Eintritt dieser Veränderung. Klin Monatsbl Augenheilkd 44:228–242
[4] Lavezzo MM, Sakata VM, Morita C, Rodriguez EE, Abdallah SF, da Silva FT et al (2016) Vogt-Koyanagi-Harada disease: review of a rare autoimmune disease targeting antigens of melanocytes. Orphanet J Rare Dis 11:29
[5] Koyanagi Y (1929) Dysakusis, Alopecia und Poliosis bei schwerer Uveitis nicht traumatischen Ursprungs. Klin Monatsbl Augenheilkd 82:194–2

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