Multidisciplinary approach leading to a diagnosis of Vogt – Koyanagi Harada Disease with a Cutaneous Presentation: A Case report

Alsharif M. Muhanna[1], Hussam Al issa[2], Adam Almuhisen[3], Abdullah Alhasanat[4], Anas Alshudeifat[5], Sara abdullah alzyadna[6]

[1, 2, 3]Dermatology specialist - Royal medical services- Department: Dermatology clinic Irbid
[4]Dermatology specialist - Royal medical services- Department: Dermatology clinic Aqaba
[5]Dermatology specialist - Royal medical services- Department: Dermatology clinic Amman
[6]Royal medical services - Specialist Nurse- Department: Dermatology clinic Amman
Email: Dr.Alsharifmohammed@gmail.com
Email: Drhussamalissa@gmail.com
Email: Adamalmohiesen@yahoo.com

Abstract

Vogt-Koyanagi Harada Disease (VKHD) is a rare multisystem autoimmune inflammatory condition targeting melanocytes, causing dermatological, neurological, ophthalmological, and auditory manifestations. Severe bilateral granulomatous panuveitis is the primary clinical feature that characterizes VKH (inflammation throughout the uveal tract in the eye).

Cutaneous features such as vitiligenous patches, alopecia, and whitening of the hair (poliosis) can be observed. Meningism (meningitis symptoms without inflammation), hearing loss, and tinnitus are examples of neurological characteristics. Prodromal and constitutional symptoms such as fatigue, malaise, low-grade fever, and headache may precede the classic picture. VKHD is reported in darker skin populations in addition to Asian and Mediterranean origins. VKHD has four stages: prodromal, acute, chronic convalescent, and chronic recurrent. There are three categories of VKH: complete, incomplete, and probable. VKHD is treated aggressively with a systemic corticosteroid to suppress the inflammatory response and prevent further ocular complications. We report a 43-year-old male patient referred by an ophthalmologist with a diagnosis of Uveitis who developed hypopigmented patches over the face and mid trunk, poliosis, and alopecia in addition to headache, neck stiffness, and auditory abnormalities.

Keywords: Vogt-Koyanagi Harada Disease (VKHD

1. Introduction

First documented in 1906 by Alfred Vogt in Switzerland, the patient had bilateral subacute iridocyclitis and rapid, premature whitening of the eyelashes. A case series with bilateral serous retinal detachment and cerebrospinal fluid (CSF) pleocytosis was reported by Harada in 1926, 20 years later. Shortly after that (1929), Koyanagi published a review article in which he made a strong case for the relationship between auditory and integumentary symptoms and posterior eye involvement. It was suggested by Babel in 1932 that these cases were all part of the same condition, which was known as Vogt-Koyanagi-Harada disease.

There is speculation that Francisco José Goya y Lucientes (1746–1828), a famous painter, may have experienced the illness in the middle of his career (1792). Loss of vision and hearing, ringing in the ears, dizziness, disorientation, abdominal discomfort, malaise, and weakness on one side of the body were its prominent symptoms. Goya was mostly able to regain his vision, but he remained permanently deaf [3].

VKHD is a significant cause of noninfectious uveitis, affecting people with darker skin more frequently than Caucasians and those of Turkish ancestry. For populations of Asians, Middle Easterners, Hispanics, and Native Americans, epidemiological statistics have been described [2]. In Europe and among persons of African heritage, the sickness is not common.

VKHD is found to have significant regional and global variance, and its incidence varies [1].

VKHD affects between 1.5 to 6 out of every 1 million individuals in the US, but it affects about 800 new patients every year in Japan [1, 10].

According to the majority of research, VKH affects women twice as much as it does men [3]. noting that the majority of patients are adults and middle-aged patients between the ages of 20 and 50, with a mean age of 38.7 years, however reports of onset in infancy or old age have also been made [4-6]. Women make up between 57% to 78% of VKHD patients in the US and around 38% in Japan, demonstrating regional differences in gender predilection [1, 10].

A systemic granulomatous autoimmune disease that affects melanocyte-rich tissues in various body organs, including the eye, inner ear, meninges, skin, and hair, Vogt-Koyanagi-Harada disease (VKHD) is a rare and uncommon multisystem inflammatory disease. It was first identified as a

doi.org/10.31838/hiv23.01.66 Received: 05.09.22, Revised: 08.10.22, Accepted: 03.12.22

uveomeningoencephalitic syndrome.
In most cases, meningeal or ocular symptoms come on first, although in a few instances, skin abnormalities come on before uveitis. VKH's etiology has not yet been determined. It is an autoimmune inflammatory disorder with melanocytes as its target. There could be a connection between genetic predisposition, allergic reactions, and unidentified viral exposure. Due to ocular morbidity, early detection is crucial [6].
In this case report, we describe a 43-year-old male patient who had been referred to our clinic due to the presence of skin lesions and hair abnormalities and was later diagnosed with Vogt-Koyanagi Harada Disease (VKHD) after a physical and laboratory examination. The patient had been diagnosed by an ophthalmologist as having uveitis.

Case report

We describe the case of a 43-year-old male patient who was medically healthy but suddenly experienced hazy vision. He was sent to us by the ophthalmology clinic, where he was given a systemic corticosteroid for bilateral uveitis (prednisolone 30 mg daily). Two distinguishing features on an ophthalmologic exam include an exudative retinal detachment and a sunset glow fundus (caused by choroid depigmentation). The most crucial characteristic of VKHD that distinguished uveitis from non-VKHS causes was diagnosis confirmation. Given that there were numerous asymptomatic depigmented macules and patches throughout the scalp, face, anterior and posterior trunk, as well as the sacral areas, the ophthalmological findings provided a clue to the diagnosis of VKHD. Fig (1)

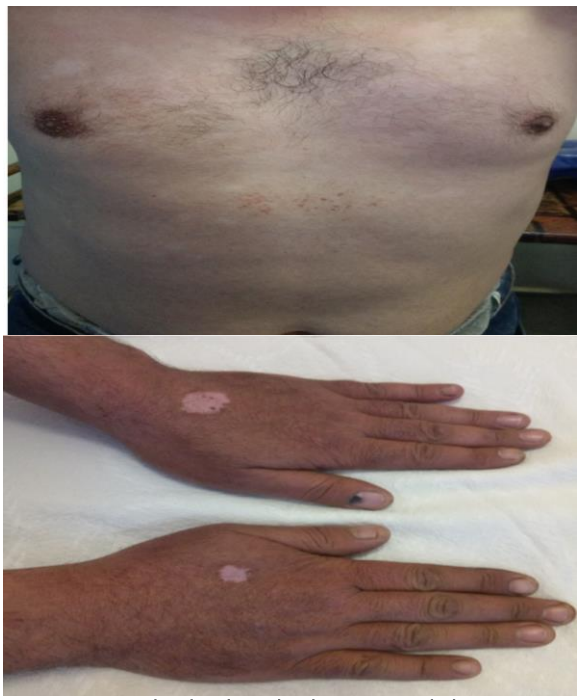

Fig (1) Multiple sharply demarcated depigmented macules and patches over the anterior trunk and dorsum aspect of the hands.

Following a thorough dermatological examination, localized areas of the scalp displayed Prominent Whitening of the Hair (Poliosis). Fig (2)
In addition to alopecia (area devoid of hair) over the temporal scalp Fig (3)

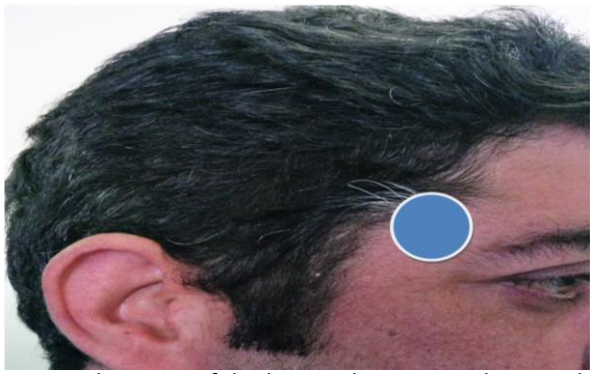

Fig (2) Whitening of the hair (poliosis) over the temple.

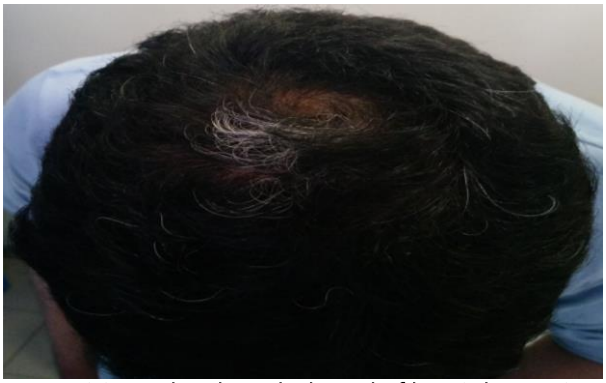

Fig (3) Localized patch devoid of hair (Alopecia)

There were no nails, mucous membrane, or genital involvement the added to previously mentioned symptoms and signs.
Reduced pigmentation was visible during Wood's lamp examination, which also revealed loss of pigmentation in the vitiliginous patches, which glow brilliant blue-white.
Dermoscopic examination of the dermatological lesions revealed a reduced pigment network and sharp border appearance of white regions devoid of structure (absence of pigment network). Perilesional and perifollicular hyperpigmentation as well as comet-tail appearance and micro-koebnerization.
Laboratory investigations showed normal levels of blood count and leukocytes in addition to normal biochemical and endocrinological tests.
Ordered diagnostic tests for HLA subtypes that are thought to be supportive of our primary diagnosis of VKHD revealed positive results for DR4, DR11, DR15, DR52, and DR53.
SSOP (Sequence-Specific Oligonucleotide Probes) and SSP (Polymerase Chain Reaction) were used in the laboratory section to conduct the testing (Sequence-specific Primers).
We classified the patient as having VKHS and suggested the necessity for a multidisciplinary approach based on the patient's combination of symptoms, indicators, and HLA subtype.
Upon medical review, the patient was free of any medical condition.
A neurological examination revealed no meningeal

signs and there were no neurological deficits.
Cranial nerves, reflexes, cerebellar, and coordination tests were normal.
Auditory and hearing assessments were normal.
With a successful clinical response for his eye and dermatological findings, the patient was kept on systemic steroids for several months to control his eye inflammation in addition to topical steroids alternated with topical calcineurin inhibitors as a therapy option for his skin disease.
Regular follow-up visits were planned to monitor for potential relapses or additional improvements.

2. Discussion

It has been misdiagnosed as vitiligo due to a lack of understanding of the disease's typical presentation.
However, the presence of melanocyte specific autoreactive CD8+ and CD4+ T lymphocytes in the blood and CSF is correlated with the disease activity, indicating that there is no known cause for VKHS.
Activated T cells are discovered adjacent to melanocytes when studying the histologic sections of the afflicted skin and eyes. These T cells release Th1-type cytokines, which have a profile similar to that of vitiligo and other autoimmune disorders that affect a particular organ. In contrast, a another study reveals that those with active VKHS have fewer and less-effective T regulatory cells.
HLA subtypes DR4, DR 11, DR 15, DR 52, DR 53, HLA-DQ4, and in particular DRB1*0405 are implicated in genetic research as risk alleles for the condition, whereas DRB1*0401 appears to be protective.
The emergence of autoimmune diseases like psoriasis, thyroiditis, type 1 diabetes, and as a component of type 1 autoimmune polyglandular syndrome has been linked to the development of VKHS.
Serologic studies to find other autoimmune disorders have been considered, and investigations and screening for autoimmune diseases are required.
According to conventional wisdom, VKHD has four clinical phases and several characteristics that differ according to the patient's gender and ethnicity:
1. Acute symptoms such as fatigue, malaise, fever, headache, neck stiffness, photophobia, nausea, vertigo, discomfort when exposed to sounds at normal volume, and tinnitus are characteristics of the prodromal phase, which is mostly neurological. These symptoms linger a few days and disappear on their own.
2. The uveitic phase (ophthalmic), also known as panuveitis or posterior uveitis, is characterized by non-traumatic inflammation of one or both eyes, as well as multifocal serous retinal detachments, choroiditis (inflammation of the central layer of the eye), or optic neuritis. The patient frequently complains of blurred or lost vision, a burning sensation, photophobia, or ocular pain. This stage often lasts a few weeks.
3. Dermatological anomalies include poliosis of the eyebrows and eyelashes, depigmentation of the skin and hair, and symmetrical depigmentation, which shows in the eye choroid with a vivid orange fundus (a "sunset glow"), are all present throughout the convalescent period [10, 11]. Hair loss in patches may be a symptom of alopecia areata..
4. This phase usually lasts for several months or years.
5. Chronic recurrent phase, characterized by persistent granulomatous anterior uveitis and choroidal thickening, which are low-grade ocular involvement. The new skin involvement will likely be depigmented during this phase, and alopecia areata may experience periods of remission and relapse. Six to nine months after the disease's initial manifestation, the chronic recurrent phase manifests [1, 2].

The diagnostic criteria for VKHD include the following
There is no proof that the current state of the eyes is caused by another ocular disease, trauma, or ocular surgery [9].
Bilateral inflammation of both eyes (ocular involvement).

Neurological findings

Auditory findings

Skin symptoms do not appear before CNS or auditory issues develop.
The illness can be divided into three different groups [8]:
1. Complete VKHD, which includes bilateral ocular involvement, neurological and dermatological indicators, as well as specific criteria based on the disease's stage. The neurological signs may go away, but the dermatological signs do not come on before the development of uveitis.
2. Incomplete VKHD, which manifests as either neurological or dermatological symptoms in addition to the same ophthalmological findings as patients with complete VKHD.
3. Probable VKHD, which lacks neurological or dermatological symptoms but has ophthalmological findings similar to those reported in patients with complete VKHD.

Most of the time, these clinical signs that damage the inner ear and CNS are temporary, but untreated uveitis can cause blindness.
The chronic convalescent stage is when dermatological characteristics are most frequently observed [1].
70% of patients experience the fourth chronic recurrent phase during the third phase (the convalescent phase).
Early diagnosis and treatment can stop the condition from progressing to the chronic convalescent and chronic recurrent stages [7].
Skin or CNS/auditory symptoms, which can be identified as "incomplete VKHD," do not emerge in all patients. The diagnosis of isolated ocular illness is "probable VKHD."
About 3–4 months following the onset of the

disease, many individuals with the acute ophthalmic phase of VKHD proceed to the chronic convalescent stage of the disease [10].

Physical examination reveals quick and severe depigmentation of the skin with obvious polio. Even though poliosis can develop in vitiligo-affected depigmented skin, it usually happens more quickly in VKHD, and it affects the eyebrows, eyelashes, and scalp.

Laboratory tests

Pleiocytosis is a common finding in the cerebral spinal fluid (CSF) of affected patients, and because VKHS is the only disease to create pigment-laden macrophages, it is simpler to distinguish it from other diseases that do as well.

According to the literature data and the associated subtypes of (HLA DR4/ HLA DRB1-04*05), the presence of this allele is linked to an increased chance of acquiring this disease.

The histopathologic appearance could be devoid of an inflammatory infiltrate because the offending T cells frequently exit the skin before there is obvious depigmentation. The inflammatory pattern would be a superficial perivascular mononuclear infiltrate with clusters at the dermal-epidermal junction and random single-cell infiltration of the basal layer of the epidermis. Similar to vitiligo, the absence of all melanocytes or a significant decrease in their number in the lesional skin is required to validate the diagnosis.

Due to the various organ involvement, managing VKHD patients is challenging, but the goal is to limit the progression by reducing inflammatory processes and avoiding future problems using corticosteroids [7].

Dermatological therapy options including topical corticosteroids, TCI, PUVA, or camouflage may assist and help in enhancing the cosmetic appearance of patients.

Patients with VKHD may experience serious ophthalmological problems include retinal detachment, secondary glaucoma, cataracts, and sub-retinal fibrosis. Further complications should be avoided and managed by routine follow-ups.

In order to monitor for flare-ups and fresh discoveries that might indicate a therapeutic response, long-term follow-up is crucial.

The diagnosis of VKHD was partial due to symptoms and signs, as per what was stated in the literature that corresponded to our situation.

3. Conclusion

Vogt-Koyanagi-Harada syndrome (VKH) is a rare multisystem disease that manifests as a combination of signs and symptoms relating to the eyes, the nervous system, the ears, and the skin.

To make a diagnosis of such a complex condition with a wide range of differential diagnoses, one needs to have a clinical suspicion, accompanying test findings, and the implications of a multidisciplinary approach.

The elevated prevalence of various autoimmune conditions in affected patients and the success of immunosuppressive medication are evidence that VKHS has an autoimmune etiology.

The prognosis of related morbidities, particularly ophthalmological disorders, may be positively impacted by the early initiation of corticosteroids and other immunosuppressive therapy.

According to data gathered from the reported cases in the literature, VKHD represents a disease with multi-organ involvement that is composed of complex signs and symptoms and a variety of associated clinical features in several phases. This raises the importance of making a diagnosis of the disease because it harbors many potential chronic clinical sequelae and improves the patient's quality of life.

References

1.Arevalo J, Lasave A, Gupta V, et al. Clinical outcomes of patients with Vogt–Koyanagi–Harada disease over 12 years at a tertiary center. Ocul Immunol Inflamm 2015; 24: 521–9. DOI: 10.3109/09273948.2015.1025984. Journal

2. Read R, Rechodouni A, Butani N, et al. Complications and prognostic factors in Vogt–Koyanagi–Harada disease. Am J Ophthalmol 2001: 131: 599–606 PubMed

3.Yang P, Ren Y, Li B, Fang W, Meng Q, Kijlstra A. Clinical characteristics of Vogt–Koyanagi–Harada syndrome in Chinese patients. Ophthalmology 2007: 114: 606–14

4.Abu El-Asrar A, Al-Kharashi A, Aldibhi H, Al-Fraykh H, Kangave D. Vogt–Koyanagi–Harada disease in children. Eye 2008: 22: 1124–31.

5.Yamamoto Y, Fukushima A, Nishino K, Koura Y, Komatsu T, Ueno H. Vogt-Koyanagi-Harada Disease with onset in elderly patients aged 68 to 89 years. Jpn J Ophthalmol 2007; 51: 60–3. DOI: doi.org/10.1007/s10384-006-0379-0. Journal

6. Norose K, Yano A. Melanoma specific Th1 cytotoxic T lymphocyte lines in Vogt-Koyanagi-Harada disease. Br J Ophthalmol 1996; 80: 1002–8. DOI: dx.doi.org/10.1136/bjo.80.11.1002. Journal

7. Sasamoto Y, Ohno S, Matsuda H. Studies on corticosteroidtherapy in Vogt-Koyanagi-Harada disease. Ophthalmologica. 1990;201:162–7.

8. Sakata VM, da Silva FT, Hirata CE, de Carvalho JF, Yamamoto JH. Diagnosis and classification of Vogt-Koyanagi-Harada disease. Autoimmun Rev. 2014; 13:550–5.

9. Lavezzo MM, Sakata VM, Morita C, Rodriguez EEC, Abdallah SF, da Silva FTG et al. Vogt-Koyanagi-Harada disease: review of a rare autoimmune disease targeting antigens of melanocytes. Orphanet J Rare Dis. 2016; 11:29.

10. Beniz J, Forster D, Lean J, Smith R, Rao N. Variations in clinical features of the Vogt-Koyanagi-Harada syndrome. Retina 1991: 11: 275–80. Europe PMC

11. O'Keefe G, Rao N. Vogt-Koyanagi-Harada disease. Surv Ophthalmology 2017; 62: 1–25.

DOI: doi.org/10.1016/j.survophthal.2016.05.002. Journal

Abbreviations used
VKHD: Vogt-Koyanagi Harada Disease
PUVA: psoralen ultraviolet A radiation
NB-UVB: narrow-band ultraviolet B radiation
CSF: cerebrospinal fluid
HLA: human leukocyte antigen
CNS: cranial nervous system
TCI: topical calcineurin inhibitors
PCR: Polymerase Chain Reaction
SSOP: Sequence Specific Oligo-nucleotide Probes technique
SSP: Sequence-specific Primers