Vogt Koyanagi Harada Syndrome

Ernawati Hidayat [1*], Milka Wulansari[1], Yosep Ferdinand Rahmat Sugianto [1], Galih Sari Damayanti[1]
Meira Dewi Kusuma Astutik[2]
[1]*Department of Derrmatovenereology, Faculty of Medicine, Diponegoro University/Dr.Kariadi Hospital*
[2]*Department of Anatomic Pathology, Faculty of Medicine, Diponegoro University/Dr.Kariadi Hospital*
**Corresponding author*

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Abstract: Vogt-Koyanagi-Harada syndrome (VKHS) is a rare autoimmune disorder involving pigmented multiorgan. VKHS reported 6-8% in Asia,1-4 % in North America, and 2-4 % in Brazil of all uveitis. Diagnosis is made based on *American Uveitis Society* (AUS) criteria; no history of eye trauma, and minimum 3 of 4 signs: bilateral chronic iridocyclitis, uveitis, neurologic signs (tinnitus, neck stiffness, CNS symptoms), and dermatologic signs (alopecia, poliosis, vitiligo). A 51-year-old female presented with generalized hypopigmented-non pruritic patches since 8-year-old. Visual impairment was reported one month before. Patches of white hair were found on the forehead and eyelashes. Tinnitus and frequent headache were reported. There was no history of eye trauma. Ophthalmologic examination revealed bilateral panuveitis and *retinal detachment* on the right eye. Histopathologic examination showed no melanin pigment in the basal layer. The patient was treated with systemic methyl-prednisolone and topical steroid creams. Prognosis is *ad malam for ad sanam and ad cosmeticam*. The diagnosis was based on AUS criteria and histopathologic examination. The precise etiology for VKHS is challenging to establish. Treatment required long term steroid administration and routine follow up to assess the progression of this disease.

1 INTRODUCTION

Vogt Koyanagi Harada Syndrome (VKHS), initially described as an uveomeningoencephalitic syndrome, is a rare granulomatous inflammatory disease that affects pigmented structures, such as eye, inner ear, meninges, skin, and hair (Geel et al, 2016; Lavezzo et al, 2016). The disease is defined as a non-infectious, bilateral, and granulomatous panuveitis that occurs with or without extraocular manifestations, and it typically affects young adults (Ando et al, 2018). In 1906, Vogt reported a patient with atraumatic, idiopathic uveitis, poliosis, and alopecia, a syndrome that in time would be associated with his name. In 1926, Harada reported five cases of bilateral posterior uveitis and retinal detachment. In 1929, Koyanagi reported 16 patients with headache, fever, dysgeusia, vitiligo, poliosis, alopecia, bilateral anterior uveitis with occasional exudative retinal detachment. Koyanagi published a review article associating the posterior eye involvement unequivocally with auditory and integumentary manifestations. In 1932, Babel suggested that these cases represented a single entity, which was then named Vogt-Koyanagi-Harada Disease (Geel et al, 2016; Lavezzo et al, 2016; Ando et al, 2018).

VKHS more frequently affects individuals of pigmented skin, such as Asians, Middle Easterners, Hispanics, and Native Americans (Ando et al, 2018; O'Keefe et al, 2018; Silpa-Archa et al, 2016; Emily et al, 2018). The incidence of VKHS varies. Among all cases of uveitis, it was reported 6-8% in Asia,1-4 % in North America, and 2-4 % in Brazil of all uveitis. In China, VKHS is one of the most common uveitis entities. In the United States, the incidence of VKHS is approximately 1.5 to 6 per 1 million patients, while in Japan, it is seen in approximately 800 new patients each year. Most studies have found that women were affected more frequently than men and that most patients were in the second to fifth decades of life at the onset of the disease. However, children and the elderly may also be affected. Women account for 55 to 78 % of VKHS patients in

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the United States and approximately 38 % in Japan, showing a global variation in gender predilection (Lavezzo et al, 2016; Giannakourasa et al, 2017).

The exact etiology of VKHS is still a matter of inquiry. The most accepted mechanism involves autoimmune aggression against antigens associated with melanocytes in a genetically susceptible individual after a virus infection trigger. Immunological and histopathological studies suggest that VKH is an autoimmune inflammatory condition mediated by CD4þ T cells that target melanocytes. These activated T cells likely initiate the inflammatory process through generation of cytokines, IL 17 and IL 23,35 in individuals with altered tolerance to melanocytes from deficient T regulatory cells (Lavezzo et al, 2016; Emily et al, 2018; Baltmr et al, 2017).

Diagnosis is made based on *American Uveitis Society* (AUS) criteria; no history of eye trauma or surgery, and minimum 3 of 4 signs: Bilateral chronic iridocyclitis, posterior uveitis (multifocal exudative retinal or RPE detachments; disc hyperemia or edema; or "sunset glow fundus", which is a yellow-orange appearance of the fundus due to depigmentation of the RPE and choroid), Neurologic signs (tinnitus, neck stiffness, cranial nerve or central nervous system symptoms or cerebral spinal fluid pleocytosis) and Cutaneous findings (alopecia, poliosis or vitiligo) (Geel et al, 2016; Lavezzo et al, 2016; O'Keefe at al, 2017; Coutinho et al, 2017).

Early diagnosis and prompt immunosuppressive treatment with corticosteroids and other immunosuppressives can halt the progression and prevent recurrence and vision loss. The mainstay of treatment of VKHS is prompt, high-dose systemic corticosteroids, followed by slow tapering of oral corticosteroids throughout a minimum 6-month period (Lavezzo et al, 2016; Joanne et al, 2014). Localized lesions of vitiligo can be treated with a high-potency fluorinated corticosteroid for 1–2 months. Treatment can be gradually tapered to a lower potency corticosteroid (Birlea et al, 2012).

2 CASE

A 12-year-old girl came to Dermato-venereology Departement Dr.Kariadi Hospital with generalized hypopigmented-non pruritic patches since 8-year-old. Visual impairment was reported one month before. Patches of white hair were found on the forehead and eyelashes. Tinnitus and frequent headache were reported. There was no history of eye trauma or surgery. Ophthalmologic examination revealed bilateral panuveitis and *retinal detachment* on the right eye. No similar history or symptoms in his family. Physical examination showed body height 165 cm, and bodyweight 65kg, blood pressure is 120/70 mmHg, respiratory rate 18x/m, heart rate 88x/m, and axilla temperature 36°C. Skin lesions are generalized hypopigmented macules, poliosis on forehead and eyelashes.

The routine laboratory examination result was typical. Histopathologic examination showed no melanin pigment on the basal layer. The working diagnosis is Vogt Koyanagi Harada Syndrome. The patient was given oral methylprednisolone 16mg 2-0-1 long term and followed by tapering off and fluticasone propionate 0,05%/ twice daily. Prognosis*, quo ad sanam dubia ad malam, quo ad kosmetikam dubia ad malam.*

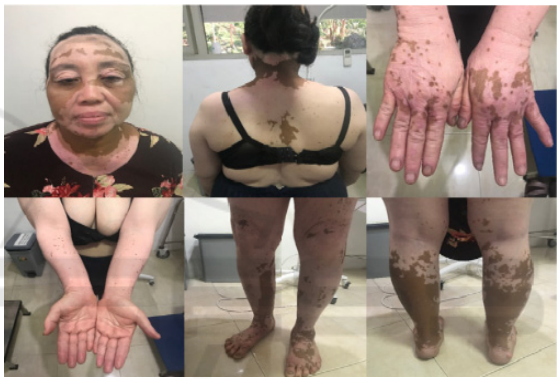

Figure 1. Generalized hypopigmented patches

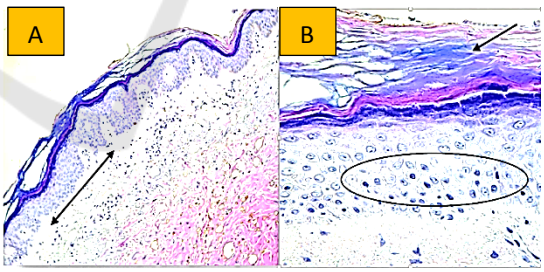

Figure 2. Histopathologic examination **A)** no melanin pigment on the basal layer. **B)** Hyperkeratosis and no melanin pigment

3 DISCUSSION

The diagnosis of Vogt Koyanagi Harada Syndrome in the patient was established by history, physical examination, and histopathological examination. Anamnesis a 51-year-old female presented with generalized hypopigmented-non pruritic patches since 8-year-old. Visual impairment was reported

one month before. Patches of white hair were found on the forehead and eyelashes. Tinnitus and frequent headache were reported. There was no history of eye trauma or surgery. Ophthalmologic examination revealed bilateral panuveitis and *retinal detachment* on the right eye. No similar history or symptoms in his family. VKHS presents clinically in 4 different phases: prodromal, acute uveitis, convalescent, and chronic recurrent.

The prodromal phase may present a viral infection and last anywhere between a few days to a few weeks. In this phase, before ocular involvement, clinical manifestations are predominantly extraocular and include headache (82%), meningismus (55%), fever (18%), nausea (9%), vertigo (9%), orbital pain, auditory disturbances, photophobia, and tinnitus. However, some patients present with typical clinical features of VKH without the prodromal symptoms. The acute uveitic phase is following the prodromal phase, blurring of vision develops in patients in both eyes, although the involvement of 1 eye may be delayed. The convalescent phase is Several weeks to months after the acute uveitic phase, depigmentation of the choroid, vitiligo, and poliosis occurs. The convalescent phase usually lasts for months. Chronic recurrent intraocular inflammation develops in some of the patients and is characterized by exacerbations of granulomatous anterior uveitis that is usually resistant to systemic steroid therapy. This chronic recurrent phase usually develops 6 to 9 months after initial presentation and is also marked by complications such as retinal pigment epithelium (RPE) proliferation, subretinal fibrosis subretinal neovascular membranes, posterior subcapsular cataract, posterior synechiae, open-angle glaucoma and, occasionally, angle-closure glaucoma, as well as band keratopathy (Lavezzo et al, 2016; Silpa-Archa et al, 2016)

Physical examination revealed skin lesions are generalized hypopigmented macules, poliosis on forehead and eyelashes. Based on literature VKHS have founded skin and hair changes: alopecia, vitiligo, and poliosis.(Geel et al, 2016;Lavezzo et al, 2016; Silpa-Archa et al, 2016)

Histopathologic examination, in this case, showed no melanin pigment in the basal layer. A skin biopsy is rarely necessary to confirm the diagnosis of vitiligo. Generally, histology shows an epidermis devoid of melanocytes in lesional areas and sometimes sparse dermal, perivascular, and perifollicular lymphocytic infiltrates at the margins of early vitiligo lesions and active lesions, consistent with cell-mediated immune processes destroying melanocytes in situ.(Birlea et al,2012)

The patient was given oral methylprednisolone 16mg 2-0-1 long term and followed by tapering off and fluticasone propionate 0,05% cream/ twice daily. Based on literature treatment of VKHS is prompt, high-dose systemic corticosteroids, administered either orally (prednisone 1–1.5 mg/kg per day) or through a short course of intravenous delivery (methylprednisolone 1000 mg per day, intravenously, during 3 days), followed by slow tapering of oral corticosteroids throughout a minimum 6-month period. Timing to initiate therapy, corticosteroid dosing, and duration of therapy are the key factors in reducing the chance of recurrences. (Lavezzo et al, 2016.Joanne et al,2014) Localized lesions of vitiligo can be treated with a high-potency fluorinated corticosteroid (e.g., clobetasol propionate ointment, 0.05%) for 1–2 months. Treatment can be gradually tapered to a lower potency corticosteroid (e.g., hydrocortisone butyrate cream, 0.1%). (Birlea et al,2012) Prognosis, *quo ad sanam dubia ad malam, quo ad kosmetikam dubia ad malam.*

4 CONCLUSION

Has been reported a case of Vogt Koyanagi Harada Syndrome in a 51-year-old female presented with generalized hypopigmented-non pruritic patches since 8-year-old. Visual impairment was reported one month before. Patches of white hair were found on the forehead and eyelashes. Tinnitus and frequent headache were reported. Physical examination revealed Skin lesions are generalized hypopigmented macules, poliosis on forehead and eyelashes. Histopathologic examination, in this case, showed no melanin pigment in the basal layer. The mainstay of treatment of VKHS is prompt, high-dose systemic corticosteroids, followed by slow tapering of oral corticosteroids throughout a minimum 6-month period. Localized lesions of vitiligo can be treated with a high-potency fluorinated corticosteroid for 1–2 months. Treatment can be gradually tapered to a lower potency corticosteroid. Prognosis *quo ad sanam dubia ad malam, quo ad kosmetikam dubia ad malam.*

REFERENCES

Ando T, Kato H, Mochizuki K, Ozawa K, Goshima S, Matsuo M. 2018. *MR findings of the orbit in patients with Vogt–Koyanagi–Harada disease*. Feb 23;1-6.

Baltmr A, , Lightman S, Netzer OT. 2016. *Vogt Koyanagi Harada syndrome- current perspectives*. Clinical Ophthalmology. 10 2345–2361

Birlea AS, Spritz RA, Norris DA Vitiligo. 2012. *In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors*. Fitzpatrick's dermatology in general medicine. 8th Ed. New York : Mc Graw Hill. 1680-90p

Coutinho I, Pedrosa C, Santos C, et al. 2017. *A challenged case of Vogt_Koyanagi_Harada syndrome: when dermatological manifestations came first*. Springer Science Business Media Dordrecht. 1- 6

Emily Su, Vikash S. Oza, Paul Latkany. 2018. *A case of recalcitrant pediatric Vogt-Koyanagi-Harada disease successfully controlled with adalimumab*. Journal of the Formosan Medical Association. 1-6

Geel NV, Speeckaert R. 2016. *Acquired Pigmentary Disorders*. In: Burns T, Breathnach S, Cox N, Griffiths C. Rook's Textbook of Dermatology. 8th Ed. Volume 1. Oxford: Blackwell scientific Publication. 88.43p.

Giannakourasa P, Andreanosa K, Giavia B, Diagourtas A. 2017. *Optical Coherence Tomography Angiography: Employing a Novel Technique for Investigation in Vogt-Koyanagi-Harada Disease*. Case Rep Ophthalmol. 8:362–369

Joanne YW Ng, Fiona OJ Luk, Timothy YY Lai, Chi-Pui Pan. 2014. *Influence of molecular genetics in Vogt-Koyanagi-Harada disease*. Journal of Ophthalmic Inflammation and Infection. 4:20

Lavezzo MM, Sakata VM, Morita C, Rodriguez EE, Abdallah SF, da Silva FT, Hirata CE, Yamamoto JH. 2016. *Vogt-Koyanagi-Harada disease: review of a rare autoimmune disease targeting antigens of melanocytes*. Orphanet J Rare Dis.1-21

O'Keefe GA, Rao NA. 2017. *Vogt-Koyanagi-Harada disease*. Surv Ophthalmol. 62(1):1–25

Silpa-Archa S, Silpa-Archa N, Preble JM, Foster CS. 2016. *Vogt- Koyanagi-Harada syndrome: perspectives for immunogenetics, multimodal imaging, and therapeutic options*. Autoimmun Rev. 15(8):809–819