International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Vogt-Koyanagi-Harada Syndrome following Anti-SARS-COV2 Vaccine

Dr. Hrutuja Kantrao Dhumale[1], Dr. Satish S. Desai[2], Dr. Swapnali Bandgar[3]

Junior Resident 3, Department of Ophthalmology, Government Medical College and Hospital Miraj
Corresponding Author Email id: *dhumalehrutuja[at]gmail.com*
Mobile: 9665629469

Head Of Department, Department of Ophthalmology, Government Medical College and Hospital Miraj

Assistant Professor, Department of Ophthalmology, Government Medical College and Hospital Miraj

Abstract: ***Vogt-Koyanagi-Harada syndrome is a multisystem disorder with chronic, bilateral, non-necrotizing, diffuse granulomatous panuveitis and exudative retinal detachment associated with neurological, audiovestibular, dermatological abnormalities. Aim and objective: 1) to determine Possibility of anti-SARS-COV 2 vaccination associated with triggering VKH syndrome. 2) Role of early diagnosis and treatment. We are reporting on patient treated Early and in sustained fashion who was asymptomatic and developed symptoms after anti-SARS-COV 2 vaccination. Conclusion: Vogt-Koyanagi-Harada syndrome results from an autoimmune inflammatory process which can be controlled with early diagnosis and treatment. Immunological mechanisms and dysregulation of the immune system may play a significant role in association between VKH syndrome and vaccination. Although it is difficult to determine causality, this report enlightens possible association between VKH and vaccination.***

Keywords: VKH, Vogt-Koyanagi-Harada, IL - Interleukin, HLA - Human Leukocyte antigen, OCT - Optical Coherence Tomography, OD - Oculus Dexter, OS - Oculus Sinister

1. Introduction

Vogt-Koyanagi-Harada (VKH) syndrome is a multisystem disorder with chronic, bilateral, non-necrotizing, granulomatous panuveitis and exudative retinal detachment associated with neurological, audiovestibular, and dermatological abnormalities. [1–5].

Although the exact pathogenesis is still uncertain It is considered to be an autoimmune disease against melanocyte and mainly mediated by cellular immune response [6] immunological and histopathological studies suggest that VKH is mediated by CD4+T cells that target melanocytes, these activated T cells likely initiate the inflammatory process through generation of cytokines, IL-17 and IL23. Genetic factors and viral infections are likely involved [7-12]

Association with HLA DR4/ HLA DRB1–04*05 has been reported in the Japanese population [13].

VKH disease has a variable incidence, more frequent in people from East Asia, Hindus, Hispanics, Mediterranean and Native Americans; it is infrequent in Caucasians and usually affects patients between the ages of 20 and 50 years, although it also occurs in children. [14] Studies indicate that women are more committed than men, with a 2: 1 ratio, except some studies from Japan and China, which showed no differences in prevalence by gender The Median age at diagnosis is around 33±8 Only few studies are available to estimate prevalence of ethnic characteristics in the European population [14]

VKH disease usually manifests as four distinct clinical phases: prodromal, acute uveitis, convalescent, and chronic recurrent. [15]

1) In the prodromal phase, symptoms may mimic a viral infection presented with flu-like symptoms that lasts for a few days
2) The acute uveitic stage occurs within three to five days of the first stage as patients may experience blurred vision in both eyes due to diffuse choroiditis
3) The convalescent stage usually follows a few months later. At this stage, depigmentation of the integument and choroid occurs
4) The chronic stage may develop by interrupting the convalescent stage in 17% to 73% of patients. Ocular Complications such as cataract, choroidal neovascularization, glaucoma, and retinal fibrosis can be observed in this stage

We are reporting on two cases treated Early and in sustained fashion at tertiary care hospital who was asymptomatic and developed symptoms after anti-SARS-COV 2 Recently, cases of VKH disease following Covid-19 mRNA and adenovirus vector vaccine have been reported [24]We report a case of bilateral VKH like disease following an inactivated Covid-19 virus vaccine

Case Report 1

A 32 year old female came with chief complaints of blurring of vision in both eyes and floaters in left eye. The patient was examined 2 days after development of symptoms. No h/o trauma No h/o spectacle use No h/o similar episode in past. Patient had history of covid 19 infection. Patient had received 1 st dose of an inactivated covid-19 virus vaccine one year after covid infection, after which patient developed mild fever, myalgia 3-4 hours later and subsequently developed ocular symptoms 11 days after vaccination. No H/o Diabetes mellitus, Hypertension, tuberculosis or any other chronic illness. Family history was not significant. On

examination vitals and systemic examination was within normal limits.

On ocular examination right eye visual acuity was 6/18, Left eye visual acuity was 6/36 both eye Anterior segment was within normal limit, Intraocular pressure was within normal limit.

Fundus examination revealed both eye exudative retinal detachment with subretinal fluid as shown in fig-1 which was confirmed by Optical coherence tomography (OCT) as shown in fig-2 Fundus Fluorescein angiography fig-3 revealed multiple areas of pinpoint leakage Hematological and serological investigation were unremarkable

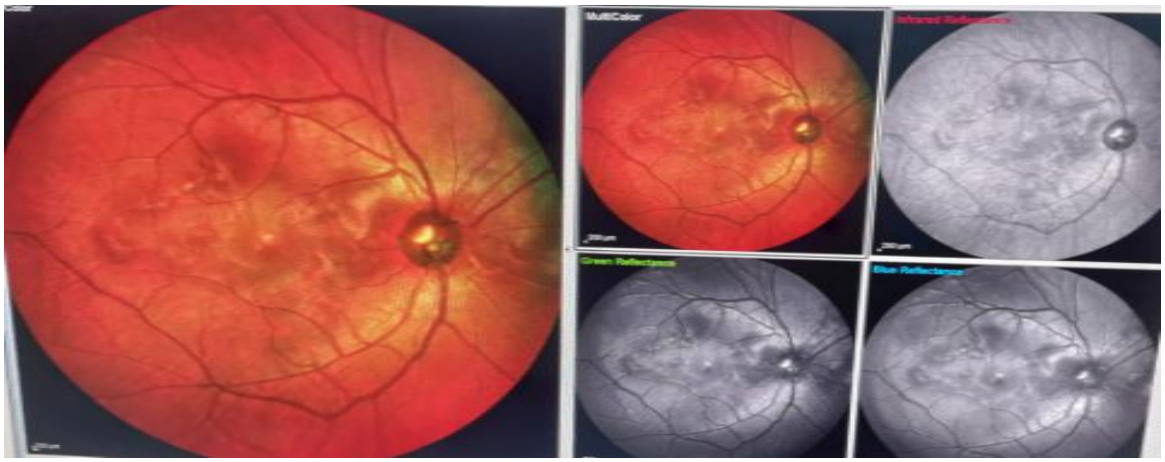

Figure 1 (A): OD fundus photograph shows exudative retinal detachment

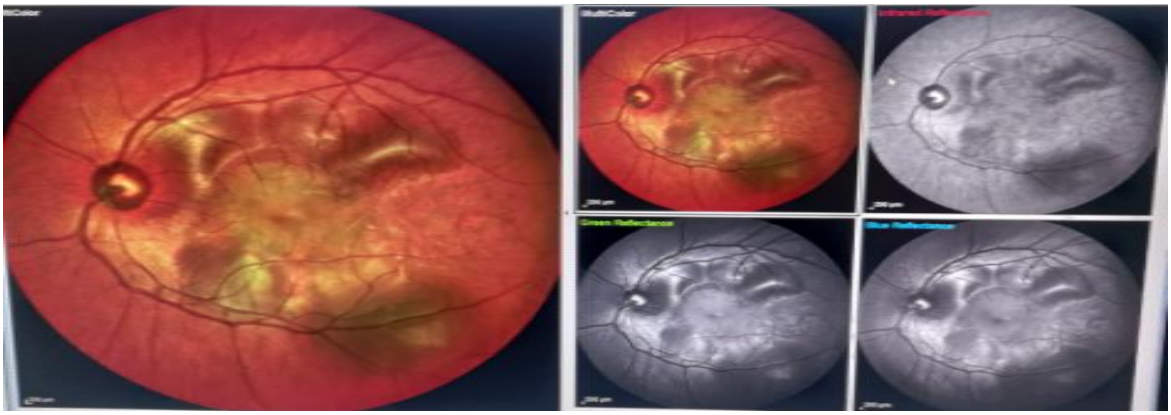

Figure 1 (B): OS fundus photograph shows exudative retinal detachment

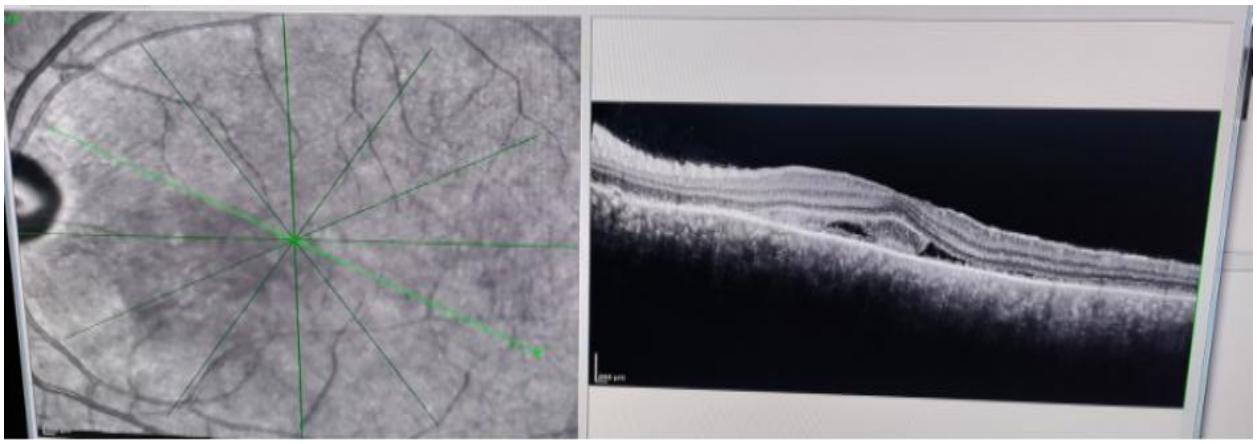

Figure 2 (A): OCT picture of OD showing subretinal fluid on macula

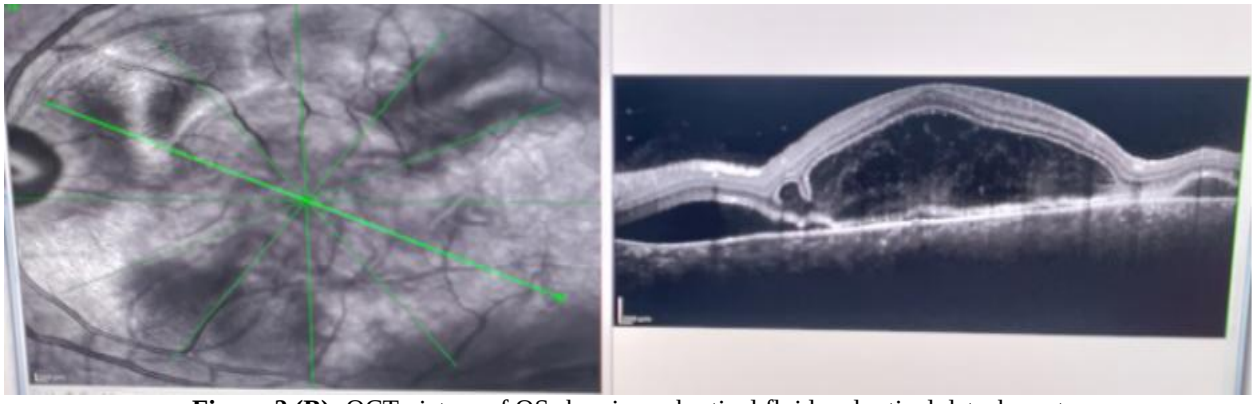

Figure 2 (B): OCT picture of OS showing subretinal fluid and retinal detachment

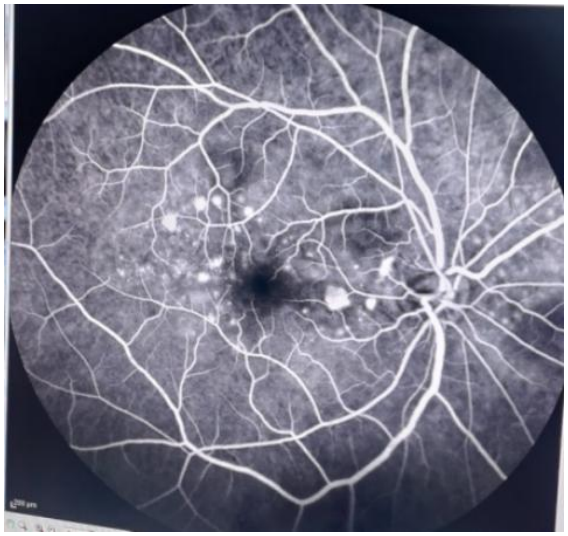

Figure 3 (A): OS FFA showing multiple area of pinpoint exudates

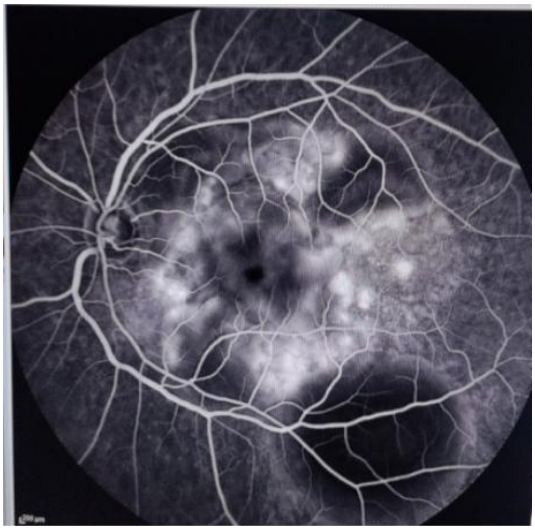

Figure 3 (B): OD FFA shows multiple area of pinpoint exudates

After evaluation the patient was treated for non infectious panuveitis treatment. Patient was given intravenous injection methylprednisolone 8 mg x 5 days starting treatment one day after onset of symptoms After which Oral corticosteroid started with 75mg for 7 days, tapering done with 5mg every every week for month followed by every 15 days for one month followed by monthly tapering with 5mg and thereafter sustained 5mg daily dose of oral corticosteroid maintained Weekly follow up maintained for 1 st two months followed by monthly follow up of patient maintained Subretinal fluid significantly resolved within 3 days of initiation of treatment and blurring of vision improved within a week, Retinal detachment resolved within 2 months of treatment and best corrected visual acuity improved to 6/6

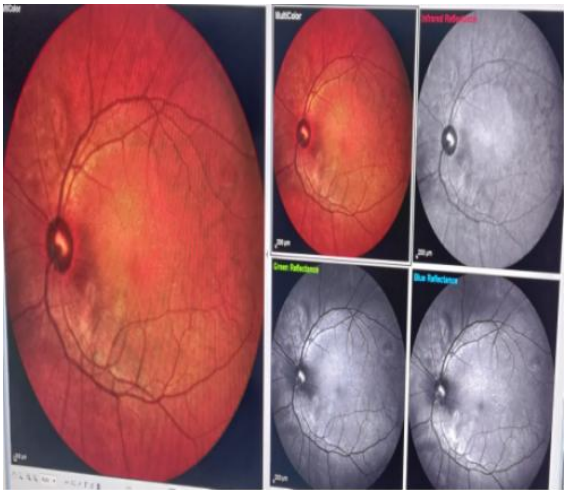

Figure 4 (A): fundus photograph OD shows resolved retinal detachment

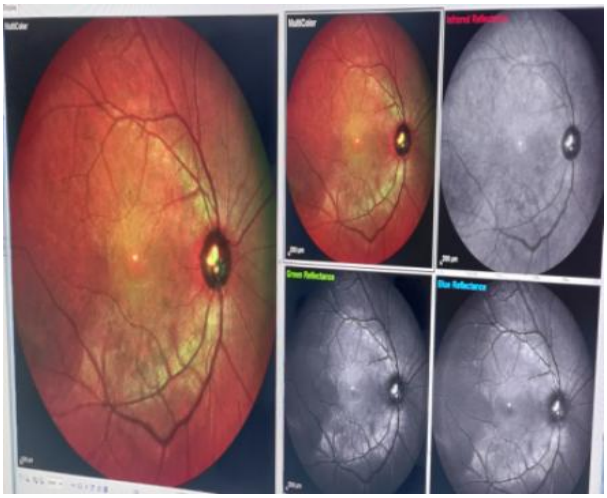

Figure 4 (B): Fundus photograph OS shows resolved retinal detachment

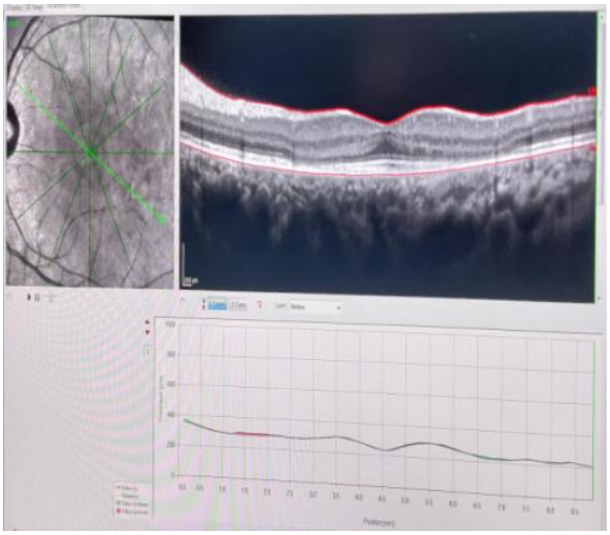

Figure 5 (A): OCT picture OD with thickness after 5 months of treatment shows complete recovery

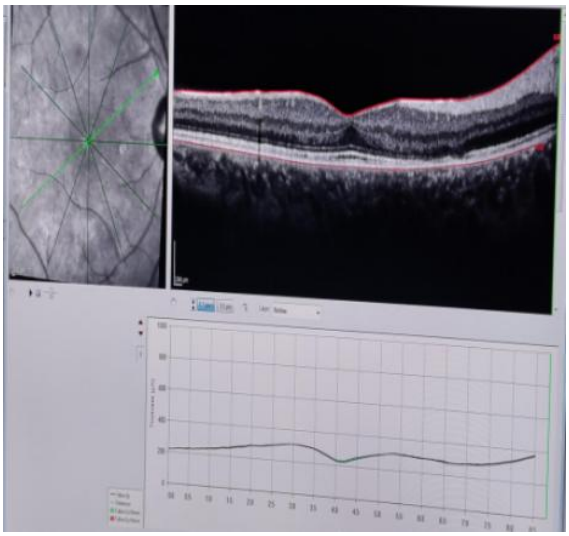

Figure 5 (B): OCT picture OS with thickness after 5 months of initiation of treatment shows complete recovery

Case Report 2

42 year old female came with chief complaints of diminution of vision in both eyes, redness and tenderness in periorbital region, patient examined 6 days after onset of symptoms there was H/o headache No H/o trauma No H/o photophobia/colored halos Past history of similar episode 7 years back and was diagnosed with VKH syndrome treated for same and was on oral corticosteroid for one year after which patient stopped medication on own No h/o recurrence after that Patient had received inactivated covid-19 virus vaccine of which following 2 hours she developed headache and periorbital pain and subsequently after 5 days developed diminution of vision in both eyes. Family history was not significant. General and systemic examination was within normal limits. On ocular examination right eye visual acuity was 6/60 and left eye visual acuity was 6/24. anterior segment and intra ocular pressure of both eye were within normal limits.

Fundus examination of both eyes revealed vitreous haze with exudative retinal detachment and subretinal fluid which was further confirmed by OCT as shown in fig 6A and 6B and fluorescein fundus angiography as shown in fig 7A and 7B

After detailed evaluation, she was treated with Intravenous methylprednisolone For 5 days after which oral corticosteroid started with tapering dose After initiation of treatment symptoms resolved within 2 weeks, vitreous haze and subretinal fluid reduced significantly Retinal detachment resolved after 6 months of treatment with visual acuity of both eyes was 6/9

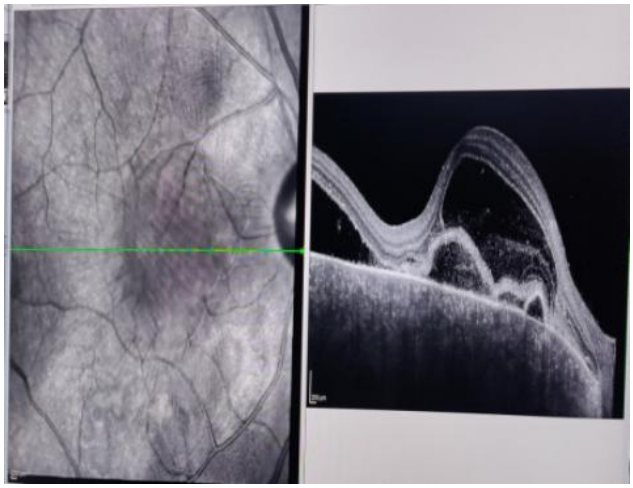

Figure 6 (A): OD OCT picture showing serous retinal detachment

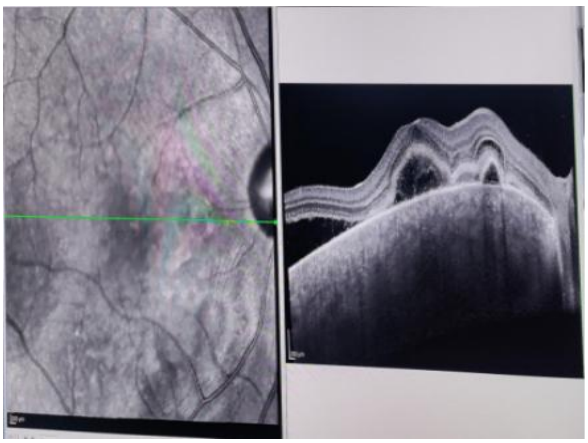

Figure 6 (B): OCT picture OS shows serous retinal detachment

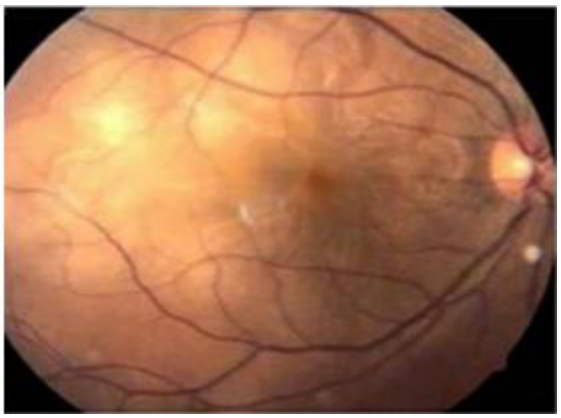

Figure 7 (A): Fundus photograph OD showing serous retinal detachment

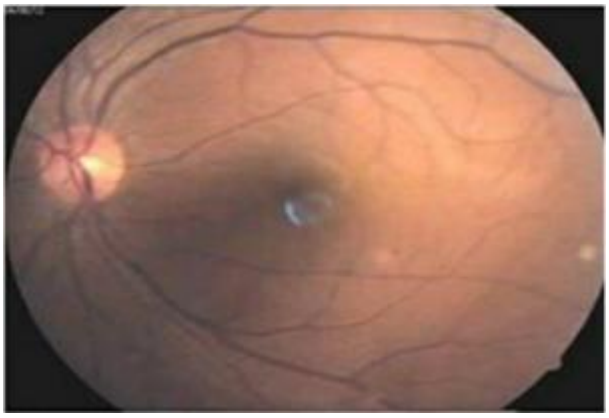

Figure 7 (B): Fundus photograph OD showing serous retinal detachment

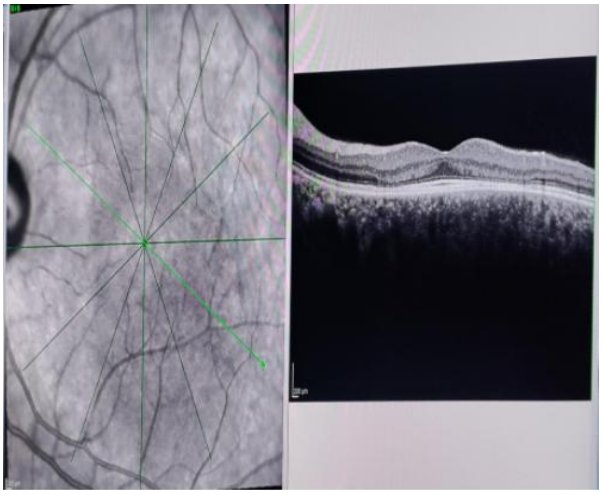

Figure 8 (A): OCT OD show resolved retinal detachment after treatment

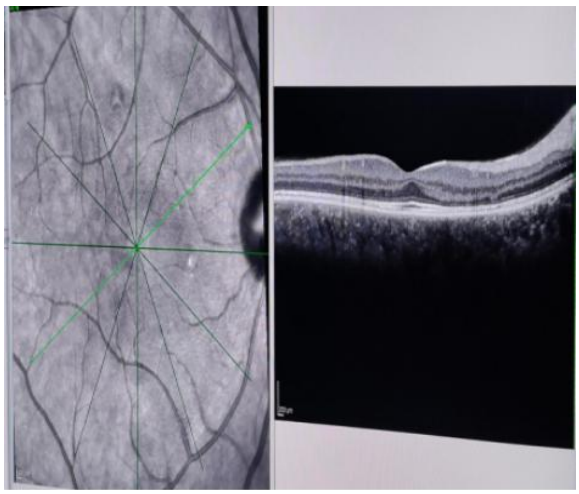

Figure 8 (B): OCT OS shows resolved retinal detachment a 9 months of months of treatment

2. Discussion

VKH disease results from an autoimmune process directed against melanocyte-associated antigens, which can be controlled when early and sustained corticoid/ immunosuppressive treatment is followed [16]

Here, we describe the case of a patient with VKH like uveitis developed within 2 weeks of COVID-19 vaccination and case of patient with VKH disease whose exacerbation within few hours of COVID-19 vaccination showed possible relationship with the COVID-19 vaccine administration that it was likely this vaccine was the causative or triggering factor.

Our case highlights the possibility of panuveitis following administration of an inactivated Covid-19 vaccine. While the rapid resolution of the disease with excellent visual recovery reassured us that this type of adverse event could be transient and treatable, the mechanism underlying vaccine-associated uveitis is unclear, and it is difficult to prove causality in these rare cases. Commonly proposed mechanisms of inflammation may be induced by the adjuvants that are routinely used in inactivated or subunit vaccines to enhance the immunogenicity of the virus. [17]

Like our case, VKH-like uveitis is reported to occur mostly in association with the inactivated vaccinates against yellow fever, influenza, BCG and HPV. [18-20]

There have been previous cases of vaccine associated uveitis from reported cases of hepatitis B vaccine, human papillomavirus vaccine and influenza vaccine [21-23]

3. Conclusion

Vogt-Koyanagi-Harada (VKH) syndrome results from an autoimmune process directed against melanocyte associated antigen which can be controlled when early and sustained immunosuppressive treatment is introduced. Although it is difficult to determine causality, our cases raise the possibility of vaccination and COVID-19 triggering-or even causing—VKH. This report enlightens possible causative mechanisms involved in VKH pathogenesis. SARS-CoV-2 vaccination can be at the origin of reactivation of long-time controlled disease. Reactivation of VKH disease is another potential side effect of anti-SARSCoV-2 vaccination to be added to the list of effects due to this vaccination Early diagnosis and treatment result in rapid resolution of disease and excellent visual recovery which reassure us that this type of adverse effect could be transient and treatable. The mechanism underlying vaccine-associated uveitis is unclear, and it is difficult to prove causality in these rare cases. Commonly proposed mechanisms of inflammation may be induced by the adjuvants that are routinely used in inactivated or subunit vaccines to enhance the immunogenicity of the virus. Immunological mechanism and dysregulation of immune system may play important role in association between VKH and covid 19 vaccination

Abbreviations

VKH-Vogt-Koyanagi-Harada
SARS-Severe Acute Respiratory Syndrome
IL-Interleukin
HLA-Human Leukocyte antigen
H/O-History of
OCT-Optical Coherence Tomography
OD-Oculus Dexter
OS-Oculus Sinister
BCG-Bacille Calmette-Guerin
HPV-Human papillomavirus

References

[1] Greco A, Fusconi M, Gallo A, et al. Vogt-Koyanagi-Harada syndrome. Autoimmun Rev.2013; 12 (11): 1033–8.
[2] O'Keefe GAD, Rao NA. Vogt-Koyanagi-Harada disease. Surv Ophthalmol.2017; 62 (1): 1–25.
[3] Read RW, Holland GN, Rao NA, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an international committee on nomenclature. Am J Ophthalmol.2001; 131 (5): 647–52.
[4] O'Keefe GA, Rao NA. Vogt-Koyanagi-Harada disease. Surv Ophthalmol.2017; 62 (1): 1–25. https: //doi. org/10.1016/j. survophthal.2016.05.002 (Epub 016 May 27).
[5] Liu XY, Peng XY, Wang S, et al. Features of optical coherence tomography for the diagnosis of Vogt-Koyanagi-Harada disease. Retina.2016; 36 (11): 2116–23.6. Chi W, Yang P, Li B, et al. IL-23 promotes CD4+ T cells to produce
[6] Yamaki K, Gocho K, Hayakawa K, Kondo I. Tyrosinase family proteins are antigens specific to Vogt-Koyanagi-Harada disease. J Immunol 2000; 165: 7323–7329 Cited Here
[7] Greco A, Fusconi M, Gallo A, et al. Vogt-Koyanagi-Harada syndrome. Autoimmun Rev.2013; 12 (11): 1033–8.
[8] O'Keefe GAD, Rao NA. Vogt-Koyanagi-Harada disease. Surv Ophthalmol.2017; 62 (1): 1–25
[9] Read RW, Holland GN, Rao NA, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an international committee on nomenclature. Am J Ophthalmol.2001; 131 (5): 647–52.
[10] O'Keefe GA, Rao NA. Vogt-Koyanagi-Harada disease. Surv Ophthalmol.2017; 62 (1): 1–25. https: //doi. org/10.1016/j. phthaphthal.2016.05.002 (Epub 2016 May 27).5. Liu XY, Peng XY, Wang S, et al. Features of optical coherence tomography for the diagnosis of Vogt-Koyanagi-Harada disease. Retina.2016; 36 (11): 2116–23.
[11] Chi W, Yang P, Li B, et al. IL-23 promotes CD4+ T cells to produce IL-17 in Vogt-KoyanagiHarada disease. J Allergy Clin Immunol.2007; 119 (5): 1218–24.
[12] Li F, Yang P, Liu X, Wang C, Hou S, Kijlstra A. Upregulation of interleukin 21 and promotion of interleukin 17 production in chronic or recurrent VogtKoyanagi-Harada disease. Arch Ophthalmol.2010; 128 (11): 1449–54
[13] Shi T, Lv W, Zhang L, Chen J, Chen H. Association of HLA-DR4/HLA-DRB1*04 with VogtKoyanagi-Harada disease: a systematic review and metaanalysis. Koong LR, Chee WK, Toh ZH, et al. Vogt-koyanagi-harada disease
[14] R. Ch Walton. Vogt-Koyanagi-Harada Disease. Medscape [Internet], (2016), pp.3 – 18 https: //reference. medscape. com/article/1229432-overview
[15] Rao N. Vogt-Koyanagi-Harada Disease. In: J YMaD, editor. *Ophthalmology*. New York, New York: Elsevier; 2014; chapter 7.17; p.761-763
[16] O'Keefe, G. A.; Rao, N. A. Vogt-Koyanagi-Harada disease. *Surv. Ophthalmol.*2**017**, *62*, 1–25. [CrossRef] [PubMed]
[17] Watad A, Quaresma M, Brown S, et al. Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome)-an update. *Lupus*.2017; 26 (7): 675–681. https: //doi. org/10.1177/0961203316686406 [published Online First: 2017/01/07].
[18] Dogan B, Erol MK, Cengiz A. Vogt-Koyanagi-Harada disease following BCG vaccination and tuberculosis. *SpringerPlus*.2016; 5. https: //doi. org/10.1186/ s40064-016-2223-4, 603-3.
[19] Kim M. Vogt-K oyanagi-Harada Syndrome following influenza vaccination. *Indian J Ophthalmol*.2016; 64 (1): 98. https: //doi. org/10.4103/0301-4738.178141, 98.
[20] Sood AB, O'Keefe G, Bui D, et al. Vogt-koyanagi-harada disease associated with hepatitis B vaccination. *Ocul Immunol Inflamm*.2019; 27 (4): 524–527. https: //doi. org/10.1080/09273948.2018.1483520 [published Online First: 2018/06/29].
[21] Benage M, Fraunfelder FW. Vaccine-associated uveitis. Mo Med.2016; 113 (1): 48–52.
[22] Holt HD, Hinkle DM, Falk NS, Fraunfelder FT, Fraunfelder FW. Human papilloma virus vaccine associated uveitis. Curr Drug Saf 2014; 9 (1): 65–8. doi: 10.2174/1574886311308660062
[23] Cunningham ET, Jr., Moorthy RS. Vaccine-Associated Posterior Uveitis. Retina 2020; 40 (4): 595–8. doi: 10.1097/IAE.0000000000002816
[24] COVID-19 mRNA vaccine. Ocul Immunol Inflamm.2021: 1–4. https: //doi. org/ 10.1080/09273948.2021.1974492 [published Online First: 2021/09/11].