Case Reports in Ophthalmology

Case Rep Ophthalmol 2021;12:804–808
DOI: 10.1159/000518834
Received: June 21, 2021
Accepted: August 1, 2021
Published online: September 21, 2021

Case Report

Vogt-Koyanagi-Harada Disease Following COVID-19 Infection

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Keywords
COVID-19 · Vogt-Koyanagi-Harada disease · SARS-CoV-2 · Serous retinal detachment

Abstract
A 29-year-old female presented to the emergency clinic with gradual visual disturbance in both eyes for 15 days duration, accompanied by bilateral tinnitus, and ocular pain that increased with ocular movements. One month prior to presentation, the patient had tested positive for severe acute respiratory syndrome coronavirus-2 but without complications. Visual acuity was 20/100 in the right eye and 20/300 in the left eye. Funduscopy demonstrated optic nerve swelling, radial nerve fiber striation disruption, and bilateral retinal folds. Optical coherence tomography showed serous (bacillary) retinal detachment and multifocal areas of hyper-reflective changes in the inner and outer plexiform layer with inner nuclear layer thickening and disruption of the interdigitation zone bilaterally. We present a case of incomplete Vogt-Koyanagi-Harada disease following COVID-19 infection.

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Introduction

Vogt-Koyanagi-Harada (VKH) disease is a chronic, bilateral granulomatous panuveitis characterized by exudative retinal detachments associated with poliosis, vitiligo, alopecia, and central nervous system, and auditory signs [1]. The etiology of VKH disease remains unknown, yet evidence suggests a T-lymphocyte-mediated autoimmune process directed against one or more antigens found on or associated with melanocytes. Research indicates that tyrosinase family proteins are the antigens specific to VKH disease [2] and that VKH disease is characterized by a T helper type 1 cell-mediated immune response [2].

At the time of writing, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is an RNA encapsulated virus that has infected >170 million people worldwide [3]. The main ocular manifestations of SARS-CoV-2 infection include dry eye, tearing, itching, redness, ocular pain, and foreign body sensation [4]. Optic neuritis, uveitis, acute macular neuroretinopathy, and paracentral acute middle maculopathy have been reported after SARS-CoV-2 infection [5–7]. Here, we report a case of incomplete VKH in a patient with a previous SARS-CoV-2 (COVID-19), which, to the best of our knowledge is the first report in the literature.

Case Report

A 29-year-old female presented to the emergency clinic with gradual visual disturbance in both eyes of 15 days duration, accompanied by bilateral tinnitus, and ocular pain that increased with ocular movements. One month prior to presentation, the patient had a positive serology test for SARS-CoV-2 immunoglobulin G with positive polymerase chain reaction for COVID-19 from a nasopharyngeal swab with a COVID-19 Spike Ab 45.12 H (<0.80 U/mL). She reported no complications from COVID-19 infection. Her family history was unremarkable, and she denied diabetes, hypertension, connective tissue disease, tuberculosis, hematologic disease, or cardiovascular disease. The patient was not taking any oral medications.

On initial examination, best-corrected visual acuity was 20/100 in the right eye and 20/300 in the left eye. Intraocular pressure was 14 mm Hg bilaterally. Slit-lamp examination of the anterior segment was within normal limits bilaterally, including the absence of cells and flare. Fundoscopy demonstrated, optic nerve swelling, and radial nerve fiber striation disruption, and retinal folds in both eyes (Fig. 1). B-scan ultrasound was normal, and a T sign was ruled out. Spectral-domain optical coherence tomography (SD-OCT) indicated serous (bacillary) retinal detachment and multifocal areas of hyper-reflective changes in the inner and outer plexiform layer with inner nuclear layer thickening and disruption of the interdigitation zone in both eyes (Fig. 2). Fluorescein angiography indicated pinpoint hyperfluorescence and late leakage (Fig. 3). The patient received systemic treatment with methylprednisolone 1 g intravenously for 3 days, followed by oral prednisolone 1 mg/kg. One month of treatment the serous retinal detachment had resolved and visual acuity had improved to 20/60 in the right eye and 20/80 in the left eye.

Discussion/Conclusion

In this report, we describe a young female with VKH disease following COVID-19 infection. Many ocular diseases have been associated with SARS-Cov-2. However, demonstrating an association between SARS-Cov-2 and ocular diseases is tenuous because it a single disease does not always cause it [8]. Zapata et al. [9] published retinal microvascular abnormalities in patients after SARS-Cov-2. In animals, coronaviruses cause various ocular infections such as conjunctivitis, anterior uveitis, retinitis, and optic neuritis [10].

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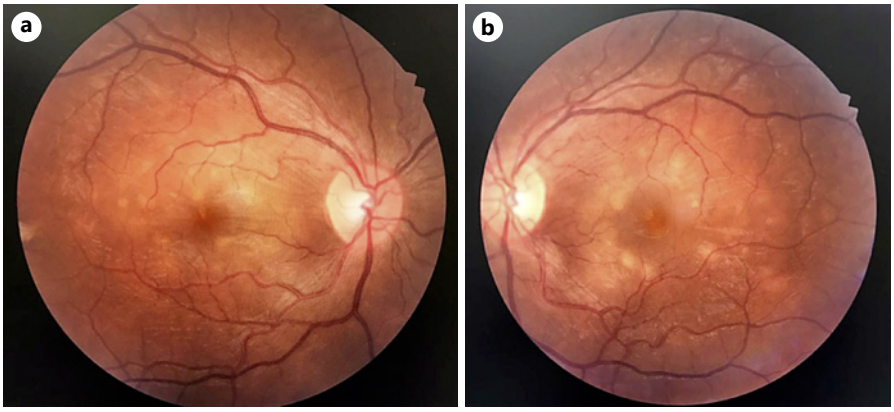

Fig. 1. a A color retinal photograph of the right eye showing slightly swollen optic disc, with choroidal folds and radial disc nerve fiber striation disruption. **b** A color retinal photograph of left eye showing slightly swollen optic disc, with choroidal folds and radial disc nerve fiber striation disruption.

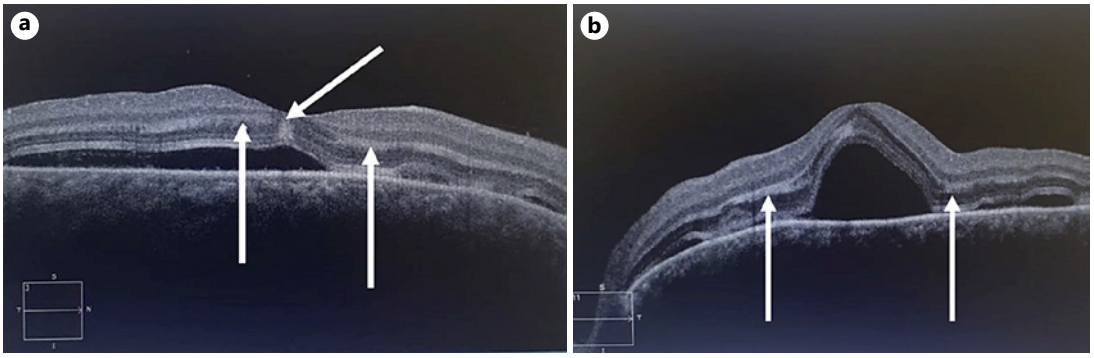

Fig. 2. a SD-OCT of the right eye demonstrates, serous (bacillary) retinal detachment and placoid parafoveal hyper-reflective bands at the level of the inner nuclear layer (white arrows). **b** SD-OCT of the left eye demonstrates, serous (bacillary) retinal detachment and placoid parafoveal hyper-reflective bands at the level of the inner nuclear layer (white arrows). SD-OCT, spectral-domain optical coherence tomography.

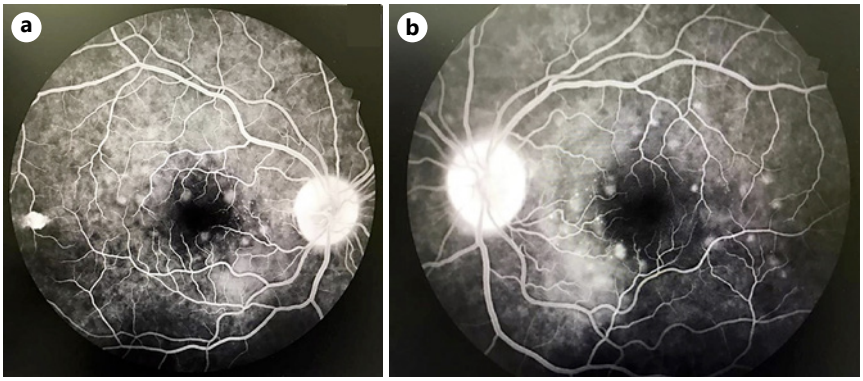

Fig. 3. a Fluorescein angiogram of the right eye, demonstrating optic disc leakage and numerous pinpoint hyperfluorescent foci of leakage at the level of the retinal pigment epithelium. **b** Fluorescein angiogram of the left eye, demonstrating optic disc leakage and numerous pinpoint hyperfluorescent foci of leakage at the level of the retinal pigment epithelium.

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The clinical manifestations of VKH disease are caused by an autoimmune response directed against melanin-associated antigens in the target organs, that is, the eye, inner ear, meninges, and skin. Evidence indicates that genetic factors, including VKH disease-specific risk factors (HLA-DR4) and general risk factors for immune-mediated diseases (IL-23R), dysfunction of immune responses, involving the innate and adaptive immune system and environmental triggering factors are all involved in the development of VKH disease [11].

Recently, prior SARS-CoV-2 infection has been associated to the appearance of various autoimmune and autoinflammatory diseases, including pediatric inflammatory syndrome and Guillain-Barre syndrome [8, 12]. This could explain the relationship with autoimmune and autoinflammatory response. Infectious diseases have been considered one of the triggers for autoimmune and autoinflammatory diseases, mostly via molecular mimicry. We believe that in the current case, an autoimmune response to the recent SARS-CoV-2 infection played a role in the development of VKH [8, 12].

Recently, Benito et al. [5] reported a case with unilateral panuveitis and optic neuritis as the initial manifestation of SARS-CoV-2 infection. Their initial clinical impression of unilateral VKH was ruled out due to the absence of meningism, and the existence of structural and functional damage at the level of the optic disc compatible with optic neuritis. Our patient presented with tinnitus, SD-OCT bacillary retinal detachment, and mid-phase pinpoint hyperfluorescent and late leakage on fluorescein angiography at the level of the RPE with retinal serous detachment consistent with VKH. On SD-OCT, our patient presented with bilateral perifoveal hyper-reflectivity in the inner retinal layers.

VKH is a disease that has been well studied, with precise diagnostic criteria. Despite having a regular and consistent pattern of clinical presentation, case reports or reviews of VKH with SARS-Cov-2 have not been reported in the medical literature.

The management of VKH involves the use of corticosteroids in the acute uveitic phase. Evidence-based therapy recommends the use of methylprednisolone pulses of 1 g intravenously per day for 3–5 days, followed by oral prednisolone 1 mg/kg per day, combined with conventional immunomodulatory therapy (cyclosporine, methotrexate, tacrolimus, azathioprine, or mycophenolate mofetil) [8].

To the best our knowledge, we present the first case with incomplete VKH disease following COVID-19 infection. There remains the possibility that VKH may not be associated with COVID and that the association is coincidental.

Acknowledgement

This manuscript does not include any nonauthor contributors to acknowledge.

Statement of Ethics

This study adhered to the tenets of the World Medical Association Declaration of Helsinki. The patient gave written informed consent to publish their case (including publication of images). Ethics board approval was not required for this study (Wilmer Eye Institute).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This manuscript did not receive any funding.

Author Contributions

J.F.A., J.B.Y., and F.A.M. were involved in the conception and design of the article and the analysis and interpretation of data; M.P. and J.D.Y. acquired the data; J.M.G., J.R., A.P., and S.V. interpreted the data; J.F.A., J.R., and Y.B.Y. drafted the article; all the authors critically revised the paper; all authors approved the final version of the article submitted for publication. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed in this study are included in this article. Further enquiries can be directed to the corresponding author.

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