

## Case Report

# Recurrence of Vogt-Koyanagi-Harada Disease after Rapid Tapering of Corticosteroids: A Case Report

Mhd Bassel Aljunaidi<sup>1</sup>, Majd Karkouki<sup>1</sup>, Zeina Aljunaidi<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Al-Rawda Syrian Specialty Hospital, Damascus University, Damascus, Syria

Corresponding Author: Majd Karkouki, Damascus, Syria, [majd.karkouki@hotmail.com](mailto:majd.karkouki@hotmail.com)

Department of Ophthalmology, Al-Rawda Syrian Specialty Hospital, Damascus, Syria

Financial support: None

Conflict of Interest: None

### Abstract

**Background:** *Vogt-Koyanagi-Harada's disease* (VKHD) is an autoimmune disorder that targets melanocyte-rich tissues in genetically susceptible individuals. It can affect the eyes, inner ears, skin, hair, and meninges. When VKHD affects the eye, it can cause bilateral granulomatous panuveitis with exudative bullous retinal detachment and is usually associated with meningismus. It may lead to permanent loss of visual acuity. While the pathogenesis remains unknown, viral infection has been implicated. The most accepted theory remains a T-cell mediated autoimmune reaction against one or more antigens associated with melanocytes, melanin, and retinal pigment epithelium (RPE).

**Case presentation:** We report the case of a 17-year-old male patient presenting to our outpatient department for vision loss. The patient reported a 2-week history of hearing loss, tinnitus, and episodic headaches associated with vomiting. Physical examination showed white lashes (poliosis) and a bilateral decrease in visual acuity. Fluorescein angiography showed bullous exudative retinal detachments. The patient was diagnosed with VKHD. His symptoms resolved following a course of oral prednisolone that was initiated at 60 mg per day (1mg/Kg/day), then tapered down over 6 weeks. Six months later, the patient presented again with more pronounced symptoms. His Best Corrected Visual Acuity (BCVA) was lower than it was on his first presentation, and the retinal exam showed a sunset glow fundus and degenerative changes in the RPE. Combined therapy with prednisolone and methotrexate resulted in a complete resolution of symptoms, and his BCVA returned to more than 20/40.

**Conclusion:** This case emphasizes the importance of avoiding the rapid tapering of corticosteroids in VKHD due to the high risk of disease recurrence.

**Keywords:** Vogt-Koyanagi-Harada disease, VKHD, case report, recurrence, corticosteroids, uveitis

## Background

Vogt-Koyanagi-Harada disease (VKHD) is a multisystem autoimmune disease characterized by inflammation of melanocyte-containing tissues. The disease is sometimes divided into (1) Vogt-Koyanagi disease, which is mainly limited to dermatologic changes and anterior uveitis, and (2) Harada disease, in which neurological manifestations and exudative retinal detachments predominate [1,2].

The disease typically begins with a *prodromal phase* which lasts a few days and consists of neurologic and auditory features. A patient in this phase commonly complains of fever, episodic headache, and frequent nausea. Tinnitus, vertigo, deafness, cranial nerve palsies, optic neuritis, and meningitis can occur. This phase is followed by the *acute uveitic phase*, in which bilateral granulomatous panuveitis, diffuse choroidal infiltration, Dalen-Fuchs nodules, vitritis, and exudative retinal detachments with blurry vision may occur [1-3]. When adequately treated with high-dose systemic corticosteroids, patients undergo resolution in this phase. A *convalescent phase* may follow, with localized alopecia, poliosis, vitiligo, "sunset glow" fundus and depigmented limbal lesions. Some patients may enter a chronic stage due to delayed or inadequate treatment. The *chronic recurrent phase* is characterized by smoldering uveitis (most commonly anterior) with exacerbations [1]. Some vision-threatening complications such as severe chorioretinal atrophy and glaucoma may occur [1, 3].

The first description of VKHD goes back to the 10th century when an Arab ophthalmologist Ali-Ibn-Isa first described it in his book "*Notebook of the Oculists*" [4]. In the 19th century, several physicians like Nettelship, Tay, and Jacobi reported entities with different aspects of the disease. In the 20th century, a Swiss physician, Alfred Vogt, and two Japanese researchers, Yoshizo Koyanagi and Einosuke Harada described it again, separately [4]. Vogt reported the association of ocular inflammation and poliosis, Harada described primary exudative retinal detachments with posterior uveitis, and Koyanagi described patchy depigmentation of the skin with whitening of the hair, hair loss, and bilateral chronic iridocyclitis. In 1949, Bruno and McPherson combined the findings of Vogt, Koyanagi, and Harada and suggested the same disease, that became recognized as VKHD [3-5].

VKHD is a rare disease. It more commonly affects certain ethnic groups such as Asian, Middle

Eastern, Native American, Indian and Hispanic populations. The incidence of the disease is variable but is highest in Japan, where 7-8% of all uveitis cases are attributed to VKHD, and around 800 new cases are diagnosed every year [4,6]. In the USA, VKHD accounts for 1-4% of all uveitis cases, and it has been reported that two-thirds of the patients affected are of Hispanic origin [6,7]. In Middle Eastern countries, such as Saudi Arabia, VKHD accounts for 2.5% of uveitis cases, and in India, VKHD accounts for around 2% of all cases [4,6,7].

VKHD predominantly affects those in their third decade of life. Cases have also been reported in children, and among 193 cases of uveitis in children in Saudi Arabia, 16% were attributed to VKHD [8].

Revised diagnostic criteria of VKHD published in 2001 include 1) Absence of penetrating eye trauma, 2) Absence of other ocular diseases, 3) Bilateral disease involvement, 4) Auditory and neurological signs such as meningismus, cerebrospinal fluid (CSF) pleocytosis, or tinnitus and 5) Integumentary findings such as alopecia, vitiligo, and poliosis [1,9].

Based on how many criteria the patient has, the diagnosis of complete (criteria 1 to 5 present), incomplete (criteria 1 to 3 present plus criterion 4 or 5) or probable (criteria 1 to 3 present only) VKHD can be made [1].

In this article, we report the case of a 17-year-old male patient who was diagnosed and treated for complete VKHD but soon developed a recurrent attack. This case was presented to emphasize the importance of avoiding the rapid tapering of corticosteroids in VKHD due to the risk of disease recurrence.

## Case Report

A 17-year-old Middle Easterner male patient presented to our outpatient clinic complaining of vision loss. The patient reported that 2 weeks prior to presentation, he started having hearing loss, tinnitus, and episodic headaches with vomiting. Visual acuity recently started decreasing, and whitening of the eyelashes occurred. The patient also reports episodes of joint pains and recurrent oral ulcers before the onset of ocular manifestations. He denies any history of eye trauma or a family history of ocular diseases.

On examination, photophobia and poliosis (whitening of the eyelashes) were noted (Fig. 1). Visual acuity was decreased in both eyes, with 20/80 in the right eye and 20/40 in the left eye. Slit



Figure 1: Poliosis (whitening of the eyelashes)

lamp examination showed clear cornea bilaterally with evidence of mild anterior chamber (AC) inflammation (1+ cells) without any keratic precipitates. Retinal examination using a 90D lens showed moderate vitreous inflammation (2+).

Folds of retinal detachment centered around the macula were also detected during the clinical examination (Fig. 2), and fluorescein angiography (FA) revealed multiple serous detachments with pinpoint leakages (Fig. 3). The decreased visual acuity was therefore attributed to bullous neurosensory retinal detachment and the subretinal fluid accumulation.

With all 5 diagnostic criteria present, the 17-year-old patient was diagnosed with complete VKHD. Treatment with topical steroids and systemic corticosteroids was initiated with oral prednisolone 60 mg/day (1mg/Kg/day). The dose was then reduced by 10 mg every week until reaching 10 mg/day during week 6. The patient was also taking lansoprazole 30 mg twice daily during this period. After 6 weeks of treatment, the patient's symptoms resolved and reattachment of the neurosensory retina was seen (Fig. 4).

However, six months later, the patient presented again, this time with a visual acuity of 20/100 in the right eye and 20/70 in the left eye. The AC activity was more pronounced (3+), vitritis was moderate (2+), and there were posterior

synechiae between the iris and the anterior capsule of the lens. The intraocular pressure of both eyes was normal.

On indirect ophthalmoscopy, a depigmented fundus appearance (sunset glow fundus) was noted, the right optic disc was not visible due to vitreous haze, and Dalen Fuchs nodules were noticed on the retinal periphery (Fig. 5). B-scan ultrasonography showed thickening of the sclera and choroid, serous detachment of the retina, and accumulation of subretinal fluid (Fig. 6). Fundus photographs showed a sunset glow fundus and revealed degenerative changes in the retinal pigmented epithelium (RPE) (Fig. 7). Fluorescein angiography (FA) showed areas of hyper and hypo-fluorescence (Fig. 8). Optical Coherence Tomography (OCT) revealed multiple neurosensory retinal detachments and sub-retinal fluid accumulation (Fig. 9).

The patient was prescribed high-dose intravenous methylprednisolone pulse therapy for 3 days (1 g/day), followed by daily 60 mg oral prednisone (1 mg/Kg/day), which was maintained for 2 weeks, then tapered by 10 mg every week, until reaching the corticosteroid-sparing effect, defined as an ability to reduce the dose to 10 mg/day with the absence of active uveitis, stabilization of visual acuity and patient tolerance of any drug-related side effects. To further prevent relapses, the patient also received cytotoxic treatment of methotrexate 7.5 mg/week.

In 4 weeks, the patient's visual acuity began to improve, the subretinal fluid disappeared, and the OCT revealed reattachment of the neurosensory retina (Figure 10).

During 24 months follow-up after the combination therapy, the patient had only one recurrent mild anterior uveitis with a best corrected visual acuity (BCVA) of more than 20/40.

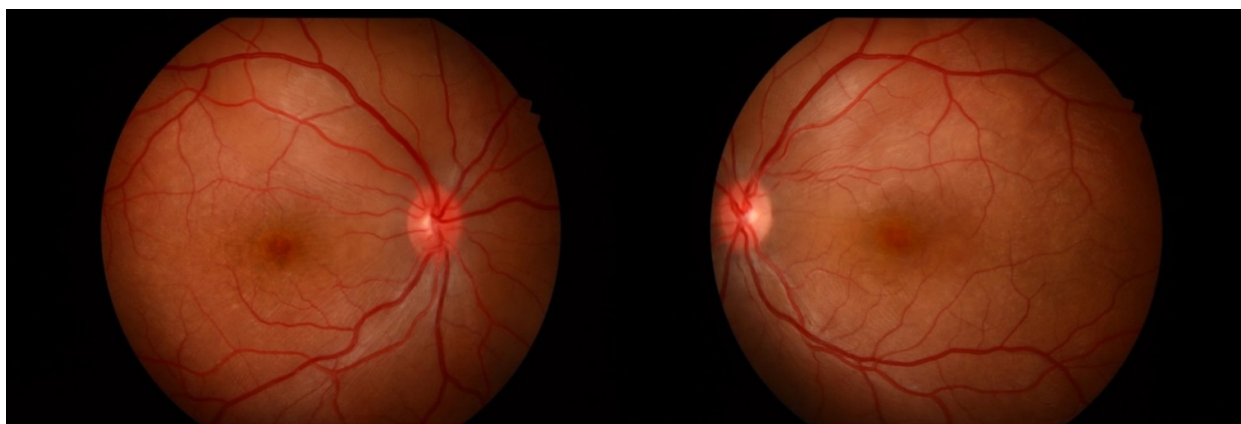


Figure 2: Fundus of the patient showing folds of sensory retinal detachment centered around the macula.

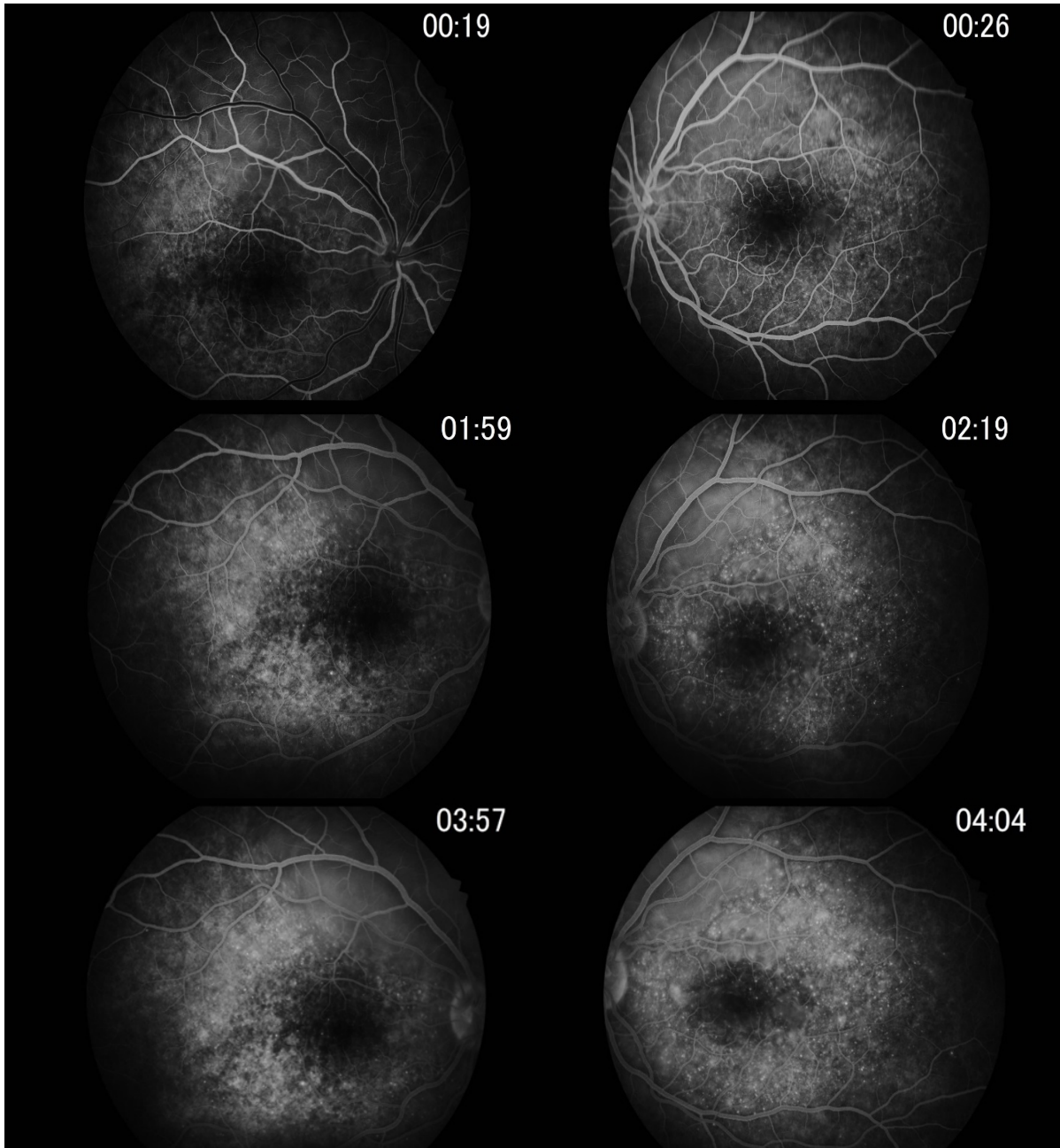


Figure 3: Fluorescein angiography in acute uveitic stage shows leakage and pooling of dye in the sub-retinal space giving the typical pinpoint hyperfluorescence, and the classic “starry sky” appearance of Harada disease

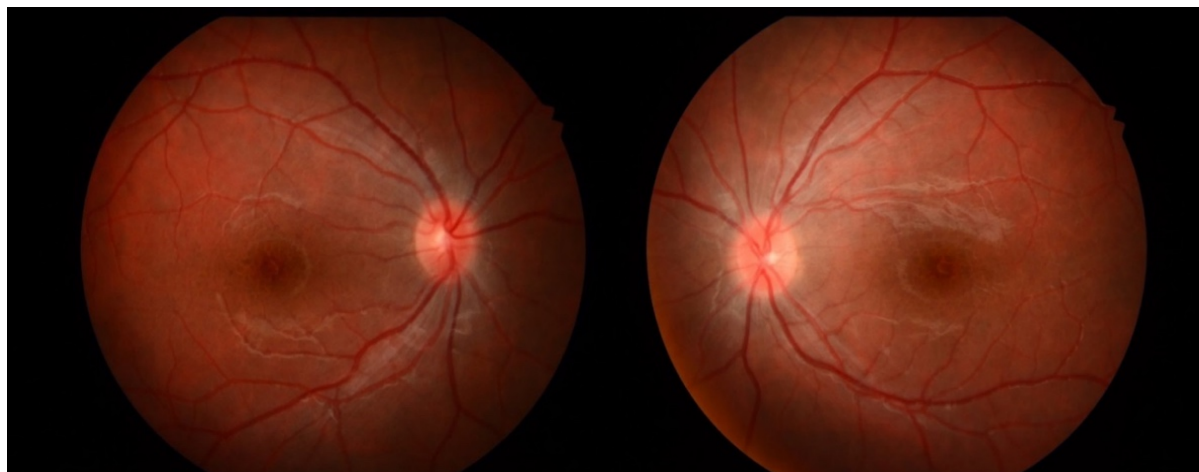


Figure 4: Retinal exam at 6 weeks showing re-attachment of neurosensory retina.

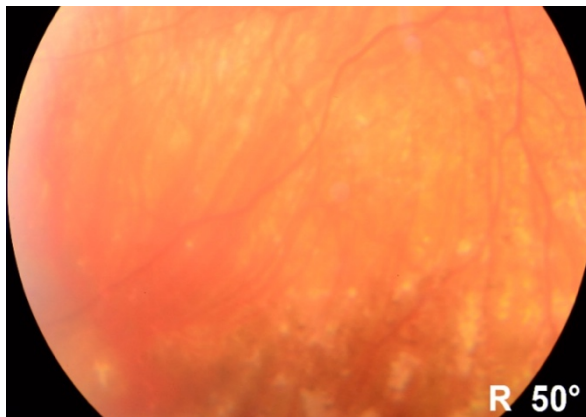


Figure 5: Dalen Fuchs nodules in the retinal periphery.

## Discussion

VKHD is a rare inflammatory disease that affects pigmented tissues and manifests initially by nonspecific symptoms. This prodromal stage with symptoms like malaise, fever, headache, and dizziness usually lasts 1-2 weeks and is followed by the acute uveitis stage in which our patient presented complaining of vision impairment [10]. The patient did report a 2-week history of headache, tinnitus, vertigo, and hearing loss that may be symptoms of the prodromal stage [1, 11]

The patient had all 5 criteria and was diagnosed with complete VKHD. He received prednisolone for a total of 6 weeks and had full resolution of symptoms. However, he then presented with a more aggressive episode after 6 months. It's been reported that a longer duration of treatment lasting for at least 3-6 months is essential to decrease the risk of disease recurrence [9,10]. Rapid tapering of systemic corticosteroid is associated with not only an increased risk of recurrence of VKHD but also a worse visual prognosis [10, 12]. The treatment of acute VKHD entails long-term oral corticosteroid therapy which is slowly tapered for a total duration of therapy at least 6 months [12].

Upon recurrence, the patient was treated with a high-dose systemic corticosteroid and steroid-sparing cytotoxic drug methotrexate, for a longer duration of time. New studies show that using a combination of corticosteroids and immunomodulatory drugs as first-line therapy reduces the chances of developing the chronic recurrent stage and late ocular complications of VKHD, subsequently improving visual outcome [9, 10]. The use of immunomodulatory therapy in acute uveitis is also beneficial in minimizing corticosteroids dosage and duration, thus sparing the patient from the side effects that

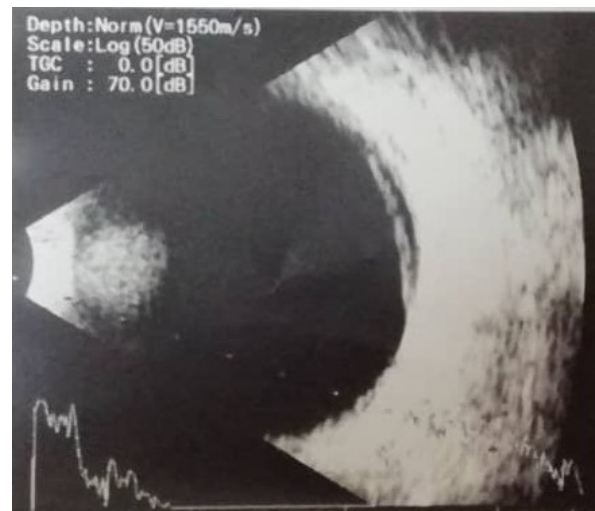


Figure 6: B-scan ultrasonography shows serous detachment of the retina and subretinal fluid

steroids can cause especially at high doses, and with long durations of treatment such as in VKHD (weight gain, osteoporosis, sleep disturbances, infections, etc.) [13].

Early and sustained aggressive treatment with a combination of corticosteroid and steroid-sparing therapy such as methotrexate during the first attack could prevent chronic uncontrolled inflammation and subsequent sunset glow fundus [14]. However, unfortunately, even with proper early aggressive treatment, recurrence rates remain high [9,10].

The risk of ocular complications also increases with recurrence, whereby irreversible damage to the structure of the retinal layers can occur. 15% of patients with VKHD develop choroidal neovascular membranes (CNVM) [15].

While ultrasonography, FA and OCT were useful in establishing the diagnosis in the case of our patient, other diagnostic methods may also be used. In case the diagnosis is uncertain, a lumbar puncture (LP) may be performed as part of the investigation of VKHD. It shows increased lymphocytes in the CSF in 2/3 of all patients with VKHD in the first week of the disease, and approximately in all patients after 3 weeks of the disease onset [16]. The Indocyanine-green angiography (ICGA) is also of great value in detecting the masked subclinical signs of choroidal inflammation during the acute episode. It was not performed due to the patient's hypersensitivity to iodide [15].

## Conclusion

This case was presented to emphasize the importance of early aggressive treatment of the acute uveitis stage in VKHD with long duration

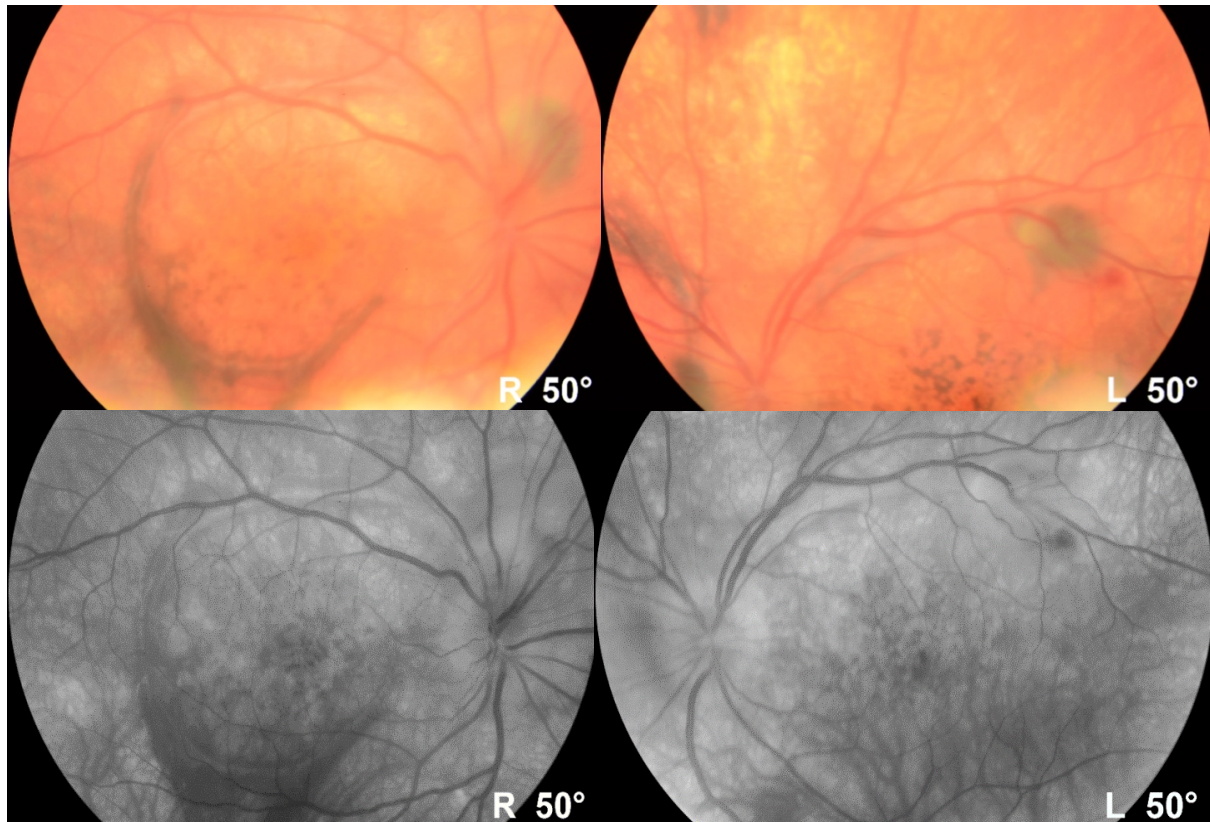


Figure 7: Upper 2 images are fundus photographs showing a "sunset-glow" fundus. The lower 2 are red-free fundus pictures showing the associated chronic changes.

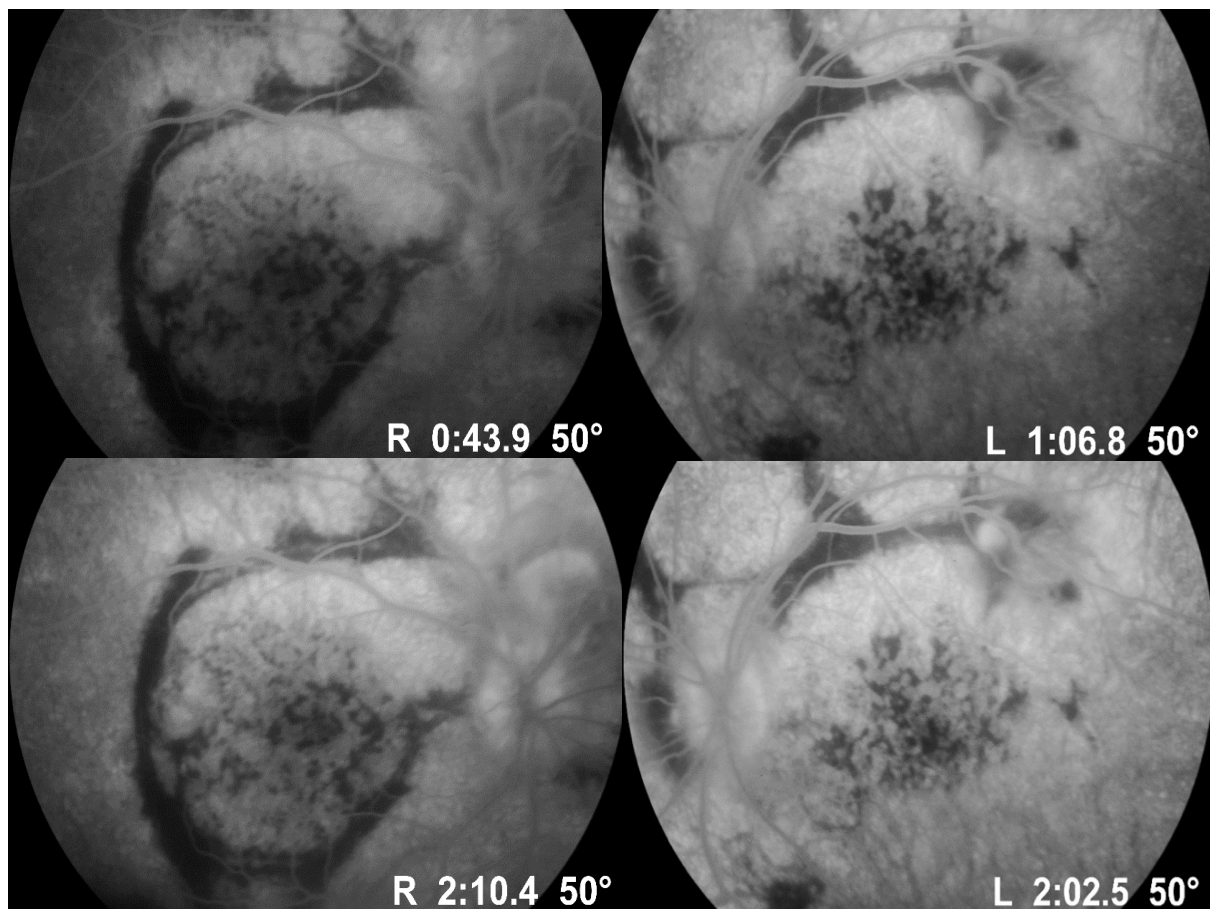


Figure 8: Fluorescein angiography in chronic phase shows degenerative changes in the RPE as well as areas of hyper- and hypo-fluorescence

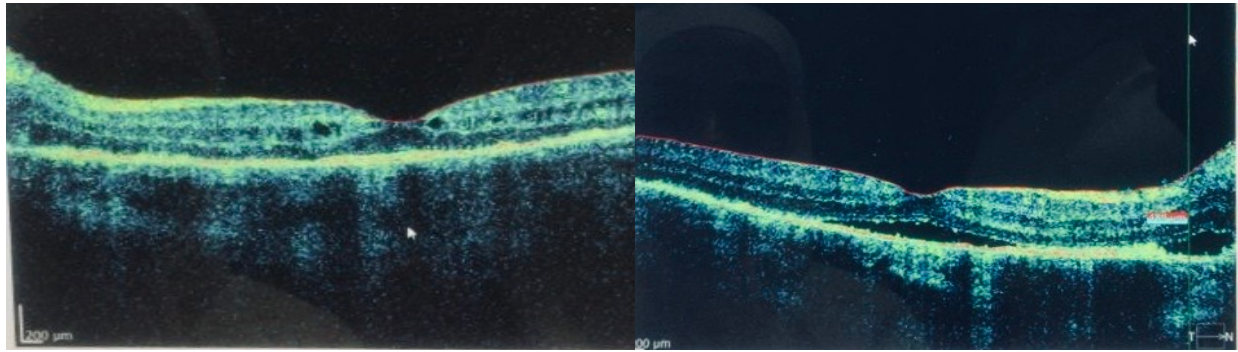


Figure 9: OCT shows multiple neurosensory retinal detachments and subretinal fluid in the chronic phase

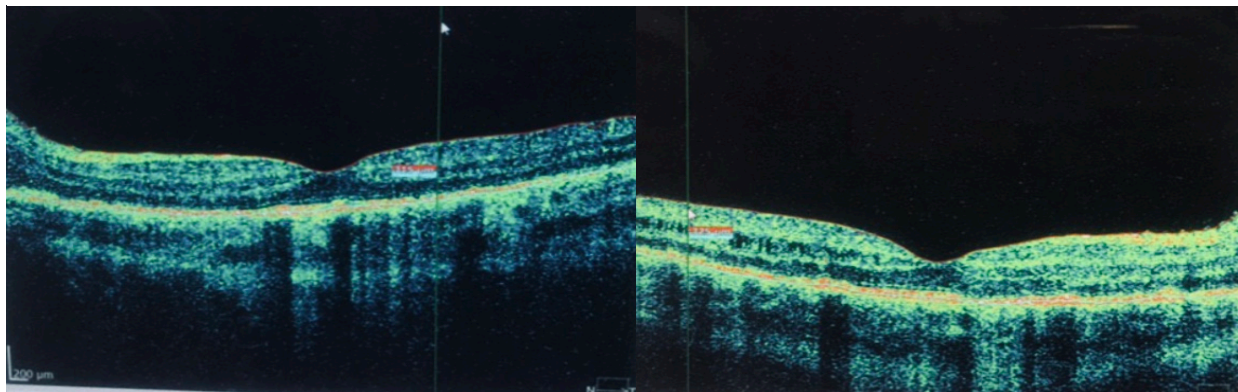


Figure 10: OCT shows anatomical improvement after the combined therapy with resolution of the subretinal fluid and re-attachment of neurosensory retina

corticosteroids and steroid sparing immunomodulators, due to the high risk of disease recurrence. Rapid tapering of corticosteroids may increase the risk of disease recurrence, and lead to worse disease prognosis and ocular complications.

## References

1. Salmon, John F. "Uveitis." *Kanski's Clinical Ophthalmology*. 9th ed. Philadelphia, PA: Elsevier (2020): 423-84. Print.
2. Rajendram, Ranjan, Monica Evans, and Narsing A. Rao. "Vogt-Koyanagi-Harada disease." *Int Ophthalmol Clin* 45.2 (2005): 115-134. <https://doi.org/10.1097/01.iio.0000155904.87679.0c>
3. García, Lourdes Arellanes, Mónica Orozco Carroll, and Manuel Alejandro Garza León. "Vogt-Koyanagi-Harada syndrome in childhood." *International ophthalmology clinics* 48.3 (2008): 107-117. <https://doi.org/10.1097/IIO.0b013e31817d9b70>
4. Mota, Luiz Alberto Alves, and Arthur Borges Dos Santos. "Vogt-Koyanagi-Harada syndrome and its multisystemic effects." *Rev Assoc Med Bras* 56.5 (2010): 590-5. <https://doi.org/10.1590/S0104-42302010000500023>
5. Andreoli, Christopher M., and C. Stephen Foster. "Vogt-Koyanagi-Harada disease." *Int Ophthalmol Clin* 46.2 (2006): 111-122. <https://doi.org/10.1097/00004397-200604620-00011>
6. Lavezzo, Marcelo Mendes, et al. "Vogt-Koyanagi-Harada disease: review of a rare autoimmune disease targeting antigens of melanocytes." *Orphanet J Rare Dis* 11.1 (2016): 29. <https://doi.org/10.1186/s13023-016-0412-4>
7. Nashtaei, Ebrahim M., et al. "Patterns of uveitis in the Middle East and Europe." *J Ophthalmic Vis Res* 6.4 (2011): 233.
8. Hamade, Issam H., et al. "Uveitis survey in children." *Br J Ophthalmol* 93.5 (2009): 569-572. <https://doi.org/10.1136/bjo.2008.148015>
9. Baltmr, Abeir, Sue Lightman, and Oren Tomkins-Netzer. "Vogt-Koyanagi-Harada syndrome-current perspectives." *Clin Ophthalmol* 10 (2016): 2345. <https://doi.org/10.2147/OPHTH.S94866>
10. Patil, Yojana B., et al. "Vogt-Koyanagi-Harada (VKH) syndrome: A new perspective for healthcare professionals." *J Family Med Prim Care* 9.1 (2020): 31. [https://doi.org/10.4103/jfmpc.jfmpc\\_787\\_19](https://doi.org/10.4103/jfmpc.jfmpc_787_19)

11. Rao, Narsing A., et al. "Frequency of distinguishing clinical features in Vogt-Koyanagi-Harada disease." *Ophthalmology* 117.3 (2010): 591-599.  
<https://doi.org/10.1016/j.opthta.2009.08.030>
12. Lai, T. Y. Y., et al. "Effects of the duration of initial oral corticosteroid treatment on the recurrence of inflammation in Vogt-Koyanagi-Harada disease." *Eye* 23.3 (2009): 543-548.  
<https://doi.org/10.1038/eye.2008.89>
13. Alan, Irmak Sayın, and Bahadır Alan. "Side Effects of Glucocorticoids." *Pharmacokinetics and Adverse Effects of Drugs-Mechanisms and Risks Factors* (2018).  
<https://doi.org/10.5772/intechopen.72019>
14. Herbort Jr, Carl P., et al. "Reappraisal of the management of Vogt-Koyanagi-Harada disease: sunset glow fundus is no more a fatality." *Int Ophthalmol* 37.6 (2017): 1383-1395.  
<https://doi.org/10.1007/s10792-016-0395-0>
15. Wu, Lihteh, et al. "Intravitreal bevacizumab for choroidal neovascularization secondary to Vogt-Koyanagi-Harada syndrome." *Jpn J Ophthalmol* 53.1 (2009): 57-60.  
<https://doi.org/10.1007/s10384-008-0600-4>
16. Sugiura, Seiji. "Vogt-Koyanagi-Harada disease." (1978).
17. Bouchenaki, Nadia, and Carl P. Herbort. "The contribution of indocyanine green angiography to the appraisal and management of Vogt-Koyanagi-Harada disease." *Ophthalmology* 108.1 (2001): 54-64. [https://doi.org/10.1016/S0161-6420\(00\)00428-0](https://doi.org/10.1016/S0161-6420(00)00428-0)