International Journal of Ophthalmology & Visual Science
2024, Vol. 9, No. 2, pp. 23-29
https://doi.org/10.11648/j.ijovs.20240902.12

Case Report

Multimodal Imaging in Diagnosis of Vogt Koyanagi Harada Disease with Reference to Choroid and Retinal Pigment Epithelium

Deepesh Arora*, Anuj Sharma, Devesh Sharma, Dinesh Sharma

Amritsar Eye Clinic, Dehradun, India

Abstract

A 48 year dark skinned North Indian male presented first time to our outpatient with history of bilateral visual decline of 3 weeks duration with associated features of headache, myalgia and rhinitus of 4 weeks duration. A detailed examination confirmed bilateral active anterior granulomatous uveitis with bilateral disc oedema with serous retinal detachment. Multimodal imaging examination was carried out with nideks mirante. Diagnosis in favour of vogt koyanagi harada disease was confirmed. The posterior segment was assessed for various changes in acute and remission phase of vogt koyanagi harada disease with fundus fluorescein angiography, fundus autoflourescence, retroillumination and optical coherence tomography. Thickness and structural change related to central macula thickness, retinal pigment epithelium and choroid were assessed pre and post treatment with additional support of optical coherence tomography and retroillumination. Both these techniques were able to document a greater value change pre and post treatment in these structures. Hence we conclude the need to include these techniques in retinal pigment epithelium and choroidal assessment in vogt koyanagi harada disease.

Keywords

Imaging, VKHD, RPE, Choroid

1. Introduction

Vogt Koyanagi Harada disease (VKHD) is a bilateral granulomatous uveitis which is frequently associated with exudative retinal detachment. Extra-ocular manifestations may form part of disease process presenting as vitiligo, poliosis, alopecia, dysacusis with involvement of cerebrospinal fluid noticed as pleocytosis [1]. It commonly affects individuals, in the second to the fifth decade of life, of pigmented races of Asian, Hispanic, American Indian and Asian Indian descent with a female preponderance. [1-3].

The disease is believed to be an auto-immune disorder with a T-cell mediated autoimmune response against the melanocytes, melanin and retinal pigment epithelium (RPE) [4]. Recent evidence points towards the utility of the RPE layer as a biomarker for the choroidal activity and inflammation in the acute stage of VKHD [5].

The RPE and the choroid were evaluated in a case of a 48 year old patient diagnosed with VKHD using Fundus Fluorescein Angiography, Optical Coherence Tomography, Fundus Auto-fluoresence and Retro-imaging and found a direct co-relation between the choroidal thickness and RPE reflec-

*Corresponding author: drda198591@gmail.com (Deepesh Arora)

Received: 22 April 2024; **Accepted:** 13 May 2024; **Published:** 30 May 2024

tivity with the inflammation noted in the disease.

2. Case Report

A 48 year old dark skinned North Indian male presented to us with a history of bilateral visual decline since the past 3 weeks associated with features of headache and myalgia of 4 weeks duration. There was no history of any prior medical or ocular consultation.

Examination revealed a best corrected visual acuity (BCVA) of 6/24 in the right eye (OD) and 6/60 in the left eye (OS) with an intra-ocular pressure of 18mmHg in both eyes. Ocular examination confirmed bilateral granulomatous anterior uveitis with 1 plus cells and flare and mutton fat keratic precipitates (KPs) in both eyes. Posterior segment examination showed vitreous cells 1+ associated with a bilateral disc swelling, serous retinal detachment and presence of bilateral retinal folds extending from disc to macula (Figures 1 and 2). Physical evaluation revealed nuchal rigidity, however there was no evidence of any hypo-pigmented skin lesions or tinnitus.

3. Materials and Methods

A Fundus fluorescein angiography was carried out which revealed blurred optic disc margins depicting leakage, multifocal pin point leaks seen at juxtapapillary and posterior pole (Figures 3 and 4) in the late phase. The periphery showed active leaks from terminal vessels extending to ora serrata (Figures 3 and 4). Fundus auto-flourescence (FAF) distinctively revealed hyper auto-fluorescence at posterior pole of both eyes highlighting RPE (Retinal pigment epithelium) involvement (Figures 5 and 6).

Retro-imaging was carried out which revealed the presence of abnormally elevated leaf pattern area of elevated retina at the posterior pole and radiating fine foveal folds suggesting RPE involvement (Figures 7 and 8).

Optical coherence tomography (Optovue - Spectral domain OCT) showed serous neurosensory detachment divided into multiple compartments by fibrous septa and presence of intra-retinal fluid accumulation appearing as cyst formation (Figures 9 and 10).

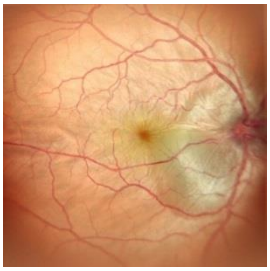

Figure 1. *Fundus OD shows disc swelling, serous retinal detachment at posterior pole with presence of retinal folds extending from disc to macula.*

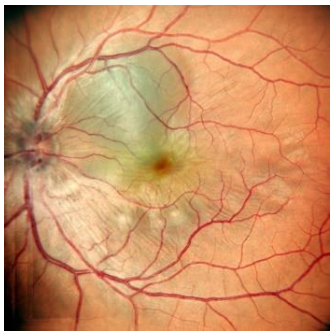

Figure 2. *Fundus OS shows disc odema with multiple pockest of serous retinal detachment involving macula.*

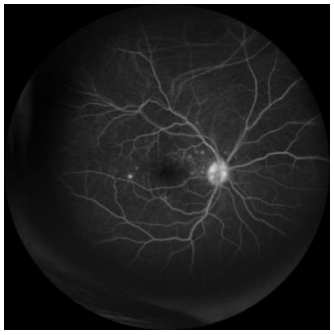

Figure 3. *Fundus fluorescein angiography OD revealed disc leakage with blurred optic disc margin, multifocal pin point leaks seen at juxtapapillary and posterior pole.*

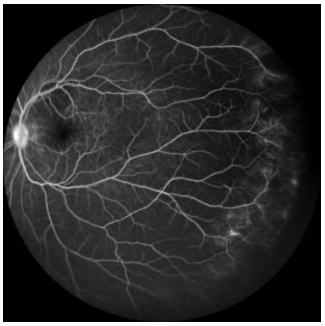

Figure 4. *FFA OS periphery shows active leaks from multiple terminal vessels extending to ora.*

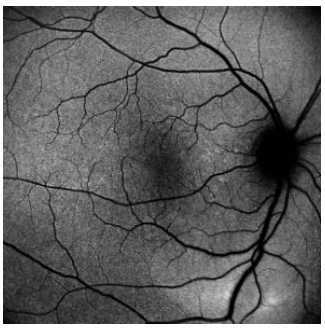

Figure 5. *Fundus auto-flourescence (FAF) OD distinctively revealed hyper auto-fluorescence at posterior pole highlighting RPE (Retinal pigment epithelium) involvement.*

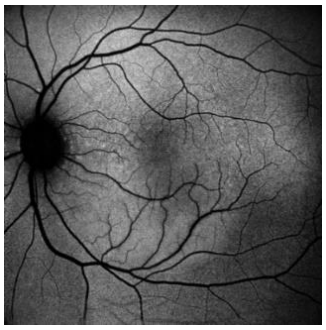

Figure 6. *Fundus auto-flourescence (FAF) OS revealed hyper auto-fluorescence at posterior pole confirming retinal pigment epithelium involvement.*

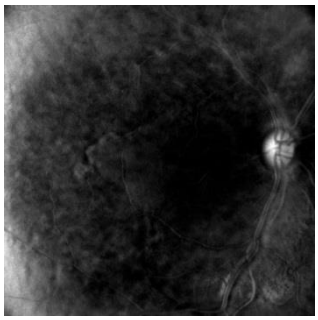

Figure 7. *Retroillumination image of acute VKHD OD shows disc florescence and a large posterior pole leaf pattern area of hypoflourescence suggesting RPE involvement with patchy hyperflourescent areas of unaffected RPE surrounding it.*

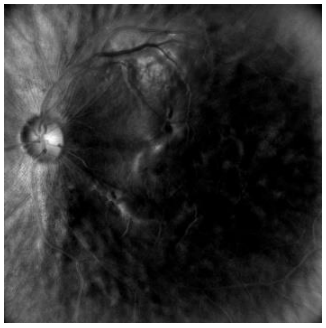

Figure 8. *Retroillumination image of OS with acute VKHD showing detailed disc flourescence with large well demarcated posterior pole hypoflourescent area of RPE involvement surrounded by normal hyperflourescent pigment epithelium.*

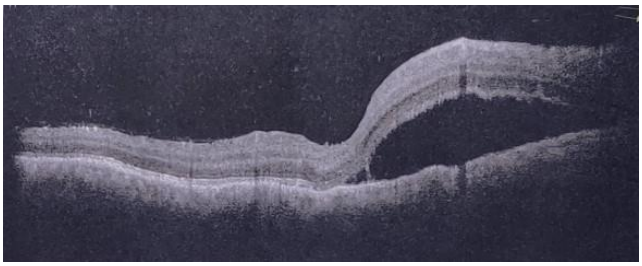

Figure 9. *OCT – Macula OD shows intra-retinal odema, neurosensory detachment (NSD), bacillary layer detachment, subretinal hyperreflective dots, choroidal hyperreflective dots and retinal pigment epithelium vacuolation.*

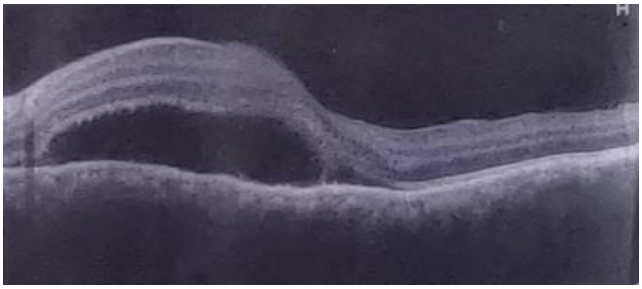

Figure 10. *OCT –Macula OS shows bacillary layer detachment, subretinal and choroidal hyperreflective dots more prominent in this eye.*

A clinical diagnosis of VKHD was made and intensive topical steroid was started with (prednisolone acetate 1%) 1 hourly application, a mydratic-cycloplegic combination (atropine sulphate 1%) 3 times a day was also initiated for pain relief and also to prevent development of synechiae. Three consecutive doses, over the course of 3 days, of methylprednisolone 1gm/day were administered intravenously in 200 ml of 20% dextrose normal saline (DNS) over 3 hours. This was followed by oral prednisolone tablets (1 mg/kg/body weight) once daily slowly tapered over 3 months to a dose less than 10mg/day.

An immunomodulator namely Mycophenolate Mofetil (MMF) in dosage of 500 mg was started in single application for one week and subsequently increased to three times a day with a strict watch on liver function test. After 3 weeks the BCVA was OD 6/9 and OS 6/12. Posterior pole depicted bilateral hyperaemic disc with pigmentation, 360 degree radiating foveal retinal folds and a large area of pigmentary disturbance at posterior pole with hypereflective outline of resolved subretinal fluid at posterior pole with pigmentary disturbance (Figures 11 and 12). FAF showed disappearance of hyper-autoflourescence at posterior pole to be replaced by hypo-autoflorescence with patchy hyper-autoflourescence at the borders (Figures 13 and 14) (suggestive of RPE disturbance). Retroillumination showed a recovery phase of VKHD depicted by resolution of the area of elevated RPE (Figures 15 and 16). The area of RPE elevation was better demarcated on the Retro-illumination photographs as compared to the colour fundus or the auto-fluoresence images. OCT showed resolution of large cystic spaces, the septae and intraretinal fluid with persistence of bilateral minimal subfoveal subretinal fluid (Figures 17 and 18). Medications were tapered after assessment of disease status involving anterior chamber and posterior segment with strict watch on retino-choroidal presentation. The OCT-macula imaging was utilized to calculate subfoveal choroidal thickness (Table 1) and optic nerve head dimension (Table 2). The retro-imaging was utilized to calculate the change in RPE elevation pre and post treatment (Table 3).

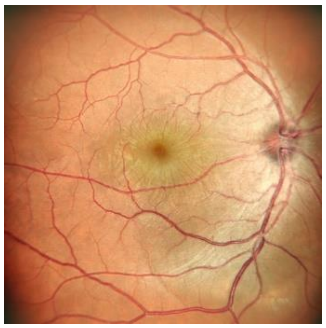

Figure 11. *Fundus photo OD 3 weeks into post treatment shows hyperemic disc and radial foveal folds with a large area of RPE at posterior pole involved in acute VKH disease.*

Figure 12. *Fundus photo OS 3 weeks into post treatment shows a hyperemic disc with radial folds and a well demarcated area of RPE previously involved in acute VKHD seen at posterior pole.*

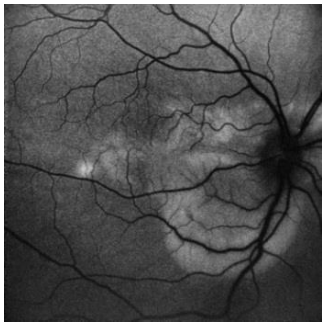

Figure 13. *FAF photo OD shows a large leaf like area of hypoflourescence depicting RPE involvement seen at posterior pole.*

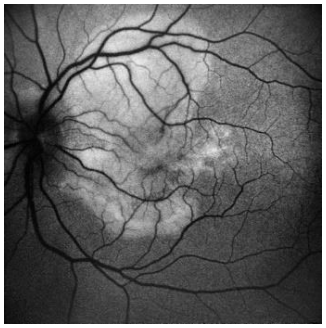

Figure 14. *FAF image OS shows a large posterior pole hypoflourescent area extending outside of superior arcade and involving fovea correlating to poor visual recovery.*

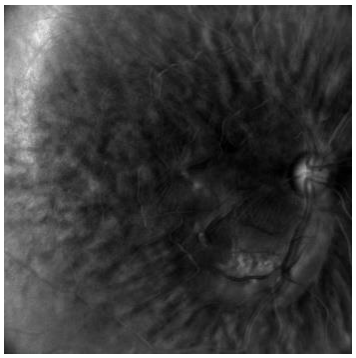

Figure 15. *Retroillumination image OD shows hyperflourescent posterior pole interspersed with recovering hypoflourescent areas seen adjacent to inferior arcade.*

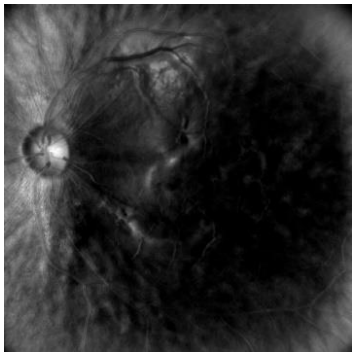

Figure 16. *Retroillumination image OS during 3 week recovery phase shows large RPE defect as hypoflourescent patch at posterior pole.*

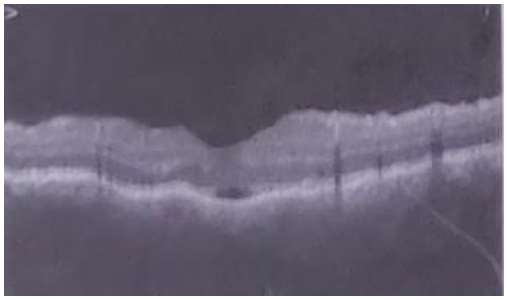

Figure 17. *OCT- Macula VKHD early post recovery with presence of subretinal fluid, reduced presence of subretinal and choroidal hyperreflective dots with altered RPE reflectivity.*

Figure 18. *OCT-Macula OS reveals irregular inner and outer retinal layers with loss of architecture, presence of subretinal fluid, persistence of choroidal hyperreflective dots.*

4. Results

The subfoveal choroidal thickness was calculated at the fovea on the OCT machine by drawing a perpendicular line extending downwards from the RPE-Bruchs membrane complex to the outer margin of the choroid as visible on the EDI-OCT. The similar process was repeated for the other eye.

Table 1. *Comparison of subfoveal choroidal thickness in the Right and the Left eye prior to and following treatment.*

Subfoveal Choroidal Thickness		
	Right Eye	**Left Eye**
At Presentation	593 microns	486 microns
After Therapy	430 microns	410 microns

A note was also made of the horizontal and vertical margins of the optic nerve head whose dimensions came out to be as mentioned below. These measurements were later used to calculate the area of the RPE elevation on the retro-imaging.

Table 2. *The horizontal and vertical measurements of the optic nerve head in the right and the left eyes.*

	Right Eye	**Left Eye**
Horizontal Diameter	1382 microns	1504 microns
Vertical Diameter	1461 microns	1636 microns

The RPE elevation was calculated on en-face retinal imaging by marking the outlines of the elevated RPE on (Image 7 and 8) and calculating the area hence forth. The disc margins were used as reference and the horizontal and vertical diameters calculated as above were used for calculating the area of involvement.

Table 3. *Comparison of RPE elevation and NSD in the Right and the Left eye prior to and following treatment.*

	Right Eye	**Left Eye**
At Presentation	42.906 mm^2	55.443 mm^2
After Therapy	14.661 mm^2	19.931 mm^2

5. Discussion

Optical Coherence Tomography is highly informative imaging tool in documenting changes at level of retinal pigment epithelium and choroid. Our patient showed subfoveal increase in choroidal thickness during acute inflammatory phase of which showed subsequent resolution following immunosuppressive therapy [6]. Similar findings with emphasis on recurrence of choroidal thickness have been documented elsewhere postulated by acute disease leading to inflammatory infiltration with increased exudation involving choroid. The outer layers of the choroid are principally involved in VKHD [7-9]. The choriocapillaris suffers from metabolic stress and hypoxemia due to insufficient perfusion the disease progresses, this leads to disturbance in its function of providing nutrition, oxygen, ions with water to RPE and outer retina [10].

A single-centre retrospective observational study showed changes in retinal pigment epithelium (RPE) reflectivity immediately above the choroid in eyes with acute VKH disease, as well as the strong association between RPE reflectivity and VKH disease recurrence [11]. With subsidence of choroidal inflammation one gets to notice histological change as focal loss of RPE [12, 13]. In chronic cases of VKHD, hyperplastic RPE may appear clinically as subretinal fibrosis, [13] confirmed on OCT. This is a significant prognostic indicator related to visual acuity in VKHD. A specific change related to melanin accumulation in the RPE at the location of granular hyper near infra-red-autoflourescence has been detected by multicontrast-OCT supporting in evaluation of RPE changes in chronic VKHD [14]. A similar change visible in convalescent stage shows focal RPE melanin accumulation (FRMA) derived from RPE melanin and sunset glow fundus derived from choroid melanin as visible changes [15]. RPE undulations seen in acute stage of VKHD is a predictor of posterior recurrences and poor visual outcomes after high-dose steroid therapy in VKHD [16]. Presence of hyper-reflective outer nuclear layer (HROL) is also poor prognostic indicator of thinning and atrophy of outer retinal layers [17].

Bacillary layer detachment (BLD) constitutes a commonly seen feature in eyes with acute stage of VKHD. Defect is seen at the level of photoreceptor layer creating a split at the inner segment myoid [18]. Serial swept source OCT has been efficient in detecting changes in acute and recovery phase in both bacillary layer and photoreceptors [17]. The role of pulse steroids in re-establishing anatomical and functional integrity and speed of recovery of bacillary layer has been reported elsewhere [19]. “Kwak JJ et al” reported that patients with BLD have high recurrence rate requiring more frequent and thorough follow up in comparison to those without BLD [20].

6. Conclusion

The Retinal Pigment Epithelium plays a pivotal role in maintaining the anatomical and functional integrity of the neurosensory retina. In cases of posterior uveitis as seen in Vogt Koyanagi Harada disease, an inflammatory assault is

noted in the outer choroidal layers and the RPE which results in both anatomical and physiological changes in the retina. The degree of inflammation directly correlates with the RPE changes and the morphological phenomenon as documented above. Immunosuppressive therapy either with steroids or immunomodulator agents helps in decreasing the inflammatory response and in restoring normalcy in the diseased retina. However, in cases of chronic inflammation this may lead to vision threatening sub-retinal fibrosis and scarring. Hence, accurate assessment of the choroid and the RPE via multimodal imaging helps in prognosticating the disease severity and follow-up.

Abbreviations

VKHD	Vogt Koyanagi Harada Disease
FAF	Fundus Auto-Flourescence
OCT	Optical Coherence Tomography
MMF	Mycophenolate Mofetil
RPE	Retinal Pigment Epithelium
BLD	Bacillary Layer Detachment
HROL	Hyper-Reflective Outer Nuclear Layer

Author Contributions

Deepesh Arora: Writing – review & editing, Writing – original draft

Anuj Sharma: Conceptualization, Investigation, Supervision, Writing – review & editing

Devesh Sharma: Data curation, Formal Analysis, Funding acquisition, Methodology, Resources, Validation, Visualization

Dinesh Sharma: Supervision, Validation, Visualization

Conflicts of Interest

The authors declare no conflicts of interest.

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