Rebound inflammation after an intravitreal injection in Vogt–Koyanagi–Harada syndrome

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A 43-year-old male with chronic Vogt–Koyanagi–Harada syndrome (VKH) presented with subfoveal choroidal neovascular membrane (CNVM) in the right eye with no evidence of active inflammation. He underwent intravitreal bevacizumab and dexamethasone injections. Postinjection he developed fresh keratic precipitates and exudative retinal detachment (RD). He received two more bevacizumab injections with oral corticosteroids and immunosuppressants causing resolution of exudative RD with scarred CNVM. We report this case to highlight that intravitreal injection may act as a trigger for rebound inflammation in VKH patients and may require anti-inflammatory drugs to be started even in the absence of an active inflammation.

Key words: Choroidal neovascular membrane, exudative retinal detachment, intravitreal injection, Vogt–Koyanagi–Harada syndrome

Vogt–Koyanagi–Harada syndrome (VKH) is a bilateral diffuse granulomatous panuveitis associated with exudative retinal detachment (RD), subretinal fibrosis, choroidal neovascular membrane (CNVM) formation and associated neurological and cutaneous manifestations.[1] CNVM is found in 2%–15% of VKH patients.[2] We report a case of chronic VKH with CNVM where the intravitreal injection given for the treatment of the CNVM triggered active inflammation.

Case Report

A 43-year-old male presented with the complaints of pain, redness, and diminution of vision in the right eye for the last 1 month. No relevant systemic history was reported. Best-corrected visual acuity (BCVA) in the right eye was 6/9, N6 and in the left eye was 6/6, N6. Applanation tonometer recorded an intraocular pressure of 16 mmHg in both the eyes. Anterior segment examination of the right eye showed posterior synechiae at 4 o'clock, and the left eye was within normal.

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Fundus examination of both the eyes showed hyperemic disc with pockets of subretinal fluid (SRF) involving the macula in both the eyes, sparing the fovea in the left eye. Fundus fluorescein angiography (FFA) showed disc leakage in both the eyes with multiple pinpoint leaks and pooling of the dye in the late phase [Fig. 1].

The patient was diagnosed as VKH and started on intravenous methylprednisolone (IVMP) 1 g/day for 3 days followed by oral corticosteroids (1 mg/kg wt.) and azathioprine (1.5 mg/kg wt.). Topical atropine 1% and prednisolone acetate 1% eye drops were added.

Follow-up at 4 months, the BCVA was 6/6, N6 with no SRF in both the eyes. The patient was continued on oral azathioprine and was stopped after 1 year due to deranged liver functions (LFT). He was then lost to follow-up.

Follow-up at 3 years, he presented with diminution of vision and seeing a central black spot in the right eye. There was no history of pain and redness in either eye. The BCVA of the right eye was 6/60, N36 and 6/6, N6 in the left eye. Anterior segment examination of the right eye showed posterior synechiae at 4 o'clock with no evidence of inflammation in either eye. Fundus examination of the right eye showed a subfoveal CNVM. FFA of the right eye showed a minimal hot disc with early hyperfluorescence and a late leakage at the macula suggestive of an active subfoveal CNVM [Fig. 2]. Optical coherence tomography (OCT) of

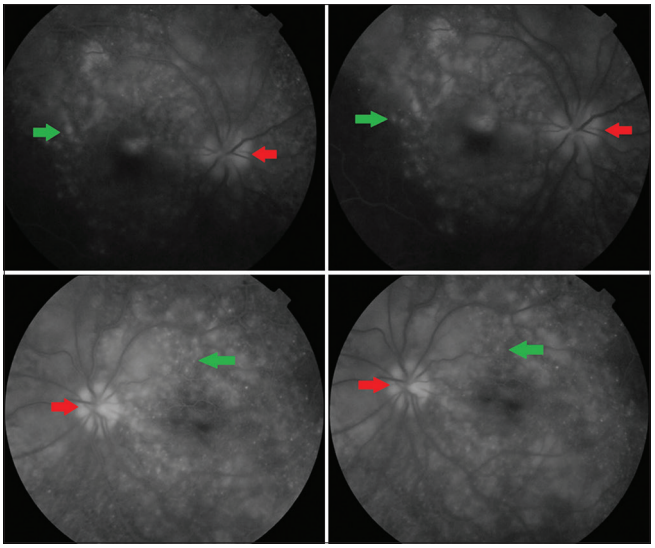

Figure 1: Fundus fluorescein angiography showing hyperemic disc leakage (red arrow) and multiple pin point leakages (green arrow) in both the eyes

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the right eye showed a subretinal high reflective lesion with intraretinal cystic spaces and a pocket of SRF [Fig. 3a-c]. Intravitreal injection of bevacizumab (1.25 mg/0.05 ml) with dexamethasone (400 µg/0.1 ml) was given in the right eye.

Follow-up at 3 days, the patient complained of mild pain in the right eye. Anterior segment examination showed fresh keratic precipitates (KPs). Fundus examination showed exudative RD in the right eye which was confirmed on ultrasound B-scan. There was no evidence of SRF in the left eye. Color fundus photo was hazy due to fresh KPs and poorly dilating pupil secondary to posterior synechiae formation and improper focusing secondary to exudative RD. The patient was photophobic and non-cooperative for performing FFA. An OCT was done of the right eye which showed increased SRF suggestive of exudative RD [Fig. 3d-f]. He was treated with IVMP 1 g for 3 days followed by oral corticosteroids and azathioprine as LFT was normal.

Follow-up at 4 months after three intravitreal injections of bevacizumab and dexamethasone, the BCVA in the right eye was 6/36, N36. Fundus examination of the right eye showed a scarred CNVM which was confirmed on OCT [Fig. 4]. Tapering dose of oral corticosteroids and immunosuppressive therapy was continued.

Follow-up at 1 year, the BCVA in the right eye is 6/36, N36 with the presence of scarred CNVM and no recurrence of inflammation.

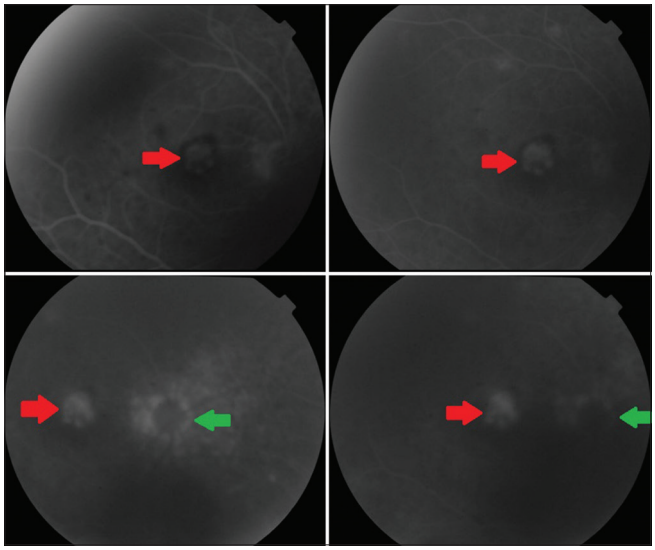

Figure 2: Fundus fluorescein angiography of the right eye showing a classic choroidal neovascular membrane (red arrow) with minimal disc leakage (green arrow)

Discussion

VKH syndrome is a bilateral diffuse granulomatous uveitis associated with neurological and cutaneous manifestations. It shows a good response to systemic and periocular steroids with a good visual prognosis in most of the patients. Late complication such as CNVM formation is reported in 2%–15% patients and is associated with poor visual prognosis.[2]

Chronic inflammatory insult in VKH patients gradually destroys the choriocapillaris and Bruch's membrane leading to CNVM formation. Vascular endothelial growth factor (VEGF) is one of the causative factors for increased vascular leakage and neovascularization.[3] Intravitreal anti-VEGF alone or with triamcinolone have been effective in managing CNVM secondary to VKH.[4-6] Our patient was a known case of VKH on immunosuppressive therapy for 1 year and no history of recurrence of inflammation for subsequent 2 years when he was lost to follow-up. However, he then presented with an active CNVM in the right eye with no evidence of active inflammation. He was treated with an intravitreal injection given through the pars plana, following which 3 days later, there was rebound inflammation in the form of fresh KPs and exudative RD. He responded to IVMP followed by oral corticosteroids and immunosuppressive therapy leading to complete resolution of the exudative RD. Subsequently, two more intravitreal anti-VEGF and dexamethasone injections were given under oral steroid cover resulting in scarring of the CNVM with no evidence of recurrence of active inflammation. However, in our patient, we did not start any anti-inflammatory drugs at the time of presentation as there was no evidence of active inflammation. Pathogenesis of VKH includes a cell-mediated autoimmune process driven by T-lymphocytes directed against self-antigens associated with melanocytes of all organ systems in genetically susceptible individuals,[7] even an indirect trauma to melanocyte-containing tissue may induce an inflammatory response in the eye.[8] Sensitization to melanocytic antigenic peptides by cutaneous injury or viral infection has been proposed

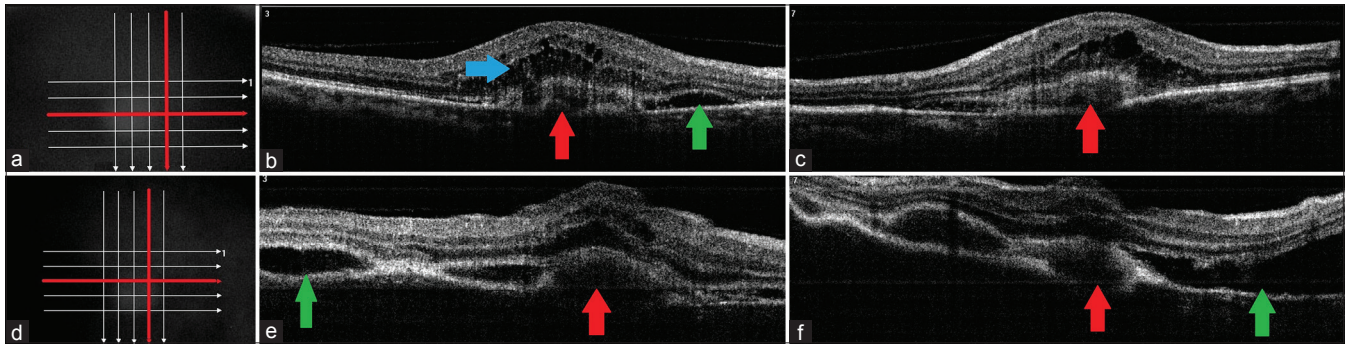

Figure 3: (a-c) Optical coherence tomography of the right eye showing subretinal choroidal neovascular membrane complex (red arrow) along with intraretinal cystic spaces (blue arrow) with subretinal fluid (green arrow) through the horizontal and vertical scans. (d-f) Optical coherence tomography of the right eye showing increase in subretinal fluid (green arrow) with choroidal neovascular membrane complex (red arrow) postintravitreal injection through the horizontal and vertical scans

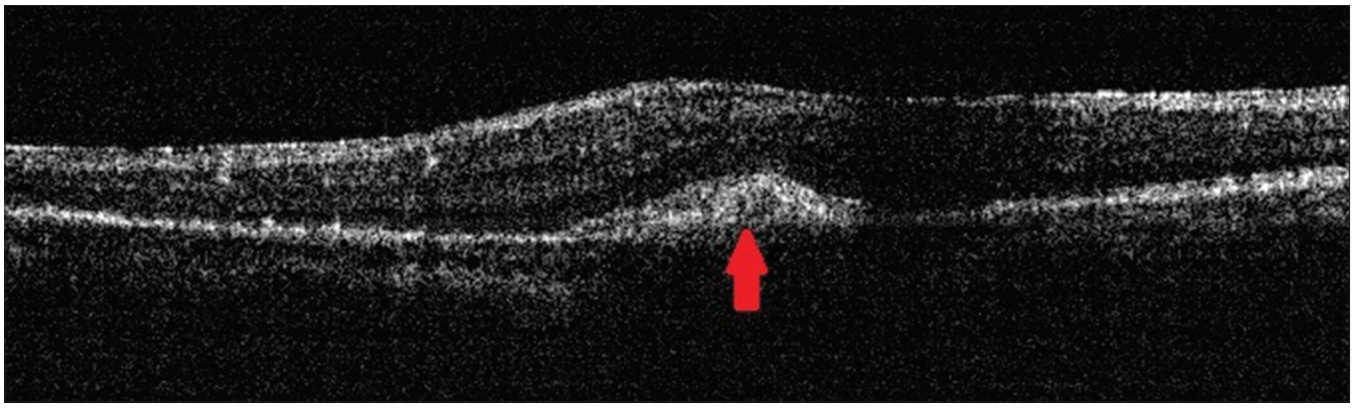

Figure 4: Optical coherence tomography of the right eye showing scarred choroidal neovascular membrane (red arrow)

as a possible trigger of this autoimmune process.[7] We postulate that the intravitreal injection through the pars plana released the uveal melanocytes in the eye which caused stimulation of the T-lymphocytes and triggered an active inflammation with an acute onset of fresh KPs and an exudative RD.

On review of literature, two cases of onset of VKH after closed head trauma have been reported,[7] however, to the best of our knowledge, this is the first report of acute onset of inflammation in VKH after an intravitreal injection.

Conclusion

We report this case to highlight that an intravitreal injection through the pars plana route may act as a trigger for inflammation in a VKH-CNVM patient; therefore, even in the absence of any signs of active inflammation, a better therapeutic approach would be to start oral corticosteroids and immunosuppressants before giving an intravitreal injection. The limitation includes that we have a single case and more number of cases are required to optimize the therapeutic regime.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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