Commentary: Dexamethasone intravitreal implant therapy in Vogt–Koyanagi–Harada disease

Management of a chronic, relapsing non infectious uveitis with long-term systemic steroid treatment with or without immunomodulatory therapy (IMT) remains a bugbear for both treating physicians and patients. Inefficacy of the drug in controlling the inflammation as well as patient's factors like comorbidity, drug dependency, and noncompliance may result in the treatment failure or multiple recurrences of uveitis. Most of the comorbidities can be well managed with additional therapy or short term withhold or change of IMT and compliance can be improved with good counselling. However, despite all efforts situation may arise where systemic therapy cannot be administered to control the uveitis, and a local therapy is the only option. Various steroid preparations and more recently even biologics have been used as periocular or intraocular injections in the treatment of uveitis.[1] Choice of the drug depends on the duration of action and the patient's affordability.

The authors in their study "Long-term efficacy of dexamethasone intravitreal implant in the treatment of Vogt-Koyanagi-Harada (VKH) disease relapsing posterior uveitis" presented a series of 16 patients (29 eyes) of Vogt–Koyanagi–Harada (VKH) disease with systemic steroid and/or immune-suppressive agents comorbidity comorbidity, dependency, and noncompliance, which were successfully treated with intravitreal dexamethasone 0.7 mg implant (Ozurdex; Allergan Inc., CA, USA). Overall, their patients enjoyed systemic steroid free and/or IMT free control of their disease avoiding unwanted systemic side effects of steroids and IMT, although manageable ocular adverse effects such as high intraocular pressure, cataract progression including a case of intralenticular inadvertent insertion of the implant were seen. Those adverse effects should be judged against the comorbidities the patients had due to systemic medications.

The aim of the prolonged steroid therapy and a long-term IMT in VKH disease is to decrease the number of recurrences. Errera *et al*.[2] reported 73.8% recurrences in patients treated with steroids and IMT. This is comparable with the index study combining their anterior (58.3%) and posterior (27.6%) recurrences. Recurrences of anterior uveitis should not be underestimated, as they may indicate subclinical inflammation in the posterior segment. Imaging studies with indocyanine green angiography may reveal occult signs of inflammation such as progression of hypofluorescent lesions suggestive of choroidal granulomas. Appearance or progression of the sunset glow fundus is also a sign of inadequate treatment. Whether in the index study author's cases with recurrence of anterior uveitis harboured subclinical inflammation in the choroid or had progression of the sunset glow fundus remained unknown. Authors have also acknowledged that the number of recurrences before and after the implant were not studied in their series. This data will be useful to know if the implant therapy successfully prevented or reduced the number of recurrences. The onset of action of IMT requires several months; this explains more recurrences of posterior uveitis within 6 months and less thereafter as observed by Errera *et al*.[2] It would be interesting to know if the reverse can be seen with the dexamethasone implant therapy as the implant starts degrading over few months.

"Probable VKH" or "limited VKH" as reported by Chew *et al*.[3] may not have recurrence for 3–4 years once treated with systemic steroids and without IMT. Post corona virus disease -2019 (COVID-19), post vaccination, or drug-induced VKH-like disease may also have limited duration of the disease.[4-6] Index study also included patients presented during the COVID-19 pandemic. It remained unknown if any cases had preceding history of vaccination or COVID-19 infection. In such subset of VKH patients, the implant therapy can also be beneficial to avoid systemic steroid therapy "and long term IMT".

The main concern with the implant therapy lies in the management of associated systemic signs and symptoms of VKH disease. Persistence of headache, tinnitus, and progression of vitiligo would be a major concern when the disease is treated with local therapy only. Author's cases also had neurological and auditory symptoms such as headache and tinnitus in 33.3% and integumentary findings such as alopecia and vitiligo in 31.2%. It remained unknown whether these systemic manifestations of VKH progressed in the absence of systemic therapy.

Both VKH and sympathetic ophthalmia share a common pathogenesis and course of the disease. Several reports of sympathetic ophthalmia have been reported following vitreo-retinal surgery.[7] Although unreported, a theoretical risk of uveal antigen exposure to the immune system following

intraocular injection of the implant remains a distant possibility. Conversely, multiple dexamathsone implant as a sole therapy have also been used in the treatment of sympathetic ophthalmia.[8]

Overall, intravitreal dexamethasone implant therapy without systemic steroids and IMT can be a good option in noncompliant patients or patients with serious side effects due to systemic medications. It is also a good choice in "limited VKH," "incomplete VKH," or drug-induced VKH-like disease or in combination with IMT in "complete VKH" syndrome. The cost, invasive procedure, and inability to control systemic manifestations of the disease could be the noteworthy limitation of implant only therapy.

Ankush Kawali, Sanjay Srinivasan, Padmamalini Mahendradas, Rohit Shetty[1]

Departments of Uveitis and Ocular Immunology, [1]Cornea and Refractive, Narayana Nethralaya, Bangalore, Karnataka, India

Correspondence to: Dr. Ankush Kawali, Narayana Nethralaya, Chord Road, Rajajinagar, Bangalore, Karnataka, India.
E-mail: akawali332@gmail.com

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