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Short-Term Successfully Management Therapy of Neovascular Glaucoma in Vogt- Koyanagi- Harada Syndrome: A Case Report

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ABSTRACT- Neovascular glaucoma (NVG) is one of many complications in Vogt-Koyanagi-Harada Syndrome (VKHS) patient. It will potentially blind if it is not treated properly A – 44 year old female presented to Hasanuddin University Hospital with decreased of vision since four months prior and an intermittent headache. Both eyes visual acuity showed hand movement, with IOP were 53 and 43 mmHg respectively. We found chronic uveitis, vitritis, exudative retinal detachment in BE and iris neovascularization only in right eye (RE). Patient received systemic methylprednisolone and carbonic–anhydrase also topical steroid and ß-blocker. Exudative retinal detachments resolved in both eyes after management. Iris neovascularization diminished after an intracameral anti VEGF injection. Trabeculectomy with Mitomycin (MMC) performed in BE within 1-month interval. Synechiolisis, membranectomy and cataract extraction with implantation intraocular lens performed in LE 2 months later. Best corrected visual acuity (BCVA) in LE improved to 20/30 but decreased to 20/400 in 4 months. During 4 months follow-up, BE IOP remained stable in 16 mmHg and 11 mmHg respectively. Inflammation management is needed before any surgical procedure. Anti VEGF injection performed to deteriorate new vessels for transient effect and change in bleb vascularity. Trabeculectomy + MMC performed to enhance filtration and improve long-term bleb function. Visual acuity decreased after 4 months presumably because the chronic recurrent phase of VKHS. Managing ocular complication in VKHS is challenging due to chronic recurrences. An adequate inflammation therapy and comprehensive management are needed for controlling visual outcome and IOP in VKHS patient.

Keywords: **Vogt-Koyanagi-Harada Syndrome, Neovascular Glaucoma, anti-VEGF**

I. INTRODUCTION

VKHS is a systemic autoimmune disorders in which T- cell lymphocytes are directed against melanocytes, mostly in the eye, auditory, skin and integument (Sakata et al., 2014; Pandey et al., 2016; Almobarak et al., 2016). The most common complications associated with chronic inflammation such as cataract, glaucoma integument (Sakata et al., 2014; Pandey et al., 2016; Almobarak et al., 2016). Neovascular glaucoma may occur in VKHS because of the inflammation with or without retinal ischemia. Anti–VEGF known as an inhibitor of the pathologic neovascularization, therefore it has the effectiveness in controlling intraocular pressure in neovascular glaucoma (AlBloushi et al., 2021). Hereby we report the management therapy in vogt koyanagi harada syndrome with cataract and neovascular glaucoma complications.

CASE REPORT

A–44 year old female referred to our Eye Clinic with the main complain decreased of her vision associated with intermittent headache four months prior. No history of trauma or surgery. Two months after those symptoms, she had focal hair loss (alopecia), whitish hair and eyelashes (poliosis), followed by hearing loss both of her ear.

Both Eyes visual acuity showed hand movement with IOP 53 mmHg and 43 mmHg respectively. The eye examination revealed, mild redness at both conjunctiva, keratic precipitates, shallow anterior chambers with Van Herrick 1 and 2 respectively, iris were bombans with multiple synechiae anterior and posterior, and the opacification of the lenses (fig. 2).

Gonioscopy (fig.3) revealed at RE showed schwalbe's Line for the whole quadran, and LE showed multiple peripheral anterior posterior synechiae. Ocular ultrasonography showed bilateral exudative retinal detachments. Laboratory findings such as complete blood count, TORCH infection were within normal limit. Chest x-ray also showed normal limit. Patient consulted to the ENT department and an audiogram revealed moderate to severe bilateral sensorineural hearing loss.

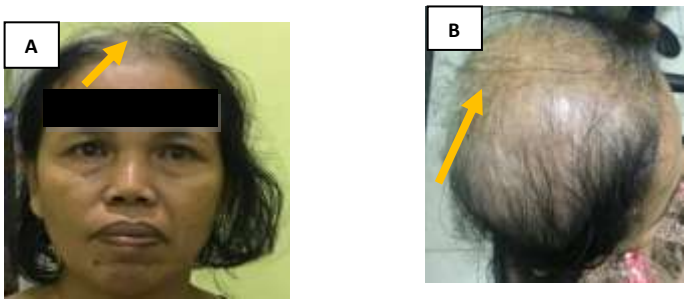


Figure 1. Both pictures showed alopecia (hair loss) and poliosis (whitish hair) of the scalp.

Based on the clinical manifestation such as an intermittent headache with no history of trauma or surgery, decreased vision, poliosis, alopecia, hearing impairment, chronic uveitis, exudative retinal detachment and laboratory findings, the diagnosis of VKHS was made.

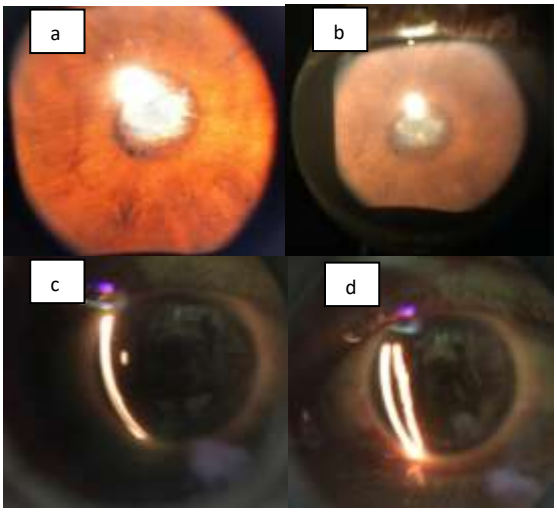


Figure 2. (A, B) Both RE and LE showed 360° posterior synechiae. (C) RE showed anterior chamber's depth was Van Herrick 1 and (D) LE showed anterior chamber's depth Van Herrick 2.

Infection and immunology subdivision gave an oral methyl prednisolone 16 mg/8 hours and gradually tapered for three months with topical prednisolone acetate eye drop/4 hours and β-blocker drugs, Timol eye drop/12 hours and an oral carbonic anhydrase inhibitor/12 hours with KSR 600 mg/24 hours. The IOP in LE remained stable only with anti-glaucomatous medications.

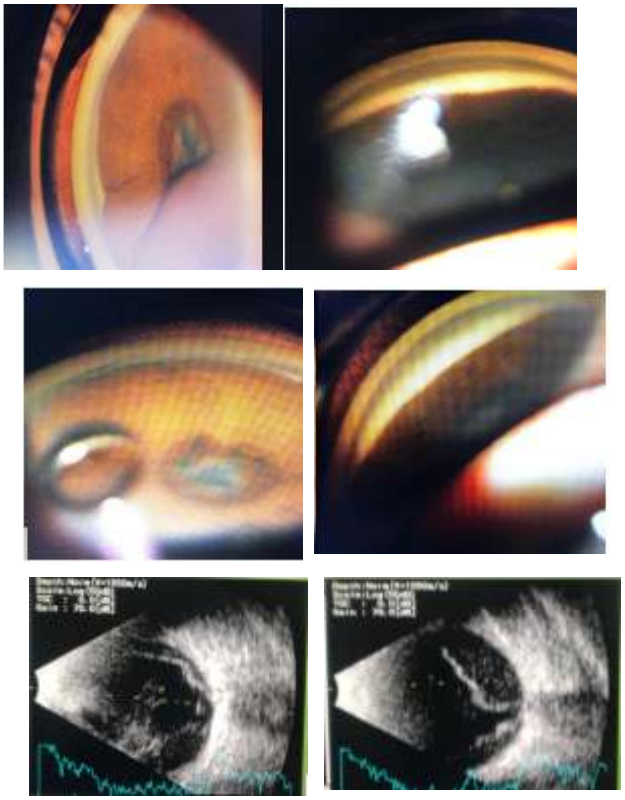
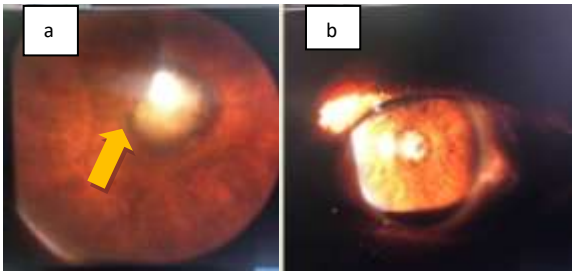


Figure 3. (upper and middle) RE and LE Gonioscopy showed schwalbe's line and Peripheral anterior synechiae. (bottom) initial ocular ultrasonography showed bilateral retinal detachments

Three months later, patient presented to the eye clinic with rubeosis iris developed in RE with ocular ultrasonography control confirmed that bilateral exudative retinal detachments had reabsorbed in BE (Fig.4). Visual acuity in BE still showed hand movement and IOP remained at 65 mmHg and 51 mmHg respectively. Patient consulted to the glaucoma subdivision and received an add - on cycloplegic eye drop/12 hours, oral methylprednisolone tapered at 4 mg/8 hours, prednisolone eye drop for/ 6 hours, alongside with topical β - blocker /12 hours, topical carbonic anhydrase inhibitor/12 hours, and an oral carbonic anhydrase inhibitor/12 hours with KSR 600 mg/24 hours.

One month follow-up, visual acuity only improved into counting finger for BE, with IOP became 53 mmHg and 11 mmHg, respectively and therefore trabeculectomy with MMC was performed in LE. Patient discharged after surgery with antibiotic topical eye drops/4 hours and prednisolone eye drops/3 hours for LE, and for RE, β-blocker eye drops/12 hours, carbonic anhydrase eye drops/8 hours, cycloplegic eye drops/12 hours, oral carbonic anhydrase inhibitor/8 hours, KSR/ 24 hours and oral methyl prednisolone 16 mg/8 hours were given.

One month interval VA remained the same, with IOP 60 mmHg and 16 mmHg respectively**.** An oral Methyl prednisolone tapered into 12mg/8h, and an 0,05 cc intracameral and subconjunctiva anti-VEGF was performed in her RE, rubeosis iris in RE dissolved then trabeculectomy with MMC was performed.



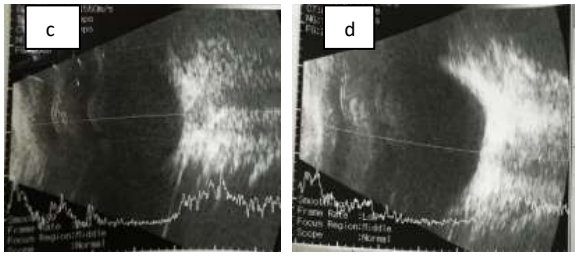


Figure 4. (a). Two months after the corticosteroid was given, rubeosis iris (yellow arrow) developed in her RE. (b). LE complicated cataracts (c and d) Ocular ultrasonography showing exudative retinal detachments had reabsorbed after 3 months of corticosteroid topical and systemic.

Two days after, patient controlled to our clinic, VA remained the same hand movement and counting finger respectively. IOP in RE elevated into 54 mmHg, while in LE was 18 mmHg, bleb consistency was flat, so we massage but it still remained high, then operator decided to exchange the treatment into bleb repaired. Intraocular pressure remained stable for both eyes with no anti glaucoma drugs therapy, only with an oral Methyl prednisolone 16 mg/8 hours.

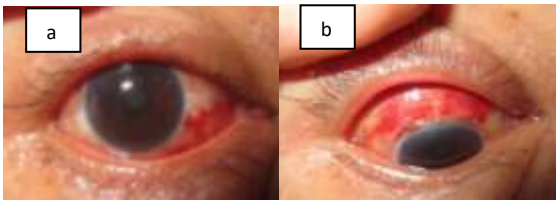


Figure 5. (a,b) Post bleb repaired day one in the right eye. Intraocular pressure decreased to 7 mmHg with medium bleb consistency.

The next month, both VA for LE remained at hand movement, while RE improved to counting finger and IOP stable 16 mmHg and 15mmHg respectively (Fig.6) so we performed a cataract extraction with implantation intraocular lens and synechiolisis and membranectomy in LE. Visual acuity improved with BCVA 20/30 and IOP remained stable in BE , both 15 mmHg and 16 mmHg respectively.

Unfortunately, due to many reasons our patients were not able to perform cataract extraction in her RE. Patient presented to our eye clinic three months after last surgery with visual acuity decreased into 20/400 in her LE, nonetheless IOP remained stable 20 mmHg and 19 mmHg in BE with no anti-glaucoma medications add-on. Slit lamp examination revealed keratic precipitate with no cells and flares in BE and RE posterior synechiae almost 360 °. Patient discharged with an oral methyl prednisolone 12mg/8 hours, prednisolone eye drops/4 hours and cycloplegic eye drops/12 hours. A chronic recurrent bilateral uveitis due to VKHS diagnosis was made.

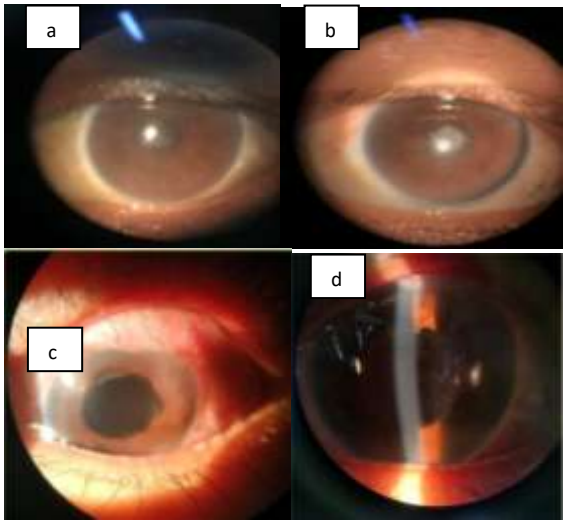


Figure 6. (a) RE one month after anti-VEGF injection + Trabeculectomy + MMC, Rubeosis had regressed. (b) LE complicated cataract (c and d) LE post operation extraction cataracts + membranectomy + synechiolisis + implantation IOL.

II. DISCUSSION

According to the Revised Diagnostic Criteria of Vogt-Koyanagi-Harada Syndrome proposed by the International Nomenclature Committee (Table 1), so our patient fulfilled the complete criteria of VKHS because there was no history of trauma (separated this to from sympathetic ophthalmica) and surgery, no clinical or laboratory result suggestive of other ocular disease, bilateral ocular involvement including bilateral panuveitis, exudative retinal detachment, with intermitten headache as a neurological sign, alopecia, poliosis and hearing impairment.

Table 1. Revised diagnostic criteria by the First International Workshop on VKH disease (Almobarak et al., 2016).

Complete disease (criteria 1 to 5 must be present)
1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis.
2. No clinical or laboratory evidence suggestive of other ocular disease entities.
3. Bilateral ocular involvement (a or b must be met, depending on the stage of disease when the patient is examined)
a. Early manifestations of disease.
– Diffuse choroiditis (focal areas of subretinal fluid, bullous serous retinal detachments)
– OR, characteristics fluorescein angiography findings AND echography evidence of diffuse choroidal thickening
b. Late manifestations of disease.
– History suggestive of prior uveitis with the above described characteristics AND, ocular depigmentation (sunset glow fundus, Sugiura sign)
– AND other ocular signs (nummular chorioretinal depigmented scars, retinal pigment epithelium clumping and/or migration, or recurrent or chronic anterior uveitis)
4. Neurological/auditory findings.
– Meningismus, OR tinnitus, OR cerebrospinal fluid pleocytosis
5. Integumentary finding (*not* preceding onset of central nervous system or ocular disease).
– Alopecia, OR poliosis OR vitiligo
Incomplete disease (criteria 1 to 3 and either 4 or 5 must be present)
Probable disease (isolated ocular disease; criteria 1 to 3 must be present)

The most common complication in VKHS are glaucoma and cataract, and glaucoma is one of the most severe complication other than cataract (Pandey et al., 2016; Almobarak et al., 2016; Ganesh et al., 2004). The more severe inflammation in the anterior chamber, more likely it is to develop in to glaucoma together with the duration of the disease, although the average time needed to develop the glaucoma has not been reported yet. Neovascular glaucoma is caused by the formation of fibrovascular membrane secondary to angiogenesis stimuly in trabecular meshwork that could obstruct the acquoeus humor outflow resulting elevated intraocular pressure (Ganesh et al., 2004; Simha et al., 2020).

The inflammation process release many cytokines such as interleukin (IL)-β, Tumor necrosis factor (TNF)-α, IL-6, IL-8, NF-kβ, TGF-β2 and VEGF which could break blood ocular barrier results in accumulation of inflammatory cells (Simha et al., 2020; Gulati et al., 2011; Katsanos et al., 2018). Those numerous cytokines also induce more VEGF to be released , and it is and therefore could increase vascular permeability and pathological angiogenesis (AlBloushi et al., 2021). Those VEGF products may diffuse into the anterior chamber through Long posterior ciliary artery, resulting pathological neovascularization in iris and corpus ciliary.

In the anterior chamber those cytokines products may result an elevated IOP due to trabeculitis, progressive synechial angle – closure, and iris bombe, those presumably could be the leading factors of elevated IOP in LE.

As mentioned before, because the cytokines induce more VEGF to be released, While in RE, the presence of neovascular glaucoma, multiple anterior and posterior synechiae also seclusio pupil and iris bombe are probably the factors in causing elevated IOP. Thereby, inhibitor product of VEGF plays an important role in treating secondary angiogenesis (Simha et al., 2020).

The ocular inflammation in our patient was quite impressive therefore our goal therapy is to treat the inflammation rapidly and aggressively. Our goals in treating Neovascular glaucoma are to treat the underlying disease, therefore not only corticosteroid to reduce the inflammation but also an Anti-VEGF both plays an important factors. Anti VEGF agents have been proven not only to cause deterioration of new vessels in the anterior chamber but also could diminish the IOP and corticosteroid to reduce the inflammation (Quek et al., 2011). Because of the rapid onset, Anti-VEGF was promoted as a standard therapy for NVG treatment (Ha et al., 2017). An anti-VEGF used in our patient was bevacizumab. Bevacizumab is a humanized monoclonal antibody against towards all VEGF subtypes ((Ha et al., 2017) Bevacizumab widely used to treat VEGF-related conditions, here in our patient was an inflammation process (Ha et al., 2017). Although ranibizumab likely said to be more effective, bevacizumab had lower cost compare to ranibizumab. In most cases, an intracameral injection shows shorter half-life duration than those performed intravitreal injection. Nevertheless an intracameral injection can be performed in the presence of media opacities and studies reported that an intracameral injection could provide better IOP-lowering effects than those performed with intravitreal injection (Ha et al., 2017) An intracameral and superior subconjunctival of anti VEGF 25mg/ml (0,05 cc) (Bevacizumab) in right eyes was performed, and the rubeosis iris had completely resolved. However because of the transient effect of anti-VEGF, therefore we performed prior to trabeculectomy with MMC, before injections, patient was paracentesis to avoid the IOP elevation .

Two days after performed surgery, the bleb needs to be repaired because of the fibrous membrane developed.

The limitation of this case report, due to many reasons, we only performed cataract extraction and synechiolisis in left eyes because patient refused it. The visual acuity improved to 20/30 BCVA. However IOP remained stable for BE after the surgery performed.

In Vogt-Koyanagi-Harada Patient, many factors may cause the formation of cataract. Long standing usage of corticosteroid, and the chronic inflammation take prosess in leading its formation (Simha et al., 2020; Gulati et al., 2011).) At initial presentation, we believe that our patient was in the acute VKH phases, in which there were keratic precipitate, posterior synechiae, vitritis and exudative retinal detachments. According to the literature says that patient with VKH syndrome more likely to get cataract if initial presentation with anterior segment inflammation (AlBloushi et al., 2021;Ji et al) also said that the perfect timing for doing the cataract surgery shows no significant differences in 1 months or 3 months after the inflammation therapy for visual outcome (Ji et al., 2018).There were no significant differences in outcome between eyes that underwent cataract extraction by manual nuclear extraction compare to eyes that underwent phacoemulsification, although previous study mentioned that phacoemulsification provides better result however both techniques equally efficacious and safe (Quek et al., 2011). Also unfortunately, Patient controlled to our eye clinic with decreased in visual acuity in her left eye, we presumed due to her chronic recurrent phase of uveitic, as besides Posterior capsular opasification and cystoid macular edema recurrent uveitic is one of the most cautious sight-threatening complication after cataract surgery in VKHS (Ganesh et al.,2004). The usage of immunomodulatory therapy should be considered when controlling chronic recurrent phase in VKHS (AlBloushi et al., 2021).

III. CONCLUSION

It is quite challenging in managing the ocular complication in VKHS because of its chronic recurrences and it is often leading to rapid visual acuity regression. An adequate timely therapy and strictly follow-up are needed for controlling visual outcome and IOP in VKHS patient.

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