Ophthalmol Ina 2023;Supplement Ed.: 323-328

CASE REPORT

METHOTREXATE FOR REBOUND PHENOMENON OF VOGT-KOYANAGI-HARADA IN JUVENILE: A RARE CASE REPORT

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ABSTRACT

Introduction: *Vogt-Koyanagi-Harada (VKH), an auto-immune disorder driven by melanocyte antigen, is rare in children. The mainstay treatments are corticosteroid and immunomodulators. Methotrexate is one of immunomodulator that widely used due to its effectiveness with minimal side effects.*

Case Report: *A 9-years-old boy get diagnosed Vogt-Koyanagi-Harada. His best corrected visual acuities (BCVA) were 20/400 in both eyes. Anterior segment examination showed granulomatous uveitis. Posterior segment examination revealed optic disk swelling, Dallen Fuch's nodule and exudative retinal detachment. We also found poliosis and vitiligo in his lips. He had been previously treated with topical corticosteroids, oral corticosteroids and topical cycloplegics. The dose was tapered every month. After taking medication for 5 months with the last dose oral corticosteroid 16 mg/day and topical corticosteroid every 8 hours, his BCVA recovered to 20/25 RE and 20/40 LE. During the treatment time, the patient discontinued the medication due to parental disobedience and then came with decrease of vision. Based on the consideration of rebound phenomenon and the use of maximum dose of corticosteroids, we consulted the patient to the pediatrician, and decided to give methotrexate as an immunosuppressant. After receiving 15 mg/week of methotrexate for 3 months, inflammation calmed down but unfortunately the vision did not improve.*

Discussion: *In children, the main treatment for VKH disease is high-dose corticosteroids. Considering the side effects of prolonged systemic corticosteroid therapy, methotrexate become the first line of corticosteroid sparing agent, especially in chronic stage.*

Conclusion: *Methotrexate can be an effective treatment option for rebound VKH.*

Keywords: *Juvenile Vogt-Koyanagi-Harada, Steroid Sparing Agents, Rebound Phenomenon, Methotrexate.*

INTRODUCTION

Vogt-Koyanagi-Harada (VKH) is an auto-immune disorder driven by melanocyte antigen-reactive T-cells [1]. It is known that patients with VKH disease often suffer bilateral uveitis accompanied with serous retinal detachments and papillitis, following aseptic meningitis and deafness at early phase, and if the treatments are deficient or the induction of the treatments is delayed, they suffer poliosis and vitiligo at late phase. The onset age of VKH disease tends to be approximately from 20 to 50 years. Therefore, VKH disease in children is very rare [2]. We experienced a nine-years-old boy affirmatively diagnosed with VKH disease. The patient

had previously recovered, but had a rebound phenomenon due to discontinuation of the treatment. Early immunomodulatory treatment in patient with VKH rebound phenomenon has become first option especially in children. Methotrexate is most widely used than other IMT and seems to be effective with minimal side effects.

CASE ILUSTRATION

A 9-years-old boy admitted to eye clinic with blurred vision and redness in both eyes. He also complained flu like illness and headache prior to eye symptoms. Best corrected visual acuities (BCVA) were 20/400 in both eyes. Anterior segment examination showed mutton fat (figure 1), cells and flare in the anterior chamber, and posterior synechiae of the iris. The posterior segment examination revealed optic disc swelling, Dalen Fuch's nodule, and exudative retinal detachment in both eyes (figure 2). B-scan ultrasonography showed exudative retinal detachment (figure 3). Optical Coherence Topography (OCT) of the macula showed hyperreflective lesion underneath retina suggested choroidal fibrosis (figure 4). We also found poliosis and vitiligo in his lips (figure 5). Blood cell count, mantoux test, antigen immune serology Ana's Profile and thorax imaging was normal. Therefore, he was diagnosed with VKH disease. He was treated with topical corticosteroids every 3 hours, topical cycloplegics every 12 hours and oral corticosteroids 32 mg/day. After 5 months taking medication with the last dose of 16 mg/day oral corticosteroid, and topical corticosteroid every 8 hours, his BCVA recovered to 20/25 RE and 20/40 and his anterior segment became quieter. During the treatment time, the patient discontinued the medication due to parental disobedience for 1 week and then came with decrease of vision. His vision was 1/300 in both eyes with severe inflammation in the anterior and posterior segments. The patient was immediately given topical corticosteroids every 3 hours, topical cycloplegics every 12 hours, and oral corticosteroids with a maximum dose (32 mg/day) but there is no improvement after one week. Therefore, we consulted him to a pediatrician to get immunosuppressant therapy. The pediatrician recommends several examinations before giving the treatment, including blood cell count, erythrocyte sedimentation rate, kidney function, liver function, weight, height and body surface area. All the examinations results were normal and we decided to give him methotrexate as a steroid sparring agent. He received methotrexate 15 mg/week and folic acid once daily with continuation of tapered dose topical steroid and oral corticosteroid (20% tapered every week). After first month of taking methotrexate, we did blood tests, including blood cell count, erythrocyte sedimentation rate, kidney function, and liver function, to follow up the side effect of methotrexate and found

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normal results. After 3 months of taking methotrexate with minimal dose of corticosteroid, the inflammation calmed down but unfortunately vision did not improve.

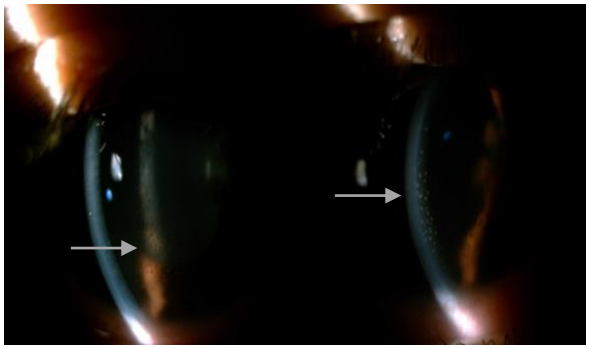

Figure 1. Mutton fat in the Anterior Chamber.

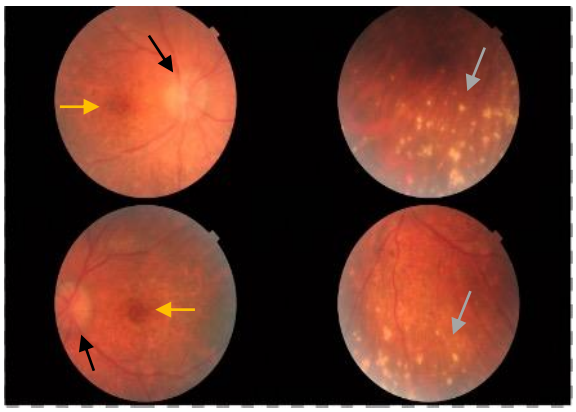

Figure 2. Optic disc swelling (black arrow), Punched out chorioretinal scars around the macula (yellow arrow), and Dalen Fuch's nodule in funduscopy examination (grey arrow).

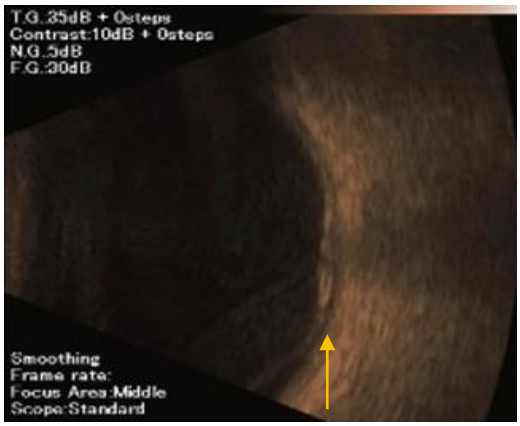

Figure 3. Ocular ultrasonography showed exudative retinal detachment.

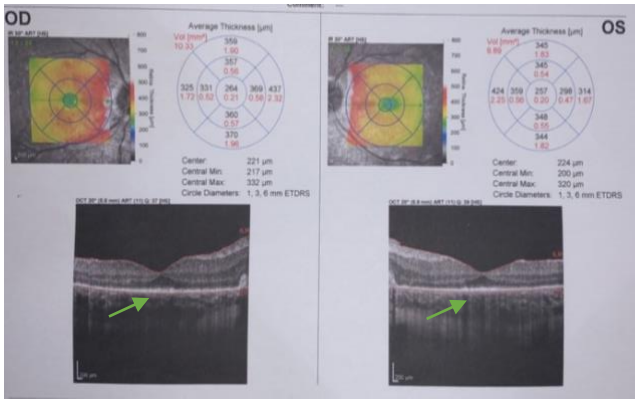

Figure 4. Sub RPE hyperreflective lesion suggested as choroidal fibrosis.

DISCUSSION

VKH is an uncommon multisystem inflammatory disease in pediatric group (only 13%–15% VKH in children). [4,5] Visual prognosis in this population has been described differently in the literature, with the poor visual prognosis attributed to the younger age at presentation and the high rate of complications. A shorter time between disease onset and initiation of therapy (< 2 weeks) has been reported to be associated with better visual outcomes and fewer complications. [3]

The etiology of VKH disease is an auto-immune disorder driven by melanocyte antigen-reactive T-cells which triggered by certain factors and has four clinical stages: prodormal, uveitic, convalescence and chronic or recurrent. Extraocular signs typically happen during the prodormal, convalecens, and chronic stages. The prodromal phase is characterized by fever, nausea, and headache lasting 3 to 5 days. A few symptoms, including dysacousia, tinnitus, high-frequency hearing problems, and vertigo, are caused by the involvement of the auditory system. Our patient was at this stage initially because before complaining about his eyes, he complained of a fever, headache, and flu-like symptoms. [7,9,10]

The onset of photophobia, impaired vision, and the presence of ocular discomfort are signs of the uveitic stage experienced one week after the prodromal stage. On examination, we found granulomatous anterior uveitis in both eyes with fat deposits (mutton fat precipitates keratic) and nodules in the iris. Uveal granulomatous inflammation causes choroidal thickening due to the presence of epithelioid histiocytes in the layer between the retinal pigment epithelium (RPE) and Bruch's membrane which gives the appearance of Dalen Fuch's nodules and exudative retinal detachment filled with protein fluid. [7,9,10]

If patients receive the right care throughout the convalescence stage, their eye problems and exudative diffuse retinal detachment will eventually improve. In this stage, the retinal

pigment epithelium is migrating and there are many depigmentation lesions of the retinal epithelium scattered on the mid-peripheral fundus, which together give the appearance of a "sunset glow" (the fundus is red-orange). These show that melanocytes and pigmented tissue are acting aggressively. A depigmented limbus known as the "sugiura sign" could be seen at this point. Depigmentation on the skin such as vitiligo and poliosis, which causes whitening of the eyelashes. [7,9,10].

In later stages, the chronic stage is characterized by mild panuveitis with recurrent episodes of anterior uveitis. This stage is usually considered to be the result of inadequate or delayed treatment with corticosteroids for the disease. As in this patient who has not received adequate treatment and has stopped. On anterior examination, relapsed anterior uveitis, the inflammation gradually changed from non-granulomatous to granulomatous. Keratic precipitate of Mutton fat on the corneal endothelial surface, flare and cells in the anterior chamber are characteristic features of this stage. We also found Busacca nodules in the iris. [11].

This patient has reached the chronic recurrent stage of the disease because has had improved vision previously but because the treatment has not been adequate so that the rebound phenomenon occurs.

High-dose corticosteroids are the principal treatment for acute VKH in children. Recent studies have shown that immunosuppressive medications such methotrexate, cyclosporine, azathioprine, and cyclophosphamide can successfully treat children with VKH disease, taking into account the side effects of extended systemic corticosteroid therapy, particularly growth retardation [11]. In comparison to other IMT, methotrexate is used most frequently in newborns and appears to be beneficial with little adverse effects. Patients with active panuveitis who were unable to tolerate or respond to systemic corticosteroids or who experienced steroid-related adverse effects had methotrexate added to their treatment plan. At the start of the methotrexate therapy, oral corticosteroids (0.5–1 mg/kg) were given to reduce inflammation before methotrexate started working. [11]

In light of the side effects of methotrexate that have been documented, such as leukocytopenia, thrombocytopenia, and anemia, patients were assessed to rule out treatment contraindications, such as abnormal blood cell counts and liver or renal function tests. According to the American College of Rheumatology's (ACR) recommendations, patients who were taking methotrexate were examined every two months, and laboratory tests like blood cell counts, bilirubin, liver aminotransferase, and serum creatinine were monitored every six weeks. If any anomaly in the aforementioned tests was found, methotrexate was stopped. Methotrexate was administered once weekly in doses of 5 to 7.5 mg. Patients who experienced nausea and

vomiting were prescribed oral antacids. Folic acid was administered orally at 1 mg daily. Methotrexate doses were adjusted based on treatment response and the potential for steroid dose reduction after 6 to 9 weeks of treatment. Methotrexate dosage, duration of treatment, clinical response, and side effects of treatment were recorded. To determine the efficacy of methotrexate treatment, data from the last pre-treatment laboratory test were compared with data from the last follow-up test while on methotrexate. [11,12]

With VKH syndrome, visual loss can happen, usually through cataract, glaucoma, RPE atrophy or in rare cases, choroidal neovascularization.

CONCLUSION

We consider the report of this clinical case to be of utmost importance, in order to raise awareness of one more form of clinical presentation of VKH disease. Early diagnosis and treatment of the disease can prevent most of the complications and lead to a favorable visual outcome. Methotrexate can be an effective treatment option for recurrent VKH in children and needs to be used as soon as possible without delay.

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