A Clinical Study on Vogt-Koyanagi-Harada Disease

Periyanayagi Murugananthan[1], Maria Deepika Krishna Moorthi[2], Arthi Mohankumar[3]

[1]Associate Professor, Department of Ophthalmology, Thoothukudi Medical College, Thoothukudi, Tamilnadu, India. [2]Postgradutae Student, Department of Ophthalmology, Regional Institute of Ophthalmology, Chennai, Tamilnadu, India. [3]Fellow, Department of Ophthalmology, Aravind Eye Hospital, Pondicherry, India.

ABSTRACT

BACKGROUND

This is a bilateral condition where there is a chronic granulomatous iridocyclitis with an exudative choroiditis which often leads to an exudative detachment of the retina. We wanted to study the demographic features, and the clinical outcomes in patients of Vogt-Koyanagi Harada Disease.

METHODS

This is a prospective study in which patients between 8 and 50 years were seen and treated at RIO-GOH, Chennai, from 2008 to 2018, and followed-up subsequently. All patients were treated with a dose of bolus of intravenous methylprednisolone for 3 days followed by high-dose oral prednisolone. Few patients needed further intervention with immunosuppressants. One patient treated with immunosuppressants required further injections of anti-VEGF when he further developed choroidal neovascularisation. Periodic review of the patients was done monthly for assessing reduction of the vitreous inflammation and assessing the response to treatment.

RESULTS

Most patients responded well to steroids and there was less recurrence of inflammation. Few patients had repeated episodes and were started on immunosuppressants. Some of them were started on azathioprine and few of them needed cyclosporine and mycophenolate mofetil. One patient further developed choroidal neovascular membrane, and injection Anti-VEGF was administered to reduce complications.

CONCLUSIONS

IV methylprednisolone followed by oral prednisolone is a first line approach to Immunosuppression where there is steroid intolerance or inadequate response to steroid.

KEYWORDS

Vogt-Koyanagi-Harada, Panuveitis, Exudative Retinal Detachment, Corticosteroid Immunosuppression

Corresponding Author:
Dr. Periyanayagi Murugananthan
5/55 Teachers Street,
N. A. Nagar Redhills,
Chennai-52, Tamilnadu, India.
E-mail: m.periyanayagi@gmail.com

DOI: 10.18410/jebmh/2020/345

How to Cite This Article:
Murugananthan P, Moorthi MDK, Mohankumar A. A clinical study on Vogt-Koyanagi-harada disease. J Evid Based Med Healthc 2020; 7(33), 1652-1656. DOI: 10.18410/jebmh/2020/345

Submission 07-02-2020,
Peer Review 12-02-2020,
Acceptance 28-06-2020,
Published 17-08-2020.

BACKGROUND

Vogt-Koyanagi-Harada disease is a rare, autoimmune multisystemic syndrome, that has a varied spectrum of manifestations ranging from ocular involvement that presents as bilateral granulomatous panuveitis associated with integumentary involvement such as poliosis and vitiligo and central nervous system involvement presenting as cerebrospinal fluid pleocytosis and meningismus. Case reports were first described by Vogt in 1906 and Koyanagi in 1929 of patients presenting with bilateral anterior uveitis, vitiligo, poliosis, alopecia and dysacusis. This became known as Vogt-Koyanagi-syndrome.[1] In 1926 a similar condition was described in Japan by Harada where posterior uveitis was associated with exudative retinal detachment and CSF pleocytosis. This syndrome was called Harada disease. As both of these conditions were variations of the same disorders, the entity became accepted as VKH syndrome.

The causative factors leading to VKH syndrome remains uncertain. The two most attractive theories remaining have been a viral etiology and an autoimmune or hypersensitivity process. The prodromal stages manifest with headache, fever, orbital pain, nausea, dizziness and light sensitivity, blurred vision and photophobia.[1] The Uveitic stage presents with blurred visual acuity in both eyes. Thickening of the posterior choroid manifested by elevation of the peripapillary retino-choroid layer, hyperemia and edema of the optic disc, with multiple serous retinal detachments seen. Further progression to a panuveitis picture will ensue. The convalescent stage is characterized by the development of vitiligo, poliosis and depigmentation of the choroid. Nodular yellowish lesions at the level of the choroid can be present in the peripheries which appear similar to Dalen-Fuchs nodules of sympathetic ophthalmia.[2,3]

Later in the course of the disease, neovascularization of the optic nerve head and retina can occur which may cause vitreous hemorrhage. Subretinal neovascular membrane both in peripapillary region and macula are seen in approximately 10 percent of the patients in VKH syndrome.[4]

The treatment of VKH during the initial stages include corticosteroids and long-term treatment involves addition of immunomodulators like cyclosporine, antimetabolites, and alkylating agents.[1,5] Secondary glaucoma and cataract occur in the chronic recurrent phase which can cause visual debilitation. The aim of this study is to provide a detailed report on the clinical spectrum of Vogt-Koyanagi-Harada disease.

METHODS

Study population included the patients who presented to the Uvea-retina services of RIO-GOH, Chennai during the period of 2008-2018. 20 patients were included in the study. Though 35 patients were registered and treated, only 20 patients with minimum of 1 year follow up were included in the study. The approval of the institutional ethical committee was obtained before proceeding with the study and the study adhered to the Tenets of Helsinki. Informed consent obtained from all patients. Patients were given intravenous steroids followed by tapering doses of oral prednisolone with immunosuppressants with periodic review done to assess recurrence. Anterior segment inflammation was also treated by topical steroids and cycloplegics. Further treatment with immunosuppressants was necessitated when patients had recurrences.

Inclusion Criteria

All patients with clinical evidence of active anterior chamber and vitreous inflammation, bilateral optic disc oedema and serous retinal detachments. Patients who have had multiple recurrences despite high-dose steroids and immunosuppressant therapy.

Exclusion Criteria

Patients with H/O ocular trauma, ocular surgery, rheumatological disorders, hypercalcemia, non-caseating granulomas and non-caseating lymphadenopathy, exposure to tuberculosis and venereal diseases.

All patients underwent a detailed examination to assess the uncorrected and best corrected visual acuity, intraocular pressure measured with Goldmann applanation tonometry and a detailed anterior segment examination done with slit lamp biomicroscopy. Fundus evaluation was done by slit lamp bio microscopy with a +90 D lens and indirect ophthalmoscopy. All patients underwent fundus fluorescein angiography to assess early pinpoint peripapillary hyperfluorescence with pooling in late stages. Patients were subjected to Optical Coherence Tomography to quantify the extent of serous detachments and for further monitoring to assess the response to treatment. Once the diagnosis of Vogt-Koyanagi-Harada disease was made, patients were started on intravenous methylprednisolone 500 mg bd dose for three days followed by oral prednisolone 1 mg/Kg body weight in tapering doses.

RESULTS

40 eyes of 20 patients were included in the study. Our study also included a paediatric patient with VKH – who was 8 years of age. The mean age of the study population was 39.21 years (range 8-50 years, standard deviation 10.8, median 29) (Table 1).

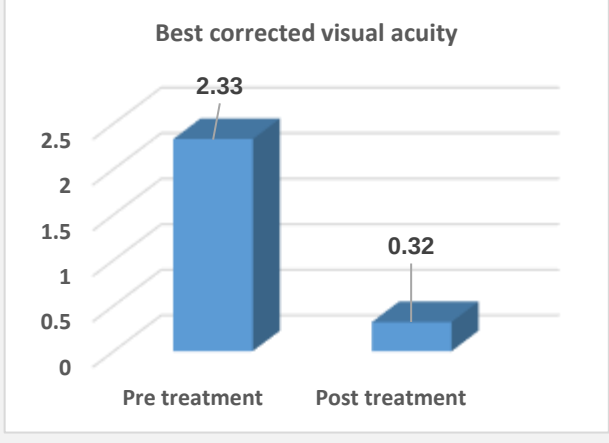
Number of Patients	20
No. of eyes	40
No. of males	17
No. of females	3
Mean age	39.21 years
Median age	29
Age range	8 - 50 years

Table 1. Demographic Features of Our Study Population

Prodromal symptoms included headache in 12 patients (60%), ocular pain in 6 patients (30%) and tinnitus and hearing loss in 2 patients (10%). There was no evidence of fever or neck rigidity in any patient.

All patients presented with complaints of bilateral defective vision. Three patients (15%) had poliosis and vitiligo and two patients (10%) had alopecia.

The mean Best Corrected Visual Acuity (BCVA) at presentation was 2.33 LogMAR units. The mean post-treatment BCVA was 0.32 LogMAR units. The improvement in visual acuity following treatment was found to be statistically significant with a 'p' value <0.05. This indicates that the visual prognosis of patients with VKHS was fairly good following adequate treatment (Figure 1).



Visual Recovery after Steroids

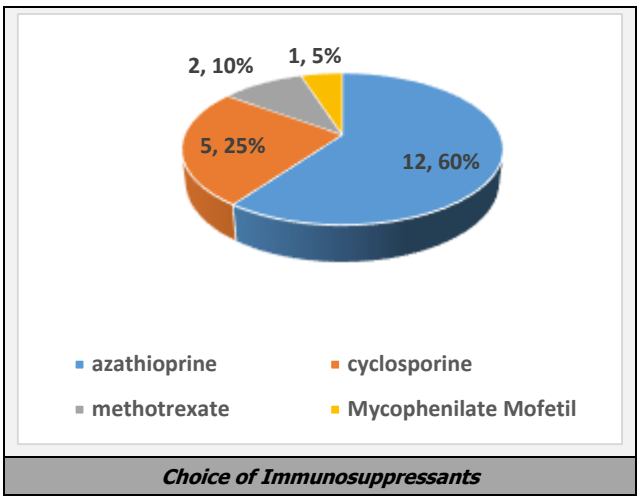
All patients presented with bilateral multifocal serous detachments. All patients developed bilateral sunset glow fundus during the course of follow up. All eyes had bilateral anterior uveitis and vitreous cells. The mean intraocular pressure was 12.68 mmHg (SD 3.58). None of the patients had Dalen-Fuchs nodules or Sugiura's sign.

Clinical Features	Number of Eyes (%)
Extensive exudative RD	Nil
Multifocal exudative RD	100%
Anterior uveitis	100%
Vitreous cells	100%
Optic disc oedema	100%

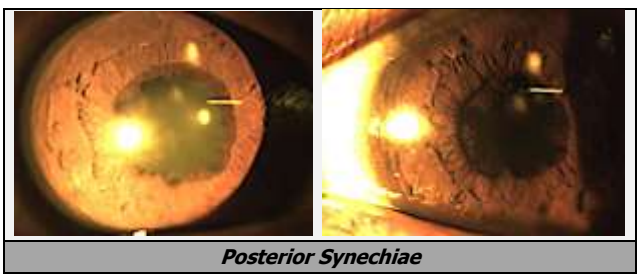
Table 2. Clinical Features in Patients with VKHS Syndrome

Once the diagnosis of Vogt-Koyanagi-Harada disease was made after FFA and OCT, patients were started on intravenous methylprednisolone 1 g BD dose for three days followed by oral prednisolone 1 mg/Kg body weight. Patients were followed up monthly for reduction of anterior chamber and vitreous inflammation. A minimum follow-up period of 1 year was done for each of the patients.

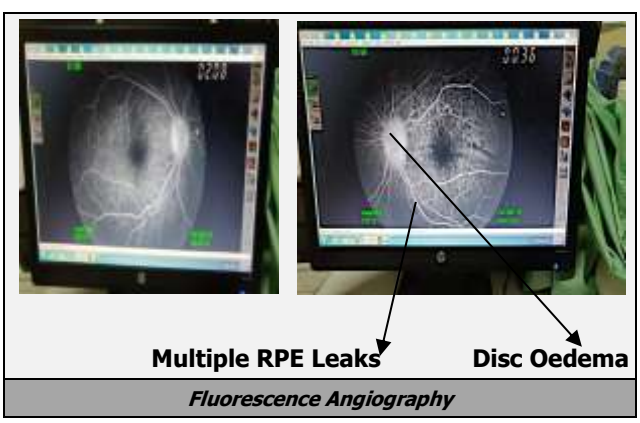
12 (60%) patients needed azathioprine, 5 (25%) of them needed cyclosporine and 2 (10%) patients Methotrexate and 1 (5%) further needed mycophenolate mofetil (Figure 2). The disease was kept in remission for a longer duration when steroids were continued along with immunosuppressants.



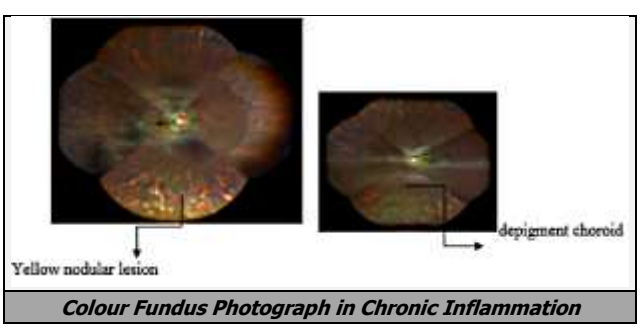
Choice of Immunosuppressants



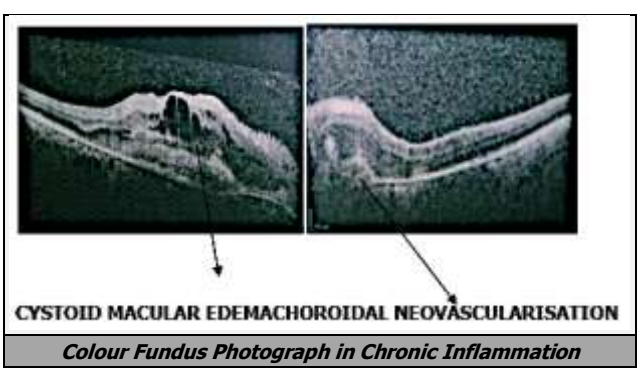
Posterior Synechiae



Fluorescence Angiography



Colour Fundus Photograph in Chronic Inflammation



Colour Fundus Photograph in Chronic Inflammation

One patient was operated for complicated cataract under steroid cover and had good vision post operatively. He was initially on steroids and azathioprine and later switched over to mycophenolate mofetil and he further developed a choroidal neovascular membrane with severe drop in vision. Multiple doses of anti-VEGF injection was given to further reduce complications.

It was also noted that this disease was more common from October to December thus giving a strong association with a viral aetiology or an upper respiratory tract infection associated with the development of the disease. Studies associating a probable viral aetiology with disease onset is still going on to show an increased likelihood of upper respiratory cause with disease onset.

DISCUSSION

VKH disease is a systemic, autoimmune disorder with antibodies directed against antigens present in the melanocytes in choroid, meninges, inner ear and skin. It presents as a bilateral, diffuse granulomatous uveitis with a chronic course. It is seen in adults between 20 to 50 years with a predilection for females. The diagnostic criteria includes no history of accidental or surgical prior ocular trauma, no clinical or laboratory evidence suggesting presence of other ocular conditions and bilateral ocular involvement. Studies have shown that Male patients have a higher risk of chorioretinal degeneration and poor visual outcomes after treatment. The oestrogen / progesterone fluctuations during pregnancy and the menstrual cycle as well as higher levels of TGF- beta are protective in females in studies conducted by Yujuan Wang and Chi-Chao Chan. Marked chorioretinal thickening is widely considered to be the hallmark of this disease. Studies have also proven that prompt initiation of high-dose corticosteroid treatment was associated with improved prognosis for visual function.[1,5,6]

Newer studies have made breakthroughs in finding out a causal association with VKH syndrome. A strong association with HLA antigens DR4, DRw53, and Bw54 is seen in these patients.[4] Studies have shown an association between decrease in the glyceraldehyde derived advanced glycation end products and decreased 1, 25-dihydroxyvitamin D3 level in the pathogenesis of VKH disease.

In our study, cases were reported between the months of October to January. In our study the youngest patient was 8 years old. We found that younger the age of disease onset, more was the severity of symptoms and the aggressiveness of the disease. In our study, these young patients presented with early cataract as compared to adult cases. All patients who tolerated steroids from 6 months to 1 year had good visual recovery with low rate of recurrences. Patients in whom steroids was tapered early and patients who developed intolerance to steroids developed repeated recurrences with frequent reactivation of anterior uveitis and also became resistant to steroids. 50 % of patients needed immunosuppressive drugs. Azathioprine was chosen as the first-line immunosuppressive agent. In few patients cyclosporine was also added with azathioprine. A few were started on methotrexate and mycophenolate mofetil. Patients responded equally well to all immunosuppressive agents and no one drug was found to be superior to the other. In spite of all these steroid and immunosuppressant treatment, one 19-year-old male patient developed choroidal neovascular membrane and required multiple doses of anti-VEGF. Thus we concluded that steroids should never be discontinued and a continued low dose steroids of dose 30 mg/ day should be given to the patient along with concurrent immunosuppressant therapy.[7,8] Abrupt discontinuation of steroids is detrimental to the patient as it doesn't improve in visual rehabilitation even when steroids are restarted during reactivation of the disease. Thus we concluded that steroids act not only as an induction therapy but it is also helpful in maintaining relatively disease-free periods and provides reasonably functional vision to the patient.[8]

CONCLUSIONS

In Vogt Koyanagi Harada syndrome, corticosteroid therapy is the first line treatment, with maintenance for six months to one year, with very slow tapering as patient's response to steroids decreases during each recurrence for immunosuppression only when there is inadequate response to steroid therapy as well as to steroid intolerance. Azathioprine was started as the first choice of immunosuppression in most of the patients. None of the immunosuppressives can be preferred as the best choice to suppress the disease activity. As diagnosis of the disease is based on clinical decision, the choice of immunosuppression is also the same. As patients present with recurrence of active anterior uveitis on tapering steroids, very slow tapering after six months to one year may help to prevent complications like CNVM and subretinal fibrosis.

Financial or Other Competing Interests: None.

REFERENCES

[1] Lodhi SAK, Reddy JML, Peram V. Clinical spectrum and management options in Vogt–Koyanagi–Harada disease. J Clin Ophthalmol 2017;11:1399-1406.
[2] Mondkar SV, Biswas J, Ganesh SK. Analysis of 87 cases with Vogt-Koyanagi-Harada disease. Jpn J Ophthalmol 2000;44(3):296-301.
[3] Giordano VE, Ariel Schlaen A, Guzmán-Sánchez MJ, et al. Spectrum and visual outcomes of Vogt-Koyanagi-Harada disease in Argentina. Int J Ophthalmol 2017;10(1):98-102.
[4] Sheu SJ, Kou HK, Chen JF. Prognostic factors for Vogt-Koyanagi-Harada disease. J Chin Med Assoc 2003;66(3):148-154.
[5] Wang C, Cao S, Zhang D, et al. Increased complement 3a receptor is associated with Behcet's disease and Vogt-Koyanagi-Harada disease. Sci Rep 2017;7:15579.

[6] Soheilian M, Aletaha M, Yazdani S, et al. Management of pediatric Vogt-Koyanagi- Harada (VKH)-associated panuveitis. Ocul Immunol Inflamm 2006;14(2):91-98.
[7] Storey PP, Tan JJ, Aziz HA, et al. Early versus late immunomodulatory therapy in Vogt-Koyanagi-Harada disease. Journal of Ophthalmic Science 2017;1(4):6-14. ISSN:2470-0436.
[8] Kunihiko Y, Kiyoko G, Shozo S. Pathogenesis of Vogt-Koyanagi-Harada disease. International Ophthalmology Clinics 2002;42(1):13-23.