

Analysis of 87 Cases with Vogt-Koyanagi-Harada Disease

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Purpose: Vogt-Koyanagi-Harada (VKH) disease is known to have varied manifestations in different ethnic groups. In order to analyze the clinical profile of VKH cases in the Indian population, we studied 87 consecutive cases of VKH disease treated in an uveitis clinic in South India between 1985 and 1996.

Methods: Retrospective analysis and review of charts of consecutive new VKH cases diagnosed in a referral clinic.

Results: VKH disease comprised 2.2% of all uveitis referrals. Extraocular symptoms or signs were seen in 64% of cases at the time of presentation. Most common was meningism (95.9%). However, subsequently all patients developed extraocular manifestations. Panuveitis (92%) was the commonest presentation. Systemic corticosteroid was the usual form of therapy (50.3%) followed by immunosuppressive therapy (39%); surgical treatment was needed in 8% of the cases. Complicated cataract (33%) and glaucoma (24%) were major complications. Final vision was between 6/60 and 6/18 in 88% of the cases and 6/18 and better in 15.4%; there was no improvement in 11% of the cases.

Conclusions: VKH disease occurs less frequently in India than in Japan and about as commonly as in the United States. Extraocular signs are far less common than in the Japanese population. Visual prognosis is good in patients presenting within 1 month of onset of symptoms. Immunosuppressive agents and vitreoretinal surgery are needed in advanced cases and in cases reported later. **Jpn J Ophthalmol 2000;44:296-301** © 2000 Japanese Ophthalmological Society

Key Words: Complicated cataract, glaucoma, panuveitis, Vogt-Koyanagi-Harada disease.

Introduction

Vogt-Koyanagi-Harada (VKH) disease is a panuveitis of autoimmune nature where the melanocytes act both as an inducer and as a target. The condition has several extraocular manifestations, and is a common uveitic entity in Japanese, relatively less common in Hispanics and Indians, and rarely seen in White patients. The disease has been reported to present varied manifestations in different racial groups. In order to study any racial differences in clinical characteristics, we analyzed all VKH cases seen in our uveitis clinic between 1985 and 1996. To the best of our knowledge, our study is the first to report a large series of VKH cases in India.

Materials and Methods

Eighty-seven patients were diagnosed as having VKH disease between 1985 and 1996. They comprised 2.2% of all uveitis patients seen in our Institute (4,329 cases). The diagnosis of VKH was based on the specific clinical findings recommended by the American Uveitis Society (Second Annual Meeting, Kansas City, MO, 1978).¹ These include the absence of previous ocular trauma or surgery, and findings in at least three of the following four groups of signs and symptoms:

1. bilateral iridocyclitis;
2. posterior uveitis, including exudative retinal detachment or sunset glow fundus;
3. central nervous system problems (tinnitus/dysacusia, meningism, cranial nerve involvement) or cerebrospinal fluid pleocytosis;
4. cutaneous findings (alopecia, poliosis, vitiligo).

Patients were followed up for a period ranging from 1 month to 128 weeks, mean 15.6 weeks.

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Results

In our series of 87 patients, 33 were men (37.9%) and 54 (62.1%) were women. The age at onset ranged from 10 to 70 years (Figure 1). In the majority of cases, the initial complaint was marked diminution of vision. Most patients had initial bilateral (92%) involvement with vision in the worst eye being less than 6/60 in 81.4% of the cases. Extraocular signs or symptoms were seen in 64% of the cases (Figures 2 and 3), the most common sign being meningism in 41 cases (47.1%). Auditory disturbances were seen in 13 cases (14.9%); vitiligo in 5 (5.7%), alopecia in 8 (9.2%), and poliosis in 2 (2.3%). Slit-lamp examination revealed associated anterior uveitis in the majority of the cases (92%). The anterior uveitis was mostly nongranulomatous in nature. Fundus examination showed total/partial exudative retinal detachment in 44 (50.6%) cases, retinal edema in 25 (28.7%) cases. The fundus was not visible due to lenticular haze in 16 (18.4%) cases. Investigations carried out on these patients included ultrasound examination in 46 cases (52.9%), fundus fluorescein angiography in 37 (42.5%), and electroretinogram in 10 (11.5%) cases. Ultrasound examination revealed bullous retinal detachment with or without choroidal thickening depending on the stage of the disease. Fundus fluorescein angiography was done in selected cases only. It showed multiple hyperfluorescence in the early stage, increasing in intensity in the mid-arterio-venous phase and staining

in the late stages. We also observed staining of disc margin in patients who presented with papillitis. Electroretinography was done in selected cases only where there was extensive depigmentation. Electroretinographic findings ranged from normal to extinguished pattern, depending on the stage of the disease and depigmentation.

Management of most of these cases was done medically with systemic steroid as the first line of therapy. The most common regimen given was systemic steroid (1 to 1.5 mg/kg of body weight) in the form of prednisolone tablets. We adopted a single morning-after-breakfast-dose of 80 to 100 mg/day. This was given in 49 cases (56.3%).

Following oral prednisolone therapy, 61.6% showed improvement of vision, 24.4% maintained their vision, and 14.1% experienced deterioration of vision (Figure 4). Those cases who were unresponsive to steroid therapy were put on immunosuppressive agents. Immunosuppressive agent with low dose systemic steroid was given in 34 (39.1%) cases. Many patients had been treated earlier with systemic steroid by a local ophthalmologist without significant improvement. The immunosuppressive agent used in all cases was azathioprine (The Wellcome Foundation Ltd., London, UK) in an initial dosage of 50 mg 3 times daily. The reason for choosing this particular immunosuppressive agent was our experience in other uveitic conditions and familiarity with its side effects.

Following immunosuppressive therapy, visual acu-

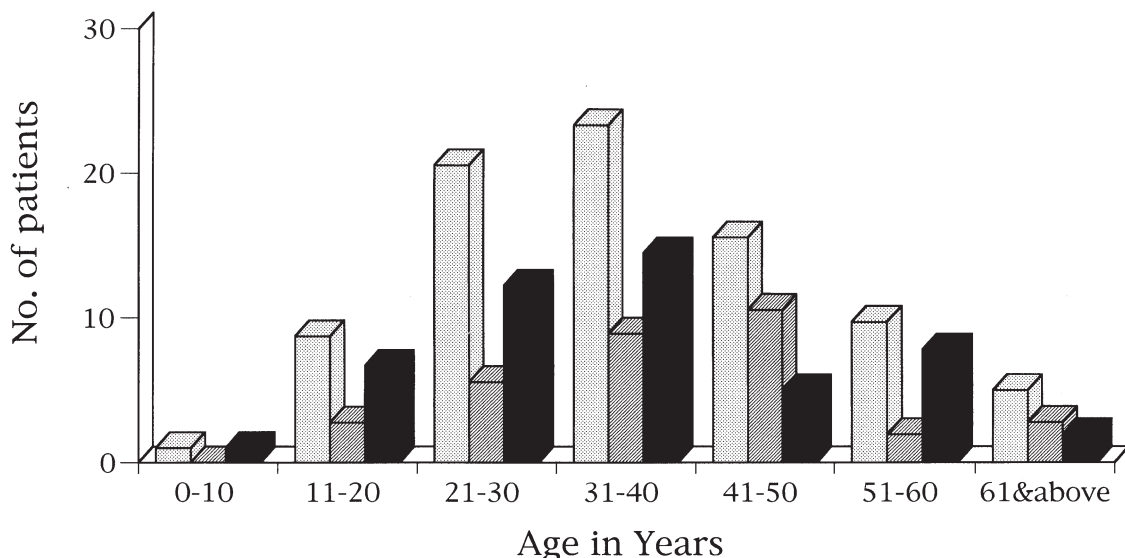


Figure 1. Age and sex distribution of Vogt-Koyanagi-Harada disease in Indian clinic. Note majority of patients were in 4th decade when seen. Total: □; Male: ▨; Female: ■.

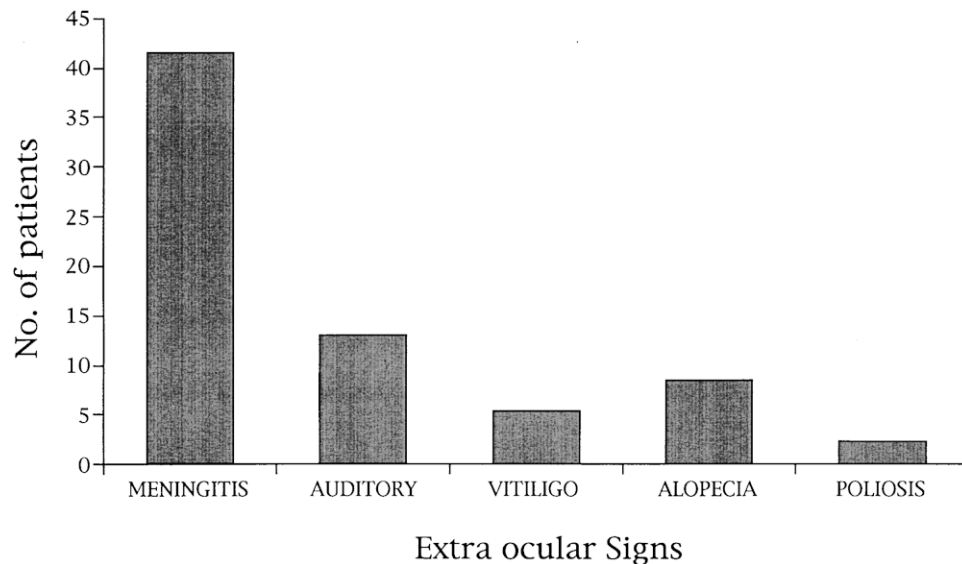


Figure 2. Extraocular signs and symptoms in Vogt-Koyanagi-Harada disease. Some patients had more than one extraocular sign or symptom.

ity improved in 62.5% of cases, was maintained in 19.4% of cases, and deteriorated in 18.1% of cases (Figure 5). Seven eyes of 6 patients underwent surgical treatment. Vitrectomy and membranectomy were conducted in 3 eyes; lensectomy and vitrectomy, in 2 eyes; cataract extraction, vitrectomy, and scleral buckling, in 1 eye. Vision improved in 5 eyes and was maintained in 2 eyes. Three eyes had 6/24 or better vision and 2 eyes had visual acuity of 6/60. Eight patients were seen in the healed stage and did not require any treatment.

The follow-up period ranged from 4 to 128 weeks (mean = 15.6 weeks). Of these 87 cases, 73.6% had final vision between 6/60 and 6/18, and 15.04% had vision of 6/18 or better. Ten cases (11.5%) had visual acuity of less than 6/18. Various ocular complications (60.9%) were encountered in these patients. They

were complicated cataract (33.3%), glaucoma (24.1%), subretinal fibrosis and macular scar, and cystoid macular edema in 1 case each. The period from onset of symptoms to presentation at our institute ranged between 7 to 13 months (mean = 10 months). We compared the visual acuity at the time of presentation with the final visual acuity. Final visual acuity improved in 104 eyes (59.8%), was maintained in 37 eyes (21.3%), and showed deterioration in 24 eyes (13.8%).

The majority of the cases (48 cases) (55.2%) were seen within 3 months of onset of symptoms. About 15% of the cases presented after 1 year (Table 1). Eleven cases (12.6%) were seen 4 months to less than 6 months after onset of symptoms. Fifteen cases (17.2%) were seen 6 months to less than 1 year after onset of symptoms, and 13 cases (14.9%) were seen over 1 year after the onset of symptoms.

Discussion

We report here for the first time a large series of VKH cases among Indians from a major referral eye institute in India. In our series, 64% of cases showed extraocular signs at the time of presentation. This is in contrast to reports of extraocular symptoms in Japanese (40%)² and in White patients (55%).³ Meningeal symptoms were most common and seen in 46% of cases. Dermatological manifestations were seen in only 5.7% of patients. Auditory disturbance

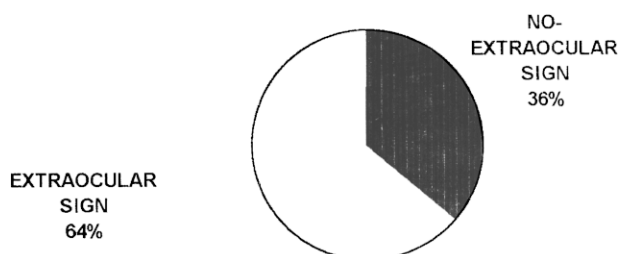


Figure 3. Comparison of extraocular signs in Vogt-Koyanagi-Harada cases at time of presentation.

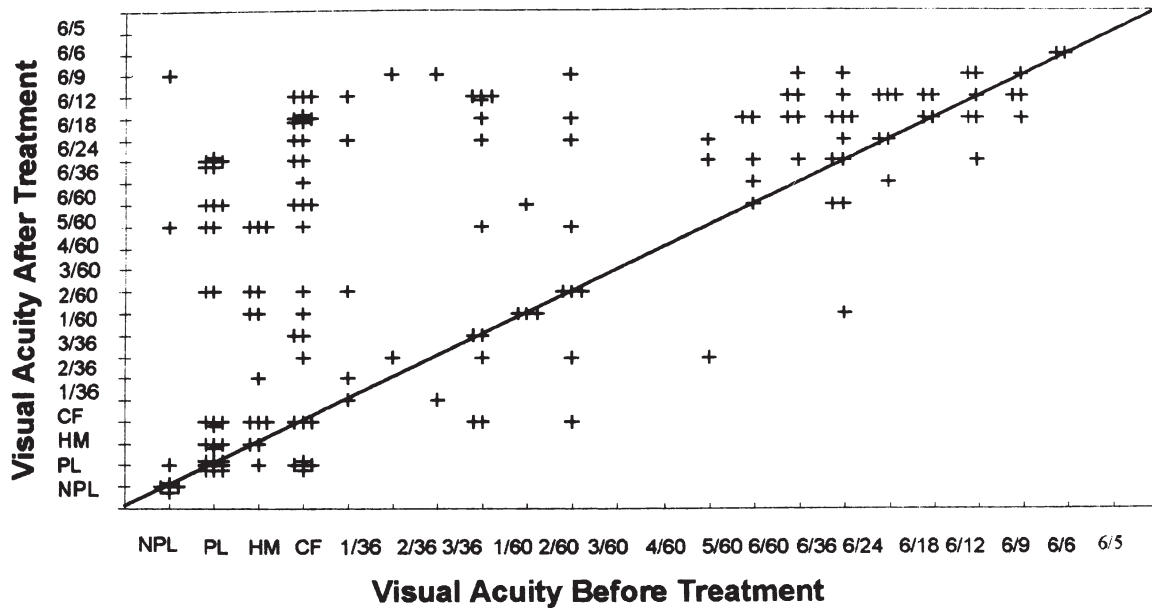


Figure 4. Visual acuity following oral corticosteroid therapy alone in Vogt-Koyanagi-Harada cases: 61.6% of cases improved, 24.4% maintained vision, and in 14% vision deteriorated. CF: counting fingers; HM: hand motion; PL: perception of light; NPL: no perception of light.

was also less (13%) in comparison to the study of Japanese patients (74%). Such a low incidence of extraocular findings was observed in Hispanic patients by Beniz et al.¹ This could be due to different genetic

predisposition and the role of medical treatment. Ohno first reported HLA-DR4 and DW53 in Japanese patients in VKH.⁴ In a study of Japanese patients with VKH disease, the prevalence of the HLA

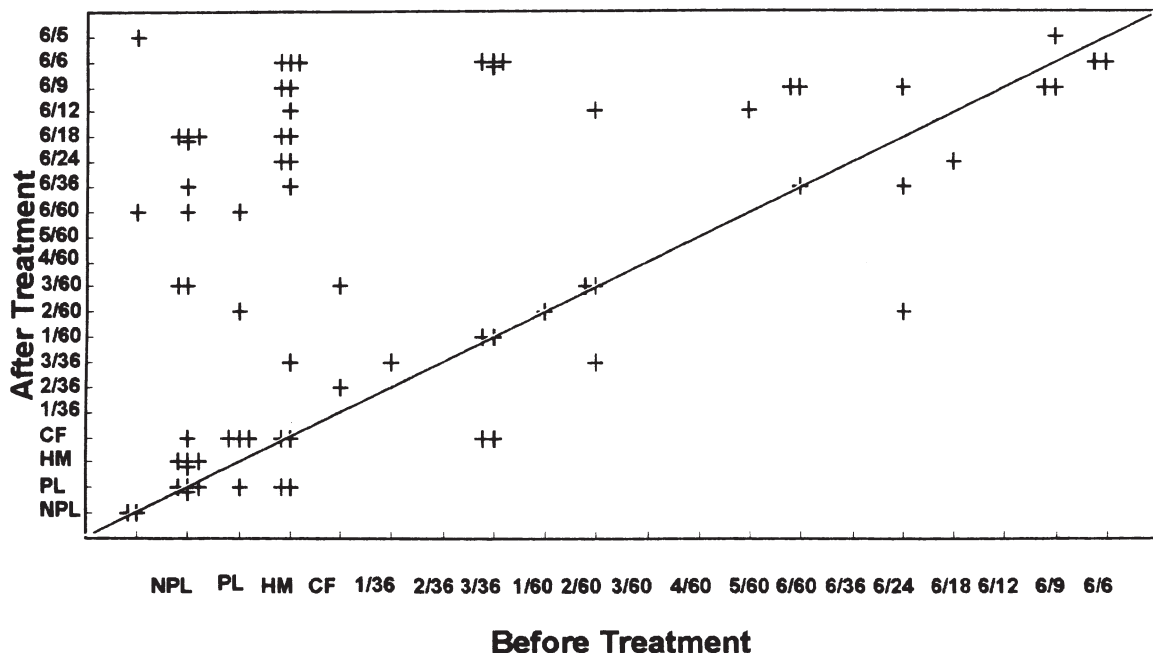


Figure 5. Visual acuity after immunosuppressive therapy; 62.5% of cases improved, 19.4% maintained vision, and in 18.1% vision deteriorated. CF: counting fingers; HM: hand motion; PL: perception of light; NPL: no perception of light.

Table 1. Interval Between Onset of Symptoms and Presentation at Our Institute

Interval Between Symptoms and Presentation (in Months)	No. of Cases
0-3	48 (55.2%)
>3-6	11 (12.6%)
>6-12	15 (17.2%)
>12	13 (14.9%)

DRB1*0405 gene was significantly higher in the chronic phase of the illness.⁵ Shindo and coworkers reported the same HLA association, HLA-DRB1*04 and DQB1*04, in Japanese patients with VKH disease and sympathetic ophthalmia.⁶ In a study of patients with VKH and sympathetic ophthalmia in the United States, an increased prevalence of HLA-DR4 and HLA-DW53 was found.⁷ No HLA study has been conducted in Indian VKH patients.

The incidence of anterior uveitis (92%) in our VKH patients was similar to findings in other studies.¹⁻³ However, many of our anterior uveitis cases were not the typical granulomatous type but non-granulomatous. Exudative retinal detachment was a common finding and marked retinal edema with disc edema was also a frequent finding and seen in 28.7% of our cases. These cases probably represent the early stage or incomplete presentation of the Harada component. We found ultrasound and fluorescein angiography particularly helpful in ruling out several entities like uveal effusion, metastatic carcinoma, and posterior scleritis.

In our series, systemic corticosteroid was the mainstay of therapy (Figures 4 and 5). However, 39.1% of cases required immunosuppressive therapy. Beniz et al¹ in their study reported that only 10% of patients required immunosuppressive therapy.

A small percentage of patients, 7.6%, required vitreoretinal surgery in our series, indicating that some patients might show poor response to medical treatment. Of these, only 2 patients showed an improvement of more than two lines following vitreoretinal surgery. We also encountered a high rate of complications in our series. The most serious was complicated cataract. Persistent intraocular inflammation and prolonged treatment with systemic steroid led to cataract formation in these patients. Moorthy and coworkers¹⁰ have reported cataract in 40% of their patients in the United States. Glaucoma was also another major complication and was seen in 23.9% of cases. These incidences were lower than seen in White patients (38.1%) by Forster et al.¹¹ Cataracts

can be operated on once the inflammation has completely subsided. After the eye is quiet, we wait for 3 months before undertaking cataract surgery in these patients.

Final visual outcome was 6/12 or better in 30.9% of our cases. Visual acuity of patients presenting 3 months after onset of symptoms was: 7 eyes (9.6%) showed improvement, 24 eyes (32.9%) remained stable, and 42 eyes deteriorated (57.5%). Visual acuity was better in patients who presented within 1 month after onset of symptoms. Of 31 such cases, 71.7% showed improvement of more than two lines. Systemic steroid in high doses was the mainstay of therapy in these cases. These results are compatible with other studies.^{1-3,8,9} Visual outcome was poor in those patients who had already marked scarring with subretinal fibrosis, complicated cataract, or secondary glaucoma. Visual improvement was not good following vitreoretinal surgery in those cases with evidence of subretinal fibrosis. Beniz et al¹ reported 59% of their patients having final visual acuity of 6/12 or better. Yoshida et al⁹ reported vision of 6/12 or better in 42% of their cases.

Our study indicated that VKH disease in India is much less common than in Japanese patients and similar to that seen in the United States.¹⁰ We also showed that extraocular signs are far less common than in Japan. Due to the referral nature of our institute, a significant proportion of the patients presented in an advanced stage of the disease. The need for immunosuppressive agents and vitreoretinal surgery was therefore higher in our series. We also encountered increased incidence of complications, especially cataract and glaucoma.

There were fewer dermatological symptoms in our Indian VKH patients. This could be due to several factors. One such factor could be race, as the Indians are mostly darkly pigmented with more melanin in the skin. Our study indicates that VKH presents different clinical aspects in India.

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