Vogt-Koyanagi-Harada Disease Managed With Immunomodulatory Therapy Within 3 Months of Disease Onset

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• PURPOSE: To study the outcome of high-dose corticosteroids with early addition of immunomodulatory therapy (IMT) in patients with Vogt-Koyanagi-Harada (VKH) disease.
• DESIGN: Retrospective, interventional case series.
• METHODS: Patients with VKH seen at Singapore National Eye Centre from 2008-2018 were studied. The standardized clinical protocol was intravenous methyl prednisolone followed by/or oral prednisolone 1 mg/kg daily with slow taper plus IMT within 3 months. We collected data on demographics, clinical features, and indocyanine green angiography (ICGA). Uveitis activity was assessed clinically and by ICGA. Results were compared when IMT was given before vs after 6 weeks (late IMT) and with historical data (IMT added when uveitis uncontrolled).
• RESULTS: Fifty-eight eyes of 29 patients were studied. Half of the patients were Chinese (15, 51.7%). The mean age ± standard deviation was 42.2 ± 13.3 years. Twenty-five patients required 1 IMT and 4 needed 2 drugs. Sunset glow fundus occurred in 34 of 58 eyes (58.6%). Uveitis resolved in 24 of 58 eyes (41.4%), became chronic in 30 (51.7%), and required chronic recurrent in 4 eyes (6.9%). *Eyes with IMT initiated within 6 weeks had better visual outcome that was significant at 4 years ($P = .036$; Mann-Whitney U test)* but had a similar occurrence of sunset glow fundus and uveitis. Compared with historical data, visual outcome was better and was significant at 3 years ($P = .04$; t test), and significantly fewer patients developed chronic recurrent disease ($P < .001$; χ^2 test).
• CONCLUSION: High-dose corticosteroids with IMT within 3 months resulted in improved visual outcomes and a reduced risk of developing chronic recurrent uveitis compared with IMT given as clinically indicated. (Am J Ophthalmol 2020;220:37–44. © 2020 Elsevier Inc. All rights reserved.)

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VOGT-KOYANAGI-HARADA (VKH) DISEASE IS A multisystem T cell–mediated autoimmune disorder directed against various melanocyte-containing organs, causing bilateral granulomatous panuveitis, choroiditis, and exudative retinal detachment. Systemic manifestations include central nervous system, auditory, and integumentary abnormalities that may be present to varying extent. It was previously thought that cases developing ocular signs, such as sunset glow (SSG) fundus or vitiligo, were a part of the natural course of the disease.[1,2] However, there is sufficient evidence to suggest that many of these chronic signs are preventable if the disease is adequately treated, preventing the development of manifestations of chronic disease.[3–5] Early diagnosis, timely initiation of treatment, and appropriate and adequate therapy are key to the optimal management of VKH. A delay in diagnosis and in initiating adequate treatment may result in a higher risk of developing disease chronicity, complications, and visual impairment.[3]

VKH is a common cause of panuveitis in Singapore. In a previous study,[2] we found that despite starting patients on high doses of corticosteroids orally or intravenously (IV) within 2 weeks of onset of uveitis, the disease continued to evolve in >35% of cases. This resulted in patients presenting as probable or incomplete VKH deteriorating ≥1 category steps. Clearly, administering corticosteroids alone was not adequate for some patients. These findings have also been reported by other authors.[1,3,5]

In this study, we aim to evaluate the outcome of VKH treated with a combination of oral corticosteroids and immunomodulatory therapy (IMT) initiated within 3 months of disease onset. In addition, we intend to compare the results with our previous study,[2] where IMT was only used when corticosteroids were clinically inadequate to control the uveitis.

METHODS

THIS WAS A RETROSPECTIVE REVIEW OF PATIENTS WITH VKH seen at the Singapore National Eye Centre

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(SNEC) between January 1, 2008 and December 31, 2018. The diagnosis of VKH was made based on the VKH International Committee criteria.[6] Consecutive patients were identified from the SNEC uveitis database. Only eyes with a minimum follow-up of 6 months were included. Patients treated with only corticosteroids were excluded. Informed participation consent was taken from patients whose follow-up extended beyond November 2017. The data were anonymized by a third party before analysis. The study and data accumulation were in conformity with the Singapore Personal Data Protection Act and this study was approved by the SingHealth Centralized Institutional Review Board (protocol number: CIRB, reference number: 2019/2811). The research adhered to the tenets of the Declaration of Helsinki.

We documented patient demographics, clinical features at presentation, complications, and imaging data (indocyanine green angiography [ICGA] and enhanced depth imaging optical coherence tomography [OCT] findings) at presentation and various time intervals. Uveitis activity was assessed clinically and by ICGA findings. Details of the type and duration of therapy were recorded.

The patients were divided into acute phase and chronic phase based on the interval between onset of symptoms and presentation. According to International Study Committee categories, patients were further classified as complete, incomplete, or probable VKH.[6]

Disease activity was categorized based on both clinical signs as well as ICGA signs defined above. Clinical quiescence was defined as the absence of anterior chamber cells and vitreous haze according to the Standardization of Uveitis Nomenclature,[7] with resolution of the choroiditis and subretinal fluid. OCT was performed at every clinic visit. ICGA was performed once or twice within the first 6 months until the disease was quiescent, each time when medication was stepped down, and at a minimum of 6-12 monthly intervals. Complications documented included posterior synechiae, new onset cataract, glaucoma, SSG fundus, retinal pigment epithelial disturbance, subretinal fibrosis, choroidal neovascular membrane, and chorioretinal atrophy.

• **IMAGING:** We used enhanced depth imaging OCT (Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany). For study purposes, we captured the presence or absence of subretinal fluid and choroidal thickness at the fovea. The subfoveal choroidal thickness measurements were taken from the retinal pigment epithelium/Bruch reflective complex to the sclerochoroidal interface using manual calipers.

ICGA was performed using the Topcon 50 IA camera (Tokyo, Japan) coupled to an image digitalizing system (Topcon Imagenet 2000, v 2.15, Tokyo, Japan), according to a standard protocol, whenever the OCT showed no improvement and when IMT adjustment was planned. Following a bolus injection of 50 mg of indocyanine green in 4 mL normal saline, images were captured from the start until 20 minutes. The ICGA was assessed for the presence of the following signs of disease activity according to Kawaguchi and associates[3]: 1) early choroidal stromal vessel hyperfluorescence and leakage; 2) hypofluorescent dark dots; 3) fuzzy vascular pattern of large stromal vessels; and 4) disc hyperfluorescence, with ICGA quiescence being defined as the absence of any of these ICGA signs. The ICGA was deemed to show evidence of active disease if any of these 4 signs were present. In addition, ICGA was assigned a score from 0-4 based on the number of positive signs present as described in a previous study.[8]

• **TREATMENT:** Patients were admitted at the time of presentation for investigations and initiation of treatment. They were discharged when their vision began to improve and they could mobilize. They were typically followed-up initially at weeks 1, 2, 3, and 4 then monthly for first 3 months, every 2-3 months for 1 year, every 3-4 months until stable on IMT, and then every 6 months.

During this period, all patients received treatment according to a standardized protocol: IV methylprednisolone 1 g daily for 3 days followed by/or ≥1 mg/kg body weight prednisolone daily tapered over a minimum of 6 months. The initiation of prednisolone therapy was followed by IMT within 3 months with antimetabolite drugs (azathioprine, methotrexate, or mycophenolate mofetil [MMF]) or cyclosporin. Patients treated only with corticosteroids were excluded from the study. Prednisolone was gradually tapered off and immunomodulatory agent was increased as indicated. This was increased to the maximum tolerable dosage before it was switched to another agent or another agent was added, depending on the response to therapy. Monitoring tests were done regularly and as indicated.

To understand the effect of timing of initiation of IMT on the course of VKH, patients were divided into 2 groups based on when IMT was added: IMT received ≤6 weeks of onset of disease (early IMT) and IMT received >6 weeks of onset of disease (late IMT). The prevalence of SSG fundus at various time points (6 months then yearly), uveitis outcome (resolved, chronic, or chronic recurrent), and visual outcome at various time points (6 months then yearly) was compared between the 2 groups.

• **COMPARISON OF OUTCOME WITH HISTORICAL DATA:** To facilitate comparison with previous published data,[2] study eyes were also classified based on the therapy received at presentation. High-dose therapy (HD) was defined as prednisolone administered at ≥1 mg/kg/day given orally or IV. In early-high (EH) group, HD therapy was given within 2 weeks after onset of the symptoms of VKH. The eyes that received HD therapy at >2 weeks but <1 month after symptom onset were labeled as late-high (LH). Low-dose therapy (LD) was labeled in eyes that were treated with lower doses or with no systemic

corticosteroid at all or which received HD corticosteroids, but >1 month after symptom onset.

We compared the prevalence of SSG fundus, uveitis outcome (resolved, chronic, or chronic recurrent), and visual outcome between the 2 groups with differing treatment approach.

Statistical analyses of continuous variables were conducted with paired tests using the Wilcoxon signed rank test to analyze the effect of baseline visual acuity (VA) logarithm of minimal angle of resolution (logMAR) vs each time point VA logMAR. The Mann-Whitney *U* test was used to compare independent groups. For categorical data, χ^2 or Fisher exact tests were conducted where appropriate. The statistical analysis was performed using IBM SPSS software (v 24.0; IBM Corp, Armonk, New York, USA). Means with standard deviations (SDs) were calculated for continuous variables and frequency with percentage were tabulated for categorical variables.

Kaplan-Meier survival plots were used to illustrate the difference of survival probability between EH and LH. The log rank test was used to compare 2 survival curves. Event was based on the event of having best-corrected VA logMAR ≥0.3 among treatment groups. Statistical significance was defined as $P < .05$.

RESULTS

DURING THE STUDY PERIOD, 68 EYES OF 34 PATIENTS DIAGnosed with VKH were identified. Five patients were excluded because they had been treated with systemic corticosteroids only, leaving 29 patients included in this study. The reasons for not giving systemic steroids only include patient refusal ($n = 3$), history of breast carcinoma ($n = 1$), and treatment initially by a medical retina specialist who did not offer IMT, with subsequent referral to our clinic for management. Half of the patients were Chinese (15, 51.7%), 4 were Malay (13.8%), 2 were Indian (6.9%), and 8 were other races. There was male predominance (19, 58.6%) and the mean age ± SD at presentation was 42.2 ± 13.3 years. The median duration of follow-up was 5.3 years (range 0.51-13.6 years).

Among the study patients, 3 patients were initially partially treated elsewhere, while others presented to the SNEC because they were symptomatic. Slit-lamp examination revealed keratic precipitates in 28 eyes of 14 patients (48.3%). The keratic precipitates were fine in 14 eyes, small in 12 eyes, and granulomatous in 2 eyes. Anterior chamber activity was present in 35 eyes (60.3%), 8 eyes had flare 2+, and 4 had flare 1+. No eyes developed posterior synechiae. Posterior segment examination revealed vitritis in 10 eyes (17.2%), disc swelling in 10 eyes of 5 patients (17.2%), and exudative detachment of the retina in 44 eyes (75.9%) at initial presentation. Eyes without clinical exudative detachment had OCT and ICGA signs of active VKH. Systemic manifestations included 3 patients with tinnitus, but none had hearing loss, meningism, vitiligo, poliosis, or alopecia. Cerebrospinal fluid analysis was conducted in 13 patients, revealing pleocytosis in 9 patients (69.2%).

VKH was classified as incomplete VKH in 9 patients (31.0%) and probable VKH in 20 patients (69.0%). No patients had complete VKH. According to treatment category, 24 patients (82.8%) received EH. Three patients were treated with low-dose corticosteroids elsewhere and 2 patients received high doses of corticosteroids but treatment was delayed >4 weeks. These 5 patients were categorized as LD.

Average time to treatment was 9.0 ± 16.7 days, with a median of 5.0 days (range 0-89 days). Eighteen patients were initially treated with IV methyl prednisolone 1 g once a day for 3 days while the remaining 11 received high-dose oral prednisolone. The median duration of prednisolone was 21 months (interquartile range 14-33.3 months) and the average duration of prednisolone therapy at a dose of >10 mg daily was 5 months. Prednisolone was ultimately discontinued in 17 patients (58.6%).

• **IMMUNOMODULATORY THERAPY:** One immunomodulatory drug was used in 25 patients and 2 immunomodulatory drugs in 4 patients (azathioprine and cyclosporin A). Uveitis resolved and all medication was discontinued completely in 2 patients at a mean of 1.71 years.

Azathioprine was used in 27 patients. Fifteen patients (55.6%) discontinued because of intolerance (6 patients) and deranged blood test results (9 patients). VKH resolved in 2 patients. The average duration of treatment was 46.8 ± 36.4 months.

Methotrexate was prescribed to 12 patients. It was discontinued in 3 patients because of lack of efficacy. The average duration of treatment was 51 ± 23.3 months. None of the patients resolved with methotrexate.

MMF was used to treat 7 patients. Three patients were intolerant (42.9%). The average duration of treatment was 26 months (SD 17.5 monts) and uveitis did not resolve in any of the patients taking MMF.

Cyclosporin was used in 4 patients for an average of 38 months. None of the patients had remission of uveitis. One patient with recalcitrant VKH was treated with cyclophosphamide. Despite this, the patient became clinically quiescent but persistently active on imaging. The patient refused further adjustments of IMT. None of the patients in this study used biologic therapies.

• **TREATMENT OUTCOME:** The VA of most patients did not fall below logMAR 0.3 throughout their follow-up. Mean logMAR vision improved for both eyes at all time points compared with baseline ($P < .01$, pairwise Wilcoxon signed rank tests; Figure 1). With treatment, the subfoveal choroidal thickness on OCT decreased over time in all patients. The mean choroidal thickness readings on enhanced depth imaging OCT at baseline (first readable),

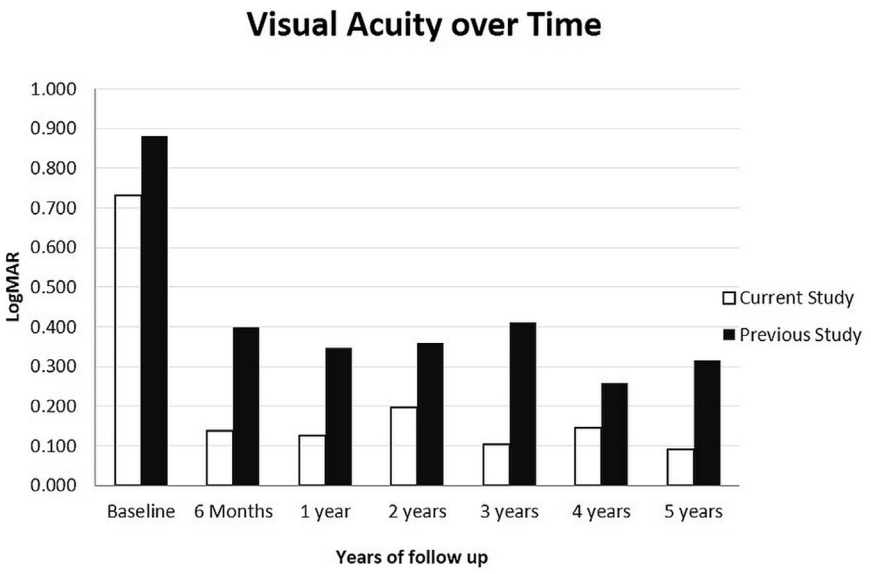

FIGURE 1. Differences in visual acuity outcome (logarithm of minimal angle of resolution [logMAR]) between the current study and previous study[2] cohorts. The differences were only statistically significant at year 3 ($P = .039$, χ^2 test).

initiation of IMT, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years were as follows: 635 μm (SD 200 μm), 612 μm (SD 114 μm), 343 μm (SD 107 μm), 311 μm (SD 108 μm), 291 μm (SD 95 μm), 278 μm (SD 79 μm), 274 μm (SD 70 μm), and 285 μm (SD 62 μm), respectively. The mean choroidal thickness at the start of IMT and at 6 months was significantly different ($P < .001$, *Wilcoxon signed rank test)*.

Apart from 1 patient who received LD treatment initially seen elsewhere who presented quiescent to SNEC, all patients had clinically active uveitis at presentation. Over the next 5 years of follow-up, 2 patients were still active at 6 months (7.6%); and 1 patient each had a relapse at year 3 and year 4 of follow-up.

Twenty-eight of 29 patients had ICGA activity at presentation and 1 patient had no ICGA signs (the patient who had corticosteroid therapy initiated elsewhere). Four patients (8 eyes, 14.3%) had early hyperfluorescent choroidal vessels, 11 patients (22 eyes, 39.3%) had hypofluorescent dark dots, 11 patients (22 eyes, 39.3%) had fuzzy choroidal vessels, and 2 patients (4 eyes, 7.1%) had disc hyperfluorescence. The average ICGA score decreased throughout follow-up period. At the 5-year follow-up, 2 patients had persistent hypofluorescent dark dots (Figure 2).

SSG fundus at presentation were seen in 3 patients even though they were in the acute uveitic phase and were excluded from analysis of development of SSG fundus. Thirty eyes (57.7%) developed SSG fundus on treatment. It eventually occurred in 34 of 58 eyes (58.6%). Thus, of the 29 patients (58 eyes) presenting with acute VKH, features of chronic VKH occurred in 30 eyes (51.7%), and 4 eyes (6.9%) went on to chronic recurrent uveitis. Twenty-four of 58 eyes (41.4%) resolved.

Complications included 8 eyes of 4 patients with cataracts and 2 eyes of 1 patient with retinal pigment epithelial disturbances. None had glaucoma, subretinal fibrosis, choroidal neovascular membrane, or chorioretinal atrophy.

Kaplan-Meier survival analysis based on the event of having best-corrected VA logMAR 0.3 or better among treatment groups revealed that at 1 year, survival of the EH eyes was 100% and the LD eyes was 88.3% although the comparisons were not significant (log rank $P = .842$; Figure 3).

• **COMPARISON BETWEEN EARLY AND LATE IMT:** Of the 29 patients with VKH, 15 (51.7%) received early IMT and the remaining (14, 48.3%) received late IMT. The prevalence of SSG fundus at various time points were analyzed between early and late IMT (18 eyes [60.0%] and 16 eyes [57.1%], respectively) and found to be similar at all time points. We looked at the uveitis outcomes based on resolved, chronic recurrent, and chronic categories for IMT initiated before and after 6 weeks of onset of disease. There was no difference in the proportion of eyes with resolved uveitis (12 eyes each in early [42.9%] and late [40.0%] IMT). Two eyes each in the early and late IMT groups developed chronic recurrent inflammation. Comparison of the visual outcomes between the early and late IMT groups was better overall in the early IMT group, but was statistically significant only at 4 years (logMAR 0.06 [SD 0.07] and logMAR 0.2 [SD 0.2], respectively; $P = .036$, *Mann-Whitney U test)*. The nonsignificant findings for other years may be related to the small sample size comparisons.

• **COMPARISON WITH HISTORICAL DATA:** In the 2007 study,[2] 120 acute VKH eyes were treated with

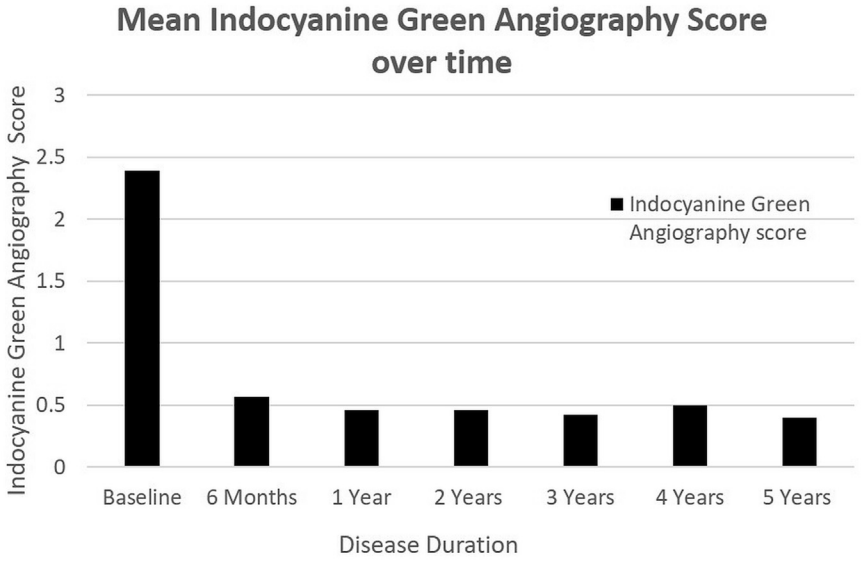

FIGURE 2. Mean indocyanine green angiography score reducing over time with treatment.

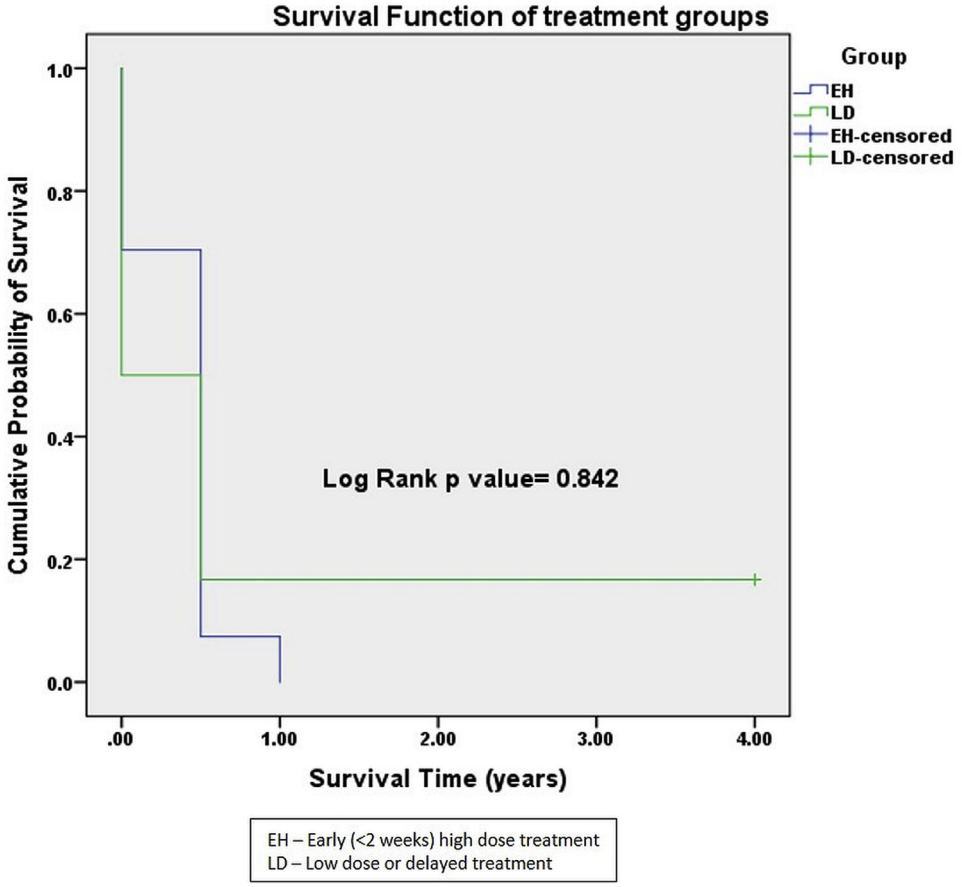

FIGURE 3. Kaplan-Meier survival analysis based on the event of having a visual outcome of logarithm of minimal angle of resolution (logMAR) ≥0.3. For patients receiving high doses of corticosteroid within 2 weeks of disease onset (EH), 100% achieved logMAR ≥0.3 at year 1. In patients who received low-dose corticosteroids or those whose treatment was initiated 4 weeks after the disease onset (LD), 16.7% achieved logMAR ≥0.3 up to 4 years.

corticosteroid predominantly and IMT was added only when uveitis was clinically uncontrolled. Of these, 40 eyes resolved (33.3%), 34 became chronic (28.3%), and 46 became chronic recurrent (38.4%). In this study, of the 58 acute eyes receiving systemic corticosteroid and IMT given within 3 months of disease onset, 24 eyes resolved (41.4%), 30 eyes became chronic (51.7%), and 4 eyes became chronic recurrent (6.9%).

Comparing the studies, significantly more eyes became chronic ($P = .008$, χ^2 test) but fewer chronic recurrent ($P < .001$, χ^2 test) with administering IMT within 3 months. Although the prevalence of SSG fundus in the current study was lower (34 eyes, 58.6%) than in the previous study (95 eyes, 68.34%), this was not statistically different ($P = .168$, χ^2 test).

The logMAR comparison of VA outcomes between the cohorts of this study and previous study[2] that treated patients predominantly with corticosteroids showed that there were differences in outcomes between the cohorts. However, these differences were only statistically significant at year 3 ($P = .039$, χ^2 test). The nonsignificant findings for other years may be related to the small sample size comparisons.

DISCUSSION

VKH IS A RELENTLESSLY PROGRESSIVE PANUVEITIS THAT leads to chronic recurrent disease and visual loss if inadequately treated, and is one of the indications for starting IMT.[9] Almost 2 decades ago, IMT was recommended for the treatment of uveitis when the corticosteroid dose could not be lowered to a safe level of ≤10 mg/day. Adding IMT to spare the corticosteroid dose or when the uveitis could not be adequately managed with corticosteroids only was practiced when managing patients with VKH in a previous study,[2] which found that only a third of acutely presenting patients resolved with this treatment approach. Indeed, more than a quarter became chronic and 38.4% became chronic recurrent. We also found that using ICGA to monitor VKH disease activity did not significantly improve uveitis outcomes and reasoned that this was because the ICGAs had not been performed frequently enough to allow for adequate adjustment of therapy.[10] In this article, we studied a similar population but a different cohort of patients with VKH who were treated initially with a similar regimen of systemic corticosteroids. IMT was added within 3 months of disease onset for all patients. In addition, the disease was monitored not only by clinical means but also with the help of choroidal imaging using OCT and frequent ICGA for assessment of choroidal activity. The mean choroidal thickness was observed to reduce from baseline to initiation of IMT, and by 6 months the swelling was significantly thinner ($P < .001$, Wilcoxon signed rank test). The mean choroidal thickness continued to decrease until 1 year and thereafter appeared to stabilize. A similar trend was seen in the mean ICGA score over time. This management resulted in better visual outcome, significant at 3 years ($P = .039$, t test) and also significantly fewer eyes progressing to chronic recurrent disease (6.9% vs 38.4%; $P < .001$, χ^2 test).

Abu El-Asrar and associates[11] recently showed that they were able to prevent the development of SSG fundus in a cohort of patients with VKH treated with MMF as first-line therapy combined with systemic corticosteroids at the onset of acute VKH. Although the choice of IMT rather than the timing of its initiation may have been the key factor, we believe that the latter was the main reason for their success. In rheumatologic and other immune diseases, it is well known that there exists a therapeutic window of opportunity.[3,12] Unless adequate therapy is administered during this time interval, the disease progresses to a chronic state and subsequent addition of therapy or switching to more costly therapy may not result in the reversal of the damage nor the desired outcome.[13] Indeed, in contrast to their study, MMF was discontinued as it was not tolerated by 3 of the 7 patients in our study who received it. Patients who were tolerant used it for an average of 26 months without achieving disease resolution.

The choice of IMT in our practice is azathioprine. This is cheap, easily available, and safe for use during pregnancy. It is, however, not always well tolerated, and most who are intolerant experience undesirable gastrointestinal effects. A third of patients develop deranged blood test results, either drug-induced hepatitis (elevation of liver enzymes) or leukopenia. Testing for the enzyme thiopurine methyltransferase, which metabolizes thiopurines, unfortunately is not available in Singapore. For this reason, azathioprine is introduced at a low dose of 25 mg/day and only when the initial blood results are reviewed and found to be normal is the dose increased. Using azathioprine, disease resolution was achieved in 2 patients but not with using other IMT in our series. The average duration of therapy was close to 4 years, suggesting that in patients who were tolerant to the drug, generally, they would be able to use it over the long term.

The use of IMT early in the disease process in our study certainly had a role in preserving vision in these eyes and minimizing clinical relapse as is evidenced by the improved outcomes. However, despite introducing IMT within the first 3 months of onset of VKH in cases who received HD systemic corticosteroids, SSG fundus occurred in more than half (58.6%) of our patients. In majority of the patients, we were unable to achieve disease resolution to achieve cure of uveitis that would have enabled us to discontinue IMT completely without relapse. In our previous study,[2] we had shown that VKH should be treated within 2 weeks of onset of disease, this being the therapeutic window. Initiating therapy beyond this time interval resulted in poorer prognosis and a higher risk of developing chronic disease. From the findings of this study, adding IMT within

3 months improved the outcome but did not prevent chronic disease. When we compared early IMT with late IMT, we did not detect any difference in the incidence of SSG fundus nor in the uveitis outcome. However, the visual outcome was better, reaching statistical significance at 4 years ($P = .036$, *Mann-Whitney U* test). Thus, initiating IMT before 6 weeks appears to be beneficial, but is yet unable to prevent the development of SSG fundus. Perhaps initiating corticosteroid therapy alone respecting the therapeutic window of 2 weeks is inadequate because the severity of the disease warrants the addition of IMT to bring the immune response under control. As IMT does not take effect immediately, often taking months to have maximal effect,[9] being quicker in onset in MMF than MTX or azathioprine, introducing it as soon as possible rather than when the dose of corticosteroid has been decreased is likely to achieve a better outcome over the long term. *Indeed, our current practice is to start IMT with the oral steroids.*

This study has several limitations. Despite its retrospective nature, the small number of cases, the suboptimal use of ICGA to monitor disease activity due to cost, and the lack of use of more quick-acting and powerful therapies, such as biologics, our study has several important findings. First, adding IMT within 3 months to HD systemic corticosteroids initiated within 2 weeks of onset of VKH is inadequate in preventing the development of SSG fundus in >50% of our patients. Second, we were able to statistically compare the outcome of the patients in this study with a historical cohort because we had used a standard though different clinical protocol at each time, and because we had archived the previous study data. We found that patients who had received IMT within 3 months with HD corticosteroid therapy achieved better outcomes. Third, the choice of IMT in our patients reflects the real-world situation where the long-term cost of the medication is of grave concern for the many who pay out of pocket. Although the numbers were small, we saw resolution of VKH in patients who had been treated with azathioprine.

In conclusion, our study found that the use of IMT in addition to HD systemic corticosteroids was beneficial when introduced within 3 months of VKH onset. Although this led to outcomes that were better than adding IMT only when disease was clinically active, this regimen did not prevent the development of SSG fundus in >50% of patients. In addition, we found that starting IMT before 6 weeks improved the visual outcome but did not prevent SSG fundus. Thus, we recommend starting IMT as soon as is possible. Larger prospective studies are required to determine the ideal immunomodulatory drug and the optimal time this should be introduced in the management of acute VKH.

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