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Predictors of Recurrence in Vogt-Koyanagi-Harada Disease

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Purpose: Normally, Vogt-Koyanagi-Harada (VKH) disease has a good prognosis with adequate treatment. However, VKH disease recurs more frequently if diagnosis is delayed or treatment is inadequate. As soon as VKH disease recurs, inflammation is harder to control and the prognosis worsens. Our objective was to study predictors of recurrence in patients with VKH disease.

Design: Retrospective case series.

Participants: Forty-one eyes of 41 patients (25 women, 16 men) were included in this study. Patients with recurrent attacks of inflammation were classified as recurrent, whereas patients needing only steroid treatment, without any recurrent attacks, were classified as nonrecurrent.

Methods: Descriptive and bivariate analyses were used to characterize disease and outcomes. A blood-flow analysis was performed with laser speckle flowgraphy on days 0, 14, 30, and 60. Choroidal thickness was measured with swept-source OCT, using a 12-radial scan protocol, on the same day as mean blur rate (MBR) measurement. Flare in the anterior chamber also was measured on the same day, using a flare cell meter.

Main Outcome Measures: Prevalence of each type of disease pattern and flare, MBR, and thickness of the choroidal layers.

Results: The recurrent group initially had lower visual acuity (VA) and higher flare than the nonrecurrent group, but these parameters improved over time and were similar in the groups on days 14, 30, and 60. However, on these days, MBR was significantly lower in the recurrent group than in the nonrecurrent group. Choroidal thickness was not significantly different in the 2 groups at any time point.

Conclusions: We found that patients with recurrent VKH disease had lower VA, higher initial flare number, and a lower response of MBR to treatment than patients with nonrecurrent VKH disease. Thus, VA and flare number during the initial phase, as well as the MBR response to treatment, may be useful in determining the prognosis for VKH disease and choosing therapeutic options. *Ophthalmology Retina 2017;■:1–8 © 2017 by the American Academy of Ophthalmology*

Vogt-Koyanagi-Harada disease (VKH) is a common type of uveitis in Japan.[1] The symptoms usually appear suddenly, without any precursors, although the disease has been reported to occur sometimes after systemic viral infections.[2,3] Vogt-Koyanagi-Harada disease is a T-cell–mediated autoimmune disease directed against melanocytes.[4] Therefore, symptoms can be located in several different organs and tissues, appearing as uveitis, skin depigmentation, sensory deafness, or meningitis. The prognosis for VKH disease is usually good with steroid treatment. However, VKH disease frequently recurs because of poor initial visual acuity (VA), anterior chamber reaction of more than 2+ at initial presentation, delayed diagnosis, and insufficient treatment (i.e., too-rapid systemic tapering of steroids).[1,2] Iwahashi et al[5] reported that posterior recurrence mostly occurred within half a year of disease onset. Rubsamen and Gass[6] also reported that almost all recurrence within 6 months of presentation was associated with a too-rapid or premature decrease in steroid dose. Specifically, posterior recurrence developed when treatment with 5 to 30 mg corticosteroid was tapered between 1.5 and 5 months after the onset of symptoms. When VKH disease becomes recurrent, inflammation becomes difficult to control, and additional treatments, such as increasing the steroid dose or adding immune-suppressive drugs, become necessary. Currently, even with the best diagnostic and treatment strategies, 20% of VKH disease patients experience recurrence.[1] Thus, it would be very useful to identify quickly those patients whose disease is likely to become recurrent, but currently it is difficult to do so.

Aqueous flare and cell counts usually are considered to be important indicators of ocular inflammation in VKH disease, because they reflect the breakdown of the barrier between the ocular tissue and the blood vessels. These parameters usually are measured as the Standardization of Uveitis Nomenclature score, which is determined in a slit-lamp examination.[7] However, the accuracy of this method relies on the experience of the examiner, and thus usually requires an attending uveitis specialist. Therefore, measurements of inflammation obtained by general ophthalmologists can be inadequate, and moreover,

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slit-lamp observations lack objectivity. To overcome these limitations, laser flare cell meters have been introduced to provide objective measurements of inflammation-induced flare in the anterior chamber.[8–10] Furthermore, a study based on laser speckle flowgraphy (LSFG) has reported that choroidal blood flow, especially the microcirculation of the choroid, is an index of disease activity for VKH disease after treatment with steroids.[11] Laser speckle flowgraphy is a noninvasive technique for measuring blood flow velocity in the choroidal layers.[12] This technique requires just a few seconds to acquire an image of choroidal circulation, and it has excellent reproducibility.[11,13] The key measurement parameter of LSFG is mean blur rate (MBR), which represents the relative velocity of erythrocytes in the blood vessels.[14] Laser speckle flowgraphy has been reported to provide measurements of ocular microcirculation that are equivalent to those obtained using the microsphere method.[15]

Thus, the present study set out to determine new biomarkers of future recurrence in VKH disease, allowing clinical prediction of the need for advanced treatment. To achieve this goal, this study measured choroidal blood flow with LSFG, flare with a flare-cell meter, and choroidal thickness with swept-source OCT, and compared these measurements over the clinical course of VKH disease in groups of patients with recurrent and nonrecurrent types of the disease.

Methods

Patients and Diagnosis

This study included 41 eyes of 41 patients (25 women, 16 men) who were diagnosed with VKH disease based on clinical data from a slit-lamp examination, OCT, angiography, and lumbar puncture analysis.[3] The patient detail is provided in Table 1. All patients were admitted to Tohoku University Hospital between October 2012 and May 2016. Their medical records were analyzed retrospectively. Recurrent VKH disease was defined by the need for additional treatment, such as immune suppressive drugs, as a result of recurrent inflammation (defined according to the Standardization of Uveitis Nomenclature score)[4] or other complications, such as serous retinal detachment or choroidal neovascularization. Patients needing only steroid treatment were classified as nonrecurrent. This study was approved by the ethics committee of Tohoku University Hospital and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants for chart review after the nature and possible consequences of the study had been explained.

Table 1. Patient Details

Patient No.	Gender	Age (yrs)	Objective Eye	Time to Treatment (days)	Prednisolone Dose (mg) at Recurrence
1	F	43	Left	17	2.5
2	F	66	Right	38	5
3	F	76	Right	6	20
4	M	60	Left	13	5
5	F	58	Right	8	35
6	M	40	Right	36	20
7	M	78	Left	195	40
8	F	60	Left	33	40
9	F	62	Left	64	40
10	M	25	Left	8	20
11	F	19	Right	18	40
12	M	37	Right	5	20
13	F	37	Left	33	20
14	M	66	Right	2	10
15	F	48	Left	2	15
16	M	58	Right	4	15
17	F	56	Right	8	15
18	F	28	Right	15	5
19	M	70	Left	9	15
20	M	51	Left	6	0
21	F	66	Left	5	0
22	F	29	Right	6	25
23	F	72	Right	6	—
24	F	57	Left	8	—
25	M	40	Left	18	—
26	M	59	Right	50	—
27	F	30	Right	8	—
28	F	30	Left	11	—
29	F	35	Right	6	—
30	F	41	Left	15	—
31	F	35	Right	3	—
32	M	38	Right	6	—
33	F	47	Left	4	—
34	F	56	Right	73	—
35	M	39	Left	7	—
36	F	23	Right	2	—
37	M	38	Right	35	—
38	M	64	Left	12	—
39	F	41	Left	7	—
40	M	58	Left	19	—
41	F	13	Left	3	—

F = female; M = male.
Dashes indicate no recurrence.

Clinical Examination

General clinical examinations for uveitis were performed throughout the clinical course, including measurements of VA, intraocular pressure, flare number, retinal and choroidal thickness, and MBR. Initial examinations and follow-up examinations at 3 and 6 months (or at the time of recurrence) included fluorescence and indocyanine green (ICG) angiography.

Treatment

Initial treatment comprised a daily intravenous injection of prednisolone (1 g) for 3 days. After the intravenous injection, oral prednisolone was started (60 mg/day or 1 mg/kg daily if the patient's body weight was less than 50 kg). The tapering schedule for prednisolone was as follows: 60 mg/day for 7 days, 50 mg/day for 7 days, 40 mg/day for 14 days, 35 mg/day for 14 days, 30 mg/day for 14 days, 25 mg/day for 14 days, 20 mg/day for 14 days, 17.5 mg/day for 14 days, 15 mg/day for 14 days, 12.5 mg/day for 14 days, 10 mg/day for 14 days, 7.5 mg/day for 14 days, 5 mg/day for 14 days, and 2.5 mg/day for 14 days. Immune-suppressive drugs, if prescribed, were administered at the first treatment. Patients with recurrent VKH disease received additional treatment comprising a single daily dose of 3 mg/kg cyclosporine, starting with a schedule of 30 mg/day prednisolone treatment. The trough level of cyclosporine was kept at 100 to 120 mg/ml during the clinical course.