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A Case of Vogt-Koyanagi-Harada Disease with Good Visual Acuity in Spite of Subfoveal Fold

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Background: Vogt-Koyanagi-Harada (VKH) disease patients with the complication of subretinal pigmented proliferative tissue tend to have a poor visual prognosis.

Case: We herein report a case of VKH with good visual acuity despite a prominent subretinal fold.

Observations: A 24-year-old woman, who experienced several recurrent episodes of VKH disease, had bilateral serous retinal detachment with poor vision (RE 20/40 and LE 20/25). After the administration of high doses of systemic corticosteroids and D-mannitol, the subretinal fluid disappeared and the sensory retinas gradually became reattached. During the course of therapy, prominent pigmented subretinal strands were formed in both eyes. Optical coherence tomography disclosed that the strands existed at the retinal pigment epithelium level. Amazingly, we observed a change in the location of the fold in the posterior retina during the course of the disease. The patient finally showed the ''sunset glow'' fundi and a subretinal fold that was located almost directly beneath both fovea. Fortunately, this patient was able to recover and finally achieve a good visual acuity (RE 20/17 and LE 20/17).

Conclusion: We reported a VKH disease patient with a good visual acuity despite a remarkable subfoveal fold, which changed its location during the course of the disease. **Jpn J Ophthalmol 2003;47:591–594** © 2003 Japanese Ophthalmological Society

Key Words: Optical coherence tomography, subfoveal fold, Vogt-Koyanagi-Harada disease.

Introduction

Vogt-Koyanagi-Harada (VKH) disease is bilateral, chronic panuveitis with systemic involvement including skin, meningismus, and dysacousia.[1] Although the exact cause of VKH disease remains unknown, T-cell–mediated autoimmunity against melanocytes shared by all areas of involvement is believed to play a major role.[2,3]

VKH disease patients generally have a good visual outcome;[1] however, some patients can have a poor visual prognosis because of a number of complications after prolonged inflammation.[4] Some complications, such as subretinal fibrosis and choroidal neovascularization, result in irreversible vision loss.[5–8] Subretinal fibrosis in VKH is often associated with a longer duration of disease and frequent relapses.[5] An insufficient dose of systemic corticosteroid tends to cause this situation. VKH disease patients with this complication are difficult to treat and usually have a poor visual prognosis.[5]

We herein report a 24-year-old VKH disease patient with a good visual acuity despite a remarkable subfoveal fold. It is notable and novel that the fold changed its location in the posterior retina during the course of the disease.

Case Report

A 24-year-old Japanese woman noticed bilateral blurred vision on December 13, 1999, and visited a local hospital. Her past medical history was noncontributory; she had experienced no trauma to her eyes. On examination, her visual acuity was RE 20/25, LE 20/30 and intraocular

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pressure was RE 9 and LE 11 mm Hg. The bilateral corneas and lenses appeared to be transparent. A few cells were found in the anterior chamber and vitreous. Serous retinal detachment was seen bilaterally at the posterior fundus and several leaking points were observed by fluorescein angiography (Figure 1). No optic disc edema was found. A diagnosis of VKH disease was made at the previous hospital, and systemic corticosteroid (dexamethasone 15 mg/day) was prescribed. However, this primary treatment was not sufficiently effective and her symptoms became exacerbated twice within a short span of time. Although the dose of systemic corticosteroids was increased, only a temporary effect was achieved. As a result, she was referred to our hospital on January 12, 2000.

At the first medical examination in our hospital, her visual acuity was RE 20/40 and LE 20/25, intraocular pressure was RE 11 and LE 12 mm Hg. An ophthalmoscopic examination disclosed bilateral bullous retinal detachment (Figure 2A), and a B-mode ultrasound examination also revealed retinal detachment (Figure 2B). She had aseptic meningitis (cell number 147/3 in cerebrospinal fluid despite no sign of infectious disease). Human lymphocyte antigens (HLA) were DR4-DR53-DQ4, which was compatible with VKH disease. The serum antibody titers for herpes simplex virus, varicella-zoster virus, Epstein-Barr virus, and *Toxoplasma gondii* were either negative or in the normal range. The test results of blood cell count, blood chemistry, the level of C-reactive protein, angiotensin-converting enzyme, and antinuclear antibody were also either negative or in the normal range. There were no abnormal signs in the chest x-ray. She had no dysacousia or pathologic skin lesions.

We administered high doses of systemic corticosteroids (dexamethasone 20 mg/day) with the addition of bilateral topical steroid eye drops (0.1% dexamethasone three times a day). We also administered D-mannitol 500 mL/day for 5 days to reduce the degree of serous retinal detachment. While the subretinal fluid decreased, bilateral subretinal folds became apparent. Figure 3A shows a fundus photograph 10 days after retreatment. These folds gradually changed location in an upper temporal direction with associated advanced pigmentation (Figure 3C). On fluorescein angiography, fluorescence was blocked on the pigmented proliferative tissue and on its periphery (Figures 3B and 3D). Systemic corticosteroids were administered for 6 months. At 9 months after undergoing the above therapy, her visual acuity in both eyes was 20/17, although prominent subretinal pigmented strands seemed to exist just under the fovea. Finally, the fundi became largely depigmented, and the ''sunset glow'' appearance was observed (Figures 4A and 4B). As shown in Figures 4C and 4D, an Optical Coherence Tomography (OCT) analysis revealed that the pigmented strands were limited to the retinal pigment epithelium (RPE), which seemed similar to the thickening of the pigment epithelial layer. Using OCT, we confirmed that there were no abnormal signs in the retina (such as edema, deposit, or hemorrhage) above the thickened RPE. We have followed-up the patient for 36 months and she has shown no signs of a recurrence of inflammation and no further abnormal signs, such as choroidal neovascularization.

Discussion

The symptoms and signs of this case are compatible with those of VKH disease. The patient had aseptic meningitis. HLA were DR4-DR53-DQ4. The fundi finally showed a typical ''sunset glow'' appearance.

It is notable that the newly formed subretinal fold actually changed position in the posterior retina and then finally located under the fovea bilaterally. The precise mechanism for the movement of the subretinal fold is still largely unknown. We speculate that some pigment epithelial cells might have left the RPE layer, and proliferated in the subretinal space when the retina detached, and then gradually formed the fold. The fold might have moved due to a decrease in the subretinal fluid.

Tsukahara et al reported that a patient suffered similar serous retinal detachment with subretinal proliferative tissue, or so-called multifocal posterior pigment epitheliopathy (MPPE).[9] Although photocoagulation therapy has been effective in some particular cases, the spontaneous healing of serous retinal detachment has also been observed to leave submacular scars and a marked visual loss in most patients. It is interesting to note that the shapes of the scars in MPPE were quite similar to those in the present case. In our case, primary steroid therapy did not sufficiently reduce the serous retinal detachment. We assume that the prolonged serous detachment will cause this type of subretinal proliferation of pigment epithelial cells.

We would like to emphasize that this patient maintained a good visual acuity in spite of the subretinal fold at the fovea. VKH disease patients generally have a good visual prognosis if they are successfully treated with systemic corticosteroids. However, the formation of subretinal fibrosis and choroidal neovascularization tend to carry a poor visual prognosis.[5,7] Up to now, the presence of a subretinal fold has been considered to correlate with a longer duration of disease and more severe ocular inflammation. Sternberg et al proposed that RPE migration and proliferation could lead to the development of

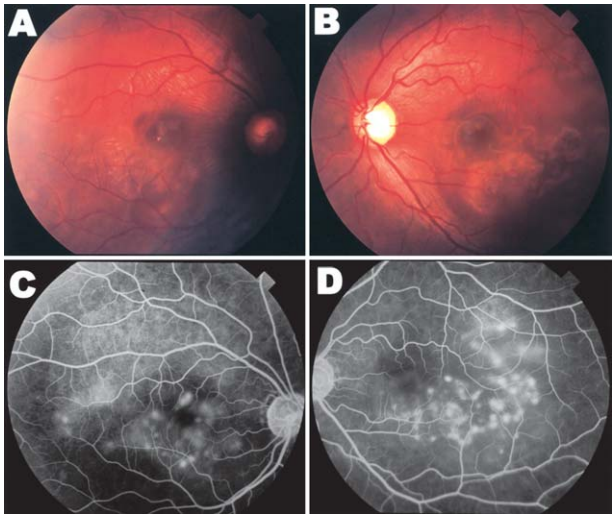

Figure 1. Color fundus photographs in a 24-year-old woman with Vogt-Koyanagi-Harada (VKH) disease (**A**: right fundus, **B**: left fundus) and fluorescein angiograms (**C**: right, **D**: left) on December 15, 1999 (at onset). Visual acuity was RE 20/25, LE 20/30. Note bilateral serous retinal detachment and several fluorescein leaking points.

subretinal folds during chronic retinal detachment.[10] Because chronic retinal detachment is a well-known feature in patients with severe VKH disease, it is possible that patients with chronic and/or untreated disease are at risk of developing subretinal fold.

The reason why our patient recovered and achieved a good visual acuity in spite of a subretinal fold at the fovea

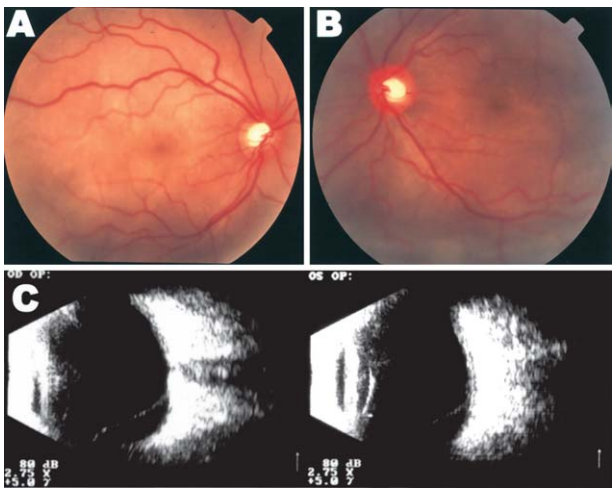

Figure 2. Color fundus photographs (**A**: right fundus, **B**: left fundus) and B-mode echo (**C**) on January 12, 2000 (at recurrence). Visual acuity was RE 20/40, LE 20/25. Note the remarkable bilateral retinal detachments.

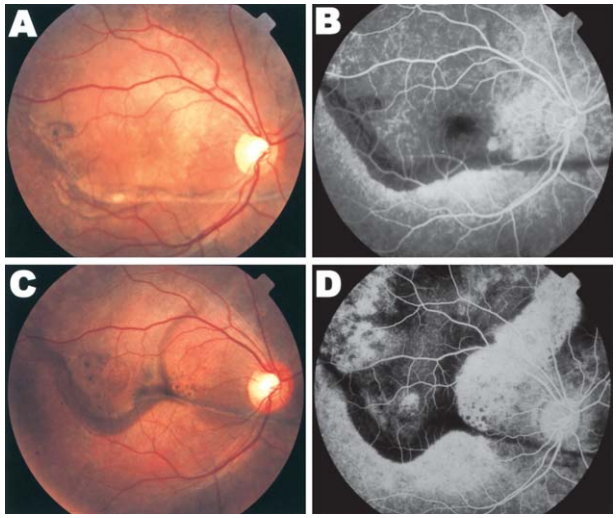

Figure 3. Color fundus photographs in patient's right eye on January 27, 2000 (**A**), and on February 23, 2000 (**C**). Fluorescein angiograms on January 27, 2000 (**B**), and on February 23, 2000 (**D**). Visual acuity was 20/33 (**A**), 20/30 (**C**), respectively. Note the prominent subretinal fold and the change in its location in both eyes. Retinal detachment ranged from nasal of the optic disc to lateral of the posterior arch in both eyes.

still needs to be explored. One of the possible reasons is that no angiogenic lesions were observed at the fovea by fluorescein angiography in this case (data not shown). The angiogenic features are usually described as irregular

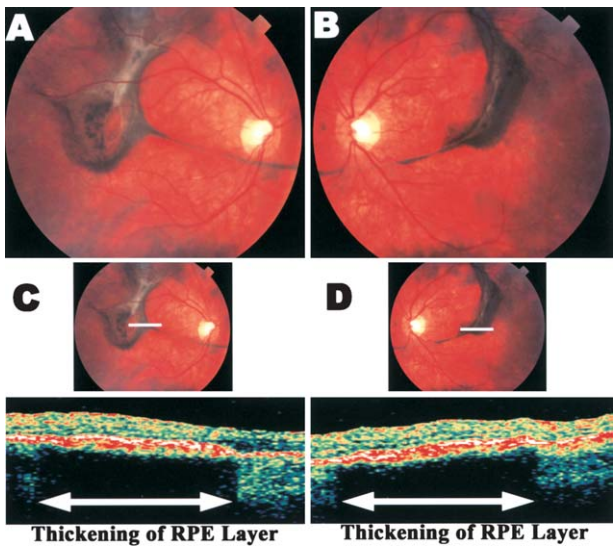

Figure 4. Color fundus photographs on July 28, 2000 (**A**: right fundus, **B**: left fundus) and results of optical coherence tomography (OCT) on the same day (**C**: right fundus, **D**: left fundus). The white bars show the scanning lines. Visual acuity was 20/17 in both eyes. Both fundi demonstrate the "sunset glow" appearance. Note the thickening of pigment epithelial layer in the lesion.

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early hyperfluorescence with late intense staining. In addition, an OCT analysis revealed that the subretinal fold seemed to be a simple thickening of RPE cells (Figures 4C and 4D). We assume that if the subretinal fold is accompanied by choroidal neovascularization it would cause a severe dysfunction of the fovea and a loss of visual acuity. We have previously reported that subretinal folds and disciform scars are due to the proliferation of RPE cells associated with choroidal neovascularization in severe cases of VKH disease.[8] Another explanation is that such subretinal folds are not located just beneath the fovea, and therefore the fovea is attached to the normal RPE layer. Especially in the right fundus of the present patient, the fovea is not observed on the thickened RPE layer by an OCT examination (Figure 4C). Another possibility is that even though the subretinal fold existed just beneath the fovea, the fold was covered by the normally functioning RPE. As a result, the fovea became attached to the functioning RPE in the same manner as previously observed.

For the treatment of a severe serous detachment of the retina in VKH, the intravenous injection of systemic D-mannitol was effective and promptly removed the subretinal fluid in our case. We believe D-mannitol therapy is an extremely effective modality for the treatment of prolonged retinal detachment and might thus be a useful method in addition to corticosteroid therapy for VKH disease. Previously, D-mannitol therapy was reported to be used in the treatment of serous retinal detachment associated with VKH disease.[11] The rapid reduction of retinal detachment by this treatment may thus be one of the reasons that a good visual acuity was obtained in this case.

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