European Journal of Ophthalmology / Vol. 15 no. 2, 2005 / pp. 277-283

Iris atrophy, serous detachment of the ciliary body, and ocular hypotony in chronic phase of Vogt-Koyanagi-Harada disease

J.M. SAARI[1], K. NUMMELIN[2]

[1]Department of Computational Engineering, Helsinki University of Technology, Helsinki
[2]Department of Ophthalmology, University of Turku - Finland

PURPOSE. *To describe iris atrophy, serous detachment of the ciliary body, and ocular hypotony in a patient with chronic phase of Vogt-Koyanagi-Harada (VKH) disease.*
METHODS. *Ocular examination and follow-up including digital infrared transillumination imaging of the iris was done in a 52-year-old woman with chronic phase of VKH disease.*
RESULTS. *Infrared transillumination imaging showed extensive atrophy of the iris stroma and occasional pigment clumps both in the pupillary and ciliary zones of the iris, and detachment of the ciliary body in both eyes. Conventional transpupillary transillumination using white light showed only minute patchy atrophy of the pigment epithelium in the pupillary zone. Treatment did not normalize bilateral shallow retinal detachment of the posterior pole, serous detachment of the ciliary body, or severe ocular hypotony.*
CONCLUSIONS. *Severe atrophy of the iris stroma, retinal detachment of the posterior pole, serous detachment of the ciliary body, and ocular hypotony may occur in chronic phase of VKH disease. (Eur J Ophthalmol 2005; 15: 277-83)*

KEY WORDS. *Detachment of the ciliary body, Infrared transillumination, Iris atrophy, Ocular hypotony, Uveitis, Vogt-Koyanagi-Harada disease*

Accepted: November, 1 2004

INTRODUCTION

The long-term complications of Vogt-Koyanagi-Harada (VKH) disease include cataract, secondary glaucoma, subretinal neovascular membranes, subretinal fibrosis, optic atrophy, and chronic pigmentary changes in the fundus known as sunset glow fundus (1-3).

We used digital infrared transillumination imaging of the iris to demonstrate iris atrophy and serous detachment of the ciliary body in both eyes of a patient with chronic phase of VKH disease. Our patient also showed persistent severe ocular hypotony, which has not been reported earlier in VKH disease.

METHODS

We performed a careful ophthalmologic examination and follow-up on a 52-year-old woman with bilateral chronic panuveitis, vitiligo, cerebrospinal fluid pleocytosis, and dysacousis, fulfilling the criteria defined by an international committee for VKH disease (4).

 1120-6721/277-07$15.00/0

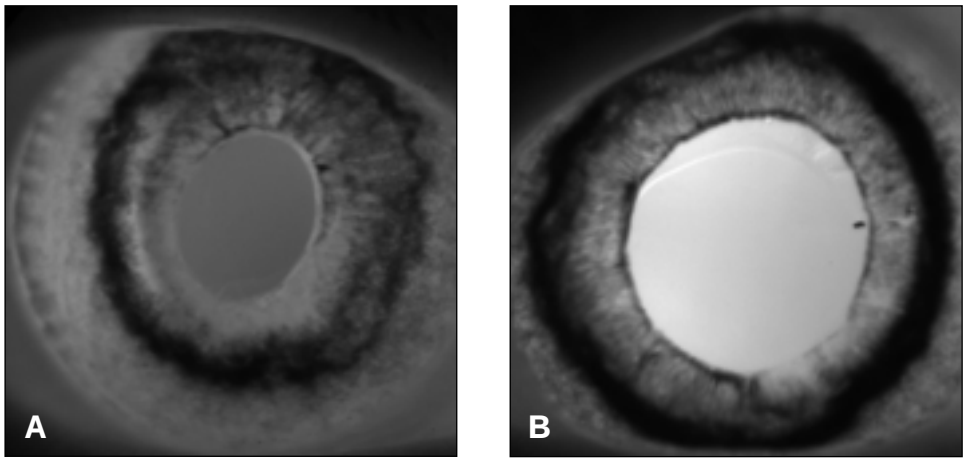

Fig. 1 - *Digital infrared transillumination images of right* **(A)** *and left* **(B)** *iris of a patient with Vogt-Koyanagi-Harada disease 2 years after beginning of the uveitic phase showing atrophy both in pupillary and ciliary zones and gathering of pigment in inner half of ciliary zone. Detachment of ciliary body seen as light band temporally.*

Imaging methods

Digital color images of the anterior eye and digital transpupillary imaging of the iris using white light were taken using the Zeiss photo slitlamp digital camera body (Kodak DCS 315). For digital infrared transillumination imaging (5) the examination light from the Zeiss slitlamp was passed through a Kodak Wratten gelatin filter No 87 transmitting only infrared light via light fiber optic cable through the lateral wall of the globe. Digital infrared transillumination imaging of the iris was done using the digital Topcon retinal camera (TRC 50 IA) with its indocyanine green (ICG) angiography filters focused on the iris. A Topcon TRC 50 IA camera (Topcon Optical Co. Ltd., Japan) was used for digital 50º color (768 x 576 pixels), blue light, red-free, red light, and fluorescein angiography imaging of the ocular fundus. The red-free light, monochrome, black-and-white images (1320 x 1032 pixels) were taken using the green filter supplied by the manufacturer.

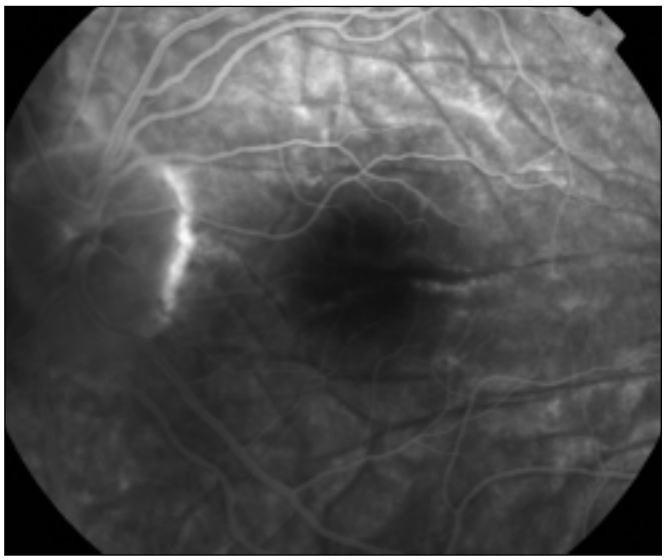

Fig. 2 - *Fluorescein angiogram of left fundus of a patient with chronic phase of Vogt-Koyanagi-Harada disease showing chorioretinal folds and edema of optic disc and retina.*

Case report

A 52-year-old woman, who had been treated by an ophthalmologist due to visual deterioration, photophobia, hypotony, iris atrophy, and posterior subcapsular cataract for 1 year, was admitted to a private eye center for cataract extraction on June 29, 1999. Corrected visual acuity was 0.01 in the right eye and 0.3 in the left. The intraocular pressure (IOP) was 2 mmHg in the right eye and 4 mmHg in the left. Both eyes showed folds of Descemet's membrane, 3+ aqueous flare and 1+ cells, atrophy of the iris, posterior synechiae, and dense posterior subcapsular cataract. The right fundus could not be seen but the left fundus showed pigment changes in the macular area.

The patient underwent cataract extraction using phacoemulsification and intraocular lens implantation of the right eye on July 5, 1999, and of the left eye on August 30, 1999. On the first postoperative day the operated eye showed 2+ flare, 2+ cells, and edema of the optic disc and macular area. The corrected visual acuity was 0.3 in the right eye and 0.6 in the left, and the IOP varied between 2 mmHg and 6 mmHg in both eyes during the first month postoperatively.

During the following year the patient complained of vi-

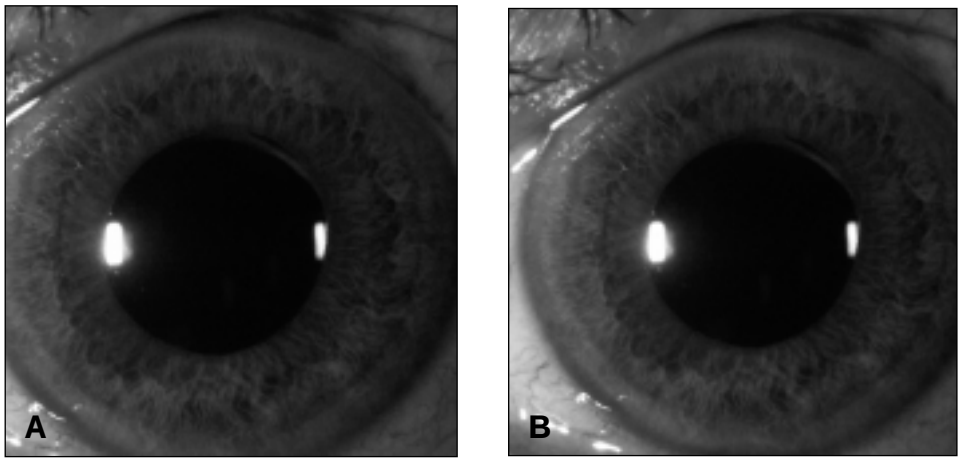

Fig. 3 - *Anterior surface of iris seen in black-and-white prints of digital color images of right* **(A)** *and left* **(B)** *eye in a patient with chronic phase of Vogt-Koyanagi-Harada disease.*

sual deterioration, photophobia, and wrinkling of straight lines. Both eyes showed aqueous flare, cells, hypotony, iris atrophy, and edema of the optic disc and macular area. The uveitis was treated with topical prednisolone acetate eye drops 3 to 4 times daily in both eyes.

The patient was referred to the Department of Ophthalmology, Turku University Central Hospital on August 21, 2000. Visual acuity was 0.04 in the right eye and 0.6 in the left, the IOP was 0 to 1 mmHg in the right eye and 2 to 3 mmHg in the left.

The iris was grayish in both eyes showing 3+ aqueous flare and 1+ cells. Digital infrared transillumination imaging showed in both eyes small and large patches of atrophy both in the pupillary and ciliary zones of the iris and gathering of pigment in the inner half of the ciliary zone, and circumferential detachment of the ciliary body (Fig. 1). In both eyes there were edema of the optic disc and a pale fundus.

The macular area was edematous showing chorioretinal folds. In the posterior pole between the superior and inferior temporal vessels the sensory retina showed a shallow elevation. In the midperiphery the fundus showed mottled hyperpigmentation and small patches of depigmentation. Fluorescein angiography showed chorioretinal folds in the posterior fundus, slight accumulation of fluorescein in the subretinal space, some diffusely scattered dots of hyperfluorescence due to window defects of retinal pigment epithelium, and diffuse fluorescence of the disc in the late phase (Fig. 2). Ultrasonography showed shallow serous detachment of the retina in the posterior pole.

The patient had vitiligo in both forearms, upper arms, thighs, legs, and on the left wrist. The audiogram showed sensorineural hearing loss in both ears. In serologic tests the patient had elevated levels of herpes simplex virus antibodies and elevated *Chlamydia pneumoniae* IgA antibodies. The cerebrospinal fluid showed 3 leukocytes/field. HLA phenotypes were A2, 68 (28); B5, 13, w4; w6; DR BI* 04, *07.

Treatment was started using 80 mg prednisolone a day, topical prednisolone eye drops every hour daily to both eyes and prednisolone ointment at night, and scopolamine eye drops twice daily. The eye condition did not respond to the prednisolone treatment. Cyclosporine A with a daily dose of 250 mg (3 mg/kg) was added to the treatment and continued for 2 years. Chlamydia pneumoniae was treated using roxithromycin 150 mg twice daily for 10 days.

On May 16, 2002, corrected visual acuity was 0.6 in both eyes. There was 1+ aqueous flare but no cells in both eyes. IOP was 4 mmHg in the right eye and 5 mmHg in the left.

The iris was grayish blue in both eyes (Fig. 3). Transpupillary transillumination with white light showed minute patches of atrophy in the pigment epithelium of the iris in the pupillary zone (Fig. 4). Digital infrared transillumination imaging showed extensive atrophy and occasional small pigment clumps both in the pupillary and ciliary zones of the iris, and atrophic changes of the ciliary processes and circumferential detachment of the ciliary body in both eyes (Fig. 5). During the last visit on October 31, 2002, corrected visual acuity was 0.5 in both eyes, the conjunctiva showed some chemosis and subconjunctival hemorrhages, there was 1+ aqueous flare but no cells, IOP was 1 mmHg in the right eye and 2 mmHg in the left, there were edema of the optic disc and macular area with chorioretinal folds, and the peripheral retina showed patches of chorioretinal atrophy and hyperpigmentation.

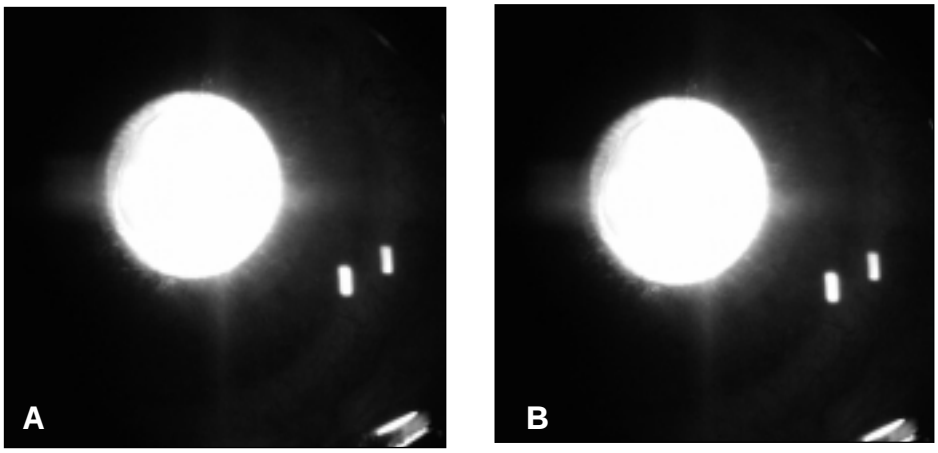

Fig. 4 - *Transpupillary transillumination with white light shows some small atrophic patches of pigment epithelium in right* **(A)** *and left* **(B)** *iris.*

DISCUSSION

This is the first study to show extensive atrophy of the iris stroma, circumferential detachment of the ciliary body, shallow detachment of the retina in the posterior pole, and ocular hypotony in chronic phase of VKH disease. In VKH disease it is important to suppress the initial intraocular inflammation with early and aggressive use of systemic corticosteroids, followed by slow tapering over 3 to 6 months (1, 6). This treatment may shorten the duration of the disease and prevent progression into chronic stage. Steroid-resistant recurrences may respond only to cytotoxic/immunosuppressive agents (1, 6). In the present case the patient was admitted to the University Hospital in chronic phase. The patient was treated for 2 years with peroral and topical prednisolone and with peroral cyclosporine. During the treatment the aqueous cells disappeared but the treatment did not have any improving effect on the iris atrophy, serous detachment of the ciliary body, and ocular hypotony, and the ocular fundus still showed edema of the optic disc and shallow detachment of the retina in the posterior pole.

In acute phase of VKH disease serous retinal detachment was confined to the posterior fundus within the temporal vascular arcades (in 44% of eyes) or it extended to the midperipheral fundus (in 56% of eyes) (7). With aggressive therapy in the early uveitic phase of VKH disease the exudative retinal detachments usually reattach over 6 to 17 (mean 11) days (7) and do not persist after the initial presentation although the other signs of inflammation continue to be present (6). Our patient with chronic VKH disease showed shallow detachment of the retina and subtle chorioretinal folds in the posterior pole, and patches of depigmentation and mottled hyperpigmentation causing a blond sunset glow fundus (6). The patient was treated in chronic phase of VKH disease with aggressive therapy for 2 years but the shallow detachment of the retina in the posterior pole did not reattach. Poor function of the pigment epithelium, chorioretinal folds, and ocular hypotony precluded normal reattachment of the sensory retina in the posterior pole.

Ultrasound biomicroscopic examination showed in Japanese patients serous detachment of the ciliary body in the acute phase of Harada disease in about 60% of eyes (7-9). The circumference of the ciliary body was detached from 20% to 250% of the scleral thickness and the ciliary detachment was more prominent in eyes with more extensive retinal detachment (7). In over half of the eyes the ciliary detachment disappeared on day 3 of treatment and in all eyes it had disappeared before day 21. Ciliary detachment recurred in eyes with recurrent serous retinal detachment (7). In VKH disease it is important to continue steroid therapy until ciliochoroidal detachment completely disappears. If steroid therapy is stopped too soon, recurrence or progression of disease may ensue (9). The present patient remained without any systemic corticosteroid treatment for 2 years after beginning the uveitic phase of the disease. Infrared transillumination images showed circumferential detachment of the ciliary body in both eyes 2 and 4 years after beginning of the uveitic phase.

Cataracts may develop in 10.5 to 40% of patients with VKH disease (1, 3, 10, 11). In VKH disease cataract operation can be recommended only in eyes where the inflammation has been controlled for at least 2 to 3 months with high dose systemic corticosteroids (1). The present case

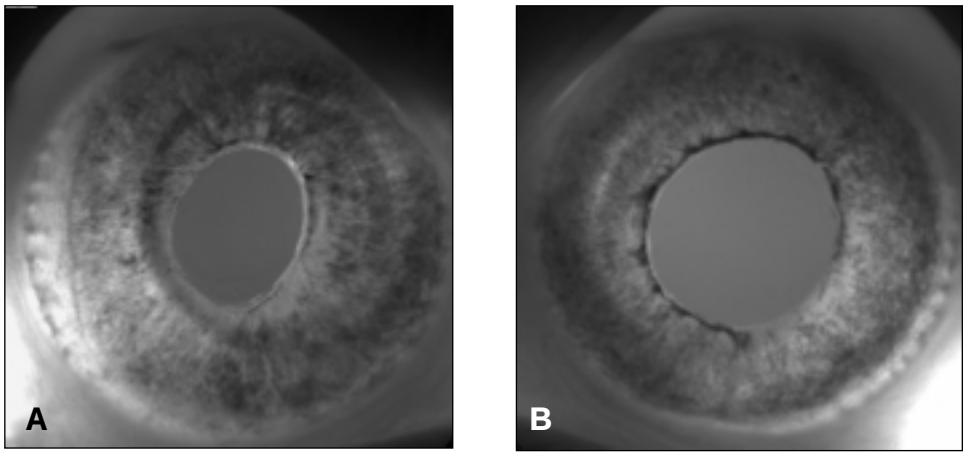

Fig. 5 - *Digital infrared transillumination images of right* **(A)** *and left* **(B)** *eye of a patient with chronic phase of Vogt-Koyanagi-Harada disease (4 years after beginning of the uveitic phase) showing extensive atrophy and occasional pigment clumps in pupillary and ciliary zones of the iris, and detachment of ciliary body seen as temporal light band.*

had cataract for 2 years, and was operated in a private eye center during the active uveitic phase without any preoperative control of inflammation 1 year before admittance to the Turku University Central Hospital. Detachment of the ciliary body may occur as a complication of cataract surgery (7). Thus cataract operation during the active uveitic phase may have further deteriorated the uveitis, barrier of the choroidal vessels, shallow detachment of the retina in the posterior pole, and detachment of the ciliary body. VKH disease is uncommon in Finland (12) and only one case has been reported previously (13).

Glaucoma may occur in VKH disease in 6 to 45% of cases (1, 3, 10, 14). Of these 56% had open angle glaucoma and 44% angle closure glaucoma (14). On the other hand, severe inflammation of the anterior uvea may cause edema of the ciliary body and swelling of the ciliary processes early in VKH disease (15), and may occasionally lead to transient hypotony in the uveitic phase of the disease (6). However, we are not aware of any reported cases of persistent hypotony in VKH disease. The present patient remained without any systemic corticosteroid treatment for 2 years after beginning of the uveitic phase of the disease. In addition, during this time she underwent cataract extraction and intraocular lens implantation in both eyes, which may have further deteriorated the situation. Infrared transillumination images showed atrophy of the ciliary processes and circumferential detachment of the ciliary body in both eyes 2 and 4 years after beginning of the uveitic phase. Atrophy of the ciliary processes, cyclitis as part of the severe chronic anterior uveitis, and detachment of the ciliary body may explain the ocular hypotony in this case.

The present case helps us to understand the morphologic changes of the iris stroma in VKH disease. In the uveitic phase the iris is thickened (6) by diffuse infiltration of lymphocytes, macrophages, and epithelioid cells (16). Iris nodules may be noted on the pupillary margin, as well as in the iris stroma in 5% of cases in the uveitic phase and in 29% of cases in the chronic phase of VKH disease (6, 10). These nodules transmit infrared light and may be seen in uveitic phase as round light patches in infrared transillumination images of the iris in the same manner as reported in sarcoid uveitis (17). In this study 2 years after beginning of the uveitic phase of VKH disease the nodules had become atrophic and appeared as small and large patches of atrophy in infrared transillumination images. Melanocyte destruction was seen as large gathering of pigment in the inner half of the ciliary zone (Fig. 1). Two years later in the chronic phase of VKH disease there was extensive atrophy of the iris stroma, but most of the pigment gathering had disappeared, and only occasional small pigment clumps were seen in the pupillary and ciliary zones of the iris in both eyes (Fig. 5).

The chronic phase of VKH disease has been characterized by depigmentation of the fundus (sunset glow fundus) and limbus (Sugiura sign) (2, 3). Sugiura sign does not occur in white patients with VKH disease (6, 10). The present study suggests that characteristic findings of chronic phase of VKH disease may include, along with the sunset glow fundus, the depigmentation and atrophy of the iris stroma.

This study shows the usefulness of digital infrared transillumination imaging for examination of the iris and ciliary body in VKH disease. In the chronic phase of VKH disease both biomicroscopy and conventional digital color imaging showed the iris to be normal overall (Fig. 3, a and

b) and conventional transpupillary transillumination technique by using the white light revealed only minute patches of atrophy of the pigment epithelium in the pupillary zone of the iris (Fig. 4). Digital infrared transillumination imaging (5) can be used to study the normal structure of the stroma and posterior surface of the iris including the radial contraction and structural folds of Schwalbe and the circular contraction furrows (5, 18), or different pathologic changes including atrophy, cysts, tumors, foreign bodies, granulomas, and nodules of the iris (5, 17-21). In this study it showed 2 and 4 years after beginning of the uveitic phase of VKH disease in both eyes extensive atrophy of the iris stroma (Figs. 1 and 5). In addition, infrared transillumination images showed circumferential detachment of the ciliary body in both eyes (Figs.1 and 5). Infrared transillumination imaging reveals in the iris stroma the nodules and atrophic patches more clearly than by using other clinical methods. Thus it can be used in the diagnosis and follow-up not only in VKH disease, but also in sarcoid uveitis (17) and in Fuchs' heterochromic cyclitis (20). Infrared transillumination imaging does not harm the patient, is easy to repeat, and does not require any stain injection.

In the etiology of VKH disease viral infection and autoimmunity against melanocytes have been suggested (1, 6, 13, 16). Autoreactive T-cells against tyrosinase-related protein may contribute to the development of VKH disease (22). The trigger that causes the autoimmune response is unknown. Our patient had elevated antibodies against herpes simplex virus and *Chlamydia pneumoniae*, which might have triggered the inflammatory reaction. Her HLA phenotype was A2; 68(28); B5, 13, w4, w6, DR B1* 04, *07, which may be related to the prolonged form of VKH uveitis. A strong association of VKH disease with HLA DRB1* 0405 and/or DRB1* 0410 has been described in Japanese patients (23).

In summary, we describe extensive iris atrophy, persistent circumferential serous detachment of the ciliary body, ocular hypotony, and shallow retinal detachment of the posterior pole in a patient with chronic phase of VKH disease.

ACKNOWLEDGEMENTS

This study was supported in part by the Research Fund of Turku University Hospital, Turku, Finland. The authors thank Professor K.M. Saari, MD, Department of Ophthalmology, University of Turku, for advice in this study.

Reprint requests to:
Jukka M. Saari, MD
Pihlajatie 11 B 24
FI-00270 Helsinki, Finland
jzsaari@medscape.com

REFERENCES

1. Moorthy RS, Inomata H, Rao NA. Vogt-Koyanagi-Harada syndrome. Surv Ophthalmol 1995; 39: 265-92.
2. Inomata H, Rao NA. Depigmented atrophic lesions in sunset glow fundi of Vogt-Koyanagi-Harada disease. Am J Ophthalmol 2001; 131: 607-14.
3. Read RW, Rechodouni A, Butani N, et al. Complications and prognostic factors in Vogt-Koyanagi-Harada disease. Am J Ophthalmol 2001; 131: 599-606.
4. Read RW, Holland GN, Rao NA, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an international committee on nomenclature. Am J Ophthalmol 2001; 131: 647-52.
5. Saari JM, Nummelin K. Digital infrared transillumination imaging of iris. J Ophthalmic Photography 2005; 27 (in print).
6. Nussenblatt RB. Vogt-Koyanagi-Harada syndrome. In: Nussenblatt RB, Whitcup SM, eds. Uveitis. Fundamentals and Clinical Practice, 3rd ed. Philadelphia: Mosby; 2004: 324-38.
7. Maruyama Y, Kimura Y, Kishi S, Shimizu K. Serous detachment of the ciliary body in Harada disease. Am J Ophthalmol 1998; 125: 666-72.
8. Kawano Y-J, Tawara A, Nishioka Y, et al. Ultrasound biomicroscopic analysis of transient shallow anterior chamber in Vogt-Koyanagi-Harada syndrome. Am J Ophthalmol 1996; 121: 720-3.
9. Nakamura H, Tsukamoto H, Shibahara R, Nagai M, Mishima HK. Ultrasound biomicroscopy in the management of Vogt-Koyanagi-Harada disease. Acta Ophthalmol Scand 2000; 78: 718-9.
10. Rubsamen PE, Gass JDM. Vogt-Koyanagi-Harada syndrome. Arch Ophthalmol 1991; 109: 682-7.
11. Moorthy RS, Rajeev B, Smith RE, Rao NA. Incidence and management of cataracts in Vogt-Koyanagi-Harada syndrome. Am J Ophthalmol 1994; 118: 197-204.
12. Päivönsalo-Hietanen T, Tuominen J, Vaahtoranta-Lehtonen H, Saari KM. Incidence and prevalence of different uveitis entities in Finland. Acta Ophthalmol Scand 1997; 75: 76-81.

13. Saari M. Vogt-Koyanagi-Harada syndrome. Report of a case with many recurrences. Ophthalmologica 1974; 169: 326-32.
14. Forster DJ, Rao NA, Hill RA, Nguyen QH, Baerveldt G. Incidence and management of glaucoma in Vogt-Koyanagi-Harada syndrome. Ophthalmology 1993; 100: 613-8.
15. Kimura R, Kasei M, Shoji K, et al. Swollen ciliary processes as an initial symptom in Vogt-Koyanagi-Harada syndrome. Am J Ophthalmol 1983; 95: 402-3.
16. Inomata H. Vogt-Koyanagi-Harada disease. In: Yanoff M, Duker JS, eds. Ophthalmology, 2nd ed. St. Louis: Mosby; 2004: 1196-9.
17. Karma A. Ophthalmic changes in sarcoidosis. Acta Ophthalmol Scand Suppl 1979; 141 (Suppl): S 1-94.
18. Saari M, Vuorre I, Nieminen H. Infrared transillumination stereophotography of normal iris. Can J Ophthalmol 1977; 12: 308-11.
19. Saari M, Vuorre I, Kaila J, Lahti R. Family studies of ocular manifestations in arthritis. Can J Ophthalmol 1978; 13: 144-51.
20. Saari M, Vuorre I, Nieminen H. Infrared transillumination stereophotography of the iris in Fuchs's heterochromic iridocyclitis. Br J Ophthalmol 1978; 62: 110-5.
21. Vuorre I, Saari M, Tiilikainen A, Räsänen O. Fuchs' heterochromic cyclitis associated with retinitis pigmentosa: a family study. Can J Ophthalmol 1979; 14: 10-6.
22. Gocho K, Kondo I, Yamaki K. Identification of autoreactive T-cells in Vogt-Koyanagi-Harada disease. Invest Ophthalmol Vis Sci 2001; 42: 2004-9.
23. Shindo Y, Inoko H, Tuji K, et al. HLA-DRB1 typing of Vogt-Koyanagi-Harada's disease by PCR-RFLP and the strong association with DRBI*0405 and DRB1* 0410. Br J Ophthalmol 1994; 78: 223-6.