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Two Cases of Harada's Syndrome Including One Preceded by Symptoms of Glaucoma

(uveitis/glaucoma/papilledema)

YUKARI YAMAMOTO, TOSHINORI NOUMI, and TOMOICHI SETOGAWA

Department of Ophthalmology, Shimane Medical University, Izumo 693, Japan

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We report 2 cases of Harada's syndrome found to be difficult to diagnose in the initial stage.

In one patient, there was an elevation of intraocular pressure accompanied by a shallow anterior chamber depth in the very early phase of Harada's syndrome, preceding the appearance of fundic abnormality and the onset of iridocyclitis.

The shallow depth was considered to be caused by a forward movement of the lens due to ciliary changes and in this case mydriatic and steroid treatment gradually led to a normalization of the anterior chamber depth.

She had been treated with a miotic agent under the diagnosis of primary angle-closure glaucoma. This seems to have resulted from delayed detection of fundic abnormalities at the initial stage of onset and which induced a seclusion of the pupil.

In the other patient, only papilledema of optic disc was remarkably evident in initial stage. The oscillatory potential in ERG decreased but A and B waves were fairly normal.

These findings suggested the importance of differentiation between optic neuritis and brain tumor.

Harada's syndrome is relatively frequent in Japan and the acute uveitis occasionally is associated with an involvement of the central nervous system, vitiligo and whitening of the hair and eyebrows. The initial clinical signs of Harada's syndrome are inflammatory detachment of posterior pole of retina, peripapillary edema and iridocyclitis.

It is not so difficult to diagnose patients showing typical clinical signs, but, because of various initial signs, a differential diagnoses in the very early stage is difficult.

We now experienced two cases of Harada's syndrome.

In case 1, with symptoms of glaucoma, she had been treated with a miotic agent under the diagnosis of angle-closure glaucoma. As a seclusion of the pupils was induced, a protracted type of the syndrome occurred. Glaucoma secondary to Harada's syndrome is not so rare, but differentiations have to be made when symptoms of glaucoma precede other symptons, in a very early stage (1, 2).

In another patient, only conspicuous papilledema of bilateral fundus was remarkable in the early stage and there was little abnormality in the posterior pole and peripheral retina. Therefore, it seems important to differentiate between optic neuritis and brain tumor.

CASE REPORT

Case 1 : R. S. A 51-year-old housewife was initially seen on Nov. 11, 1980. She complained of bilateral visual disorders and headache. History prior to diagnosis in our department : The loss of visual acuity occurred in the left eye on Nov. 7 and in the right eye on Nov. 9 and was accompanied by headache, nausea, vomiting and ocular pain. She consulted an ophthalmologist on Nov. 10 at which time glaucoma or intracranial disorder was suspected. She was then referred to our department.

Past history : She had been on antihypertensive drugs for 20 years. Ophthalmologic findings at initial examination : The visual acuity was 0.1 (n. c.) OD and 0.05 (n. c.) OS. The intraocular pressure was 29 mmHg OD and 31 mmHg (Schiötz) OS. Perimetric examination using an intermediate isopter showed a constriction superior to the nasal side in the right eye. Measurement was not possible in the left eye. The bulbar conjunctiva was slightly congested and slight edema existed in both corneas. The anterior chamber was rather shallow but clear. The both pupils were miotic with loss of light reflex. Funduscopic examination revealed no abnormality in the papilla and no other untoward finding in each eye.

She was admitted on Nov. 18 for precise examination. Ophthalmologic examination on admission : The visual acuity was lower than at the time of initial diagnosis, i. e., V, R.=count finger/ 20cm (n. c.) and V, L.=hand motion/ 20cm (n. c.). The pressure was 32 mmHg OD and 27 mmHg (Schiötz) OS.

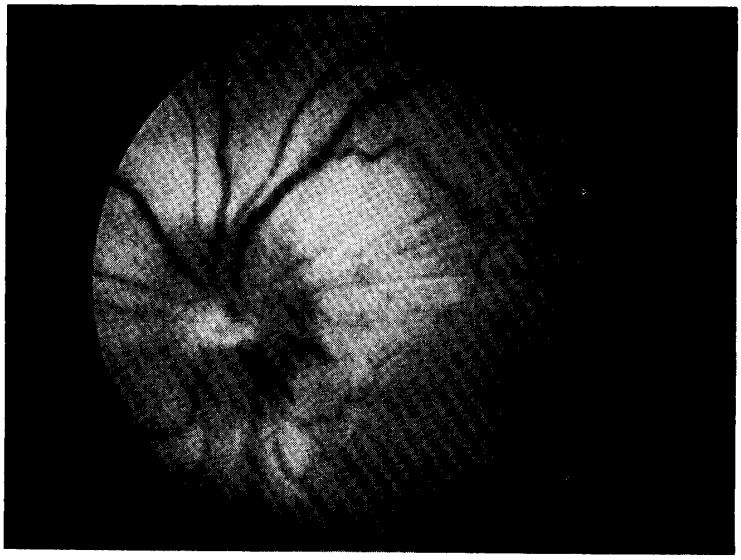

Fig. 1. Left fundus appearance of case 1. Blurred margin of optic nerve head and retinal fold of posterior pole region before the steroid therapy.

The ERG was non-recordable. The depth of both the anterior chambers was still slightly shallow with the presence of minimal flare in both eyes. The posterior pole of the fundus showed a turbidity and edema bilaterally. Retinal folds were observed in the left eye (Fig. 1). Peripheral detachment of the retina was also observed. Fluorescein fundus angiography revealed a scattered mottled effect of hypofluorescence on the pigment epithelium in the early phase and diffuse hyperfluorescence in the late phase. General examination on hospitalization : The blood pressure was 138/78 mmHg. Laboratory study showed normal erythrocytes, leukocytes and platelets in peripheral blood, CRP (++), RA (−), LE (−), ASO below 20x, serological syphilitic tests (−), IgG 1038 mg/dl and IgM 180 mg/dl. Neurological examination revealed no abnormality. There were no dermal abnormalities. Otological tests showed a bilateral sensorineural bradyacusia, of a similar degree.

The diagnosis of Harada's syndrome was established on the basis of the above mentioned results. A high dose of steroids was begun on the day after hospitalization. Administration of betamethasone was continued for 54 days and a total dose of 252.5 mg was administered. At the initial stage when conspicuous detachment of retina was observed, a hyperosmotic diuretic was also given. On the day following admission, the intraocular pressure dropped to 6 mmHg (N.C.T.), binocularly. Remission of papilledema and reduction of peripheral detachment of retina in both fundi occurred from approximately 10 days after the start of therapy. Both the fundi returned to almost normal with only a slight degree of papillary congestion 40 days later. The fundi, 2 months after the commencement of therapy, showed spots of depigmentation with a somewhat tanned appearance. The visual acuity 10 days after the treatment recovered to 0.3 (n. c.) OD and 0.2 (n. c.) OS. Four weeks later it further improved to 0.4 (n. c.). Side-effects of moon-face, acne to a slight degree and a slight posterior subcapsulor opacity of the lens occurred.

Recurrence was frequent after she was first discharged from our department (Dec. 21, 1980). She was re-admitted from Feb. 16 to Apr. 13, 1981 and again from May 12 to Aug. 2, 1981, due to recurrence with an initial symptom of iritis. A recurrence but without a lesion in the anterior portion followed and she was again prescribed steroid therapy. At the time of discharge on Aug. 2, 1981, the visual acuity was 1.0 (n. c.) OD and 0.9 (1.0×-0.5 D) OS and the intraocular pressure was 11 mmHg OD and 12 mmHg (N. C. T) OS (Fig. 2). ERG continued to show a reduced reaction throughout the entire course, with a feeble A wave and without a B wave.

Case 2 : S. N. A 55-year-old woman who worked in civil engineering and building was initially referred to our department on Sept. 22, 1981 for the primary complaint of visual disorder. History prior to diagnosis in our department : Dust entered her right eye while she was working, at the beginning of Sept. As she felt slight pain and the presence of a foreign body in her eye, she used a commercial eye-drop. However, vision gradually blurred in the right eye. Approximately one week later, she developed blurred vision

Fig. 2. Left fundus appearance of case 1. Chorioretinal atrophy after about a year.

in the left eye as well. She consulted an ophthalmologist on Sept. 16, where uveitis was diagnosed. Eye-drops and an intraocular injection were prescribed. She was referred to our department on Sept. 22. Although she complained of pain deep in the orbit there was no headache, nausea, tinnitus or difficulty of hearing.

Past history : She had been leukodermic since 10 years ago. Ophthalmologic findings at initial examination : The visual acuity was 0.2 (0.4×+0.25D) OD and 0.1 (0.4×+0.25D) OS. The intraocular pressure was 13 mmHg (N. C. T.) in both eyes. Although peripheral kinetic examination of the visual field was normal, a central scotoma with an enlarged Mariotte's spot in the right eye and an enlarged Mariotte's spot in the left eye were detected. ERG showed almost normal A and B waves in both eyes but the oscillatory potential was decreased. There were no untoward findings in the anterior portion. Precipitates were observed behind the cornea of both eyes and there were minimal flare and cells in the anterior chambers. Pupils and lenses appeared normal. Both fundi showed optic disks which were exceedingly reddened and swollen with an indistinct margin and some partial bleeding (Fig. 3). The formation of retinal folds with slight edema was seen in the posterior pole of the right fundus. Ring and foveolar reflexes in the posterior pole of the left eye were lost. Fluorescein fundus angiography revealed marked leakage from the papilla and granular leakage around peripheral retina.

General examination on admission : Her blood pressure was 140/86 mmHg. Laboratory examination showed normal erythrocytes and leukocytes in the peripheral blood, CRP (−), RA (−), LE (−), serological syphilitic tests (−), and normal levels of serum proteins, fractions and immunoglobulins. The spinal fluid with an initial pressure of 80 mmH_2O was soluble and clear with the increased number of cells of 740/3. The protein and sugar contents were within the normal range. Otological tests were normal. Depigmentation

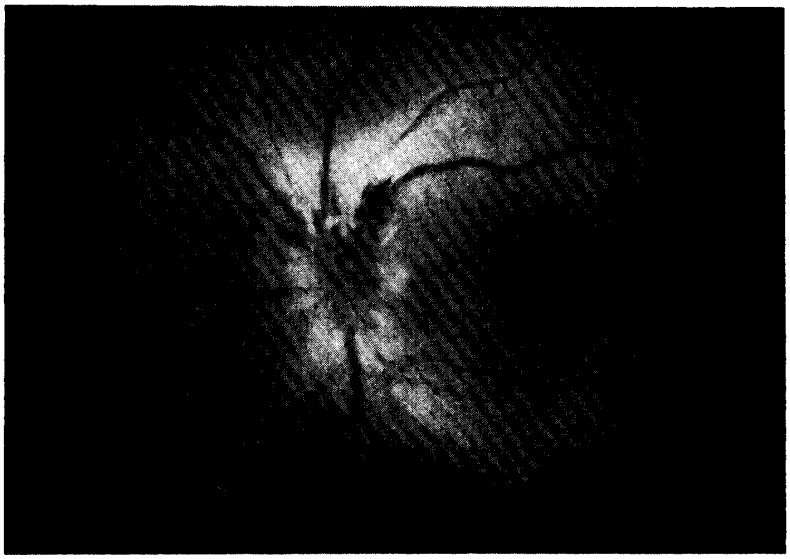

Fig. 3. Left fundus appearance of case 2. Severe congestion and blurred margin with small bleeding of optic nerve head before the steroid therapy.

spots were scattered symmetrically all over her body.

Under the diagnosis of Harada's syndrome, administration of prednisolone was continued for 47 days and a total dosage of 2045 mg was used. Ten days after the treatment, the papilledema disappeared in both fundi as did the edema in the posterior pole of the right eye. Four weeks later, the border of the papilla in both fundi became distinct and only slight congestion remained (Fig. 4). Fluorescein fundus angiopraphy no longer showed leakage

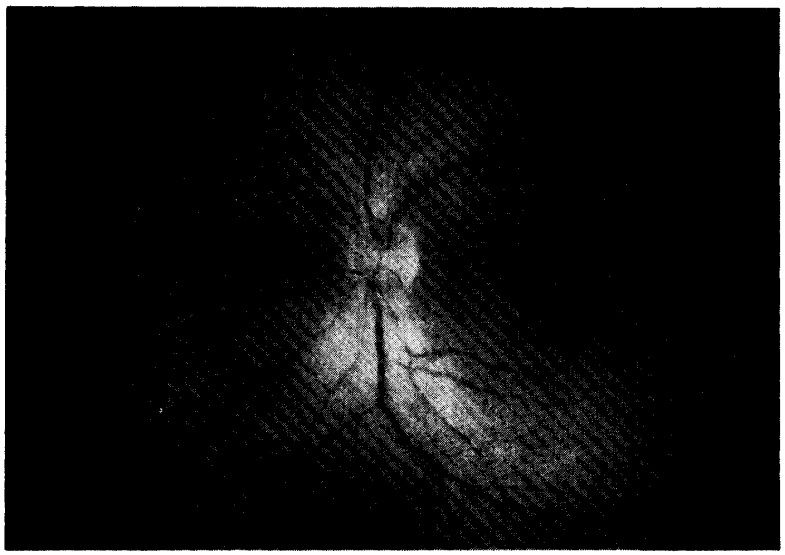

Fig. 4. Left fundus appearance of case 2. Almost normal fundus after four weeks.

from the papilla. The visual acuity recovered to 1.0 in both eyes, 4 weeks later. Steroid administration produced no side-effects whatever.

DISCUSSION

Glaucoma secondary to Harada's syndrome mostly results from posterior adhesion of the iris during development and anterior adhesion of the irinic periphery, or from steroid therapy (3). However, there are recent reports of an elevation of intraocular pressure accompanied by a shallow anterior chamber depth in the very early phase of Harada's syndrome, preceding the appearance of fundic abnormality and the onset of iritis (4, 5). In case 1 in the present paper, there was a shallow anterior chamber which was considered to be caused by a forward movement of the lens due to ciliary changes (6, 7). In this case, mydriatic and steroid treatment gradually led to a normalization of the anterior chamber depth. Shirato (3) reported that miotics produce an unfavorable prognosis. Case 1 in the present study was Harada's syndrome of a favorable prognostic type with retinal detachment at the posterior pole. The steroid therapy (in a total dose of 252.2 mg) was begun in 10 days after the loss of visual acuity, and yet it passed into a protracted type. This seems to have resulted from delayed detection of fundic abnormalities due to the use of the miotic agent at the initial stage of onset and which induced a seclusion of the pupils. Kimura *et al.* (4) reviewed 11 cases (21 eyes) of Harada's syndrome with an initial symptom of transient shallow anterior chamber that had been reported from 1930 on. These cases included 16 eyes (85.7%) with elevated intraocular pressure, 5 eyes (24.2%) diagnosed exclusively as Harada's syndrome, 10 eyes (47.5%) diagnosed exclusively as glaucoma and 6 eyes (28.5%) diagnosed as combined cases of Harada's syndrome and glaucoma. Of these 21 eyes, a miotic was used for 10 eyes (47.5%) and operation was performed for 9 eyes (42.9%) for glaucoma. However, the cases after 1977 in particular were all diagnosed initially as Harada's syndrome for which a miotic was not prescribed and surgery was not done.

Case 2 presented a conspicuous congestion of papilla in both findi but with no significant change in the posterior pole. ERG was normal except for a reduction in the rhythmic slow waves. This suggested the importance of differentiation from optic neuritis. The presence of a visual disturbance to almost the same degree bilaterally and concomitantly and with minimal flare and cells in the anterior chambers and increase in the number of cells in the spinal fluid led to a differential diagnosis of Harada's syndrome. Steroid therapy proved effective and a smooth resumption of the visual acuity followed. The fundi assumed a tanned appearance 2 months after the commencement of therapy.

Steroid therapy produces a marked improvement of visual acuity in Harada's syndrome. Although a sufficiently large dose of steroid at the early stage is generally recommended, the clinical course and findings are apt to alter. Thus, as described by Satoh (8), the dose of steroid should be carefully determined according to the clinical condition.

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