FURTHER STUDY ON FLUORESCEIN ANGIOGRAPHIC FINDING IN HARADA'S DISEASE

WITH SPECIAL REFERENCE TO THE CHANGE OF OPTIC DISC

HISAHARU YOSHIOKA, TAKASHI SUGITA, AND MASAOKI NAKANŌ

*Department of Ophthalmology, Kurume University School of Medicine,
Kurume, Japan*

(Received for publication August 29, 1973)

Twenty five patients with Harada's disease are examined with fluorescein angiography to study on the incidence and the cause of the change in the optic disc. The results obtained are as follows: 1) The fluorescein angiographic finding of the optic disc reveals two kinds of finding: true papilledema (papillitis) and pseudo-papilledema (pseudopapillitis). 2) The fluorescein leakages from the optic disc are demonstrated either from the initial stage or at recovery stage of the disease with relatively high frequency (36%). 3) It is confirmed that the cause of these fluorescein leakages in the optic disc is closely related with severity of the disease process.

From the results obtained, it is pointed out that fluorescein angiographic finding of the optic disc in the Harada's disease is of importance for determination of the severity of the disease process and prognosis.

Harada's disease is a systemic disease which affects selectively the tissues having melanin pigment cells in the body. The syndrome of this disease consists of bilateral acute uveitis, auditory disturbances (tinnitus, deafness, vertigo), alteration of the hairs (poliosis, alopecia), and skin changes (vitiligo).

The ocular symptoms have been fully described, but little is known about the change of the optic disc in this disease.

The change of the optic disc is ophthalmoscopically accompanied by the hyperemia and swelling of the optic disc soon after the onset or sometimes from the initial onset.

It has also been said that such findings seen in the optic disc of this disease attribute to the secondary retinal detachment due to the peripapillary choroiditis and they have been called papilloedema-like or papillitis-like finding²⁾.

The optic disc is usually free of pathological signs angiographically but sometimes shows the capillary dilatation and microaneurysm formation in front of the optic disc peculiar to the state of papillitis^{1) 5)}.

We have also reported two cases in which the leakages of fluorescein from the optic disc were demonstrated during from a month to four months after onset, but its exact cause and

frequency have not been determined⁷⁾.

The purpose of the present paper is to study on the incidence and cause of the change in the optic disc and to point out its importance in the Harada's disease.

MATERIALS AND METHODS

Twenty five patients were clinically diagnosed as Harada's disease at Kurume University Hospital during 69-months period from Oct., 1967 to Jul., 1973, and were examined by fluorescein fundus angiography. Of these patients 14 patients were examined angiographically over two times during the course of this disease.

RESULTS

Extravasation of the dye from optic disc was found in 9 patients (36%) out of 25 patients. These 9 patients belong to group A and the others to group B.

As shown in Table 1., ages of patients in group A was slightly older than that of group B. There was no sex difference between group A and B as

TABLE 1

Age	Group A	Group B
under 29	1	8
30-39	3	6
40-49	3	1
over 50	2	1
Total	9	16

TABLE 2

Sex	Group A	Group B
male	4	7
female	5	9
Total	9	16

seen in Table 2. The periods from the onset to the time taking fluorescein angiography was shown in Table 3, and this period in group A was more one month in many patients.

Visual acuity (Table 4): Corrected visual acuity at the time taking fluorescein angiography was no difference between group A and B. Intraocular tension at the time taking fluorescein angiography was shown in Table 5, and there was the tendency to be more hypotensive in group A than group B which showed normal intraocular tension.

TABLE 3

Duration from the onset to FAG*	Group A	Group B
under 1 month	4	13
1-2	4	2
2-3	1	1
over 3	0	0
Total	9	16

* Fluorescein Angiography

TABLE 4

Corrected visual acuity	Group A	Group B
under 0.1	2	8
0.2-0.6	12	17
0.7-1.2	4	7
Total	18	32

TABLE 5

Intraocular tension (Schiotz's Tonometer)	Group A	Group B
under 10 mmHg	6	6
10-20	12	20
over 20	0	6
Total	18	32

The results of 14 patients which could be examined with fluorescein angiography more than two times during the course of this disease were as follows: The finding of cerebro-spinal fluid revealed more marked pleocytosis in group A than that in group B (Table 6) despite this examination was almost of all carried out after systemic administration of corticosteroid except for one patient of group A.

Perceptive deafness was seen in all patients of group A, but only one of 4 patients in group B (Table 7). The duration from onset to the time of fluorescein leakages from optic disc was shown in Table 8. In almost of all, extravasation of dye were disappeared within 3 months after onset. There were two types of leakage of dye from optic disc, that is, one type in the early stage of the onset, and the other in a month or more after onset.

Relation of the period in leakage of dye from optic disc and choroid in group A was shown in Table 9. Leakages of

TABLE 6

Cell in cerebro-spinal fluid	Group A	Group B
under 10/3	0	2
10/3 - 100/3	3	1
over 100/3	4	0
Total	7	3

the dye from optic disc and choroid were generally found to be parallel but leakages of the dye from only optic disc were still seen in 3 eyes even after leakages from the choroid into subretinal space disappeared.

The period of leakage of the dye from choroid into subretinal space in group A was compared with those in group B (Table 10). In group B the leakage from the choroid disappeared within about one month from onset. On the other hand, in group A there was a tendency continuing fairly long time over 2 months.

TABLE 7

Fl. leakage of optic disc	Name	Age	Sex	Period from the onset to steroid therapy (day)	Cell in cerebro-spinal fluid	Duration from steroid therapy to CSF* examination (day)	Perceptive deafness
Group A (+)	F. I.	44	F	30	85/3	3	+
	Y. T.	41	M	12	1430/3	0	+
	M. I.	33	M	3	70/3	4	+
	M. K.	57	F	12			+
	M. Y.	51	M	100	11/3	90	+
	N. N.	31	F	9	254/3	8	+
	T. N.	44	F	5			+
	T. F.	23	M	30	245/3	5	+
	M. S.	39	F	11	175/3	4	+
Group B (-)	R. S.	25	F		6/3		-
	H. I.	38	M	3	8/3	6	-
	F. S.	23	F	4	64/3	2	-
	T. N.	28	M	11			+
	T. I.	41	M	24			

* CSF Cerebro-Spinal Fluid

TABLE 8
Fluorescein findings at various periods after onset

Fl. leakage of optic disc	Name	Day			Month						
		0-9	10-19	20-29	1	2	3	4	5	6	7 -
Group A (+)	F. I.			-○	+○	+●			-●		-●
	Y. T.		-○ -○	+○	-●						
	M. H.	-○		+○	+○	+●		-● -●		-● -●	
	M. K.		+○ +○		-● -●		-●				
	M. Y.					+○ +●		+●			
	N. N.				+○	-●					
	T. N.	+○ +○							-●		
	T. F.				+○	+○ +○					
	M. S.		+○ +○		+○						
Group B (-)	R. S.				-○				-● -●		
	H. I.	-○							-●		
	F. S.	-○ -○			-● -●						
	T. N.		-○		-●	-●					
	T. I.		-○ -●	-● -●							

+ : leakage of optic disc. - : no leakage of optic disc.
 ○ : leakage from choroidal vessel. ● : no leakage from choroidal vessel.
 Upper Step : right eye. Under Step : left eye.

TABLE 9

Period of leakage of the dye	From optic disc. (number of eye)	From choroid (number of eye)
under 1 month	2	3
1 - 2 months	2	3
2 - 3 months	6	4
over 3 months	1	0
Total	11	10

TABLE 10

Period of leakage of the dye from choroid into subretinal space	Group A (number of eye)	Group B (number of eye)
under 1 month	3	6
1 - 2 months	3	1
over 2 months	4	0
Total	10	7

DISCUSSION

In patient with Harada's disease which could be repeatedly examined angiographically the leakage of the dye in the optic disc was found to be more frequent than would be anticipated. This indicates that the finding of the optic disc in this disease is of importance.

The fluorescein leakages in the optic disc were demonstrated not only in patients of the initial stage but also in patients of recovery stage during the course of this disease. In these patients with fluorescein leakages in the optic disc the visual acuity decreased markedly associated with secondary retinal detachment at the initial stage but it showed more improvement with disappearance of secondary retinal detachment at the recovery stage. Furthermore, the fluorescein angiographic findings of the optic disc in both initial and recovery stage show same pattern as dilatation and increase in the number of capillaries, extravasation of fluorescein, and occasionally microaneurysm formation.

Considering the facts that the fluorescein finding in papillitis is indistinguishable from that in papilledema, and good visual acuity is always found even with the fluorescein leakages of the optic disc, it seems likely that the ophthalmoscopic findings such as hyperemia, blurred margin, and swelling of the optic disc associated with fluorescein leakages are clearly considered of a true papilledema (papillitis) and on the other hand, the similar ophthalmoscopic findings without any leakages of fluorescein in the optic disc are considered of a pseudopapilledema (pseudopapillitis) attributed to the secondary retinal detachment due to peripapillary choroiditis.

Thus the fluorescein angiography is

very helpful for differentiating whether these findings in the optic disc are a true papilledema (papillitis) or pseudopapilledema (pseudopapillitis).

Next we should like to discuss on the cause of the fluorescein leakages in the optic disc. For this purpose, the patients with leakages in the optic disc were compared with patients without leakages in the optic disc. As the results, the patients with leakages in the optic disc at the initial stage or recovery stage revealed more marked pleocytosis of the cerebro-spinal fluid and the presence of perceptive deafness than patients without leakages in the optic disc even after the steroid therapy. In general, as the number of cell in the cerebro-spinal fluid is an indicator suggesting the severity of inflammation in this disease³⁾, marked increase in cellular content of the cerebro-spinal fluid in patients with leakages of fluorescein in the optic disc strongly suggests that the grade of inflammation of the peripapillary choroid is severe. The presence of fluorescein leakages in the optic disc at the recovery stage of some patients without any fluorescein leakages at the initial stage may also be strongly suggested an evidence which patients with marked increase of cellular content of the cerebro-spinal fluid become more severe even when the low grade of inflammatory sign is observed at the initial stage.

The other factors such as the age of the patients, the periods after onset, intraocular pressure, and the pressure of the cerebro-spinal fluid may not be related to the development of fluorescein leakages in the optic disc because of the results in patients examined with repeated fluorescein angiography performed during the course of the same individuals.

At any rate, the presence or absence of fluorescein leakages in the optic disc

as well as the number of cell in the cerebro-spinal fluid is very significant for determination of the severity of inflammation and of the dosis of steroid about this disease.

As we have also already experienced few patients misdiagnosed as brain tumor because of choked disc appearance, every patients showing any degree of papilloedema in both eyes should always be performed careful slit-lamp examination in order to look for cells in the vitreous or aqueous and examination of cerebro-spinal fluid or hearing test⁴⁾.

The mechanism of the fluorescein leakages in the optic disc of the Harada's disease may be explained by the collateral edema and dilatation of the capillaries of the optic disc⁶⁾ including the radial peripapillary capillaries due to severe inflammation in the peripapillary choroid, because of evidence that retinal hemorrhages in the peripapillary region or within the distribution of radial peripapillary capillaris may be observed as a rare occurrence.

The exact mechanism of these phenomena still remains unresolvably.

REFERENCES

- 1) IGARASHI, M. and TANAKA, N. : Fluorescein fundus angiography on Morbus Haradai. Jap. J. Clin. Ophthal. **26**, 741-747, 1972.
- 2) IKUI, H. : New Textbook of Ophthalmology. Second Ed., Igaku Shoin Ltd., Tokyo, 1970, p. 203.
- 3) IKUI, H. : Edited by Ishiyama, S., Hinohara, S. and Watanabe, Y. : Today's Therapy. Igaku Shoin Ltd., Tokyo, 1971, p. 547.
- 4) MANOR, R. S. : Particular aspects of the Vogt-Koyanagi Harada syndrome. Ophthalmologica. **165**, 425-437, 1972.
- 5) SHIKANO, S. and SHIMIZU, K. : Atlas of fluorescence fundus angiography. Igaku Shoin Ltd., Tokyo, 1968, p. 125.
- 6) SHIMIZU, K. : Fluorescein fundus photography. Part 6. Fluorescence of the optic disc. Jap. J. Clin. Ophthal. **26**, 717-724, 1972.
- 7) YOSHIOKA, H. and SUGITA, T. : Fluorescein angiographic findings of optic disc in Harada's disease. Acta Soc. Ophthal. Jap. **75**, 2116-2119, 1971.