Fluorescein Angiogram in Diabetic Dogs

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ABSTRACT. Fluorescein angiography was carried out to see retinal vascular changes of the ocular fundus in 4 spontaneously occurring diabetic dogs. In all 4 cases, several hypofluorescent areas were determined to be filling defects of the retinal capillary bed of the tapetal fundi during the arteriovenous phase. Around these hypofluorescent areas, many dots of hyperfluorescence were also observed to be microaneurysms. However, no leaking of fluorescein was detected during angiography. These findings of 4 diabetic dogs were similar to those reported in man with non-proliferative diabetic retinopathy.—**KEY WORDS:** diabetes, dog, fluorescein angiogram.

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It is well known that diabetic retinopathy is one of the most important vascular complications in man with diabetes mellitus [1, 7, 10]. Gepts and Toussaint [5] reported that retinal vascular changes could be demonstrated by the flat mounted whole-retina technique in 22 of 29 diabetic dogs including typical microaneurysms in 4 cases. On histopathological examination, diabetic retinopathy has been detected in spontaneous [9, 11], alloxan induced [4], and metasomatotropin induced [6] diabetic dogs. However, there are only a few reports on the ophthalmoscopic findings of diabetic retinopathy in the dog [2], since bilateral cataracts appear rapidly and commonly in the course of the disease. Detection of early lesions of diabetic retinopathy such as microaneurysms by ophthalmoscopy is complicated by hyperreflectiveness of the tapetum lucidum in the dog's retina. For detection of early lesions, fluorescein angiography is a valuable clinical technique since it reveals the characteristics of retinal vascular flow and provides additional information on retinal and choroidal lesions [10].

This report deals with the vascular changes shown with fluorescein angiography in 4 dogs with spontaneous diabetes mellitus.

After maximal dilatation of the pupil using 1% tropicamide (Mydrin-P, Santen Pharm., Co., Ltd., Osaka), 10% fluorescein dye (Kobayashi Pharm., Co., Ltd., Tokyo) was injected into the cephalic vein through a butterfly catheter (2.5 ml or 5 ml of fluorescein solution, according to the dog's size). A fluorescein angiogram of the ocular fundus was taken, using a portable fluorescent fundus camera with motorized film advancement (Kowa RC 2, Kowa, Co., Ltd., Tokyo). Two gelatin filters, Wratten No. 47B and No. 15 (Eastman-Kodak, Co., USA), were used as an exciter filter and a barrier filter, respectively. High speed photographic film (ASA 400, Tri-X Pan, Eastman-Kodak, Co., USA) was used.

Case 1 (a 12-year-old female Toy Poodle) had revealed signs of polydipsia and polyuria for 3 months. The dog had persistent glucosuria, ketonuria, fasting hyperglycemia (368 mg/dl), and a high level of

total cholesterol (436 mg/dl). An IV-glucose tolerance test (0.4 g/kg, IV-GTT) showed a prolonged glucose disappearance rate (Table 1). On the fluorescein angiogram, hypofluorescent areas were observed in the tapetal fundi and several hyperfluorescent dots were seen around the hypofluorescent areas in the early arteriovenous phase when the central retinal arteries were filled with fluorescein (Fig. 1a). These findings became more distinct as the arteriovenous phase progressed (Fig. 1b). The hypofluorescent

areas indicated non-perfusion of the capillary bed in the retina and hyperfluorescent dots identified microaneurysms. No leaking of fluorescein was seen during angiography.

Case 2 (a 9-year-old female Collie) with a history of obesity was examined because of polyuria and polydipsia of 2 months. The patient had persistent glucosuria, ketonuria, fasting hyperglycemia (352 mg/dl), a high total cholesterol level (309 mg/dl), and glucose intolerance with IV-GTT (Table 1). The fluorescein angiogram revealed re-

Table 1. Clinical and laboratory data of 4 spontaneous diabetic dogs

	Case 1	Case 2	Case 3	Case 4
Breed	Toy poodle	Collie	Maltese	Poodle
Sex	Female	Female	Female	Female
Age (year)	12	9	9	12
Chief complaint	Polyuria Polydipsia	Polyuria Polydipsia	Polyuria Polydipsia Polyphagia	Polyuria Polydipsia
Duration of diabetic state (month)	2	3	2	1
Glucosuria	+	+	+	+
Ketonuria	+	+	-	-
Fasting plasma glucose (mg/dl)	368	352	301	484
Total cholesterol (mg/dl)	436	309	226	289
Glucose tolerance test (T1/2, min)	120<	94	120<	60

Fig. 1. (a) Fluorescein angiogram (case 1) in early arteriovenous phase showing many hyperfluorescent dots (arrow heads) surrounding hypofluorescent areas (arrows), (b) Fluorescein angiogram in arteriovenous phase. Hyperfluorescent dots and hypofluorescent areas became more distinct (compare to a) as the arteriovenous phase progressed.

markable tortuosity of the retinal veins, and several hyperfluorescent dots surrounding filling defect areas of the capillary bed during the arteriovenous phase. In addition, large choroidal vessels were observed in some areas (Fig. 2).

Case 3 (a 9-year-old female Maltese) had revealed signs of polyuria and polydipsia for 2 months. The patient had persistent glucosuria, fasting hyperglycemia (310 mg/dl), a high total cholesterol level (266 mg/dl), and glucose intolerance with IV-GTT (Table 1). On the fluorescein angiogram, several hypofluorescent areas were observed and were due to filling defects in the retinal capillary bed in the arteriovenous phase. Many hyperfluorescent dots were also detected surrounding hypofluorescent areas. However, no leaking of fluorescein was noted during angiography (Fig. 3).

Case 4 (a 12-year-old female Poodle) had revealed signs of polyuria and polydipsia for a month. Persistent glucosuria, high fasting plasma glucose level (484 mg/dl), and a high total cholesterol level (289 mg/dl) were found upon examination. IV-GTT revealed glucose intolerance (Table 1). Fluorescein angiography in the arteriovenous phase showed numerous hyperfluorescent dots surrounding several hypofluorescent areas

in the tapetum lucidum (Fig. 4). The dog died due to severe pneumonia after 4 months of insulin therapy. Histopathological examinations of the retinal vessels using hematoxyline and eosine stain revealed dilatation of the capillary lumina and swelling of the capillary endothelial cells. Periodic acid Schiff staining revealed hyalinization of the capillary walls and desquamation of the endothelial cells in some areas (Figs. 5a, b).

Fluorescein angiography was sensitive in detecting microaneurysms in the dog due to the contrast between fluorescein and the background in the retina. The combination of filters (Wratten No. 47B and No. 15)

Fig. 2. Fluorescein angiogram (Case 2) showing remarkable tortuosity of the retinal veins and several hyperfluorescent dots (arrow heads) surrounding hypofluorescent areas (arrows).

Fig. 3. Fluorescein angiogram (case 3) showing many hyperfluorescent dots (arrow heads) surrounding hypofluorescent areas (arrows).

Fig. 4. Fluorescein angiogram (Case 4) showing hyperfluorescent dots (arrow heads) surrounding hypofluorescent areas (arrows).

Fig. 5. (a) Dilatation of the capillary lumina and swelling of the capillary endothelial cells (Case 4). HE stain. $\times 130$. (b) Hyalinization of the capillary walls and desquamation of endothelial cells (Case 4). PAS. $\times 130$.

used in this study eliminated completely the non-specific fluorescence of the tapetum lucidum in the dog's retina. Typical findings of diabetic retinopathy in man have been reported to be microaneurysms, dilatation and tortuosity of the veins, hemorrhage, neovascularization, fibrosis, exudates, and retinal detachment [8, 10]. Scott *et al.* [8] described proliferation with fibrosis in the retina and the resulting retinal detachment as a feature of severe diabetic retinopathy. All 4 diabetic dogs examined in this study revealed abnormal retinal vascular flow, filling defects of the capillary bed and numerous hyperfluorescent dots on the fluorescein angiogram. In addition, no proliferative lesions such as leaking of fluorescein, exudation, or neovascularization were observed. These findings are similar to those in man with non-proliferative diabetic retinopathy.

The incidence of diabetic retinopathy dramatically increases with the length of duration of the diabetic state [4]. Patz *et al.* [9] demonstrated 2 cases of diabetic retinopathy in spontaneously occurring diabetic dogs in which the duration of the diabetic state was over 1 year. The dogs examined in this study, according to their anamnesis, had been in diabetic state for from 2 to 4 months. Diabetic retinopathy apparently

occurred in the early stages of the disease in these spontaneously occurring diabetic dogs. The promoting factor in diabetic retinopathy is believed to be the persistent high blood glucose levels associated with circulating insulin deficiency [8]. Engerman [3] reported that in alloxan induced diabetic dogs, well controlled with careful and strict treatment, the incidence and severity of retinopathy was significantly reduced. Therefore, in order to prevent diabetic retinopathy it is necessary to detect the disease at an early stage and correct the hyperglycemic state with effective treatment.

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REFERENCES

1. Ashton, N. 1951. *Proc. Roy. Soc. Med.* 44: 747-753.
2. Barnett, K. C. 1981. *Brit. J. Ophthalmol.* 65: 312-314.
3. Engerman, R. L. 1976. *Tr. Am. Acad. Ophthalm. Otol.* 81: 710-715.
4. Engerman, R. L., and Bloodworth, J.M.B. 1965. *Arch. Ophthalmol.* 73: 205-210.
5. Gepts, W., and Toussaint, D. 1967. *Diabetologia* 3: 249-265.
6. Hausler, H. R., Sibay, T. M., and Campbell, J. 1964. *Diabetes* 13: 122-126.

7. Keen, H. 1960. *Vet. Rec.* 72: 555-557.
8. Lawrence, R. D., and Scott, G. I. 1951. *Proc. Roy. Soc. Med.* 44: 36-41.
9. Patz, A., Berkow, J. W., Maumenee, A. E., and Cox, J. 1965. *Diabetes* 14: 700-708.
10. Scott, D. J., Dollery, C. T., Hill, D. W., Hodge, J. V., and Fraser, R. 1964. *Brit. Med. J.* 1: 811-814.
11. Sibay, T. M., and Hausler, H. R. 1967. *Am. J. Ophthalm.* 63: 289-294.

要 約

糖尿病犬における蛍光眼底像（短報）：小野憲一郎・安田和雄¹⁾・岩田祐之・中山裕之²⁾・長谷川篤彦・友田勇（東京大学農学部家畜内科学教室，¹⁾家畜病院，²⁾家畜病理学教室）——自然発症糖尿病犬4例について蛍光眼底検査を行った。動静脈相において，毛細血管床閉塞野を示す低蛍光部位ならびにその周囲に細小血管瘤を示す点状蛍光が認められた。また蛍光色素の漏出は観察されなかった。これらの蛍光眼底像はヒトの非増殖性糖尿病性網膜症の所見と同様であった。