Pathological Observation of Six Cases of Feline Diabetes Mellitus

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Diabetes mellitus (DM) was more uncommon in feline species than in canine cases [6]. It has been well-known that islet amyloidosis was often seen in aged cats affected with DM [12, 13], but pancreatic lesions in younger cats with DM have not been well investigated. In DM cats only several reports referred to pancreatic lesions other than islet amyloidosis, including islet vacuolation [1, 3, 6], islet lymphocyte infiltration [3] and subacute pancreatitis [1]. In addition, secondary lesions of DM in the liver and kidneys have been scarcely mentioned in the cat [3]. This report describes pancreatic, hepatic and renal lesions in diabetic cats.

Of 319 cats which were autopsied at the Department of Veterinary Pathology, the University of Tokyo, between January 1984 and March 1989, 6 ones showed continuous hyperglycemia. Their clinical history and main gross lesions are shown in Tables 1 and 2. As the pancreatic lesions, several firm nodules and atrophy were noted in cases D and E, respectively.

Tissues were fixed in 10% neutral buffered formalin immediately after autopsy. Paraffin sections were stained with hematoxylin and eosin (HE), periodic acid-Schiff (PAS) and Masson's trichrome stainings. Alkaline Congo red staining

for amyloid was also done for selected sections of the pancreas. Immunohistochemistry avidin-biotin-peroxidase complex (ABC) technique for insulin, glucagon and somatostatin was applied for paraffin sections of the pancreas. Antibodies used were guineapig anti-insulin (Miles-Yeda, Elkhart, IN, U.S.A.), rabbit anti-glucagon (Miles-Yeda), rabbit anti-somatostatin (Miles-Yeda), biotinylated goat anti-guineapig Ig G (Kirkegaard and Perry Lab. (KPL), Gaithersburg, MD, U.S.A.) and biotinylated goat anti-rabbit Ig G (KPL). ABC reagent (Vector Lab., Burlingame, CA, U.S.A.) and diaminobenzidine (Sigma, St. Louis, MO, U.S.A.) were also used for visualizing the distribution of the hormones. Pancreatic sections of a healthy cat were used for controls.

Histopathology of the pancreas, liver and kidneys is summarized in Table 3. Deposition of a hyalin-like material was observed (Fig. 1) in most islets of cases A and F and in a few of case C. This hyalinous material was positively stained with alkaline Congo red and showed apple-green birefringence when observed by a polarized microscope. Therefore, the material was regarded as amyloid.

Vacuolation of islet cells was present in cases A, B, E and F. Especially in case B, severe vacuolation was seen in almost all islets, which could be called "ballooning of the islet cells"

Table 1. Clinical protocols in cases examined

Case	Breed	Sex	Age (year)	Clinical protocol
A	Siamese	M ^{b)}	6	Hyperglycemia
B	Chinchilla	M	2	Hyperglycemia, polyphagia, polydipsia
C	JDC ^{a)}	F ^{c)}	12	Hyperglycemia, obesity, acute renal failure
D	JDC	CM ^{d)}	? ^{f)}	Hyperglycemia, anemia
E	JDC	CM	7 1/3	Hyperglycemia, renal failure
F	JDC	SF ^{e)}	9	Hyperglycemia, emaciation

a) Japanese domestic cat. b) Male. c) Female. d) Castrated male.

e) Spayed female. f) Unknown.

Fig. 1. Hyalinous materials are deposited in an islet. Case F. HE. $\times 250$.

Fig. 2. A highly vacuolated islet. Only a small number of cells remain intact in the center. Case B. HE. $\times 180$.

Fig. 3. Glucagon-positive cells in the center of an islet. Case B. ABC method for glucagon counterstained with light green. $\times 200$.

Fig. 4. Lymphocyte infiltration in an islet (insulitis). Most of islet cells are destroyed. Case F. HE. $\times 250$.

Fig. 5. Chronic pancreatitis showing fibrosis and lymphocyte infiltration. Case D. HE. $\times 70$.

Fig. 6. Moderate fatty change in hepatic cells. Case B. HE. $\times 200$.

Fig. 7. Diffuse glomerular sclerosis of kidney. Case E. PAS. $\times 320$.

Fig. 8. Glycogen deposition in renal tubular epithelia. Case B. PAS. $\times 260$.

Table 2. Gross pathology in cases examined

Case	Gross lesion
A	Peritonitis, pulmonary hemorrhage
B	Pulmonary edema
C	Nephritis, gastric ulcer
D	Pancreatitis
E	Pancreatic sclerosis, icterus
F	Hepatic degeneration, gastric erosion

(Fig. 2). Only a small number of intact cells remained in the center of the islets involved. PAS-positive fine granules were often detected in the vacuoles and digested by amylase treatment. By the ABC method, unvacuolated cells in the center of the islets of such case were positively stained only for glucagon (Fig. 3). Control islets were not stained well for somatostatin, though they were clearly stained for insulin and glucagon.

In case F, there were islet amyloidosis and vacuolation, often associated with lymphocyte infiltration (Fig. 4).

Most islets in case D were affected with chronic pancreatitis consisting of proliferation of interstitial tissues, lymphocyte infiltration and duct metaplasia of acinar cells (Fig. 5).

Liver lesions observed were fatty change (3 cases) (Fig. 6), dissociation of liver cell cords (4 cases) and atrophy of hepatocytes (2 cases). Many renal glomeruli of case E showed diffuse glomerular sclerosis characterized by extension of mesangial area with collagenous materials

(Fig. 7). In case B, glycogen granules were accumulated in the epithelial cells of renal proximal tubules (Fig. 8). Cases C and D also showed slight mesangial proliferation and case A showed interstitial nephritis due probably to the causes unrelated to DM.

Islet amyloidosis has been frequently reported in diabetic aged cats and is known to be closely related to DM [12, 13]. Considerably high percentage of aged cats without apparent clinical signs of DM have islet amyloidosis, considered to be prediabetic [9, 12]. In the present report, 3 cats having islet amyloidosis were 6-, 9- and 12-years-old, which were also aged as previously reported [12, 13].

Islet vacuolation was reported in several diabetic cats of all ages [3]. In the present report, it was revealed by the immunohistochemical study; vacuolation occurred mainly in insulin-secreting cells and glucagon-secreting cells remained intact in the center of the affected islet. Granules seen in the vacuolated cells were positively stained with PAS and digested by the amylase treatment, suggesting that the vacuolation was caused by excess glycogen accumulation in B-cells of the islet. It is still unknown whether the glycogen degeneration of islets is the real cause or the result of hyperglycemia.

Gepts and Toussaint [3] observed lymphocyte infiltration in only one islet of a diabetic cat. In case F, lymphocyte infiltration was seen in several islets, some of which were associated with amyloid deposition and/or vacuolation. In man,

Table 3. Histopathology of pancreas, liver and kidneys in cases examined

Case	Histopathology		
	Pancreas	Liver	Kidneys
A	Islet vacuolation and amyloidosis	Fatty change, LC ^{a)} dissociation	Interstitial nephritis
B	Islet vacuolation	Fatty change, LC dissociation	Glycogen deposition in tubular epithelia
C	Islet amyloidosis	Fatty change	Mesangial proliferation
D	Chronic pancreatitis	LC dissociation	Mesangial proliferation
E	Fibrosis, islet vacuolation	Atrophy	Diffuse glomerular sclerosis
F	Islet vacuolation and amyloidosis, insulinitis	Atrophy, LC dissociation	No remarkable change

a) Liver cell cord.

insulinitis is the most typical histologic findings of juvenile type DM (insulin-dependent DM) [2] and suggests its virological and/or autoimmune etiology [4, 5, 8]. This feline case may suggest the possibility that viral infection and/or autoimmunity is a cause of feline DM.

Hepatic and renal lesions, which were regarded as secondary changes due to DM, were also recognized in the present cases. Hepatic fatty change was a common complication in DM of dogs [3, 6]. Dissociation of hepatic cords with atrophy of hepatocytes seen in the present cases may not be concerned with DM. Renal lesions observed here were diffuse glomerular sclerosis and glycogen accumulation in tubular epithelia. They appeared to be rarer and slighter than those in dogs [3, 7, 11]. In dogs, another diabetic complication, retinopathy was also reported [3, 10]. As there was only one insufficient study on retinopathy of diabetic cats [3], further investigation on the complication would be needed.

REFERENCES

1. Duffel, S. J. 1975. *J. Small Anim. Pract.* 16: 365-374.
2. Gepts, W. 1965. *Diabetes* 14: 619-633.
3. Gepts, W. and Toussaint, D. 1967. *Diabetologia* 3: 249-265.
4. Handwerger, B. S. 1985. pp. 287-344. In: Autoimmunity and endocrine disease (Volpe, R. ed.), Marcel Dekker, New York.
5. Irvine, W. J. 1980. pp. 249-274. In: Autoimmune aspects of endocrine disorders (Pinchea, A., Doniach, D., Fenzi, G. F., and Baschieri, L. eds.), Academic Press, London.
6. Meier, H. 1960. *Diabetes* 9: 485-489.
7. Nakayama, H., Ono, K., Takahashi, R., and Fujiwara, K. 1986. *Jpn. J. Vet. Sci.* 48: 149-153.
8. Notkins, A. L. and Yoon, J. W. 1984. pp. 241-247. In: Concepts in viral pathogenesis (Notkins, A. L. and Oldstone, M. B. A. eds.), Springer, New York.
9. O'Brien, T. D., Hayden, D. W., Johnson, K. H., and Stevens, J. B. 1985. *Vet. Pathol.* 22: 250-261.
10. Ono, K., Yasuda, K., Iwata, H., Nakayama, H., Hasegawa, A., and Tomoda, I. 1986. *Jpn. J. Vet. Sci.* 48: 1257-1261.
11. Ricketts, H. T., Petersen, E. S., Steiner, P. E., and Tupikova, N. 1953. *Diabetes* 2: 288-294.
12. Yano, B. L., Hyden, D. W., and Johnson, K. H. 1981. *Vet. Pathol.* 18: 310-315.
13. Yano, B. L., Hyden, D. W., and Johnson, K. H. 1981. *Vet. Pathol.* 18: 621-627.

要 約

ネコ糖尿病 6 例の病理学的観察(短報): 中山裕之・内田和幸・小野憲一郎¹⁾・後藤直彰(東京大学農学部獣医病理学教室, ¹⁾ 獣医臨床病理学教室)——持続的に高血糖を示したネコ 6 例について病理学的に観察した。膵病変としては膵島アミロイドーシス(3 例), 膵島空胞化(4 例), 膵島炎(1 例), 慢性膵炎(1 例)がみられた。また, 脂肪肝(3 例)や腎糸球体硬化症(1 例), 尿細管上皮グリコーゲン沈着(1 例)などの二次病変も観察された。