犬におけるインスリノーマの2例

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Two Cases of Canine Insulinoma

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Only a few canine cases of insulin-secreting neoplasm arising from pancreatic islets and causing a hypoglycemia leading to neurologic disturbance have been reported in several countries [1, 3–7, 11, 12] but not in Japan. This note is to describe histopathology and electron microscopy on two canine cases of beta cell tumors in the pancreas.

The patients were 9-year-old male Pomeranian (Case A) and 11-year-old female Maltese (Case B). As shown in Table 1, they had clinical signs of hyperinsulinism, hypoglycemia and epileptic convulsion. Case A showed a rapid recovery when tested for glucose tolerance 2 days before death. Laparotomy was performed in Case B, which died of pancreatitis and pneumonia 8 days later.

At autopsy (Case A) or laparotomy (Case B), a single spherical white-yellowish firm nodule 1 or 1.5 cm in diameter was present in the right (Case A) or the left (Case B) lobe of pancreas and encapsulated by thin fibrous connective tissue. In Case A, metastatic lesions were seen in the regional lymph node and the liver which had a few small yellowish nodules 0.3 to 1 cm in diameter on the surface.

Paraffin sections of the affected pancreas, lymph nodes and liver were made from formalin- or Bouin's-fixed tissues and stained with hematoxylin-eosin, Gomori's aldehyde fuchsin, periodic acid-Schiff and Congo red. Immunohistochemistry was done using avidin-biotin peroxidase complex for insulin, glucagon and somatostatin. Tissue samples were also fixed in

Table 1. Clinical data

	Case A	Case B
Breed	Pomeranian	Maltese
Sex, Age, B.W.	Male, 9y, 5.5kg	Female, 10y9m, 5.1kg
Clinical sign	Seizures for 3y	Seizures for 4m
Serum glucose (mg/dl)	16–35	15–52
Serum insulin (μU/m*l*)	1890–2700	109–123

Table 2. Pathologic observations

	Case A	Case B
Site (Diameter)	Right lobe (1.5 cm)	Left lobe (1 cm)
Metastasis	Liver, pancreatic lymph node	NE[a)]
Pattern of proliferation	Trabecular or glandular	Cord-like
Cell morphology	Small, polyhedral	Small, columnar
Secretory granule (Diameter)	Immature, circular (120–200 nm)	Mature, crystaloid (50–100×300–400 nm)
Desmosomal junction	−/+[b)]	+
Immunohistochemistry		
Insulin	+	+
Glucagon	−	−
Somatostatin	−	−

a) Not examined.
b) Desmosome-like structure was seen partly.

glutaraldehyde and osmium tetroxide, and embedded in Epok 812, and ultrathin sections were stained with uranyl acetate and lead nitrate and observed by a JEM-100S electron microscope.

Pathological observations of the both cases were summarized in Table 2. In autopsied Case A, neoplastic cells invaded into capillaries and the fibrous capsule, metastasizing to the pancreatic lymph node and liver parenchyma, where neoplastic cells with insulin-positive granules were in a ribbon pattern (Fig. 1). The neoplastic mass was lobulated by fine connective tissues (Fig. 2). Occasionally a considerable amount of amyloid was seen between neoplastic cells. Pancreatic islets were atrophied and decreased in number. In the tumor nodules small neoplastic cells proliferated showing trabecular, glandular (Fig. 2) or cord-like (Fig. 3) pattern resembling normal pancreatic islets, sometimes showing rosettes surrounding small vessels. They were polyhedral or columnar in shape having a small spherical or oval nucleus with a large nucleolus. Most cells had weakly eosinophilic cytoplasmic granules stained red or violet with Gomori's aldehyde fuchsin. The granular cytoplasm was shown to be positive for insulin but negative for glucagon and somatostatin. The comparatively clear cells were more strongly positive for insulin than dark cells. In Case B the neoplastic mass was composed of more differentiated type of cells than in Case A, showing a network structure. Mitotic figures were rare in both cases.

Ultrastructurally tumor cells had abundant cytoplasmic organella. Some nuclei scattered with chromatin showed an irregular outline. Some neoplastic cells resembled the normal pancreatic beta cells while they had various types of secretory granules (Fig. 4a). A large number of spherical or oval mitochondria, endoplasmic reticulum with abundant and free ribosome were seen throughout the cytoplasm. The cytoplasmic membrane of adjacent cells contacted each other desmosomes (Fig. 4b) in Case B. In Case A, however,

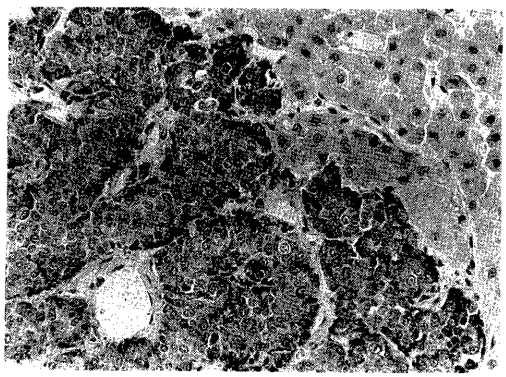

Fig. 1 Neoplastic cells with insulin-positive granules metastasized in the liver of Case A. ABC method, ×210.

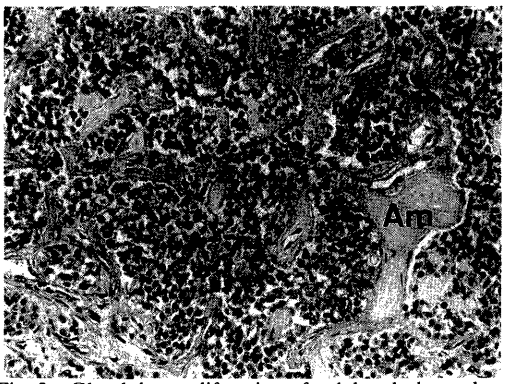

Fig. 2 Glandular proliferation of polyheadral neoplastic cells accompanied with interstitial amyloid deposition (Am) and lobulation by fine connective tissue in Case A. HE. ×80.

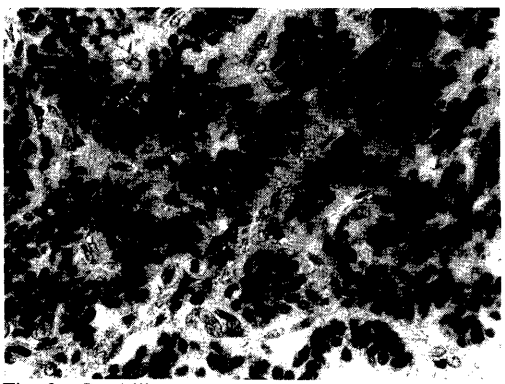

Fig. 3 Cord-like arrangement of small and columnar neoplastic cells in Case B. Arrow showed a mitotic figure. HE, ×175.

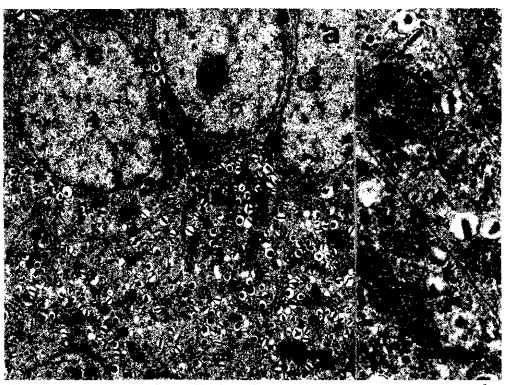

Fig. 4 Neoplastic cells having many secretory granules with crystaloid core (a) and a desmosome (b, arrowhead) in Case B. Bar=2 μm (a) or 1 μm (b).

desmosomal junctions were rare. Neoplastic cells had numerous secretory granules varying in size and shape, probably representing different stages of maturation. In Case A the granules were circular and electron-dense or pale and seemingly of immature type, while most cytoplasmic granules of Case B were supposed to be of mature type resembling those of normal beta cells [8, 10]. This type of granules had a bar- or V-shaped electron-dense core and a wide electron-lucent space under the limiting membrane (Fig. 4) sometimes contacting with the cytoplasmic membrane.

Beta cell tumors are known to be not always functioning [3, 5]. Case A with a smaller number of immature insulin-positive granules with a circular core might be malignant with hyperinsulinism and metastasis, as has been commonly seen in dogs [2, 3, 5, 6]. In contrast, tumor cells of Case B with less severe clinical signs had mature secretory granules of storing type [2, 8, 10] characterized by crystaloid cores. Some cases of this tumor were described to have heterologous cells secreting different hormone [6], but in the present cases, neoplastic cells were only positive for insulin but not for glucagon or somatostatin.

REFERENCES

1. Beck, A. M., and Krook, L. 1965. *Cornell Vet.* 55: 330–339.
2. Capen, C. C. 1978. pp. 409–414. *In*: Tumors in Domestic Animals, 2nd ed. (Moulton, J. E. ed.),Univ. California Press, Berkeler.
3. Capen, C. C., and Martin, S. L. 1969. *Pathol. Vet.* 6: 309–341.
4. Cello, R. M., and Kennedy, P. C. 1957. *Cornell Vet.* 47: 538–557.
5. Grant, C. A. 1960. *J. Comp. Pathol.* 70: 450–457.
6. Hawkins, K. L., Summer, B. A., Kuhajda, F. P., and Smith, C. A. 1987. *Vet. Pathol.* 24: 170–179.
7. Justus, H. A. 1963. *J. Am. Vet. Med. Assoc.* 142: 1413–1414.
8. Lacy, P. E. 1957. *Anat. Rec.* 128: 255–267.
9. Marcus, L. C., Bucci, T. J., and Kraner, K. L. 1964. *J. Am. Vet. Med. Assoc.* 145: 1198–1203.
10. Munger, B. L., Caramia, F. and Lacy, P. E. 1965. *Z. Zellforsch.* 67: 776–798.
11. Steinberg, H. S. 1980. *J. Am. Anim. Hosp. Assoc.* 16: 695–698.
12. Wilkinson, J. S. 1964. *J. Am. Vet. Med. Assoc.* 144: 404–412.

要　　約

犬におけるインスリノーマの2例（短報）：美土路活男・中山裕之・岡田信彦・小野憲一郎[1)]・安田和雄[1)]・沢邦彦[2)]・高橋令治・藤原公策（東京大学農学部家畜病理学教室・[1)]家畜内科学教室・[2)]開業）――低血糖とてんかん様発作を呈した犬のインスリノーマ2例について，病理学的に観察した．1例は未熟 β 細胞からなる悪性インスリノーマで，肝・膵リンパ節に転移巣を認め，他の1例は成熟 β 細胞からなる良性インスリノーマであった．両例とも腫瘍細胞は正常膵島に似た配列を示し，細胞質内には，形・大きさが不同の多数のインスリン陽性顆粒を有していたが，悪性例では未熟顆粒が，良性例では成熟顆粒が多数を占めていた．