Growth hormone (GH)-producing pituitary tumors, which induce acromegaly or gigantism, have been described in man. Immunocytochemistry revealed GH in acidophilic as well as in chromophobic pituitary tumors, which allowed classification of the pituitary tumors into several morphologically distinct entities. Pituitary tumors have been documented in the dog, cat, rat, sheep, and cow. Three acidophilic pituitary tumors associated with diabetes mellitus have been reported in the cat; elevated plasma levels of GH were demonstrated in one case.

**Case report.** An acidophilic adenoma developed in the adenohypophysis of a cat with insulin-resistant diabetes mellitus and acromegaly. This 4.5-kg 13-year-old spayed female domestic short-haired cat had a 6-week history of weight loss, polyphagia, polyuria, a large head with masculine features (prominent mandible and upper jaw), and cataracts in both eyes. Radiography revealed that both lateral malleoli of the hind legs were enlarged (0.8 cm in diameter). Hyperglycemia of 300 mg/dl led to the clinical diagnosis of diabetes mellitus. Insulin therapy was initiated at a dose of 2.5 units Long-Insulin® (Hoechst, Frankfurt, F.R.G.) per day. The dose was progressively increased to 28 units until general conditions improved and polydipsia and polyuria diminished. Treatment was sustained for 15 months. Serum glucose levels were determined every 3 to 4 weeks and ranged between 80 and 400 mg/dl. During the observation period, the cat experienced two episodes of hypoglycemia with depression and trembling, which resolved after oral glucose administration. After 15 months, the cat was presented with treatment-resistant dizziness, circling, and somnolence. The cat was euthanized and necropsied 24 hours post-mortem.

**Methods.** Tissues were fixed in Bouin's fluid and embedded in paraffin. Sections (5-µm) were mounted on albuminized glass slides and stained with hematoxylin and eosin (HE); when appropriate, Goldner's trichrome stain, Congo red, and periodic acid-Schiff (PAS) were applied. For immunocytochemistry, the peroxidase-antiperoxidase (PAP) unlabeled antibody method was applied as previously described. Rabbit antisera to the following antigens with their specified optimal dilutions were employed: canine prolactin (anti-cPRL; 3197/23 W), 1:1,500, and canine growth hormone (anti-cGH; ACGH-T-117), 1:1,500, prepared and donated by Dr. M. F. El Etreby, Schering AG, Berlin, F.R.G.; a-melanocyte-stimulating hormone (a-MSH), 1:1,000, purchased from UCB Bioproducts, Brussels, Belgium; 3α-24-cholesterol (anti-ACTH; 81/2), 1:2,250; 1-24α-N-terminal of human proopiomelanocortin (anti-h24αN-POMC; R 64-3), 1:500, donated by Dr. F. E. Estivariz, Universidad Nacional de La Plata, La Plata, Argentina.

Controls of the staining reaction included replacement of specific antisera by normal rabbit serum and omission of the second antibody or the PAP complex. In addition, anti-cGH was adsorbed in liquid phase with iodination grade cGH (AFP-1983-B) kindly supplied by Dr. A. F. Parlow through the NIADDK National Hormone and Pituitary Program at 10 and 50 µg/ml of diluted antiserum for 24 hr at 4°C and used as first antibody on adjacent sections.

Macroscopically, a tan-white multinodular mass involved most of the pituitary gland; it was approximately 0.7 cm in diameter and compressed the overlying hypothalamus. The pancreas showed multifocal nodular hyperplasia, and the liver was moderately peliotic. The tendons of extensor digitorum pedis lateralis and fibularis brevis muscles on either side were surrounded by a mantle of ossified tissue.

**Histology.** The pituitary tumor was sharply delineated with no definite capsule and replaced three-fourths of the gland with compression and atrophy of the pars distalis (PD) and focal infiltration of the pars intermedia (PI). The tumor was...
subdivided by fibrovascular stroma into several nodules composed of large polygonal cells (Fig. 1). Tumor cells had abundant finely granular acidophilic cytoplasm with HE and trichrome stains and were PAS-negative. The hyperchromatic nuclei were round to elongate. Nuclear pleomorphism was rare, and there were no mitotic figures. These findings were consistent with the diagnosis of an acidophilic adenoma of the adenohypophysis.

**Immunocytochemistry.** There was strong cytoplasmic staining for GH (Fig. 2). Preincubation of the GH antiserum with cGH at 10 and 50 ng/ml greatly attenuated and completely blocked the staining, respectively. In contrast, the tumor did not stain for PRL, α-MSH, ACTH, and POMC, which were present in different cell populations of the adjacent PD and PI. In addition, marked diffuse hyperplasia of GH-immunoreactive cells was seen in the PD.

**Other tissues.** The pancreas had extensive Congo red-positive islet amyloidosis. The remaining islet cells showed varying degrees of hydropic degeneration. Moderate nodular hyperplasia was seen in the exocrine pancreas. In the thyroids, solitary hyperplastic nodules were present, while the adenals were unremarkable. Chronic glomerulonephritis was in both kidneys. The thickened lateral malleoli showed normal architecture and consisted of lamellar bone.

Clinically, insulin-resistance was evident by high insulin requirements and persistent hyperglycemia. These findings are consistent with earlier observations by others. Furthermore, Lichtensteiger et al. demonstrated elevated plasma GH in a cat with acidophilic pituitary adenoma. The mechanism(s) responsible for the development of the growth hormone-producing pituitary adenoma and the diffuse GH cell hyperplasia in the PD described in this report remain obscure.

Diabetes mellitus with hydropic degeneration of pancreatic islet and islet amyloid deposits in this case were similar to previous reports. Diabetes may be caused by islet amyloidosis, hydropic degeneration, or GH hypersecretion of the pituitary adenoma, or a combination of all three. Amyloid was present in 65% of diabetic cats. In the present case insulin resistance was evident, posing problems in clinical treatment. In view of clinical surveys, this represents an unusual feature in feline diabetes mellitus. Diabetes mellitus may result from complex interaction of sustained GH hypersecretion with pancreatic B cells and peripheral insulin target tissues leading to permanent hormonal and metabolic derangements. Support for this concept derives from experimental data, which show the particular sensitivity of cats and dogs to the diabetogenic effect of GH. The sequence of changes induced by GH is characterized by initial hyperinsulinemia, progressively rising serum glucose, rapidly declining insulin content associated with decreasing pancreatic insulin content, and subsequent degeneration of B cells.

This case provides support for the concept of feline somatotropic diabetes mellitus caused by acidophilic pituitary tumor secreting GH.

**Acknowledgements**

The authors thank Sabine Wack, Sabine Simon, and Ute Zeller for technical and photographic assistance. This work was supported in part by grant 29-5-54 from JNO, Federal Republic of Germany.

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