CASE REPORT

Growth Hormone-producing Pituitary Adenoma, Elevated Serum Somatomedin C Concentration and Diabetes Mellitus in a Cat

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Summary

A pituitary acidophil adenoma in a domestic shorthaired cat with diabetes mellitus and elevated serum somatomedin C level is described. Growth hormone production by the neoplasm was confirmed by an appropriate reaction using an immunoperoxidase technic.

Key words: Adenoma, cat diseases, diabetes mellitus, immunoenzyme technics, pituitary neoplasms, somatomedins, somatotropin.

Résumé

Production d'hormone de croissance par un adénome de l'hypophyse, teneur sérique élevée de somatomédine C et diabète sucré, chez un chat

Les auteurs rapportent un adénome des cellules acidophiles de l'hypophyse, chez un chat domestique qui souffrait aussi de diabète sucré et affichait une teneur sérique élevée de somatomédine C. Une réaction appropriée qui employait une technique à l'immunoperoxydase confirma la production d'hormone de croissance par le néoplasme.

Mots clés: adénome, maladies félines, diabète sucré, techniques immunoenzymatiques, néoplasmes de l'hypophyse, somatomédines, somatotropine.

Introduction

Acromegaly refers to the enlargement of the extremities which occurs following prolonged endogenous hypersecretion of growth hormone (GH), usually from a pituitary acidophil adenoma. Many human acromegalics have glucose intolerance or overt diabetes mellitus (1) as GH antagonizes insulin, both by its peripheral actions and by reducing the number of insulin receptors on target cells (2). Pituitary acidophil adenomas have been identified occasionally in cats with diabetes mellitus (3), while a pituitary mass and elevated plasma GH concentration were recorded in a diabetic cat with excessive exogenous insulin requirements (4). The purpose of this paper is to document growth-hormone production of physiological significance by a pituitary adenoma in a cat with diabetes mellitus.

Case History

A ten year old neutered male shorthair cat weighing approximately 5 kg was presented to a veterinarian for recent onset of polydipsia and mild inappetence. The results of physical examination were unremarkable but urinalysis revealed severe glycosuria without ketonuria. Abnormal hematological and biochemical findings comprised eosinophilia ($3{\cdot}954 \times 10^9$ cells/L) and hyperglycemia (25·5 mmol/L). Treatment for diabetes mellitus was instituted with isophane insulin suspension, and the cat was discharged from hospital after five days with instructions for the owner to regulate the daily insulin dose on the basis of morning glycosuria. After three months the insulin requirement diminished and therapy was discontinued. An episode of right hind limb cellulitis occurred four weeks later but resolved with administration of antibiotic. After a further eight months the cat was reexamined because of polyphagia. Hyperglycemia (16·4 mmol/L) was noted and insulin therapy reinstituted. The diabetic condition was controlled uneventfully for the subsequent year by daily insulin doses of approximately 4·5 units. At this time, morning urine samples no longer contained glucose and insulin dosage was stopped. Three months later the cat was presented for vomiting and inappetence. On the basis of severe uremia (urea, 59·1 mmol/L) with urine specific gravity of 1·016, a diagnosis of uncompensated renal failure was made. There was mild fasting hyperglycemia (8 mmol/L). Diuresis by intravenous fluids failed to resolve the uremia and the cat was euthanized.

Pathological and Endocrinological Findings

The cadaver presented for autopsy was of a big, but thin, cat. Grossly, the liver was large, friable and yellow-brown. The kidneys were slightly small and firm with fine pitting of the corti-

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ces. Bilateral thickening of the adrenal cortices was noted together with extracapsular cortical nodules. There were multiple firm white masses up to 0·5 cm in diameter scattered through the pancreatic parenchyma and the parathyroid glands were enlarged. The pituitary gland was unusually firm, white, spherical and measured 6 mm in diameter.

Routine histology revealed microvesicular steatosis and prominence of the fat storage cells of Ito in the liver, severe chronic interstitial nephritis, diffuse adrenal cortical hyperplasia and hyperplastic parathyroid tissue. There was marked nodular hyperplasia of the exocrine pancreas, together with a patchy eosinophilic and lymphoid infiltrate, fibrosis and some acinar cell degeneration. Globule leukocytes were identified beneath the pancreatic duct epithelium. Many pancreatic islets were histologically normal, while others contained amyloid (green birefringence of Congo Red-stained sections under polarized light). A well-circumscribed but nonencapsulated mass consisting of well-differentiated acidophil cells replaced the normally heterogeneous cell population within the pituitary gland.

Paraffin-embedded formalin-fixed sections of the pituitary tumor and pituitary tissue from two normal cats were tested for the presence of pituitary hormones by the immunoperoxidase technique with application of the avidin-biotin-peroxidase complex (5). All the antibodies used were raised in rabbit against the human pituitary hormones, namely adrenocorticotrophic hormone (ACTH), melanocyte stimulating hormone (α-MSH), GH, thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH), luteinizing hormone (LH) and prolactin (PL). Immunoreactivity of these antibodies towards the feline antigens was confirmed in the normal feline pituitary tissue. The majority of the tumor cells showed immunoreactivity for GH, occurring in the form of fine granules in the cytoplasm but occasional cells showing strong reactivity for ACTH and PL were interspersed throughout. Tumor cells had no apparent immunoreactivity for α-MSH, TSH, FSH or LH. It could not be determined whether those cells with immunoreactivity for ACTH and PL within the neoplasm were remnants of normal tissue or whether the tumor was multihormonal. A human neoplasm with identical immunodistribution has been observed (E. Vasak, unpublished observation).

Somatomedin C (Sm-C) concentrations were measured in sera collected from the case prior to death and stored at -20°C, and from two clinically healthy cats. A double antibody radioimmunoassay technique developed for clinical use in people was employed (6). Somatomedin C levels were 5·02 U/mL in the diabetic cat, and 0·51 U/mL and 0·61 U/mL in the controls.

Growth hormone and insulin determinations were not done.

Skeletal abnormalities were not detected on radiography of several ribs and a distal forelimb.

Discussion

The somatomedins are a population of small peptides whose serum concentration is GH dependent, and which are thought to mediate the growth promoting actions of GH on the skeleton and other tissues (7). There is evidence that Sm-C measurement differentiates human acromegalics and normal patients more precisely than GH (8,9), as there is some overlap of fasting GH levels between the two groups (10,11). Somatomedin C elevations in people with acromegaly have been of the same order as that recorded for the diabetic cat (8).

Although GH concentrations in plasma may be slightly elevated in both uncontrolled diabetes mellitus and chronic renal disease (9), the Sm-C level was sufficiently high to suggest that GH production by the pituitary adenoma unmasked the diabetic state in our patient. Growth hormone is a potent diabetogenic agent in the cat (12,14); the hyperglycemia so induced is generally associated with increased plasma insulin activity (15). Similarly, glucose intolerance, diabetes mellitus and insulin resistance in human acromegalics is usually accompanied by hyperinsulinemia.

Insulin doses needed for control of overt signs of diabetes mellitus were not high in our case, which mitigates against the presence of severe insulin resistance. However, it is possible that absolute insulin deficiency, as recorded in another cat with GH-induced diabetes mellitus (15) and in some people with acromegaly (12), was an important determinant of the presence of overt diabetes in this animal. It has been suggested that, in people with GH-producing pituitary neoplasms, clinically apparent diabetes mellitus develops in those patients with inadequate pancreatic insulin reserve (9). Accumulation of amyloid in cat islets is of uncertain significance but the substance is present in larger amounts in diabetic animals than in normal cats (16). Perhaps islet amyloidosis in our patient, although mild, was coexistent with an impaired ability to enhance insulin secretion in response to prolonged elevation of plasma GH.

Hydropic degeneration of B cells has occurred in cats with pituitary acidophil adenomas (3) and in intact or partially pancreatectomized cats following administration of glucose (17) or anterior pituitary extract (18). These changes in islet morphology are probably a consequence of degranulation and glycogen deposition (19) and can be reversed with resolution of the diabetes (18). Absence of hydropic B cells in our case may be because the cat did not have marked hyperglycemia at the time of death.

Although skeletal or soft tissue changes suggestive of acromegaly were not detected in our case, these signs may be subtle in human patients and more prominent when the disorder develops in youth (9).

It would be interesting if variation in hormonal output by pituitary neoplasms was responsible for the episodic nature of diabetes mellitus in this cat, and for the variable insulin requirements reported in others (4). The possibility that GH-producing pituitary tumors are a relatively important cause of diabetes mellitus in this species does not appear to have been eliminated.

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ABSTRACTS

GROHN Y, LINDBERG LA, BRUSS ML, FARVER TB. Fatty infiltration of liver in spontaneously ketotic dairy cows. *Journal of Dairy Science* 1983; 66: 2320-2328. (Coll. Vet. Med., Helsinki, Finland).

Cows were divided into three groups (healthy, mildly ketotic, and severely ketotic) by their blood ketone body concentrations. Severely ketotic cows had a greater proportion of fat in biopsy samples of liver than healthy cows. The mildly ketotic group fell between the other two groups and differed only from the severely ketotic group. There was a positive correlation between fatty infiltration and blood ketone body concentrations, but a negative correlation with glucose concentrations. Liver-specific enzymes were positively correlated with fatty infiltration. Only ornithine carbamoyltransferase and iditol (sorbitol) dehydrogenase could separate healthy cows from those with severe ketosis. Liver biopsy seemed to be the only reliable method of measuring fatty infiltration in the liver.

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CARGILL CF, GIESECKE PR, HEAP PA, WHYTE PB. Bilateral cortical cataracts in sows. *Australian Veterinary Journal* 1983; 60: 312-313. (Vet. Sci. Div., Dep. Agric., c/o Inst. Med. Vet. Sci., Adelaide, South Australia 5000, Australia).

Blindness due to bilateral cortical cataracts occurred in 20 sows from 6 pig herds in South Australia over a 3-year period. Prevalence ranged from 8 to 40% and in 4 herds all the affected sows were over 3 years old. The sows had good reproductive performance and were otherwise clinically healthy. The only constant factors in affected herds were that dry sows were housed in dirt runs and fed hygromycin B continuously. In an experiment to test whether cataract formation was associated with ingestion of hygromycin B, sows housed in dirt runs for 3 years were fed 2.5 kg of a ration daily containing 1 kg hygromix 13/tonne of feed, being increased to 2.5 kg/t for 3 periods of 6 weeks to simulate increased feed intake during lactation. Varying degrees of corneal ulceration were present in all sows examined, but no evidence of cataract formation. The failure to reproduce the lesions indicates that other factors in addition to hygromycin may be involved. Age of pigs when first exposed to hygromycin may also be important.

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