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Acromegaly in a domestic short-haired cat: First report from Iran

Mahdieh Rezaei[1], Mehdi Saberi[1], Alireza Shafiian[2*], Mohamad Zamani-Ahmadmahmudi[1]

[1]*Department of Clinical Science, Faculty of Veterinary Medicine, Shahid Bahonar University, Kerman, Iran*

[2]*Bahman Veterinary Centre, Kerman, Iran*

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ABSTRACT

A 12-year-old cat, weighting 7.4 kg, suffering from fatigue, exercise intolerance, polyphagia, polyuria and polydipsia was presented. Obesity, a massive head, inferior prognathia and widened inter-dental spaces were noted on examination. Radiographic surveys showed organs enlargement. Labaratory results revealed hyperglycemia and glycosuria. Based on fasting hyperglycemia, concurrent hyperglycemia and glycosuria, diagnosis of diabetes mellitus was made. However, according to the poor diabetic regulation, clinical signs and the absence of other diseases, a tentative diagnosis of acromegaly was confirmed by increased plasma levels of growth hormone. Managing diabetes mellitus with increasing doses of insulin was the only possible therapeutic strategy.

1. Introduction

Acromegaly, a syndrome characterized by overgrowth of bony and soft tissue, is caused following chronic excessive production of growth hormone (GH)[1]. It is a well-recognized but rare condition in cats caused by a functional somatotroph adenoma in the anterior pituitary gland[2,3]. This disorder is encountered most often in middle-aged and elderly, predominantly male, cats[1]. Catabolic and diabetogenic effects of GH, the anabolic effects of IGF-1 and the space-occupying effect of the pituitary adenoma are responsible for clinical signs[4]. The physical changes in cats tend to be less pronounced than in dogs. Increased body size, especially large head and abdominal enlargement are prominent. Affected cats may have respiratory signs, which is due to soft tissue thickening in the pharyngeal region and consequent extrathoracic upper airway obstruction. Moreover, hypertrophic cardiomyopathy is another cause of dyspnea in these cases. Neurological signs resulting from large pituitary adenoma may also manifest[3,5]. In advanced cases, clinical manifestation may include prominent facial features, generalized bone/soft tissue enlargement, and prognathia[5].

An association between pituitary adenoma and diabetes mellitus (DM) was well described in cats[6]. More recently, feline acromegaly has been reported in several cats with concurrent insulin-resistant DM[7,8]. A GH-induced postreceptor defect in insulin action at the level of target tissues is believed to be the cause of concurrent diabetes in most cats with acromegaly[2].

Acromegaly is mainly diagnosed based upon increased serum GH concentration[9]. Computed tomography (CT) or magnetic resonance (MR) imaging of the head is also recommended to confirm the presence of a pituitary tumor[10].

Radiation therapy has been reported as the most effective treatment for feline acromegaly. It leads to improved neurologic signs and decreased insulin requirements[3,5]. This study is the first case report of a diabetic cat with acromegaly in Iran, which described historic and clinical signs and laboratory findings associated with the condition.

2. Case report

A 12-year-old, male, castrated, domestic short-haired (DSH) cat

*Corresponding author: Alireza Shafiian, Shahid Bahonar University of Kerman, Afzalipour Square, Kerman, Iran.
Tel: +983433763116
E-mail: ashafiian@yahoo.com
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weighting 7.4 kg was referred to the Veterinary Teaching Hospital, Shahid Bahonar University of Kerman, with almost a one-month history of undulating constipation. Detailed history delineated that the animal had clinical signs including fatigue, panting, exercise intolerance, polyphagia, polyuria and polydipsia (PU/PD), which developed gradually within approximately one year.

Obesity, a massive head, skin folds on the neck and inferior prognathia were prominently noted on physical examination. Oral examination revealed widened inter-dental spaces (Figure 1). Dyspnea and serous nasal discharges were also observed. The abdomen seemed to be swollen (Figure 2). No abnormalities were detected in lung auscultation except for inspiratory stridor. Cardiac examination detected an irregular rhythm. Radiographic surveys showed no abnormality other than mild heart enlargement, renomegaly and hepatomegaly (Figure 3). Considering the mentioned signs, systemic diseases, particularly endocrinopathies, were suspected. Therefore, blood and urine samples were collected for further investigations.

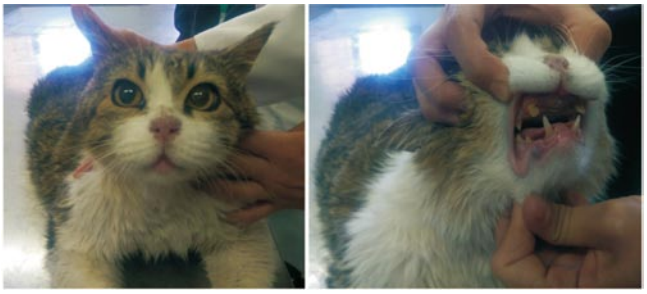

Figure 1. A 12-year-old male, castrated DSH cat with insulin-resistant DM and acromegaly. The large head, inferior prognathia and widened inter-dental spaces were noted.

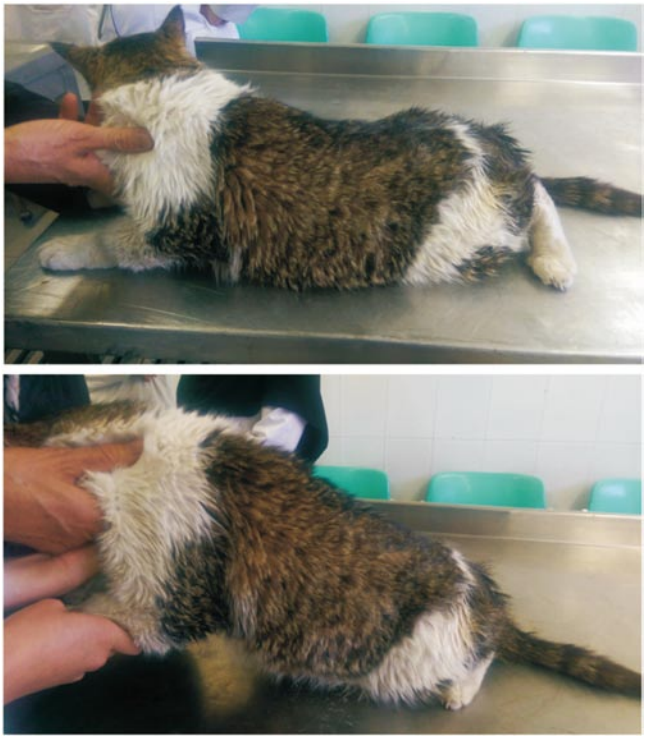

Figure 2. The increased body size and abdominal enlargement.

Hematological and biochemical parameters, as well as metabolic hormones were evaluated on the blood sample. Blood test results revealed a number of abnormalities including lymphopenia, mild neutrophilia, marked hyperglycaemia, proteinemia, and elevated levels of liver enzymes (Table 1). Glycosuria and proteinuria were also detected on the urinalysis test. Based on concurrent hyperglycemia and glycosuria, the diagnosis of DM was made.

Table 1

Complete blood count, serum biochemical parameters, hormones and endocrine function tests of a DSH cat with acromegaly.

Parameter	Values	Reference values
Hematology		
White blood cells ($\times10^3$/μL)	15.6	5.0–19.0
Red blood cells ($\times10^6$/μL)	8.6	5.0–10.0
Hemoglobin (mmol/L)	14.0	8–15
Hematocrit (%)	46.0	24–45
Platelets ($\times10^3$/μL)	585	300–700
Neutrophils ($\times10^3$/μL)	13.6	2.0–12.5
Lymphocytes ($\times10^3$/μL)	0.7	1.5–7.0
Monocytes ($\times10^3$/μL)	0.9	0.1–0.9
Eosinophils ($\times10^3$/μL)	0.4	0.0–0.8
Serum biochemistry		
Glucose (mg/dL)	315	75–130
Aspartate aminotransferase (IU/L)	54	7–38
Alanine aminotransferase (IU/L)	220	30–100
Gamma glutamyl transferase (IU/L)	3.1	1.3–5.1
Blood Urea Nitrogen (mg/dL)	38	17–32
Creatinine (mg/dL)	2	0.9–2.1
Sodium (mEq/L)	150	141–155
Potassium (mEq/L)	5.3	3.6–5.8
Phosphorus (mg/dL)	5.5	4.5–8.1
Total protein (g/dL)	8.4	5.7–8.0
Albumin (g/dL)	3.1	2.1–3.3
Total calcium (mg/dl)	9.5	6.0–10.5
Hormones		
tT4 (nmol/L)	38.4	20.0–58.0
GH (lg/L)[a]	50.5	0.8–7.2
IGF-I (lg/L)[a]	3 871	39–590
ACTH (ng/L)	22.7	4.5–90.2
Dexamethasone suppression test		
Cortisol pre-dexamethasone (nmol/L)	109.1	28–138
Cortisol 4 h after dexamethasone (nmol/L)	30.5	< 41
Cortisol 8 h after dexamethasone (nmol/L)	22.0	< 41

[a]: Basal plasma concentrations of GH and IGF-1 are means calculated from two blood samples collected 6 weeks apart.

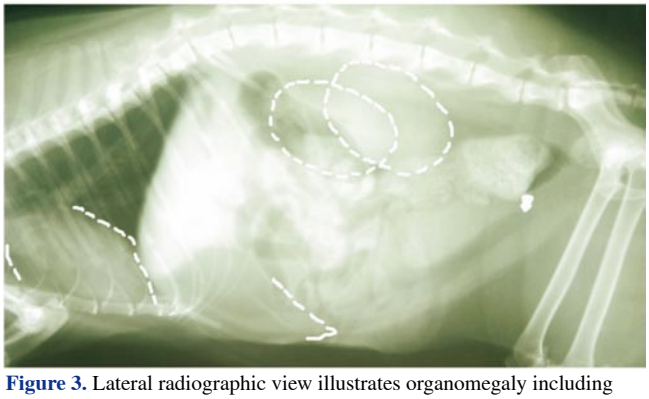

Figure 3. Lateral radiographic view illustrates organomegaly including mild heart enlargement, renomegaly and hepatomegaly.

The cat was treated with insulin (Lantus®), beginning with a dose of two units given subcutaneously, every 24 h. After one week of treatment, a mild reduction in polyuria/polydipsia and glycosuria was observed, but the clinical symptoms and hyperglycemia still remained. No improvement was achieved over the next three months by gradually increasing the dose of insulin to 8 units every 24 h. Therefore, further diagnostic tests were performed to rule out causes of insulin resistance such as hyperthyroidism and hyperadrenocorticism. Serum level of thyroxin was in the reference range and the result of low-dose dexamethasone suppression test was normal as well (Table 1).

According to the poor diabetic regulation, clinical signs and the absence of other diseases causing insulin resistance, acromegaly was suspected. A tentative diagnosis of acromegaly was confirmed by increased plasma levels of GH of 19 and 82 μg/L (reference range 0.8–7.2 μg/L; ImmuliteIGF-I, DPC) and IGF-1 of 3678 and 4064 μg/L (reference range 39–590 μg/L; ELISA kit ab 100526) in two blood samples collected 6 weeks apart (Table 1).

Considering the risk of anesthesia for older cats with cardiac disorder, unfortunately, the cat owner didn't allow us to study the cat's brain using MRI or CT scan to localize the cause of excess GH secretion. Managing DM with increasing doses of insulin was the only therapeutic strategy implemented by us. Moreover, a continuous health checkup was highly recommended.

3. Discussion

Acromegaly is caused by excess secretion of GH from a pituitary adenoma[9,11]. The average age at diagnosis is 10 years old, and 90% of the cats are male (intact or castrated)[9]. We reported acromegaly in a 12-year-old, male, castrated, DSH cat.

The present case was similar to other studies reporting large body size, weight gain, enlargement of the head, inferior prognathia and widened inter-dental spaces as the most clinical symptoms. Affected cats may have respiratory signs due to thickening of soft tissues in the pharyngeal region that results in extrathoracic upper airway obstruction. Respiratory stridor occurs in up to 53% of acromegalic cats and is due to enlargement of tongue and pharyngeal tissues. Dyspnea, serous nasal discharge and stridor were observed in the present case too. Abdominal organomegaly, cataracts, cardiac murmurs or arrhythmias, peripheral neuropathy, and central nervous signs are all attributed to acromegaly. Imaging studies may reveal organomegaly, especially of the heart, kidney, liver, and adrenal gland[10]. In the case reported here, no cardiac murmurs or arrhythmias, peripheral neuropathy, or central nervous signs were seen; however, mild heart enlargement, renomegaly and hepatomegaly were detected by radiology. Constipation was a striking feature of this cat's history. It has been reported that increased epithelial sodium channel (ENaC)-mediated sodium and water reabsorption in untreated acromegaly is the cause of constipation[12].

As we described here, one of the significant diagnostic clues to acromegaly in a cat with poorly controlled DM is weight gain. Acromegaly is proposed and demonstrated as a cause of insulin-resistant DM[7,8]. This case tolerated high doses of insulin, which confirmed our diagnosis of insulin-resistant DM. Increased secretion of IGF-1 from the liver and peripheral tissues is followed by excess GH[10]. High IGF-1 levels cause excessive soft tissue growth with bony remodeling and thickening[9,11]. Polyuria, polydipsia and polyphagia, which are associated with poor glycemic control, are included in clinical signs[10]. Polyphagia was distinctly reported by this cat's owner.

Considering the disorder's insidious onset, the cost of imaging procedures, and the lack of a readily available feline growth hormone assay, confirmation of acromegaly can be difficult[4,11]. Assays for both IGF-1 and GH have been validated in the cat, and a tentative diagnosis of acromegaly is based upon measurement of these hormones[13]. Our diagnosis was also confirmed by high and increasing GH concentrations.

Treatment should be directed at the pituitary lesion. Medical treatment, radiation therapy and hypophysectomy are the options[1]. Medical treatment with (expensive) long-acting somatostatin analogues such as octreotide and a dopamine agonist were not successful in reducing the insulin requirements in acromegalic cats[14]. Pegvisomant, a recently introduced GH receptor antagonist, has been shown to be effective in humans with acromegaly. However, this approach is not yet an option for cats because no species-specific antagonists exist[15]. Radiation therapy may improve diabetic control in cats with acromegaly following shrinking of the pituitary tumor[1]. In cats in which radiation therapy is not possible due to high expense, low availability, or other concerns, long-term survival may be achieved if DM is controlled with high doses of insulin[9]. Finally, since the owner refused any aggressive interventions, and according to high cost of medical treatment, our goal of treatment was to manage DM with insulin therapy.

Conflict of interest statement

We declare that we have no conflict of interest.

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