Acromegaly due to a pituitary tumor in a dog – diagnosis, therapy and long-term follow-up

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Abstract

Acromegaly due to a pituitary tumor has so far only been described in 3 dogs. The present case report describes a 7-year-old male-castrated Labrador Retriever which was referred because of difficult-to-control diabetes. Physical examination revealed markedly enlarged head, tongue and paws, widened interdental spaces and thickening of the skin in the head and neck area.
IGF-1 and GH were increased and the latter continued to be abnormal after somatostatin application. Computed tomography demonstrated a space-occupying lesion in the pituitary gland and the diagnosis of acromegaly due to a GH-producing tumor of the pituitary was made. The dog underwent radiation therapy with a 6MV linear accelerator (3×8Gy) and improved substantially. Two and a half years after radiation therapy the dog developed lethargy and anorexia and was euthanized. Necropsy was not permitted. This case report represents the description of a dog suffering from pituitary-dependent acromegaly which was successfully treated and had a long-term survival.

Key words: Acromegaly; pituitary tumor; diabetes mellitus; dog

Akromegalie aufgrund eines Hypophysentumors bei einem Hund – Diagnose, Therapie und Verlauf

Eine Akromegalie aufgrund eines Hypophysentumors wurde bisher erst bei drei Hunden beschrieben. Der Fallbericht beschreibt einen 7-jährigen männlich-kastrierten Labrador Retriever, der wegen eines schlecht einstellbaren Diabetes mellitus überwiesen wurde. Der Hund zeigte einen vergrösserten Kopfumfang, vergrösserte Zunge und Pfoten, erweiterte Interdentalspalten, sowie verdickte Haut im Kopf- und Halsbereich. Die IGF-1- und STH-Konzentrationen waren erhöht und die STH-Konzentration blieb nach Applikation von Somatostatin abnormal hoch. Mittels Computertomographie wurde eine Masse im Bereich der Hypophyse nachgewiesen und es wurde die Diagnose Akromegalie aufgrund eines STH-produzierenden Tumors in der Hypophyse gestellt. Der Hund erhielt eine Strahlentherapie mittels 6MV Linearbeschleuniger (3×8Gy) und sein Zustand verbesserte sich substantiell. Nach 2½ Jahren entwickelte er Anorexie und Apathie und wurde euthanasiert. Eine Obduktion konnte nicht durchgeführt werden. Es handelt sich um den Bericht eines Hundes mit einem STH-produzierenden Hypophysentumor, der erfolgreich behandelt wurde und eine lange Überlebenszeit hatte.

Schlüsselwörter: Akromegalie; Hypophysentumor; Diabetes Mellitus; Hund

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Introduction

In 1886, Pierre Marie, a French neurologist published the first description of growth hormone (GH) excess in humans and proposed the name "acromegaly".[17] The term derives from the Greek words *akron* (extreme or extremity) and *megas* (large) and is used until today to describe the disease in adult individuals, in which there is local overgrowth of bone. GH excess in childhood and adolescence leads to linear growth and large stature, which is termed gigantism. In more than 95% of affected humans acromegaly is due to a GH-producing tumor in the anterior pituitary gland. Very rarely the disease is caused by extra-pituitary disorders.[17]

The situation in cats resembles the one in humans. In the vast majority of affected cats, the disease is due to a GH-producing pituitary adenoma. In dogs with acromegaly, however, the GH excess almost always derives from the mammary gland and not from the pituitary. Mammary GH is stimulated by progesterone, which generally is a physiological event during diestrus in intact bitches.[15,21] In some elderly to old intact bitches the increase in progesterone during diestrus, however, results in an excess of mammary GH and potentially in acromegaly and diabetes mellitus. A similar effect may be seen after the administration of exogenous progesterone.[4,6] Of note, mammary GH may not only originate from normal mammary tissue, but also from mammary tumors with the potential consequence of acromegaly.[9,19]

Acromegaly due to a GH-producing pituitary tumor is extremely rare in dogs. So far, this entity has only been described in three dogs. Van Keulen et al (1996)[29] reported a 9-year-old Dobermann pinscher with difficult to regulate diabetes but without obvious physical changes of acromegaly. The dog was euthanized after a few days and necropsy revealed a pituitary adenoma with strong immunohistochemical staining for GH. More recently, Fracassi et al (2007)[8] described a 10-year-old Dalmatian dog with typical acromegalic features but with normal blood glucose concentrations. GH and IGF-1 concentrations were increased and Computed tomography (CT) revealed a pituitary mass. The dog was left untreated and was euthanized after 3 months. Necropsy confirmed the presence of pituitary adenoma, which immunostained positive for GH. Very recently, Zublena et al (2018)[31] reported a 8-year-old Border Terrier with acromegalic features and diabetes mellitus, which was successfully treated by radiotherapy and a new somatostatin analog (pasireotide).

Our case report represents the description of a dog with acromegaly due to a GH-producing pituitary tumor with successful therapeutic management and long-term survival.

Material and Methods

Analytical procedures

Haematology and serum biochemistry were run on a Sysmex XT-2000iV (Sysmex Corporation, Japan) and Cobas Integra 800 (Roche Diagnostics AG, Switzerland). Urinalysis included chemical analysis by dipstick (Combur 10, Roche), microscopic analysis of sediment and determination of the urinary protein/creatinine ratio (UPC, Cobas Integra 800). Those analyses were performed in the Clinical Laboratory of the Vetsuisse Faculty, University of Zurich. Quantitative urine culture was performed according to standard methods by the Institute of Veterinary Bacteriology of the Vetsuisse Faculty, University of Zurich.

The somatostatin suppression test was performed by collecting blood samples for measurement of GH at -15, 0, 15, 30, 45, 60, 90 min. after the intravenous administration of 10 µg/kg somatostatin (Stilamin, Merck Switzerland). Samples for GH measurement were collected in ice-chilled EDTA-coated tubes and centrifuged at 4 °C within 30 min. Plasma was stored at -80 °C until sending on dry ice by courier to the laboratory.

Blood samples for measurement of total T4 (T4), cTSH and IGF-1 concentrations were taken once and serum was stored at -20 °C until assayed.

T4 and cTSH concentrations were measured by chemiluminescence (Immulite 1000, Siemens AG, Switzerland) in the Clinical Laboratory of the Vetsuisse Faculty, University of Zurich. IGF-1 was analysed by radioimmunoassay at NationWide Specialist Laboratories, Cambridge, United Kingdom. Plasma GH concentrations were determined by a homologous radioimmunoassay at the Faculty of Veterinary Medicine, Utrecht University, The Netherlands, as described previously.[5]

Diagnostic imaging and blood pressure measurement

Two lateral thoracic radiographs (Bucky Diagnost, Philips AG, Zurich, Switzerland; FCR Profect CS, Fuji-Film AG, Dielsdorf, Switzerland) and an ultrasonographic study of the abdomen (iU22, Philips AG, Zurich, Switzerland) were acquired to screen for pathology. Conventional echocardiography was done (Vivid 7 Ultrasound system, GE Healthcare) using right and left parasternal standard views; two dimensional, motion mode and spectral Doppler images were obtained.

Indirect blood pressure was measured oscillometrically (Dinamap V 100, GE Healthcare).

A CT study (Brilliance CT 16-slice, Philips AG, Zurich, Switzerland) of the head was acquired with the following

scan parameters: 120 kVp; 280 mA; pitch, 0.688; rotation time 1 second; and detector collimation 16x0.75 mm with a rectangular field of view of 221 mm and a matrix of 512×512. The study was repeated after i.v.-injection of an iodinated contrast medium (Accupaque 350, 350 mg of I/ml, 2 ml/kg body weight, GE Healthcare, Glattbrugg, Switzerland). The raw data were reconstructed in 1 mm slices with an increment of 0.5, pre-contrast in a soft tissue and bone algorithm and post-contrast in a soft tissue algorithm exclusively. The images were reviewed with the following window settings (window width/window level: soft tissues: 140/450, brain: 100/180, and bone: 300/1500).

Radiation therapy

For the treatment planning CT and subsequent radiation therapy, the dog was under general anesthesia, immobilized in sternal recumbency. Reproducible positioning was accomplished with both, an individually shaped vacuum cushion* and a custom-made bite block.[22] On the pre- and post-contrast CT-datasets, the tumor and surrounding organs at risk (brain, brainstem, optic chiasm) were contoured in a facility internal standardized manner as previously published by our research team.[24] In brief, the gross tumor volume (GTV) was delineated using co-registered contrast-enhanced CT images. A 2 mm clinical target volume (CTV), accounting for subclinical microscopic disease extension was added into soft tissue (brain). The CTV-margin was then extended isotropically by 2 mm to define the planning target volume (PTV), accounting for setup uncertainties in daily image-guided photon treatment. Treatment planning was performed using Eclipse External Beam planning software**, applying AAA-algorithm (10.0.28). We planned radiation isocentrically and heterogeneity-corrected, using intensity-modulated radiation therapy (IMRT). Recommendations for specification of dose were adhered to as proposed by the ICRU report 83 with the PTV covered by at least the 95% isodose line.[12] The dose was prescribed to the 100% isodose line with a protocol of 3×8 Gy (24 Gy total dose).

Case Report

A 7-year-old male-castrated Labrador Retriever (30 kg) was referred to the Clinic for Small Animal Internal Medicine, Vetsuisse Faculty of the University of Zurich in 2013 because of difficult-to-control diabetes mellitus. Diabetes had been diagnosed two months before by the referring veterinarian. Initial treatment consisted of 0.5 U/kg porcine insulin (Caninsulin, MSD Animal Health) BID, due to lack of success the dose had been increased recently to 0.8 U/kg BID. The dog was fed a high-fibre diet (Prescription diet w/d, Hill's Pet Nutrition). At the time of referral, the dog showed marked polyuria/polydipsia, polyphagia, weight loss and lethargy.

On physical examination the dog was bright and alert with a reduced body condition score (BCS) of 3/9. Head, tongue and paws appeared markedly enlarged and the

Fig. 1: Labrador Retriever with acromegaly at initial presentation at the Vetsuisse Faculty, University of Zurich. Note the enlarged head and tongue.

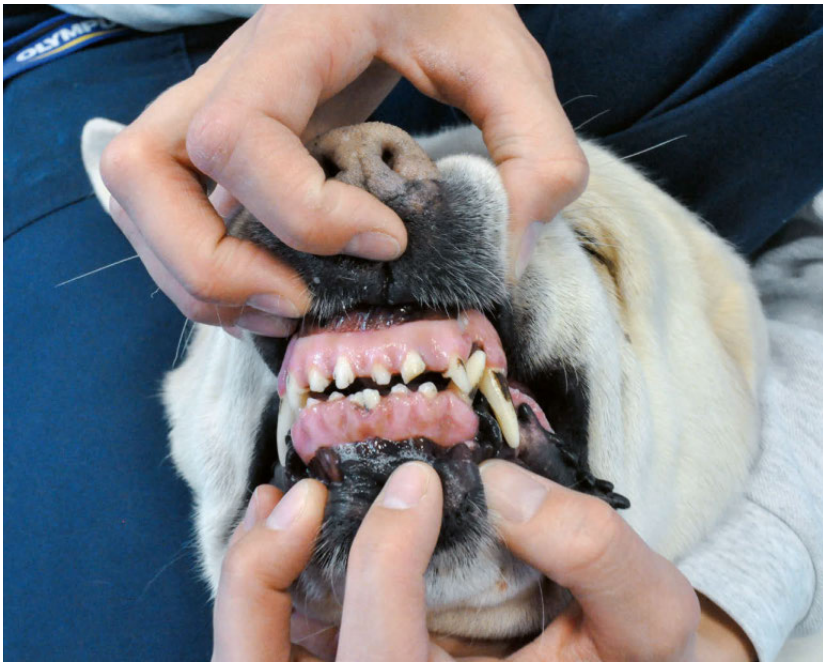

Fig. 2: Labrador Retriever with acromegaly at initial presentation at the Vetsuisse Faculty, University of Zurich. Note the widened interdental spaces.

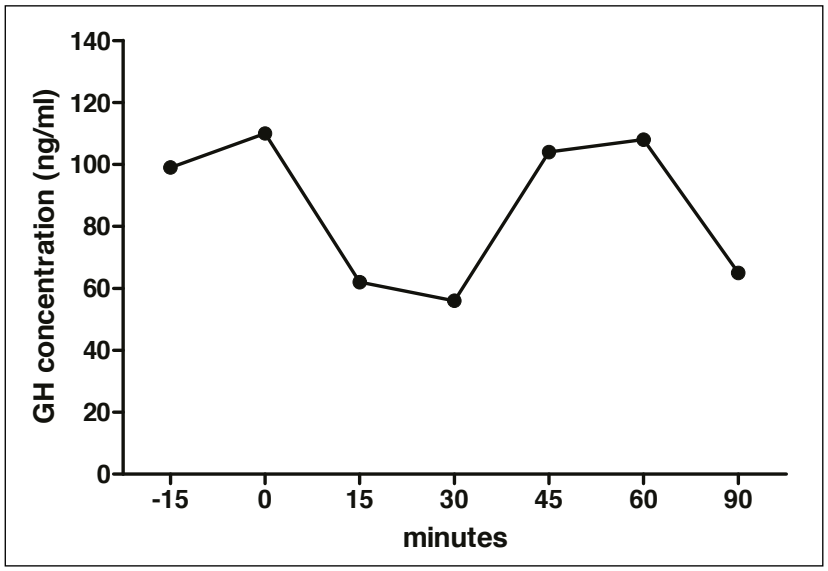

Fig. 3: Somatostatin suppression test in the Labrador Retriever with acromegaly: GH concentrations at -15, 0, 15, 30, 45, 60 and 90 minutes after the intravenous administration of somatostatin. The reference interval for baseline GH is 2-5 ng/ml. Baseline GH concentrations (-15, 0) are markedly elevated, and although there is some decrease after 15 and 30 min, GH concentrations remain very high.

interdental spaces were widened. The skin, especially in the head and neck area, was thickened with many folds. (Fig. 1 and 2). Otherwise, the clinical examination was unremarkable.

The first step in further work-up consisted in "routine" laboratory evaluation. The findings of severe hyperglycemia (21.2 mmol/l, RI 4.1-5.5), markedly increased fructosamine (774 µmol/l, RI 207–340) and severe glucosuria (4+ on dipstick) confirmed the diagnosis of poorly regulated diabetes mellitus. Ketone bodies were negative. Additional findings were mild to moderate hypercholesterolemia (14.1 mmol/l, RI 3.5-8.6), mild hyponatremia (150 mmol/l, RI 152-159) mildly increased alkaline phosphatase (258 U/L, RI 20–98) and mild normochromic normocytic anaemia (Hct 32%, RI 42–55). Those abnormalities were considered to be most likely associated with the poorly regulated diabetes. Dipstick analysis of the urine revealed proteinuria (2+), which was confirmed by the finding of a mildly increased UPC (1.1, RI: 0-0.2). Urine specific gravity was 1.037. Urine culture was negative. Blood pressure (mean of 6 measurements) was normal (systolic blood pressure 140 mm HG, normal < 150 mm HG).

Abdominal ultrasonography revealed mildly increased echogenicity of the liver and pancreas. All other abdominal organs including the adrenal glands were within normal limits.

As a next step, endocrine testing was performed. Hypothyroidism and acromegaly were considered to be the most important differential diagnosis for the striking physical changes. The T4 (18 nmo/l, RI 16-37l) and cTSH concentrations (0.04 ng/ml, RI 0.03-0.5) were normal and therefore, hypothyroidism was thought to be unlikely. The IGF-1 concentration came back as elevated (1064 ng/ml). No reference range was given on the lab report, however, it was stated that an IGF-1 concentration > 1000 ng/ml is suspicious for acromegaly. As acromegaly is extremely rare in male dogs, it was decided to confirm the diagnosis by measuring GH before and during a somatostatin suppression test. GH concentrations were markedly elevated before somatostatin administration (99 and 110 ng/ml, RI 2-5 ng/ml) and during the 60 minutes thereafter (Fig. 3). Further work-up was pursued to identify the origin of the GH excess. The mammary gland as a source seemed unlikely due to the fact that the dog had not received exogenous

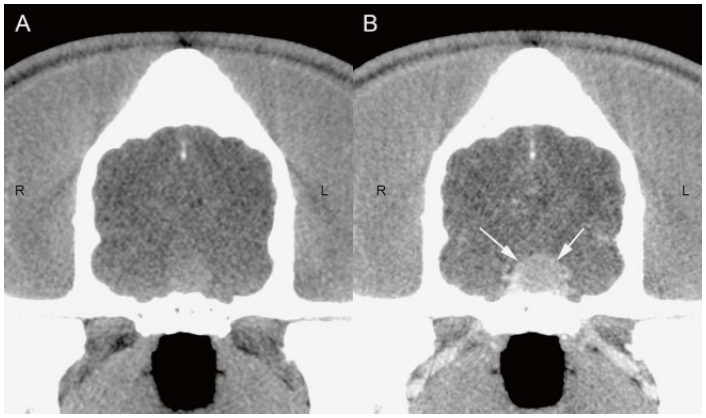

Fig. 4: Transverse images of the CT study of the head in soft tissue reconstruction; A before and B after i.v.-injection of iodinated contrast medium. Compared to white and grey matter, the pituitary space occupying lesion presented mildly hyperattenuating before contrast administration and enhanced moderately and mildly heterogeneously (white arrows) after contrast injection.

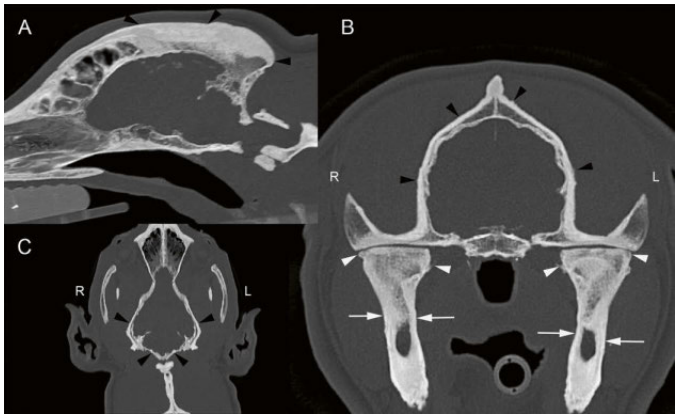

Fig. 5: Multiplanar reconstruction of the CT study of the head in a bone reconstruction; A sagittal, B transverse and C dorsal plane. Secondary to generalized hyperostosis, the calvarium (black arrow heads) and the mandible (white arrows) appeared thick and of increased attenuation with an irregular surface. Periarticular new bone formation (white arrow heads) occurred at both temporomandibular joints due to chronic osteoarthritis.

Fig. 6: Labrador Retriever with acromegaly 1½ years after radiation therapy. Note his markedly improved physical appearance.

progestagens and had no mammary tumors. Therefore, brain imaging by CT was the next step. As CT requires general anesthesia thoracic radiography and echocardiography were performed in order to rule out GH-related cardiomyopathy. Heart and lungs were unremarkable.

The CT study of the head revealed a well-defined, mildly irregular space-occupying lesion (10×16×11 mm; height × width × length) with, in comparison to the brain, a mildly increased attenuation (78.1 +/–18 HU) in the pituitary gland. The lesion underwent moderate, mildly heterogeneous contrast enhancement (98.1 +/–20 HU) after i.v.-injection of iodinated contrast medium. Additional findings of the study included moderate calvarial hyperostosis, enlarged tongue and soft palate, osteoarthritis in the temporomandibular joints and synovial joints of the cervical spine, and obliteration of both external ear canals due to mineralized thickening of the wall of the horizontal parts (Fig. 4 and 5). The diagnosis of acromegaly due to a pituitary space-occupying lesion was made. Treatment options, such as hypophysectomy and radiation therapy were discussed with the owner, who opted for radiation therapy.

Radiation was delivered with a 6MV linear accelerator*** equipped with a Millenium multileaf collimator with 120 leafs. According to the Swiss law and routine procedure in our clinic, our medical physicist dosimetrically verified and approved the treatment plan using an Octavius®-Phantom (PTW Freiburg, Germany). The dog was treated on a Monday-Wednesday-Friday schedule: Dynamic IMRT was delivered using 5 treatment fields (0°, 72°, 144°, 216°, 288°). Accuracy of positioning in daily treatments was ensured with on-board imaging (OBI) and daily orthogonal kilovolt (kV)-images.

During the time of radiation therapy the insulin preparation was changed to insulin detemir (Levemir, Novo Nordisk Pharma AG, Switzerland) at a starting dose of 0.1 U/kg BID and diet was changed to a regular diet for adult dogs.

Twenty-one days after discharge the dog was presented with acute head tilt to the right side. The owner declined any further diagnostics and a trial with prednisolone (1 mg/kg SID per os) was instituted. The head tilt disappeared within 2 weeks and prednisolone was discontinued.

Four months after radiation therapy the dog was presented with sudden blindness. Diabetic cataract was diagnosed in both eyes; after successful phacoemulsification the dog regained vision. During the following year the dog was re-checked by the referring veterinarian and by telephone consultations. Insulin dose was increased stepwise based on blood glucose curves generated by the owner at home. IGF-1 was re-measured and was still high (1354 ng/ml). Approximately 1½ years after initial presentation the dog was re-checked in our hospital. He was in a good clinical condition, bright, alert and had gained weight (BCS 5/9). The initial clinical signs of acromegaly such as large head and tongue, skin folds had improved to a large extent (Fig. 6). His diabetes was well controlled with 0.4 U/kg BID insulin detemir.

Two and a half years after radiation therapy the dog developed lethargy and anorexia. No work-up was performed and the dog was euthanized by the referring veterinarian. Necropsy was not permitted.

Discussion

In difficult-to-control diabetes a systematic work-up is required. As a first step owner-related problems (e.g. wrong syringe size, wrong injection technique) and insulin related problems (e.g. outdated insulin) need to be ruled out. Thereafter, problems with the duration of insulin action (too short, too long) and patient-related problems should be addressed. Any underlying or concurrent disease may render regulation of diabetes diffi-

cult. The referring veterinarian of the dog described here had increased the insulin dose without achieving improvement of glycemic control. After excluding pancreatitis as one of the most frequent concurrent diseases in diabetic dogs he referred the dog for further work-up. When the dog was presented in our hospital technical problems with the insulin application and too short duration of insulin effect seemed unlikely reasons for poor glycemic control. Physical examination, however, revealed striking abnormalities such as large head and tongue, thick skin with folds and widened interdental spaces. Those changes are typically found in acromegaly, however, may also be seen in some dogs with hypothyroidism. The reason why hypothyroidism sometimes mimics acromegaly, at least in part, has recently been elucidated. Primary hypothyroidism in dogs is associated with increased release of GH and IGF-1 concentrations, most likely due to transdifferentiation of TSH-producing cells to cells producing cTSH and GH.[1,13,16] As T4 and cTSH were normal, hypothyroidism was considered unlikely in our dog. It was decided to pursue work-up for acromegaly as a next step and perform any further evaluation for hypothyroidism (free T4 by dialysis, T4 autoantibodies) only if the respective test results would come back normal.

The diagnosis of hypersomatotropism requires the demonstration of GH excess and/or an increased IGF-1 concentration. Measurement of GH is difficult due to the limited availability of a homologous GH assay and the need of special sampling handling (e.g. sending sample on dry ice). Additionally, as GH is secreted in pulses a single high GH concentration may be due to a secretory pulse in a non-acromegalic dog. It is, therefore, necessary to take several blood samples. In our dog baseline GH was measured twice at 15 minutes interval and was markedly increased both times. In theory, performance of the somatostatin suppression test would not have been required, because the results were clear-cut. However, due to the expected delay in GH measurement, samples for baseline levels were taken the same day as the somatostatin test was performed and samples were sent to the lab together. Although some decline of GH was seen after somatostatin application, GH concentrations continued to stay far above the reference interval. In humans the standard diagnostic procedure for acromegaly is to evaluate GH levels during an oral glucose tolerance test. In healthy humans the sudden increase in blood glucose suppresses GH secretion below a defined threshold. In contrast, in humans with acromegaly GH levels remain unchanged, decrease only slightly or show a paradoxical increase.[17] We abstained from the glucose tolerance test because the dog was already severely hyperglycemic. In the only dog with pituitary-dependent acromegaly with extensive endocrine work-up described so far, the somatostatin suppression test as well as the oral glucose tolerance test were performed and results of both were abnormal, however, the dog was not diabetic.[8]

IGF-1 is mainly synthesized in the liver under the control of GH and is considered a valuable surrogate marker for GH. IGF-1 is not secreted in pulses therefore only a single, random blood sample is required. Its structure is conserved across species enabling measurement in assays designed for humans and the serum sample can be sent to the lab by regular mail as the molecule is stable.[21] IGF-1 concentrations in dogs vary with age and breed, therefore no reference intervals are provided by the lab for all possible combinations. Our patient had an IGF-1 concentration only slightly above 1000 ng/ml, which is considered to be the cut-off for acromegaly. However, non-acromegalic dogs usually have IGF-1 concentrations < 600 ng/ml. Taken together, the likelihood that our dog suffered from acromegaly was considered to be high.

In dogs acromegaly is usually caused by endogenous or exogenous progestagens, which give rise to GH hypersecretion from the mammary gland. GH is not only produced in normal (hyperplastic) mammary tissue but also in benign and malignant mammary tumors.[9,18,19,28] Our dog had neither received exogenous progestagens nor did he reveal any mammary masses. Therefore, the most likely source of the GH excess was thought to be the pituitary gland, and the presence of a pituitary mass was indeed confirmed by CT.

In dogs, manifestations of GH excess are quite variable. Some dogs only reveal the typical physical changes of acromegaly, some predominantly show clinical signs of diabetes and others have both categories of symptoms.[21] Part of the variability may be breed-related. For instance in Elkhound dogs, diestrus associated diabetes, but no physical changes of acromegaly have been reported; whereas in German shepherd dogs with acromegalic features only 1/11 had diabetes.[7,9]

Of the only 3 dogs with acromegaly due to a pituitary tumor published so far one had diabetes without physical changes, one had diabetes with physical changes, while the other had physical changes with normal blood glucose concentration. The latter dog revealed glucose intolerance during further testing, but did not become overtly diabetic.[8,29] The dog of the present report had both, overt diabetes mellitus and typical physical changes of acromegaly. Additionally to the clinical signs displayed by our patient, dogs with acromegaly may show inspiratory stridor, prognathia inferior, enlargement of paws, weight gain, thickening of the hair coat with long, curly hair and difficulties to rise or walk due to degenerative arthropathy as well as organomegaly.

Treatment options for a GH-producing pituitary tumor are radiation therapy and neurosurgery. Medical treatment with a new class of somatostatin analogs (pasireotide) has been successfully used in some cats with acromegaly.[10] Experience in dogs is scarce and limited to one dog with acromegaly and diabetes.[31] This dog underwent radiotherapy and was later treated with pasireotide, first with the short-acting preparation, thereafter by long-acting pasireotide with increasing time intervals. Pasireotide resulted in substantial improvement of the physical changes as well as normalization of IGF-1. Although this approach is very promising the extremely high costs of the drug are usually prohibitive.

In people with inoperable or refractory GH-producing tumors stereotactic radiosurgery is known to produce a favorable rate of endocrine remission in >54% of the patients. The median time to remission is 38 months and remains durable in about half of the patients treated.[2,27] The technique of stereotactic radiosurgery uses one single high dose fraction of radiation therapy. As the whole pituitary gland is treated, possible side effects include hypopituitarism in a modest rate of one-forth of patients treated and a low number of cranial neuropathies (4.3%), mostly to the anatomically close optic apparatus.[2,27]

In veterinary medicine, surgical removal of pituitary tumors is technically demanding, surgery is only possible in small tumors and is done in only very few centers worldwide.[20] The owner of our dog was informed about the potential good result of neurosurgery (i.e. transsphenoidal hypophysectomy) but declined this option. Pituitary masses in dogs and cats are commonly treated with radiation therapy. Radiation therapy will reduce the size of the pituitary tumors, relieve and prevent neurologic signs with long-term prognoses of >1400 days (mean), and 1-, 2-, and 3-year estimated survivals of 93, 97 and 55%, respectively.[14,23,25] While large pituitary tumors are often treated with finely-fractionated radiation therapy (10-20 fractions, over 2-4 weeks), several authors have adapted treating small tumors with excessive hormone secretion with few large fractions, making use of the high precision of newer linear accelerators.[14,23,25,26,30] In a few acromegalic cats, partial hormonal responses with subsequent easier management of diabetes mellitus has been observed in the past.[26] A more recent study with 53 cats showed a decrease in required insulin dose in 95% of patients, with 32% achieving diabetic remission but a long median duration to lowest insulin dose of 9.5 months.[30]

Treatment in few large fractions is called stereotactic radiation therapy and requires a high-precision linear accelerator and on-board imaging techniques. As the relative size of a dog brain compared to a human brain is about 1:13, the risk of complication in the surrounding brain structures with stereotactic radiosurgery is higher in pituitary macrotumors of small animals. The choice of fraction size in this dog (3×8Gy) was therefore a compromise with the aim, of possibly reducing the GH-secretion, while at the same time control further tumor growth and limiting the risk of unwanted late radiation side effects.

In this dog, three weeks after radiation therapy neurological signs were noted. Neurolocalization for those signs were considered in the thalamus region and an association with radiation therapy was considered possible. Acute radiation effects after brain tumor irradiation in human patients are rare and are seen after a single dose of >30 Gy or fractionated doses of >60 Gy.[11] The total physical dose applied here was lower but when recalculated into 2 Gy fractions (as commonly applied in human patients) for comparison of different protocols, this equivalent dose in 2 Gy fraction (EQD2) was equal to 60 Gy. Acute radiation effects are usually seen days to weeks after brain tumor irradiation, can be treated with prednisolone and are reversible. However, acute radiation effects in dogs are very rare and a possible cause of head tilt could also be attributed to a geriatric vestibular syndrome, which can also resolve spontaneously. One and a half years after radiation therapy, the IGF-1 concentration was still high. A similar finding has been seen in some cats with acromegaly, in which IGF-1 levels did not normalize after radiation therapy despite improvement in glycemic control.[3] In humans it is known that there is a long latency period to hormonal normalization after radiation therapy.[17] It is therefore possible, that the observation period was just not long enough in our dog. It is likely that although GH decreased which resulted in improvement of acromegalic signs and glycemic control, GH levels (or pulses) were not completely normal and still high enough to stimulate IGF-1 production.[21]

In summary, acromegaly due to a GH-producing pituitary tumor is very rare in dogs, although it is possible that the disease is overlooked or misdiagnosed due to the clinical similarities to hypothyroidism. This case report represents the description of an acromegalic dog due to a GH-producing pituitary tumor with successful therapeutic management and long-term survival.

* BlueBag BodyFix, Elekta AB, Stockholm, Sweden

** EclipseTM treatment planning software, Varian Oncology Systems, Palo Alto, CA, USA

*** Clinac iX, Varian, Palo Alto, CA, USA

Acromégalie cause par une tumeur hypophysaire chez un chien – diagnostic, traitement et suivi à long terme

L'acromégalie due à une tumeur hypophysaire n'a jusqu'à présent été décrite que chez 3 chiens. Le présent rapport de cas décrit un Labrador Retriever de 7 ans mâle castré, qui a été référé en raison d'un diabète difficile à contrôler. L'examen physique a révélé une tête, une langue et des pattes de taille nettement augmentée, des espaces interdentaires élargis et un épaississement de la peau dans la région de la tête et du cou.
L'IGF-1 et la GH étaient augmentées et la seconde restait anormale après l'application de somatostatine. La tomodensitométrie a mis en évidence une masse dans la région de l'hypophyse et le diagnostic d'acromégalie due à une tumeur de l'hypophyse productrice de GH a été posé. Le chien a subi une radiothérapie avec un accélérateur linéaire de 6MV (3×8Gy) et son état s'est considérablement amélioré. Deux ans et demi après la radiothérapie, le chien développa une léthargie et une anorexie et fut euthanasié. L'autopsie n'a pas été autorisée. Ce rapport de cas représente la description d'un chien souffrant d'acromégalie dépendant de l'hypophyse, traité avec succès et ayant une survie à long terme.

Mots clés: acromégalie; tumeur hypophysaire; diabète sucré; chien

Acromegalia a causa di un tumore ipofisario in un cane – diagnosi, terapia e controllo a lungo termine

L'acromegalia a causa di un tumore ipofisario è stata finora descritta solo in 3 cani. Il presente studio descrive un Labrador Retriever maschio castrato di 7 anni che è stato ammesso a causa di un diabete difficile da controllare. L'esame fisico ha rivelato un marcato ingrandimento della testa, della lingua e delle zampe, spazi interdentali più ampi e un ispessimento della pelle nella zona della testa e del collo.
I valori di IGF-1 e GH erano aumentati e il valore di GH è rimasto anormale anche dopo la somministrazione di somatostatina. La tomografia computerizzata ha mostrato una massa nella zona dell'ipofisi ed è stata diagnosticata una acromegalia causata da un tumore che produce GH nell'ipofisi. Il cane è stato sottoposto a radioterapia con un acceleratore lineare 6MV (3×8Gy) e il suo stato è migliorato sostanzialmente. Due anni e mezzo dopo la radioterapia il cane ha sviluppato letargia e anoressia ed è stato sottoposto a eutanasia. La necroscopia non è stata consentita. Questo caso mostra un cane affetto da acromegalia dipendente dall'ipofisi, che è stato trattato con successo e ha avuto una sopravvivenza a lungo termine.

Parole chiave: acromegalia; tumore pituitario; diabete mellito; cane

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