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Dynamic computed tomography of the pituitary gland using a single slice scanner in dogs with pituitary-dependent hypercortisolism

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ABSTRACT

Selective removal of the pituitary adenoma has not been advocated in dogs with pituitary-dependent hypercortisolism because the pituitary adenoma is usually not visualized on routine computed tomography (CT). Dynamic pituitary CT scanning is aimed at the detection of the pituitary flush and, indirectly, at the presence and position of the adenoma. The first aim of this retrospective study was to compare findings of a multiple slice dynamic scanning protocol with those of a single slice dynamic protocol using a single slice CT scanner. The second aim was to compare the CT findings with surgical findings, and surgical findings with histopathological findings. Computed tomography with single and multiple slice dynamic scanning protocols was performed in 86 dogs with pituitary-dependent hypercortisolism. Thirty dogs underwent transsphenoidal hypophysectomy and pituitary specimens were collected as tumor, normal, mixed and neurohypophyseal samples and processed for histology.

The pituitary flush was not detected more frequent in multiple slice dynamic scanning series than in single slice dynamic scanning series. However, in non-enlarged pituitaries, the flush was seen significantly more frequently than in enlarged pituitaries.

Prediction of the nature of the tissue during hypophysectomy by the surgeon was inconclusive.

In conclusion, when using a single slice CT scanner, both single or multiple slice dynamic scanning protocols can be used for localization of the neurohypophyseal flush, and, indirectly, the adenoma. However, based on this study, the aim of surgery in dogs with pituitary-dependent hypercortisolism remains total adenohypophysectomy, and when the neurophypophysis is recognized, it may be left in situ.

1. Introduction

Hypercortisolism is a common endocrinopathy in dogs and is caused by a pituitary corticotroph adenoma in 80% of the cases (Galac et al., 2010). The diagnosis of pituitary-dependent hypercortisolism (PDH or Cushing's disease) is based primarily on clinical signs, biochemistry and endocrinological tests (Kooistra and Galac, 2012), but pituitary imaging using computed tomography (CT) or magnetic resonance imaging (MRI) is important to determine the pituitary dimensions and to confirm the presence of an adenoma (Meij et al., 1997a; Auriemma et al., 2009; Kooistra and Galac, 2012). Pituitary imaging using contrast-enhanced CT is also a prerequisite for hypophysectomy since it enables the determination of the bony surgical landmarks in relation to the pituitary gland (Meij et al., 1997a, 1998). Pituitary imaging with CT allows the distinction between enlarged and non-enlarged pituitary glands (Kooistra et al., 1997). In dogs with pituitary-dependent hypercortisolism and non-enlarged pituitary glands, an isolated microadenoma was rarely directly visible on contrast-enhanced conventional CT (van der Vlugt-Meijer et al., 2003). In healthy dogs, dynamic contrast-enhanced CT allows the visualization of the neurohypophysis due to its early arterial enhancement, called the neurohypophyseal "flush" (van der Vlugt-Meijer et al., 2004). In dogs with pituitary-dependent hypercortisolism, the pituitary flush may be absent, displaced, or distorted, and this is considered indirect proof of a pituitary adenoma affecting the neurohypophyseal integrity (van der Vlugt-Meijer et al., 2003). Dynamic CT scanning of the pituitary gland in dogs with pituitary-dependent hypercortisolism in one slice, called single slice dynamic scanning (SSDS), may indirectly reveal the adenoma when the flush is contained in the slice. However, when the flush is outside the field of the single slice that is scanned, the position of the adenoma cannot be determined. In multiple slice dynamic scanning (MSDS), performed with a single slice helical CT scanner, the complete pituitary gland is scanned during and after maximum contrast

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enhancement. Thus, it is hypothesized that using a single slice CT scanner, the pituitary flush, and indirectly, the adenoma, will be detected more frequently using multiple slice dynamic CT series than with single slice dynamic series.

Hypophysectomy is an effective-long term treatment for pituitary-dependent hypercortisolism in dogs (Meij et al., 2002; Hanson et al., 2005) and the aim has been complete removal of the pituitary gland because of the low correlation between the dynamic CT findings on single slice dynamic CT series and the surgical and/or histological findings (van der Vlugt-Meijer et al., 2003). However, in humans selective adenomectomy is the first choice in Cushing's disease and removal of the microadenoma leaves the normal pituitary gland unaffected (Biller et al., 2008; Juszczak and Grossman, 2013). The question arises therefore whether selective removal of part of the pituitary gland based on results of multiple slice dynamic CT scanning (van der Vlugt-Meijer et al., 2007) is also an option in dogs with pituitary-dependent hypercortisolism. The hypothesis was therefore as follows: the pituitary flush, and indirectly, the adenoma, will be detected more frequently using multiple slice dynamic CT series then with a single slice dynamic series in dogs with confirmed pituitary-dependent hypercortisolism. Results of MSDS may guide the surgeon to a better distinction between normal and neoplastic tissue and therefore would allow for a more selective removal of the adenoma in dogs with PDH.

The aims of the present study using a single slice helical CT scanner were: 1) to compare the findings of multiple slice dynamic CT with those of single slice dynamic CT in a cohort of dogs with pituitary-dependent hypercortisolism, and 2) to compare the CT findings with surgical findings and to compare surgical findings with histopathological findings in a cohort of dogs with pituitary-dependent hypercortisolism that underwent single slice dynamic scanning, multiple slice dynamic scanning and hypophysectomy.

2. Materials and methods

2.1. Animals

Inclusion criteria for this retrospective, descriptive study were dogs diagnosed with pituitary-dependent hypercortisolism, referred to the Department of Clinical Sciences of Companion Animals of Utrecht University between January 2007 and November 2009. These dogs underwent pituitary imaging with CT including a contrast-enhanced spatial scanning series, and a single and multiple dynamic scanning series. A cohort of these dogs subsequently underwent hypophysectomy as primary treatment for PDH. Dogs with concurrent pituitary and adrenal neoplasia were excluded from the study.

2.2. Diagnosis

Diagnosis of PDH was based on the history, clinical signs, and results of hematology, clinical biochemistry, and the high dose dexamethasone suppression test measured by urinary corticoid/creatinine ratios (UCCRs) (Stolp et al., 1983; Rijnberk et al., 1988; Smiley and Peterson, 1993; Galac et al., 1997). In the dogs in which the suppression to dexamethasone was <50%, dexamethasone-resistant pituitary-dependent hypercortisolism was diagnosed by measurement of elevated plasma adrenocorticotropin (ACTH) concentrations (Galac et al., 2010; Feldman, 1983).

2.3. Computed tomography

CT was performed in all the dogs. Following intravenous (IV) premedication with 10–20 μg dexmedetomidine/kg BW (Dexdomitor, Orion Corporation, Espoo, Finland) and 0.1 mg butorphanol/kg BW (Dolorex, Intervet Nederland BV, Boxmeer, The Netherlands), anesthesia was induced by IV administration of 1–2 mg propofol/kg BW (Rapinovet, Mallinckrodt Veterinary, Mundelein, Illinois). The trachea was intubated and inhalation anesthesia was maintained in a semi-closed system with a mixture of isoflurane, air and oxygen. Intravenous fluids (Sterofundin ISO/Ringerfundin; Braun Melsungen AG, Germany) were administered at a rate of 10 ml/kg/h during the procedure.

CT of skull was performed with a single slice helical CT-scanner (Secura CT Scanner, Philips, Best, The Netherlands). With the dog in sternal recumbency, transverse scans of the skull base were made from the rostral clinoid processes to the dorsum sellae, using 0.45 s scanning time with 120 kV, 200 mA and 2-mm-thick consecutive slices. At a position just rostral to the dorsum sellae, a single slice dynamic scanning protocol was performed consisting of 2-mm-thick scans using 0.45 s scanning time with 1 image/s, with 120 kV and 300 mA for 80 s. The single slice dynamic scanning protocol started 10 s following the start of the IV administration of 2 ml iobitridol (Xenetix 350, Guerbet Nederland BV, Gorinchem, The Netherlands, containing 350 mg iodine/ml)/kg BW with an angiographic injector (Medrad Mark V plus, Medrad Europe BV, The Netherlands), with 4 ml/s and a pressure limit of 300 psi, through a 20 or 18 gauge vasofix certo needle (Braun Melsingen AG, Melsungen, Germany), depending on the size of the dog positioned in the antebrachium. Single slice dynamic scanning was followed by a series of scans (2-mm-thick consecutive slices) from the rostral clinoid processes to the dorsum sellae, using 0.45 s scanning time with 120 kV, 200 mA (spatial series). Ten to 12 min following single slice dynamic scanning, a multiple slice dynamic scanning protocol was performed, scanning the whole pituitary gland 8 to 10 times over a length of 13 mm with a collimation of 1 mm, 120 kV, 260 mA, a table feed of 1 mm/rotation (pitch 1), scanning time of 0.45 s, 1 rotation/s, and 11 s delay between the individual scans in this series. Multiple slice dynamic scanning started 10 s following the second IV administration of contrast medium similar to single slice dynamic scanning.

Measurements were made from the display monitor using CT computer software (Philips, Best, The Netherlands) with all images displayed at the same window setting (window width 250, window level + 80). Pituitary dimensions (height and width) were measured from the contrast-enhanced image of the spatial series that contained the largest cross-section of the pituitary gland. On the same image the edges of the brain were traced and the enclosed area was calculated by the computer. The pituitary height (mm)/brain area (mm^2) × 100 (P/B) value was calculated. Pituitaries with P/B value > 0.31 were considered enlarged and those with P/B value ≤ 0.31 were considered not enlarged (Kooistra et al., 1997). The maximum length of the pituitary gland was measured on the midsagittal reconstruction image.

The contrast enhancement pattern of the pituitary gland was assessed visually on the images of the single slice dynamic scanning series and the multiple slice dynamic scanning series by two observers (SDM and GV). The enhancement pattern of the pituitary gland was assessed in the single and in the multiple slice dynamic scanning series with special attention to the detection of the pituitary flush (early and strong enhancement of the neurohypophysis) (van der Vlugt-Meijer et al., 2004). The presence or absence of the flush sign was recorded. When the flush sign was present it was classified as: normal (central), dorsolateral displacement to the right side, dorsolateral displacement to the left side, rostral displacement or caudal displacement.

2.4. Hypophysectomy

To all owners of the dogs included in the study, medical treatment with trilostane and hypophysectomy were presented as the treatments of pituitary-dependent hypercortisolism. For various reasons, like personal preference of the owner and financial willingness, 30 of 86 dogs underwent transsphenoidal hypophysectomy as described previously (Meij et al., 1997a, 1998). All the surgeries were performed by the same boarded surgeon (BPM), using only the transverse contrast-enhanced and sagittal reconstruction CT series before surgery for orientation of the surgical landmarks. From this series, the sizes of the