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Clinical safety of percutaneous ultrasound-guided fine needle aspiration of an adrenal gland lesions in 19 dogs.

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ABSTRACT

Objective: To evaluate the safety of fine needle aspiration of adrenal gland lesions in dogs and to characterise the risks in a subset of patients with cytologically- or histopathologically-diagnosed phaeochromocytoma.

Materials and Methods: Retrospective review of medical records of dogs that underwent percutaneous ultrasound-guided fine needle aspiration of adrenal gland lesions between August 2014 and December 2016. Nineteen dogs were identified, with three undergoing bilateral adrenal gland aspiration and one dog undergoing aspiration twice, yielding 23 cytology samples in total. Data collected included signalment, concurrent medical conditions, current medications, blood pressure and heart rate before adrenal fine needle aspiration, imaging characteristics of the adrenal gland lesions and any clinically apparent procedure-related complications.

Results: Phaeochromocytoma was diagnosed in nine of 19 dogs, including one dog with bilateral phaeochromocytoma. One dog developed ventricular tachycardia following aspiration of an adrenal gland lesion cytologically consistent with a phaeochromocytoma.

Clinical Significance: Percutaneous ultrasound-guided fine needle aspiration of adrenal gland lesions appears to be relatively safe, even in phaeochromocytoma, but further data are required to lend more weight to this finding. Minimally invasive aspirates could be considered as part of the diagnostic algorithm in the investigation of an incidentally-detected adrenal gland lesion of uncertain clinical significance.

Introduction

Adrenal gland nodular or mass lesions (herein these are collectively termed 'lesions') are increasingly recognized in veterinary medicine because of improved diagnostic imaging capability, particularly abdominal ultrasound (Barthez et al. 1997, Cook et al. 2014). There are multiple potential differential diagnoses for an adrenal lesion including primary or metastatic neoplasia, nodular hyperplasia and granulomatous disease (Melian & Peterson 2000, Myers 1997). A nodule <15mm in one pole of an adrenal gland with a normal contralateral gland is usually non-functional and is typically considered benign, but some of these lesions will be early adrenocortical tumours or phaeochromocytomas (Behrend 2015).

The incidental observation of an adrenal gland lesion can cause a diagnostic dilemma for clinicians because not all of them justify extensive diagnostics (Myers 1997). It is estimated that incidental adrenal masses are detected sonographically in 4% of dogs and that prevalence increases with advancing age (Cook et al. 2014). CT detection rates are even higher: 9.3% of dogs in total (Baum 2016). A low proportion of these cases undergo histopathological examination, therefore precluding accurate assessment of the risk of malignancy of these canine 'incidentalomas' (Baum 2016). The typical diagnostic investigation of such lesions includes retinal examination, blood pressure measurement, hematology, biochemistry and urinalysis (Melian & Peterson 2000). If the minimum diagnostic investigation does not suggest an underlying aetiology, justification for further assessment depends on the clinical suspicion that the adrenal gland lesion is of clinical importance - *i.e.* functional or malignant.

Sonographic imaging characteristics of canine adrenal gland lesions used to judge potential malignancy include size, shape (mass-like rather than nodular) and vascular invasion (Besso et al. 1997). The majority of adrenal gland lesions greater than 20mm in thickness and all adrenal gland lesions greater than 40mm in thickness were malignant in one study (Besso et al. 1997). However, cautious interpretation is required given the degree of overlap in appearance between benign and malignant adrenal gland lesions and across different tumour types. Computed tomography (CT) does not perform better

than ultrasound in these aspects (Gregori et al. 2015). Mineralisation is possibly most common in adrenocortical carcinomas but occurs in both benign and malignant adrenocortical lesions, including hyperplasia, and sporadically in phaeochromocytomas (Besso et al. 1997, Yoshida et al. 2016).

Based on the clinical suspicion of a functional primary adrenocortical tumour (fAT) or phaeochromocytoma, endocrinological evaluation may assist in achieving a specific diagnosis in some cases (Melian & Peterson 2000, Salesov et al. 2015). For suspected fAT, the low dose dexamethasone suppression test is the most sensitive (95%) screening test for hyperadrenocorticism but has a relatively low specificity of 44-73% (Behrend 2015). Biochemical assessment for functional phaeochromocytoma is less widely available and samples require special handling. Plasma-free normetanephrine and urinary normetanephrine levels are the most sensitive tests, with the least overlap between dogs with phaeochromocytoma, healthy dogs and dogs with hyperadrenocorticism or non-adrenal illness (Reusch 2015). However, some overlap still occurs and levels of normetanephrine are likely to be lower for smaller tumours, which may reduce the test sensitivity for smaller phaeochromocytomas (Reusch 2015, Salesov et al. 2015; Quante 2010).

Further assessment has traditionally been limited to serial imaging of adrenal gland lesions to monitor for progression, or exploratory surgery for biopsy or adrenalectomy. Adrenalectomy is therapeutic and provides a definitive diagnosis but carries a relatively high risk of morbidity (30-43%) and mortality (12-25%) assessed across four studies (Barrera, 2013, Lang 2011, Massari 2011, Schwartz 2008).

Diagnosis of a fAT or a phaeochromocytoma before adrenalectomy aids in appropriate perioperative management. Treatment with phenoxybenzamine for a median of 20 days before adrenalectomy significantly reduces perioperative mortality from 48% to 13% for phaeochromocytomas (Herrera et al. 2008). For fAT, medical control of hyperadrenocorticism is advised for 3-4 weeks to reverse metabolic derangements and reduce the risks of complications pre-operatively, and management for acute hypocortisolism post-operatively is typically introduced during anaesthesia (Behrend

2015). Therefore, the ability to confirm either of these conditions pre-operatively may aid in appropriate preoperative planning, reduce perioperative mortality and avoid lengthy delays in proceeding to definitive treatment. Overlap in clinical signs and endocrinologic results can make this challenging. Phaeochromocytomas account for approximately 16% of adrenal tumours, while adrenocortical adenomas and carcinomas account for 53% and 22% respectively (Myers 1997).

A recent study demonstrated that cytology is accurate in distinguishing adrenocortical tumors from medullary origin neuroendocrine tumours (presumed phaeochromocytoma) in companion animals with an accuracy rate of 90-100% (Bertazzolo et al. 2014). However, the relatively benign cellular morphology in some adrenocortical carcinomas means that determining malignancy can be challenging by cytology alone (Wills 2014). Typically, a combination of imaging findings, gross surgical assessment and histopathology are required to judge malignancy (Bertazzolo et al. 2014). There are also concerns about performing percutaneous ultrasound-guided fine needle aspiration (FNA) of the adrenal glands in veterinary medicine (Pey & Saunders 2013) based on extrapolated risks from human medicine.

Complications of adrenal FNA reported in humans include inadvertent aspiration of a phaeochromocytoma leading to fatal haemorrhage, hypertensive crisis, or paradoxical hypertensive and hypotensive crises within hours of the procedure (McCorkell & Niles 1985, Casola et al. 1986). Other reported complications include pain, haematoma, delay or difficulty in definitive surgery attributed to the initial biopsy, and a missed initial diagnosis (Vanderveen et al. 2009). More recently, FNA cytology has been encouraged in non-functional, incidentally-discovered, adrenal masses in humans due to malignancy rates of 16-35% in such 'incidentalomas' and a low incidence of complications (5-8%), allowing earlier adrenalectomy in patients with malignancy (Lumachi 2007). If safe, FNA cytology may prove valuable in further classifying adrenal 'incidentalomas' in dogs.

The available veterinary literature regarding FNA cytology of adrenal glands is limited and includes strong recommendations against the procedure due to personal

observations of complications and extrapolation of potential risks from the human experience with phaeochromocytomas (Pey & Saunders 2013). The actual clinical safety of ultrasound-guided percutaneous adrenal aspiration procedures has been reported in only a few cases in veterinary medicine (Bertazzolo et al. 2014, Rosenstein 2000, Spall et al. 2011). Only six deliberate ultrasound-guided adrenal FNA were performed in the study by Bertazzolo et al. (2014) without noted complications. In the Rosenstein (2000) and Spall et al. (2011) studies, four phaeochromocytomas in total were percutaneously aspirated without complication, all being extensive masses not identified as adrenal in origin at the time of sampling. This retrospective case series aims primarily to qualitatively evaluate the clinical safety of percutaneous ultrasound-guided FNA of adrenal gland lesions in a larger series of dogs, and secondarily to assess safety in the subset of patients with a final cytologic or histopathologic diagnosis of phaeochromocytoma.

Materials and Methods

The clinical pathology database at the author's academic institution was searched by the primary author for all dogs that underwent cytological assessment of an adrenal gland lesion between August 2014 (when the database first became searchable), and December 2016. Following this, a search of the hospital medical records database was performed to determine the total number of dogs undergoing abdominal ultrasound in which adrenal nodules or masses were identified during the inclusion period. Exclusion criteria were collection of FNA cytology samples by methods other than percutaneous ultrasound-guidance, adrenal masses for which subsequent FNA did not occur, and administration of phenoxybenzamine before FNA. Use of any other medications, including other antihypertensive medications, were not considered grounds for exclusion as they are considered less likely to mask a clinically-significant hypertensive crisis following aspiration of a phaeochromocytoma.

Information relating to breed, age, sex, body weight, presenting complaint, concurrent diagnoses, medications, adrenal imaging modality and characteristics of the

adrenal gland lesion, use of procedural sedation or general anesthesia, and any medications used during the procedure was extracted from the medical records. When available, histopathological confirmation of the cytological diagnosis was also recorded.

All ultrasound examinations, CT evaluations and percutaneous ultrasound-guided aspirates of the adrenal glands were performed by specialists in diagnostic imaging or a diagnostic imaging resident under specialist supervision. Four ultrasound machines were used during this period[a,b,c,d], transducer type and frequency and the patient positioning, depended on the operator's preference. The method of FNA was not recorded but it is routine to perform abdominal FNA using a 25G x 1.5 inch (38mm) hypodermic needle at our hospital.

The original ultrasound and CT images were retrieved and reviewed by a single author with expertise in diagnostic imaging (AR). The location of the affected adrenal gland/s as well as their size and the presence or absence of vascular invasion and mineralisation were recorded. The size was defined as the maximal dimension of the lesion (Cook et al. 2014). The size of the contralateral adrenal gland was defined as the caudal pole thickness from the longitudinal image plane (Bento et al. 2016). The ultrasound images were used to acquire the imaging characteristics except in dogs that were only imaged using CT.

The clinical records were assessed for any clinically apparent complications including haemorrhage, hypertensive or hypotensive crises, tachycardia, arrhythmias or death that occurred within 12 hours of the aspirate or until the patient was discharged from the hospital, whichever occurred first.

Statistical Analysis

Characteristics of the cases were summarised using simple descriptive statistics. Though planned, inferential statistics were not applied due to the low number of observed adverse events.

Results

Adrenal nodule or mass lesions were reported in a total of 86 dogs that were presented for ultrasound imaging in the study period. The clinical pathology database identified 28 cases of adrenal gland cytology, which was confirmed by review of the hospital medical records database. After review of the cytology reports and medical records, five cytology reports from three dogs were excluded because the FNA cytology samples were acquired surgically. Twenty-three cytologies from 19 dogs, acquired at 20 separate sampling events, met the inclusion criteria. Therefore, 19 of 86 dogs (22.1%) with ultrasound identification of adrenal nodules or masses underwent percutaneous adrenal FNA. The choice as to whether to carry out a FNA of the mass was made by the attending diagnostic imager. One dog underwent percutaneous ultrasound-guided FNA of the adrenal gland twice, performed 10 months apart, with unilateral aspiration at the first assessment and bilateral aspiration at the subsequent assessment. Of the remaining cases, two underwent bilateral adrenal gland aspirates, and 16 underwent unilateral aspiration. Signalment, including breed, and pertinent results for each dog are detailed in Table 1. More males (n=14) were sampled than females (n=6). The median age was 12 years (range 7-16 years). The mean body weight was 13.4kg (range 6.6kg to 35.4kg).

The most common presenting clinical signs were gastrointestinal, including vomiting and diarrhoea (5/19, 26%), followed by collapsing episodes (2/19, 8%) and one case that presented with both gastrointestinal clinical signs and collapse (1/19, 5%). Less common signs (1/19 or 5% each) included change in behaviour, hypertension, retinal detachment, haematuria, abdominal distension, haemoabdomen, respiratory distress, diabetic ketoacidosis, vestibular disease, and referral for further assessment of an adrenal gland mass with unrecorded initial presenting clinical signs.

Concurrent disease processes were common and often multiple, reported in 15 of 19 dogs (78%). Concurrent problems included seizures, hyphaema, non-clinical cardiomyopathy, heart murmur, heart-base mass, compensated congestive heart failure, hyperadrenocorticism, pruritic skin disease, chronic otitis externa, demodicosis, recessed

vulva, idiopathic peripheral vestibular disease, cranial cruciate ligament rupture, luxating patella, diabetes mellitus, multicentric lymphoma, splenic mass, oral malignant neoplasia, and bicavitary effusion.

Multiple dogs (14/19, 73%), were receiving medications at the time of sampling, with 7/19 (37%) receiving multiple medications. These included trilostane (4/19, 21%), maropitant (4/19, 21%), amlodipine (3/19, 15%), insulin (2/19, 10%), buprenorphine (2/19, 10%) and one case each of doxorubicin, benazepril, topical aural medication, methadone, pentosan polysulfate, pantoprazole, amoxicillin-clavulanic acid, furosemide, and butorphanol.

Cardiovascular assessment including blood pressure, was recorded in all but one dog before percutaneous ultrasound-guided FNA. According to the International Renal Interest Society classification (International Renal Interest Society 2016), five dogs were normotensive (systolic blood pressure<150mm Hg), two were borderline hypertensive (systolic blood pressure 150-159mmHg), three were hypertensive (systolic blood pressure 160-179mmHg), and eight were severely hypertensive (systolic blood pressure ≥180mmHg). One dog in the severely hypertensive group had bilateral hypertensive retinopathy, confirming target organ damage. On initial physical examination on the day of FNA procedure, heart rates between 64 and 200 beats per minute were recorded, with a median of 112 bpm (n=18/19).

Four dogs were anaesthetised before aspiration of their adrenal gland lesion with the remaining cases sampled under sedation. For two dogs (one sedated and one anaesthetised), the drugs used were not recorded. The drugs used for sedation in the remaining dogs included butorphanol (Butomidor; Ausrichter), acepromazine (ACP 2; Ceva Animal Health), medetomidine (Domitor; Zoetis) and alfaxalone (Alfaxan; Jurox). Ten cases received a combination of the above medications. For the four cases that were anaesthetised, premedication included methadone (Physeptone; Aspen Pharma) and/or Alfaxalone (Alfaxan; Jurox), induction agents administered included propofol (Provive 1%; Claris) and midazolam (Hypnovel; Roche), and anaesthesia was maintained in all

cases with isoflurane (Isoflurane Inhalation Anesthetic; Pharmachem) or sevoflurane (Sevorane; Abbvie).

Twelve dogs had an abdominal ultrasound performed as their sole adrenal imaging modality. Two dogs had abdominal CT performed followed by ultrasound-guided percutaneous adrenal FNA for sample acquisition and five dogs had both abdominal ultrasound and abdominal CT performed to image the adrenals before sampling. The modality and imaging characteristics of the adrenal gland masses for each dog are presented in Table 1. A range of lesion sizes from 7 mm to 56 mm maximum dimension were sampled.

Cytology was performed on 23 adrenal aspirate samples from 19 dogs. Results were consistent with adrenocortical origin in ten cases, phaeochromocytoma in nine and were non-diagnostic in four. Histopathology was subsequently performed on five adrenal glands from four dogs. Two of the four dogs had previous non-diagnostic cytology results, in one case from both adrenal glands. In the latter case (dog 2; Table 1) the cytologic findings were no adrenal tissue in one sample and extramedullary hematopoiesis in the other. The histopathologic diagnoses were multiple areas of nodular cortical hyperplasia and adrenocortical adenoma. For the other non-diagnostic cytology case (dog 13; Table 1), necrosis, haemorrhage, mineralisation, and histiocytic inflammation was reported on cytology, with a final histopathologic diagnosis of haemangiosarcoma. A third case (dog 1; Table 1) had a histologically confirmed phaeochromocytoma misdiagnosed on cytology as being adrenocortical in origin. The fourth case (dog 9; Table 1) had agreement between cytology and histopathology results on a diagnosis of phaeochromocytoma.

A single case had a complication identified following percutaneous ultrasound-guided aspiration of the adrenal gland (dog 18; Table 1). This dog was referred for further assessment of diabetic ketoacidosis and abdominal pain. Initial physical examination identified tachycardia with a heart rate of 200 beats per minute but was otherwise recorded as unremarkable. Thoracic radiographs, an abdominal ultrasound and limited thoracic and cardiac ultrasound were performed. In addition to hepatic changes

consistent with diabetes mellitus, generalised hyperechoic mesentery, and a small volume peritoneal effusion, a complex heterogeneous mass arising from the cranial aspect of the left adrenal gland (39mm length, 22mm height and 32mm width) was noted, with the right adrenal gland within normal limits (Bento 2016). In the thorax there was an alveolar pattern in the right cranial lung lobe, mild cranial mediastinal lymphadenopathy, a small volume pleural effusion and a small volume pericardial effusion causing cardiac tamponade.

Cardiovascular monitoring after the procedure identified an irregular rhythm with pulse deficits at a rate of 170 bpm on clinical examination. A continuous electrocardiogram (ECG) was performed and identified ventricular tachycardia. A baseline ECG had not been performed before the procedures. The dog's owners subsequently elected euthanasia due to poor prognosis and necropsy was not performed. Cytology of the adrenal gland returned consistent with a phaeochromocytoma. Based on this sole complication identified in 20 separate unilateral or bilateral percutaneous ultrasound-guided adrenal FNA events, the observed complication rate in the current study is 5%.

Discussion

This study identified one complication in twenty ultrasound-guided percutaneous adrenal aspiration events (17 unilateral, three bilateral) in nineteen dogs. The complication noted, ventricular tachycardia, may be unrelated to the procedure and explained adequately by other factors including the pericardial effusion causing cardiac tamponade. The dog was tachycardic prior to sampling, and both sinus tachycardia and ventricular arrhythmia are amongst the most common ECG abnormalities in dogs with pericardial effusion (MacDonald et al. 2009). However, as the tachycardia identified before the procedure was not further characterised by electrocardiography and the ventricular tachycardia identified post-procedure could also have been triggered by aspiration of the phaeochromocytoma, it is appropriate to characterise this as a procedure-related adverse event.

Considering only the cohort with phaeochromocytoma, adverse event incidence was 10%. This observation supports the relative clinical safety of the procedure in this small case series. However, being a retrospective study, we do not know the reasons that clinicians or radiologists chose to collect FNA samples from these dogs, while the majority of adrenal masses (77.9%) were not aspirated. There was a similar range of adrenal lesion size (range 2 mm to 77 mm maximum dimension) and appearances in both populations, but the rationale concerning whether or not to perform FNA was not listed in the majority of medical records. Where a decision not to aspirate was recorded, reasons listed included lack of owner consent and clinical suspicion of hyperadrenocorticism. Therefore, the study cohort cannot be considered a random subset of the population of dogs with adrenal gland masses identified during the study period, and the possible impact of selection bias is unclear.

Considering the still undetermined likelihood of potentially fatal adverse effects of adrenal FNA including extreme alterations in heart rate, blood pressure and severe haemorrhage, the sedation or anaesthesia protocol may be relevant in minimising the risk of performing adrenal aspirates. Some anaesthetists advocate the use of acepromazine in these patients for its vasodilatory effects as well as its myocardial protective effect from catecholamine-induced arrhythmias, although concurrent disease may provide contraindications to acepromazine use (Dyson & Pettifer 1997). A previous study (Brodbelt et al. 2006) looking at all dogs anaesthetised at a referral institution in the UK demonstrated that dogs that received acepromazine were less likely to die under anesthesia than those that did not receive it, providing additional evidence to consider its use in sedation combinations for FNA of adrenal masses. Monitoring for adverse effects is also critical, and dogs should receive continuous ECG monitoring as well as periodic blood pressure monitoring during the aspiration and, ideally, for at least a few hours afterwards. Tachycardia can be effectively treated with a continuous infusion of esmolol where the rate can be adjusted in response to heart rate changes, and severe hypertension can be controlled using a continuous infusion of nitroprusside, again allowing for rate changes as necessary (Lang et al. 2011).

Bertazzolo et al. (2014) report a diagnostic accuracy of 90-100% across multiple cytopathologists of differing clinical experience for discrimination of adrenocortical tumours from phaeochromocytomas. In the current study, only five of the 23 cytologically assessed cases obtained from four dogs had concurrently performed histopathology available, limiting the assessment of the diagnostic accuracy of cytology. Of two cases with diagnostic cytology results, one agreed with histopathology and the other had been incorrectly classified. Of the three non-diagnostic samples from two dogs, one sample had no yield and repeat aspiration may have yielded a result. Extramedullary haematopoiesis in the other adrenal aspirate from this dog can occur in association with myelolipoma or adrenocortical tumours (Choi 2016), and this dog was subsequently diagnosed with an adrenocortical adenoma. This result made phaeochromocytoma unlikely. In the final case, multiple non-specific cytologic findings including haemorrhage were obtained from an adrenal with a final histopathologic diagnosis of haemangiosarcoma. Necrosis was also noted in this sample. Interestingly, in a study looking at metastatic tumors to the adrenal glands in domestic animals, necrosis was the most frequent change associated with adrenal gland metastasis, and metastasis to the adrenal gland has been reported to occur with a variety of types of neoplasia including haemangiosarcoma (Labelle & De Cock 2005).

For the case with discordant cytology and histopathology results, cytology was most consistent with an adrenocortical origin but the cellular morphology was reported to be variable within the sample. The majority of the cells had numerous distinct variably-sized vacuoles often with lacy chromatin and variably distinct nucleoli, more consistent with adrenocortical tissue. However, low numbers of cells had more eosinophilic cytoplasm containing a few fine eosinophilic granules and were suggestive of medullary origin and the final histopathologic diagnosis was phaeochromocytoma. As this is only one instance, it is challenging to draw any meaningful conclusions about the diagnostic value of cytology in adrenal gland assessment but cytology appears to be useful in achieving a non-invasive presumptive diagnosis when performed in conjunction with imaging and functional testing.

Being retrospective, external validity of this study is uncertain, particularly with regard to the potential bias due to the selection of cases which underwent percutaneous ultrasound-guided FNA of the adrenal glands *versus* cases that may not have been sampled based on the perceived risks of aspiration, reducing the observed complication rate. Assessment for complications based on extracted data from the medical records is also likely to underestimate the true rate of complications, particularly if subclinical, but is likely to have identified most or all clinically-relevant complications. Further, larger scale, prospective studies with standardised monitoring of patients for complications pre- and post- aspiration should be performed to corroborate the findings of the current study.

In conclusion, this small study suggests that percutaneous ultrasound- guided FNA of adrenal lesions, where the clinician and radiologist determine it to be feasible and carry low risk, does indeed appear to be relatively safe. These results provide a qualitative estimate of risk that can be used for planning systematic prospective studies of the procedure. Such studies are also likely to provide more information regarding the diagnostic utility of cytology in the investigation of canine adrenal gland lesions and further characterise the potential for malignancy of adrenal 'incidentalomas' in dogs, allowing a more timely surgical intervention where appropriate.

Conflicts of Interest

The authors declare no conflicts of interest.

Footnotes

[a] Siemens X300, Siemens Medical Solutions, California USA

[b] MyLab Twice, Esoate, Italy

[c] Philips CX 50, Philips Ultrasound Bothell WA, USA

[d] Philips Epiq 5, Philips Ultrasound Bothell WA, USA

[e] Computed Tomography: Siemens Emotion 16, Erlangen Germany)

[f] Microsoft Excel 2016

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Table 1 Characteristics of sampled dogs and adrenal gland lesions

Dog	Signalment	Imaging modality	Adrenal gland lesion location and maximum dimension (mm)	Mineralisation	Vascular invasion (vessel)	Contralateral adrenal gland maximal thickness (mm)	Cytological Diagnosis	Observed Complication	Histopathological Diagnosis
1	13yr MN Silky terrier 6.9Kg	CT	Right 38	Yes	No	Left 5.7	Adrenocortical origin	None	Phaeochromocytoma
2	13yr FN Shih Tzu 9.9Kg	US	Right 19 Left 9	Right No Left Yes	No	N/A	Right non-diagnostic[a] Left non-diagnostic[b]	None	Adrenocortical adenoma & nodular hyperplasia[e]
3	11yr FN Corgi 17.0Kg	US	Right 44	No	No	Left 3.9	Adrenocortical origin	None	N/A
4A*	11yr FN Cross breed 11.2Kg	US	Right 17 Left 9	Right No Left No	No	N/A	Right Adrenocortical origin Left not aspirated	None	N/A
4B*	11yr FN Cross breed 11.2Kg	US	Right 24 Left 15	Right No Left No	No	N/A	Right non-diagnostic[c] Left Adrenocortical origin	None	N/A
5	7yr MN Poodle X 27.4Kg	US+CT	Left 21	No	Yes (CVC)	Not identified	Phaeochromocytoma	None	N/A
6	13yr MN Cocker Spaniel 12.7Kg	US	Right 7	No	No	Left 6.8	Adrenocortical origin	None	N/A
7	11yr MN golden doodle 35.4Kg	US+CT	Right 52	Yes	Yes (CVC)	Left 5.4	Adrenocortical origin	None	N/A
8	8yr FN Maltese X 6.6Kg	US	Left 9	No	No	Right 6	Adrenocortical origin	None	N/A
9	8yrMN CKCS 15.6Kg	US+CT	Right 21	No	Yes (CVC)	Left 5.9	Phaeochromocytoma	None	Phaeochromocytoma

10	10yr FN Australian Cattle Dog X 12.9Kg	US	Right 9 Left: 20	No	No	N/A	Right Not aspirated Left Adrenocortical origin	None	N/A
11	13yr MN Pomeranian 9.6Kg	US+CT	Right 32	No	Yes (CVC)	Left 5.2	Phaeochromocytoma	None	N/A
12	14yr MN CKCS 13.2kg	US	Left 25	No	Yes (PA & CVC)	Right 6.9	Phaeochromocytoma	None	N/A
13	8yr MN JRT 10.4Kg	US+CT	Left 39	Yes	No	Right 7.2	Non-diagnostic[d]	None	Haemangiosarcoma
14	15yr MN JRT 8.0Kg	US	Right 24	No	No	Left 5.9	Phaeochromocytoma	None	N/A
15	11yr MN JRT 7.7Kg	US	Right 29 Left 6	Right No Left No	Right Yes (CVC) Left No	N/A	Right: Adrenocortical origin Left: Not aspirated	None	N/A
16	14yr FN Fox Terrier X 8.5Kg	US	Right 29	No	Yes (PA)	Left 8.1	Phaeochromocytoma	None	N/A
17	16yr ME Whippet 13.3Kg	US	Right 56 Left 24	Right No Left No	Right Yes (CVC) Left No	N/A	Right Phaeochromocytoma Left Phaeochromocytoma	None	N/A
18	12yr MN JRT 15.3Kg g	US	Left 39	No	No	Right 7.2	Phaeochromocytoma	Ventricular tachycardia	N/A
19	14yr MN Shih Tzu 13.6Kg	CT	Right 25 Left 47	Right Yes Left Yes	No	N/A	Right: Not aspirated Left Adrenocortical origin	None	N/A

Footnotes:
JRT= Jack Russell Terrier
CKCS= Cavalier King Charles Spaniel
CVC= Caudual Vena Cava
PA= phrenicoabdominal vein
[*] Same dog imaged ten months apart
N/A not applicable
[a] extramedullary haematopoiesis
[b] no adrenal tissue in aspirate
[c] extramedullary haematopoiesis
[d] necrosis with histiocytic inflammation, mineralisation and previous haemorrhage
[e] Unknown if left or right adrenal gland, not reported in necropsy report