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Delayed Contrast-enhanced Computed Tomography for Adrenal Masses in 3 Dogs

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Abstract : Three dogs having adrenal masses detected on ultrasonographic examination were underwent computed tomography (CT) for surgery. After adrenalectomy, each mass was diagnosed pheochromocytoma with myelolipoma, adrenocortical carcinoma and adrenal adenoma through histopathology. Five minutes were used to get delayed enhanced CT images. Attenuation value was measured in each mass and the absolute and relative percentage of enhancement washout were calculated.

Key words **:** adrenal gland mass, delayed CT, canine.

Introduction

Adenomas, carcinomas and pheochromocytomas are most common tumors of adrenal gland. Adenomas, carcinomas, myelolipomas arise from the adrenal cortex while pheochromocytomas, neuroblastomas, ganglioneuromas can be seen in medulla. Tumors of cortex are more common than medulla (5,13,11). As whole-body computed tomography (CT) examinations and evaluation of adrenal glands in ultrasonography become routine procedure, the more adrenal masses are detected.

A protocol for diagnosis and management of adrenal incidentalomas is well organized in human (8). Unenhanced CT Hounsfield units (HU), size, shape and percentage change of attenuation value in delayed enhanced CT can be used to differentiate adrenal adenomas from nonadenomas (9,10,17). Since majority of human adenomas contain large amount of intracellular lipid, they are characterized by lower attenuation value at unenhanced CT compare to nonadenomas. But 30% of adrenal adenomas are lipid-poor types and difficult to differentiate on unenhanced CT. Delayed enhanced CT is useful for differentiating lipid-poor adenomas from nonadenomas. Higher perfusion and increased capillary permeability in nonadenomas contribute to longer enhancement in delayed enhanced CT (16). Lipid-rich adrenal adenomas are not common in dogs as human, so unenhanced CT cannot be used to differentiate between adenomas and nonadenomas (12). Therefore it can be more important to establish system using delayed enhanced CT to differentiate adenomas from nonadenomas in dogs. But there is not enough database evaluating CT attenuation values of adrenal masses in dogs. In present cases, application of delayed enhanced CT on three patients with adrenal masses and characteristics of imaging findings are described.

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Case

Medical records of three dogs with adrenal masses, undergoing CT examination were reviewed at Seoul National University Veterinary Medical Teaching Hospital. After adrenalectomy, all mass samples were histopathologically confirmed.

The CT images were obtained with single slice helical scanner (GE CT/e®, General Electric Medical System, Yokogawa, Japan) at 120 kV, 45 mA, 1-3 mm slice thickness, and a 1.5 pitch. At first, unenhanced CT was performed and dynamic CT, early and delayed enhanced CT were performed in order. For dynamic CT, caudal vena cava (CVC) at the level of affected adrenal gland was targeted. Dynamic CT scans using iohexol (Omnipaque 300®, GE Healthcare, Co. Cork, Ireland) was performed at a dosage of 1 ml/kg (300 mg I/kg) and 3 ml/kg (900 mg I/kg) for contrast-enhanced CT scans, at a rate of 1 ml/sec (dog 2 and 3) or 3 ml/sec (dog 1) via power injector. For delayed enhanced CT, the images were obtained five minutes after injecting contrast media. Shorter delayed time than in human was selected for reducing the risk of anesthesia. For measuring attenuation values, circular region of interest (ROI) was used. It covered the mass in the transverse plane, avoiding the edge of the lesion to prevent partial volume artifact. Also cystic, calcified, necrotic and hemorrhagic regions were excluded. Four measurements were made in each adrenal lesion at each imaging phase and the mean attenuation value was obtained. The absolute percentage and the relative percentage of enhancement washout were calculated (4). SPSS software (IBM SPSS Statistics 22.0, IBM Corp., Armonk, NY, U.S.A) was used for statistical analysis. Mean attenuation values and the washout percentage of each mass were analyzed by Kruskal-Wallis tests.

Case 1 was an eleven year old, neutered male, weighing 6.7 kg, Shih-Tzu with a history of depression, hyperthermia, weight loss, anorexia. Neutrophilia (20960/μl, reference interval: 5200-17000) was noted on a complete blood count, but hyperthermia was not detected. Serum chemistry examina-

Table 1. Abnormal results in serum chemistry of three dogs

	Reference	Dog 1	Dog 2	Dog 3
ALT	6-90 U/l		172	127
AST	10-43 U/l	55		
ALP	8-100 U/l	> 3500	1964	188
γ-GT	0-14 U/l		55	15
Total cholesterol	21-87 mg/dl		439	
BUN	8-30 mg/dl	> 140		
Creatinine	0.5-1.5 mg/dl	2.4		
Glucose	60-120 mg/dl	189		
Total protein	5.0-7.5 g/dl	9.9		
Calcium	9.0-11.8 mg/dl	14.0		
Phosphorous	2.3-5.5 mg/dl	14.3		
Triglyceride	21-87 mg/dl		107	

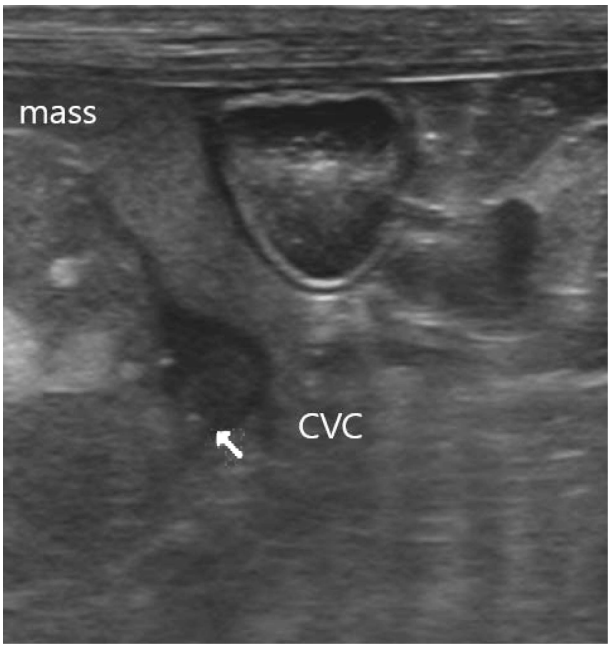

Fig 1. Transverse ultrasonographic image of mass and CVC with echogenic material within the lumen (arrow).

tion showed elevation of ALP, AST, calcium and phosphorous levels and azotemia (Table 1). Slight electrolyte imbalance was noted (decreased sodium, 142 mmol/l, reference range: 145-155). Through ACTH stimulation test, hyperadrenocorticism was detected (post-ACTH cortisol concentration: 47.3 μg/dl, reference range: 6-18).

On ultrasonographic examination, right adrenal mass at cranial pole was found with suspicion of caudal vena cava (CVC) invasion (Fig 1). For surgery, CT scan was performed after correction of azotemia. There was right adrenal gland enlargement (31 × 27 × 29 mm) and an adrenal mass had heterogeneous attenuation with containing hypoattenuation area at center of mass (Fig 2A). The mass compressed CVC, extended 40-50% of lumen with irregular contour and regional filling defect, and the invasion to CVC was suspected (Fig 2B). Hypoattenuation area was relatively large,

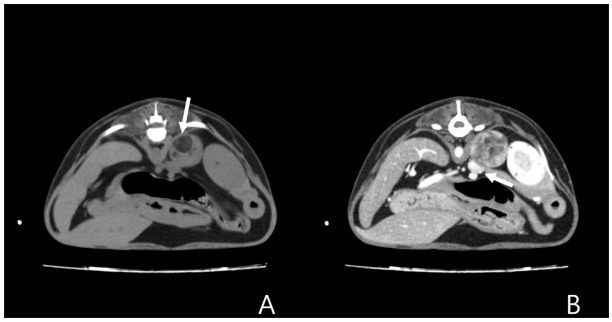

Fig 2. Transverse CT images of dog 1. (A) Mass of right adrenal gland containing hypoattenuated area (arrow). (B) Invasion to CVC suspected in mass (arrow).

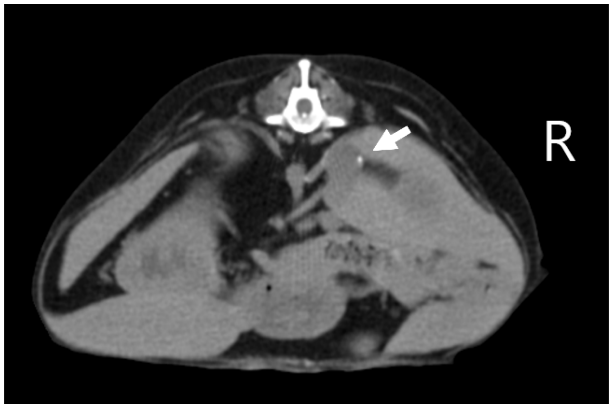

Fig 3. Transverse CT image of dog 2. Mass of right adrenal gland with mineralized area (arrow).

so attenuation values were additionally calculated for this area. Mean attenuation values were 30.1 ± 4.6 (mean ± SD) HU and −71.4 ± 2.6 HU, latter one is for hypoattenuation area. After injection contrast medium, mean attenuation values were 104.4 ± 28.6 HU and −53.0 ± 4.1 HU, ROI placed at same location as unenhanced scans. After five minutes, delayed enhanced CT scans were made and attenuation values were 115.3 ± 7.9 HU and −34.1 ± 1.8 HU.

Right adrenalectomy was performed. There was adhesion with CVC, right kidney, right lateral liver lobe and no invasion in CVC nor any other vessels on gross finding during surgery. Complications such as severe hypertension, tachycardia, arrhythmias and hemorrhage are common in pheochromocytomas patient during the perioperative period (13). In this case there was no sign of severe complication except the oliguria and hypotension temporary after surgery. After stabilization, the patient was discharged. Histopathologically, the mass was confirmed as pheochromocytoma and myelolipoma for hypoattenuation area. After the mass resection, ACTH stimulation test was performed again and there is no evidence of hyperadreocorticism (post-ACTH cortisol concentration on ACTH stimulation test: 15.6 μg/dl). At 28 weeks after adrenalectomy, there was no abnormality of activity level and no clinical sign of adrenal disease.

Case 2 was a seven year old, intact female, weighing 4.6 kg, Shih Tzu with polydipsia, polyuria, elevated liver enzyme levels and abnormal milk secretion. There were elevated liver enzyme levels, total cholesterol and triglyceride on serum

Table 2. Attenuation values of each dog in different phases of CT scans

Patient	unenhanced	early-enhanced	delayed-enhanced
Dog 1 (myelolipoma)[a]	−71.4 ± 2.6	−53.0 ± 4.1	−34.1 ± 1.8
Dog 1 (pheochromocytoma)[a]	30.1 ± 4.6	104.4 ± 28.6	115.3 ± 7.9
Dog 2 (cortical carcinoma)[a]	26.9 ± 2.7	137.0 ± 8.6	90.8 ± 3.3
Dog 3 (cortical adenoma)[a]	31.8 ± 11.2	222.8 ± 25.5	134.1 ± 10.6

[a]mean attenuation values differ significantly between three phases ($P < .05$)

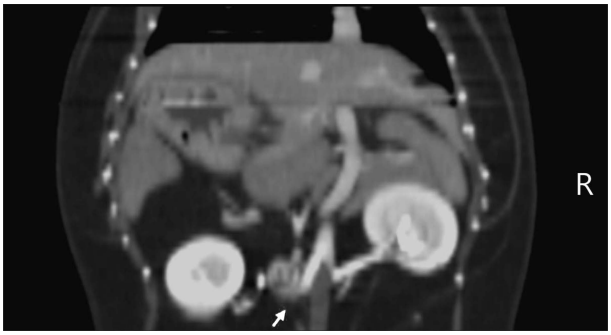

Fig 4. Dorsal CT image of dog 3. The left adrenal gland mass compressing the renal vein with rim enhancement (arrow).

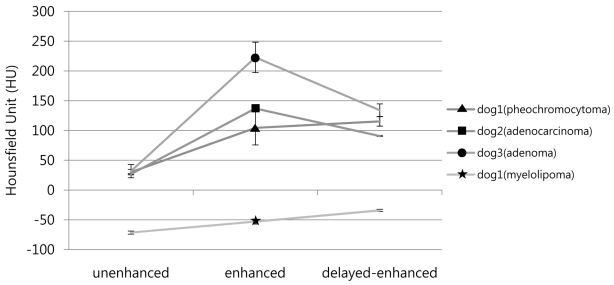

Fig 5. The mean attenuation value at the unenhanced, enhanced and delayed enhanced CT of each mass.

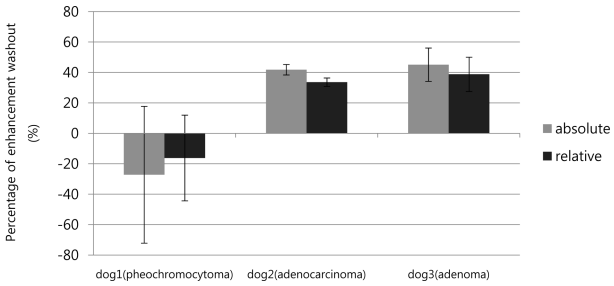

Fig 6. The enhancement washout percentage of pheochromocytoma, adenocarcinoma and adenoma. Gray bar = absolute percentage of enhancement washout, black bar = relative percentage of enhancement washout. Percentages of enhancement washout (absolute and relative) differ significantly between three masses ($P < .05$).

chemistry (Table 1). Inconclusive result in ACTH stimulation test (pre-ACTH cortisol concentration: 8.51 μg/dl, post-ACTH cortisol concentration: 10.8 μg/dl). During control clinical signs and elevated liver enzyme level, mammary gland tumor was noted. Simple mastectomy, ovariohysterectomy and liver biopsy were performed. Histopathologically, liver was diagnosed as severe diffuse vacuolar hepatopathy. After 14 months, increased cranial pole size of right adrenal gland was detected on ultrasonography. The right adrenal gland size increased progressively and adrenocortical tumor-dependent hyperadrenocorticism (ATH) was detected on low-dose dexamethasone suppression test (LDDST, pre: 7.77 μg/dl, 4 hrs post: 9.6 μg/dl, 8 hrs post: 10.6 μg/dl). Pheochromocytoma was ruled out on plasma-free metanephrine and normetanephrine measurement (6). For obtained more precise information about location, invasion, infiltration and metastasis, CT scanning was performed. A round and homogenous mass with mineralization was found at right adrenal gland at 13 × 9.5 mm in transverse diameter and height, respectively (Fig 3). Adhesions to CVC, right lateral and caudate liver lobes were suspected. In unenhanced CT scans, mean attenuation value was 26.9 ± 2.7 HU. After injection, attenuation values were 137.0 ± 8.6 HU and 90.8 ± 3.3 HU at early enhanced and delayed enhanced scans. Right adrenal gland resection and liver biopsy (caudate and left medial lobes) were performed. On histopathology, a mass was diagnosed as cortical carcinoma and liver sample was diagnosed as vacuolar hepatopathy. Adhesion to CVC was noted but no evidence of invasion to any part was detected during surgery. The dog died after 2 days after surgery and necropsy was not performed.

Case 3 was a nine year old, neutered female, weighing 4.6 kg, Pomeranian with a history of left adrenal gland mass detection on ultrasonography by referring veterinarian. There was elevated liver enzyme levels (Table 1). On LDDST, metanephrine and normetanephrine measurement were not remarkable. On CT scans, there was a round homogenous mass of the left adrenal gland. Length, height and width of a mass was 11.2 × 12.3 × 10.4 mm and contacted with left renal vein. The vein was narrowed by the mass and decreased enhancement, but no invasion was noted. The mass was well-margined and had peripheral contrast-enhancing rim on early enhanced CT scans (Fig 4). Attenuation value was 31.8 ± 11.2 HU at unenhanced CT, 222.8 ± 25.5 HU at early enhanced CT, and 134.1 ± 10.6 HU at delayed enhanced CT. This dog underwent adrenalectomy at owner's request. A mass was diagnosed as adrenal cortical adenoma through histopathology. After surgery, this patient was lost to follow-up.

All three dogs showed heterogenous enhancement after injection of contrast medium. The mean attenuation values of each dog on different phases are presented in Table 1 and Fig 5. Dog 1 did not have washout at all, instead showed increasing enhancement and Dog 2 and dog 3 presented similar percentage of washout (Fig 6).

Discussion

The percentage of enhancement washout of pheochromocytoma was consistent with finding in human medicine (14). While differentiation between adenoma and adenocarcinoma is difficult using delayed CT. The percentage of washout of Dog 2 (adenocarcinoma) was high compared to previous report (7). In this paper, delayed enhanced time was two minutes shorter than in presenting cases. Although the result is not significant ($P = 0.09$), this result showed difference between adenoma and carcinoma. So, possibility that five minutes is too long to differentiate adenoma from adrenocortical carcinoma was presented.

The mean unenhanced and enhanced attenuation values in normal dogs were reported respectively as 36.0 ± 5.3 HU, 101.5 ± 10.6 HU for left adrenal gland and 34.3 ± 7.0 HU, 97.4 ± 12.4 HU for right adrenal gland (2). Attenuation values of pheochromocytoma (52.3 ± 5 HU), adenoma (39 ± 8 and 40.8 ± 14.3 HU), adenocarcinoma (36.7 ± 11.8 HU) and myelolipoma (between -56 ± 9 and -34 ± 22 HU) were described in unenhanced phase. Also enhanced attenuation values were described in pheochromocytoma (103 ± 21.7 HU), adenoma (234 ± 20 and 66.7 ± 8.3 HU), adenocarcinoma (83.9 ± 52.7 HU) and myelolipoma (between 11 ± 27 and 26 ± 48 HU) (7, 12). Some consistent with present cases, but others showed much difference. Although p-values are not significant, these results are meaningful from point of view that there is not enough study about attenuation value of adrenal tumor. There are several factors affecting contrast enhancement, such as dose of contrast materials, duration of injection and cardiac function of patient. Longer injection duration results in longer time to arrive peak time and lesser enhancement value (1).

Besides attenuation values, CT can characterize of tumors location, relation with surrounding structures and appearance of malignancy. There is significant association between pheochromocytomas and vascular invasion with high accuracy of CT signs (7,15). In dog 1 (pheochromocytoma), vascular invasion was suspected on CT, however in operation there was no invasion to CVC. False positive can be seen when there is marked compression of the vessels by the mass with disruption the blood flow as this case. And mineralization of adrenal gland like dog 2 (carcinoma) has tendency of carcinomas or adenomas (3).

Conclusion

This report showed no significant difference between adenoma and carcinoma in delayed CT unlike in human but pheochromocytomas were consistent with previous results. However CT is still important modality to provide information on adrenal tumors with location, invasion and malignancy, etc.

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개 부신종양의 지연형 조영증강 전산화단층촬영 적용 3증례

이저순 · 윤정희[1] · 오현정 · 김보은 · 김완희 · 윤화영 · 최민철

서울대학교 수의과대학

요 약 : 복부 초음파 영상검사에서 부신 종괴가 확인된 세 마리의 개에서 지연형 조영증강 전산화단층촬영을 적용한 영상검사가 진행되었다. 조영제 주입 전과 주입 직후, 5분의 지연 시간 후에 CT 검사를 하였으며 위치, 조영 전과 후의 양상, 주변 장기와의 관계, washout 정도를 평가하였다. 세 마리 개 모두에서 부신절제술이 실시되었으며 조직병리검사 결과 골수지방종을 동반한 크롬친화세포종, 부신샘종, 부신암종으로 진단되었다. 부신암종을 가진 한 마리의 개를 제외하고는 수술 후 회복하여 퇴원하였다.

주요어 : 부신 종괴, delayed CT, 개