Canine Pheochromocytoma

Alexandra A. Brown

Mississippi State University College of Veterinary Medicine

Class of 2019

Clinicopathologic Conference

August 24, 2018

Advisors: Jason Syrcle DVM, DACVS-SA

Jon Blakely DVM

COLLEGE *of*
VETERINARY MEDICINE

MISSISSIPPI STATE UNIVERSITY™

Introduction

Pheochromocytoma is a tumor arising from chromaffin cells within the adrenal medulla that secretes excessive amounts catecholamines in a paroxysmal fashion. While pheochromocytomas are a rare neoplasia, cases have been documented in dogs, cats, horses, cattle, laboratory rats, and humans.[1,8] No breed or sex predilections exist. Dogs with pheochromocytomas are generally older with a mean age of 11 years at diagnosis.[6,8]

Clinical signs are often intermittent and vague and have been attributed to high circulating levels of catecholamines as well as tumor invasion into surrounding structures.[6] Metastasis is low with this neoplasm; however, there is a high incidence of invasion into the caudal vena cava.[6,11] Reports exist of invasion into surrounding organs, specifically the kidney.[8] The optimal therapy for pheochromocytoma is adrenalectomy. Medical management should be implemented prior to surgery with phenoxybenzamine, a non-competitive, non-selective, and irreversible alpha-1 adrenergic antagonist, to decrease the potentially life-threatening complications associated with massive catecholamine releases during surgery.[2] Prazosin, a selective and competitive alpha-1 antagonist, may be used as an alternative to phenoxybenzamine.[11] The purpose of this case report is to describe the management of one case of pheochromocytoma in a 13-year-old Cavalier King Charles Spaniel using phenoxybenzamine prior to adrenalectomy.

Case Summary

A 13-year-old, neutered male Cavalier King Charles Spaniel, presented to his primary veterinarian on Monday, December 11, 2017 for a ten-day history of polyuria, polydipsia, and lethargy. Bloodwork and urinalysis revealed hyperglycemia, with a blood glucose of 668 µg/dl, and glucosuria. He was hypertensive at 185 mmHg systolic /105 mmHg diastolic with a mean

arterial pressure of 135 mmHg. Abdominal ultrasound was performed by his primary veterinarian which revealed a large mass associated with the left adrenal gland. At this time, the patient was diagnosed with diabetes mellitus, for which he was prescribed 5 units of Vetsulin via a u-40 syringe twice daily. He was further diagnosed with left adrenal gland mass and referred to MSU-CVM Small Animal Surgery for further diagnostic testing.

Upon presentation to MSU-CVM Small Animal Surgery department on Wednesday, December 13, 2017, the patient was bright, alert, and responsive and weighed 8.3kg with a body condition score of 6/9. He was normothermic with a temperature of 102.0 degrees Fahrenheit, normocardic with a pulse of 120 beats per minute, and a precise respiratory rate was unable to be obtained as he was panting. His hydration status was normal with pink mucous membranes and a capillary refill time of less than two seconds. His lungs auscultated normally with normal bronchovesicular sounds bilaterally. A Grade IV/VI systolic murmur with maximal point of intensity over the mitral valve was auscultated. Mature cataracts were noted bilaterally on ocular examination. The rest of the physical exam was within normal limits. A blood chemistry concluded that the patient was hyperglycemic (388 mg/dl) with no other significant findings. A non-invasive blood pressure determined he was hypertensive with a systolic of 165 mmHg obtained via Doppler. Urine was collected via ultrasound guided cystocentesis; the patient's urinalysis was within normal limits and the sample submitted for culture and sensitivity showed no growth after 48 hours. Thoracic radiographs were obtained and revealed no evidence of nodular pulmonary metastatic neoplasia. Echocardiography revealed mild mitral, tricuspid, and aortic, with trace pulmonic valve insufficiency likely due to valvular degeneration. A consult with a veterinary cardiologist was recommended. The cardiologist's assessment included the following: no pathologic arrhythmias or conduction disorders documented, no evidence of

radiographic cardiomegaly, no signs of congestive heart failure, and echocardiographic findings were compatible with the presence of moderate mitral and mild tricuspid regurgitation secondary to chronic degenerative valve disease in the absence of significant cardiac remodeling or dysfunction. An abdominal CT with contrast was performed. Craniomedial to the left kidney, and surrounding the left phrenicoabdominal vein and artery, a large, ovoid, irregularly marginated, heterogeneous, soft tissue dense mass was seen measuring 4.4 x 3.8 x 4.1 cm. The left kidney was caudally displaced by the mass. The caudal vena cava was mildly displaced to the right and flattened; a thin, linear, smoothly marginated region of mineralization measuring 1.3 cm in length was within the caudal vena cava at the level of the mass. Urine was then collected and sent out for a metanephrine fractionation test. The patient's urine normetanephrine: creatine ratio measured 8194 µg/g, 21.6 times the upper end of the reference interval (380 µg/g). Based on the results from the urine metanephrine fractionation test, it was confirmed that the left adrenal gland mass was a pheochromocytoma. At this time, he was discharged and prescribed two weeks of phenoxybenzamine.

The patient returned to the MSU-CVM Small Animal Surgery department on Wednesday, January 3, 2018 to undergo a left adrenalectomy after a successful two weeks administration of phenoxybenzamine. Upon presentation, his vitals were within normal limits and he was bright, alert, and responsive. His temperature was 100.7 degrees Fahrenheit, pulse was 200 beats per minute, respiratory rate was 44 breaths per minute, and his mucous membranes were pink with a capillary refill time of less than two seconds. A Grade V/VI systolic murmur with maximal point of intensity over the mitral valve was auscultated. Blood was collected for a CBC and neuro chemistry panel and the results are as follows. No abnormalities noted on CBC. Blood chemistry abnormalities, with reference intervals in

parenthesis, included a high glucose of 270 mg/dl (75-125 mg/dl), a high BUN of 37 mg/dl (8-24 mg/dl), a high creatinine of 1.62 mg/dl (0.50-1.40 mg/dl), and a high ALP of 246 U/L (11-140 U/L). Other minimal chemistry abnormalities on the chemistry included a low chloride of 105.2 mmol/L (106.0-122.0 mmol/L), a high ANGAP of 21 mmol/L (10-20 mmol/L), a low ALT of 9 U/L (10-90 U/L), a low total protein of 5.4 g/dl (5.5-8.0 g/dl), a high cholesterol of 366 mg/dl (140-360 mg/dl), and a low magnesium of 1.5 mg/dl (1.7-2.4 mg/dl). The sample condition was determined to have a slight lipemia. A non-invasive blood pressure indicated he was normotensive with a systolic blood pressure of 100 mmHg obtained via Doppler. A coagulation profile determined he was within normal limits for PT and PTT clotting times. The patient was blood typed in preparation for surgery as was DEA 1.1 negative; he was also cross matched with a blood donor and was packed cell compatible.

The patient was taken to surgery the following day; he was placed under anesthesia and positioned in dorsal recumbency. A midline celiotomy incision was made from the xyphoid process to the pubis, curving to the right of the prepuce. Falciform fat was removed with grounded monopolar electrocautery. Moistened laparotomy sponges were placed along the abdominal wall and visualization of the left adrenal gland mass and kidney was facilitated via Balfour retractors and malleable retractors. The left adrenal mass was dark purple in color, irregularly marginated, and was heavily neovascularized and intimately associated with the surrounding structures including the aorta, caudal vena cava, cranial mesenteric artery, and left kidney. Meticulous blunt dissection and hemostasis with ligasure and bipolar cautery was used to free the renal vasculature from the mass and small vessels branching from the mass were ligated with hemoclips. There were moderate amounts of hemorrhage while hemostasis was attempted.

A blood transfusion was started from the previously cross matched donor; a total volume of 180 mls of blood was administered.

Throughout surgery, the patient experienced multiple complications including intermittent episodes of hypertension, hypotension, hypoxia, and hypothermia. He then went into cardiac arrest. Chest compressions were started and epinephrine and atropine were administered in an alternating sequence. After approximately 10 minutes, a normal sinus rhythm was obtained. Rummel tourniquets were placed and tightened around the vena cava, cranial and caudal to the mass, while the invading portion was dissected. A caudal vena cava venotomy was performed with Potts scissors to remove the tumor thrombus. Satinsky clamps were placed and Rummel tourniquets were removed to allow for continuous blood flow through the vena cava while suturing occurred. The venotomy site was closed with no appreciable hemorrhage. The abdomen was lavaged with warm, sterile saline and the incision was closed in a three layer fashion.

The patient remained on a norepinephrine constant rate infusion at 2 mcg/kg/min following removal of his pheochromocytoma to control his marked hypotension. During his anesthetic recovery, his norepinephrine constant rate infusion was slowly decreased to 0.5 mcg/kg/min and then subsequently 0.2 mcg/kg/min while monitoring blood pressures non-invasively. LRS fluids were administered at 4.7 mls/kg/hr and were discontinued in the hours following surgery. A fentanyl constant rate infusion (4 mcg/kg/hr) along with a lidocaine constant rate infusion (30 mcg/kg/min) were used to control post-operative pain. His incision was iced every 6 hours to control inflammation and swelling while also being monitored for any discharge. Enoxaparin (0.8 mg/kg SC q6hr) was used post-operatively to reduce the risk of thromboembolism. he was placed in an oxygen cage to further reduce this risk. Dexmedetomidine (2 mcg/kg/hr via CRI) was administered to help control his cage anxiety.

One day post-operatively, he was continuing to recover well from surgery but remained in an oxygen cage. His norepinephrine constant rate infusion was further decreased to 0.1 mcg/kg/min. As the day progressed, the patient was slowly weaned off norepinephrine as his blood pressure remained normotensive. No pain was elicited upon palpation of his abdomen the morning following surgery and his surgical incision was dry and uninflamed. His fentanyl constant rate infusion was decreased to 3 mcg/kg/hr and his lidocaine constant rate infusion was discontinued. Enoxaparin dosing was reduced to 0.8 mg/kg SC q8hr.

On January 6, 2018 two days post adrenalectomy, the fentanyl CRI was discontinued and he was switched to oral pain medication, Tylenol 4 (acetaminophen with codeine) at 1.7 mg/kg q8hr, to continue to control his post-operative pain. Oral clopidogrel, an anticoagulant, was added at 1.0 mg/kg q24hr. LRS fluids were administered at 1.25 ml/kg/hr and he remained in an oxygen cage. Three days post-operatively, the patient continued to remain comfortable on oral pain management. He was able to oxygenate adequately at room air and was transferred out of the oxygen cage but remained in the intensive care unit for further monitoring.

The patient was discharged and sent home on the morning of January 8, 2018 four days post left adrenalectomy. He was sent home with an additional three days of oral Tylenol 4 (1.7 mg/kg q8hr) as needed for pain and oral clopidogrel (1.0 mg/kg q24hr) for seven days to reduce the risk of thromboembolism. His owners were instructed to keep an E-collar on him at all times and to activity restrict him for the next two weeks. It was emphasized that the patient should remain on medications previously prescribed by his primary veterinarian (vetsulin and benazepril) and that his staples should be removed in 10-14 days. Since removal of his pheochromocytoma approximately eight months ago, the patient has been doing well at home and frequently visits his primary veterinarian to monitor his diabetes mellitus and overall health.

Discussion

Adrenal glands are positioned craniomedially to each kidney and are divided into two main sections, cortex and medulla. The cortex is further divided into three layers. Each layer is responsible for synthetization of different products as follows: zona glomerulosa secretes mineralocorticoids, zona fasciculata secretes glucocorticoids, and zona reticularis secretes sex hormones. The adrenal medulla naturally secretes the catecholamines epinephrine, norepinephrine, and dopamine during times of physiological stress.

Pheochromocytomas are endocrine tumors of neuroectodermal origin.[11] They arise from chromaffin cells within the adrenal medulla and account for 0.01-0.1% of all canine neoplasms.[4,10] They are functional tumors that secrete excessive amounts of catecholamines, specifically norepinephrine and epinephrine. The synthesis of catecholamines is initiated when tyrosine is hydroxylated to dopa. Dopa is then decarboxylated to dopamine at which point it is transported to the intracellular granules of chromaffin cells. Dopamine is hydroxylated to norepinephrine; norepinephrine can then be further converted to epinephrine in some cases. In adrenal glands without tumor present, norepinephrine synthesis suppresses catecholamine production via inhibition of the enzyme tyrosine hydroxylase in a negative feedback loop. Tyrosine hydroxylase is the rate limiting step in catecholamine synthesis. Pheochromocytomas result in a nonfunctional negative feedback loop. This lack of inhibition caused by the tumor leads to excessive catecholamine levels in circulation. It is hypothesized that the lack of negative feedback occurs in pheochromocytomas due to either increased activity of tyrosine hydroxylase or due to the rapid degradation of norepinephrine preventing its accumulation.[6,7]

Catecholamines that exist within circulation interact with two classes of receptors, alpha and beta. These adrenergic receptors are capable of responding to epinephrine and

norepinephrine within target tissues.[6,7] Subtypes of these receptors differ in their response circulating catecholamines. Subtypes α-1, α-2, and β-1 respond equally to norepinephrine and epinephrine; however, subtype β-2 receptors are more responsive to epinephrine.[11] Pheochromocytomas causing an overproduction of catecholamines cause these receptors to be excessively stimulated, resulting in negative, and potentially life threatening, physiological effects. Over stimulation of β-1 receptors can cause significant tachyarrhythmias. Vasoconstriction resulting in increased peripheral vascular resistance and hypertension is due to excessive α-1 receptor stimulation.[11] Clinical abnormalities such as these are frequently reported in patients with pheochromocytomas. Clinical signs may be constant or episodic depending on the pattern of catecholamine release by the tumor.[6]

The metastatic rate of pheochromocytomas are relatively low at a reported rate of less than 25% of cases.[4,11] Sites of metastasis include regional lymph nodes, liver, spleen, kidney, and lungs.[1,4] These tumors are locally expansive and invasion into the caudal vena cava is characteristic. The literature reports that caudal vena cava invasion occurs in 50% of patients with pheochromocytomas and are 7.55-times more likely to result in tumor thrombus when compared to other adrenal tumors.[5,11] Research into the prognostic biomarkers of pheochromocytomas are lacking, thus it is still not possible to predict the tumor's aggressive behavior. Mutations in the succinate dehydrogenase subunit B (SDHB) gene are associated with metastatic behavior in humans with pheochromocytomas; this same mutation has been described in dogs indicating that a common tumorigenic pathway exists.[4] Further research into these genetic mutations could help provide more insight into its pathogenesis and help predict the erratic behavior and metastasis of pheochromocytomas.

The antemortem diagnosis of pheochromocytoma can be difficult for numerous reasons. Clinical signs are usually related to the excessive secretion of catecholamines and are often vague and intermittent due to the episodic and unpredictable nature of the tumor.[4,6] Common clinical signs are due to hyperstimulation of adrenergic receptors and can result in hypertension, lethargy or weakness, tachyarrhythmias, panting, collapse, polyuria and polydipsia, as well as anorexia and weight loss in chronic disease.[2,4,6] Hypertension is the most common single finding in patients with pheochromocytoma and should be suspected in canine patients with systolic pressures greater than 160 mmHg or diastolic pressures greater than 95 mmHg.[6] However, patients with pheochromocytomas may be normotensive at the time of evaluation due to the paroxysmal secretion of catecholamines. Thus, failure to document systemic hypertension does not rule out the disease.[4,6,10]

Abnormalities in routine laboratory tests, such as blood chemistries and complete blood counts, are often nonspecific and unremarkable if present. The most frequent serum biochemical abnormalities include an elevated ALP and ALT along with a slight elevation in blood glucose. Severe hyperglycemia is not reported with pheochromocytomas unless concurrent diabetes mellitus is present. Urinalysis may show a decreased urine specific gravity due to associated polyuria and polydipsia.[6,10] Additional abnormalities observed likely reflect comorbidities as approximately 50% of dogs with pheochromocytoma have concurrent neoplasia.[4]

Several diagnostic imaging techniques have proved useful for visualization of pheochromocytomas. Diagnostic imaging often reveals the presence of an adrenal mass during investigation of a concurrent and more apparent disease. Abdominal radiography has the lowest sensitivity, revealing a mass in 26-56% of cases of canine pheochromocytomas.[6] Only 10% of pheochromocytomas are reported to have mineralization, which can aid in radiographic

visualization of these masses when present.[2] Abdominal ultrasonography is often superior to radiography as adrenal masses are detected in 50-83% of canine patients with pheochromocytomas.[6] Advantages of ultrasonography over radiography include greater resolution of the adrenal gland, better visualization of small masses, as well as assessment of adjacent structures for evidence of tumor invasion.[8] Other imaging modalities including abdominal computed tomography (CT) and magnetic resonance imaging are the most sensitive methods for detection of pheochromocytomas. CT is considered the gold standard of diagnostic imaging and has an accuracy of up to 95% in detection of adrenal masses one centimeter in diameter.[6] The use of an intravenous contrast in combination with CT can help assess the size and shape of the tumor and detect vascular invasion. The sensitivity of this technique is reported at 92% with a specificity of 89-100% and is warranted prior to surgery.[2] In human medicine, metaiodobenzylguanidine (MIBG), a contrast product that has a molecular structure similar to norepinephrine, is used to detect pheochromocytomas. MIBG is taken up via catecholamine storage vesicles which are localized within tumor tissue; thus, pheochromocytomas are expected to have an increased uptake of MIBG on scintigraphy.[2,4,6] This detection method has been used in two dogs to diagnose pheochromocytoma; however, its primary use is still within human medicine.[4]

Definitive diagnosis of pheochromocytoma is via a urine metanephrine fractionation test.[9] As epinephrine and norepinephrine are secreted from the adrenal medulla into circulation, they are metabolized to metanephrine and normetanephrine, respectively, by O-methyltransferase.[5] In humans, studies have shown that pheochromocytoma tissue contains higher levels of O-methyltransferase which in turn leads to higher levels of metanephrine and normetanephrine within the tumor tissue. Production of these tumor metabolites is independent

of circulating epinephrine and norepinephrine levels.[5] Thus, measurement of metanephrine and normetanephrine levels in urine or plasma is a more accurate biochemical test in the diagnosis of pheochromocytomas.[5,9] Dogs with pheochromocytomas have significantly higher urine normetanephrine and metanephrine to creatinine ratios in comparison to dogs without pheochromocytomas. Urine normetanephrine to creatinine is considered the best variable in differentiating pheochromocytomas from other adrenal tumors and disorders in dogs. Canine and human pheochromocytomas predominantly secrete more norepinephrine than epinephrine; however, some pheochromocytomas primarily secrete epinephrine. Studies have shown that a value of four times the upper limit of normal is diagnostic of pheochromocytoma with a probability of 100%.[9]

Cytology of pheochromocytomas is not typically recommend, as fine needle aspirate of the mass could potentially result in a massive catecholamine release. Complications of performing such aspirates include severe hypertensive crisis, tachyarrhythmias, and uncontrolled hemorrhage, all of which could result in death if not controlled. Histologically, pheochromocytomas are characterized by neoplastic cells that are polygonal, contain basophilic cytoplasm, and possess small, rounded nuclei. These cells are commonly arranged in nests or packets which are surrounded by a fibrovascular stromal network.[1,4] No histological features of a pheochromocytoma have been associated with predicting metastatic behavior.[4]

Pheochromocytoma tumors are staged following the TNM classification according to the World Health Organization. Stage T0 is defined as a tumor that is not visible macroscopically and T1 is assigned when the tumor is visible macroscopically but confined within the adrenal gland. When local invasion of adjacent structures, excluding vascular invasion, occurs, stage T2 is assigned. T3 indicates vascular invasion.[1]

Once a diagnosis of pheochromocytoma is achieved, patients should be medically managed with phenoxybenzamine for a minimum of two weeks prior to adrenalectomy. The goal of preoperative medical management is to control the hypertension associated with excessive catecholamine release by the tumor as well as allow for expansion of plasma volume by correcting the chronic vasoconstriction.[2,6] Phenoxybenzamine is a non-competitive, non-selective, irreversible alpha-1 adrenergic antagonist that can decrease the potentially life-threatening complications associated with massive catecholamine releases during surgery.[2] The recommended dose is 0.2-1.5 mg/kg twice daily. During phenoxybenzamine administration, the patient should be monitored for consequent hypotensive episodes as the tumor may secrete catecholamines episodically. It is advised that the initial dose for dogs is 0.25 mg/kg with a gradual increase until the patient is normotensive.[6] Prazosin, a selective and competitive alpha-1 antagonist, may be used as an alternative to phenoxybenzamine at dose of 0.5-2.0 mg/kg q8hr prior to surgery.[11] Treatment with phenoxybenzamine prior to tumor removal has been proven to decrease the number and severity of hypertensive episodes, ultimately lowering mortality rates.[2,6]

Adrenalectomy, the removal of one or both adrenal glands, is the treatment of choice for pheochromocytomas. Anesthesia should be carefully planned as life threatening catecholamine-induced complications can occur during induction, intubation, and surgical manipulation of the tumor.[2] Blood typing and a cross match should be performed prior to surgery in the event a transfusion is required as uncontrolled hemorrhage is an intraoperative complication due to the vascular nature of pheochromocytomas.[2] The most common intraoperative complication is hypertension. Hypertensive episodes can be controlled with a rapid-acting alpha-adrenergic blocker called phentolamine (0.02 to 0.1 mg/kg IV as needed) or with sodium nitroprusside (1-10 mcg/kg/min via constant rate infusion), a nitrate vasodilator.[6] Propranolol (0.02-0.1 mg/kg IV), a

β-blocker, can be used to manage cardiac arrhythmias and tachycardia associated with excessive secretion of catecholamines.[6,11] Close anesthetic patient monitoring is key to a successful surgical outcome; it is recommended than an intraarterial catheter be placed, to allow for direct blood pressure measurement, and cardiac rhythm be monitored via an electrocardiogram throughout the procedure.[6]

Surgical approach should be based of knowledge obtained via CT including tumor size as well as if vascular invasion is present as these are the most important criteria in choosing an approach.[4] Adrenalectomy can be performed via a ventral midline celiotomy, paralumbar incision, or through laparoscopic approach.[3,11]. A ventral midline celiotomy is recommended when the pheochromocytoma has invaded into the caudal vena cava and if an abdominal exploratory is warranted. The paralumbar approach allows for direct access to the adrenal gland; however, this approach does not allow for complete access into the abdominal cavity and should not be used if an abdominal exploratory is necessary.[3,11] Laparoscopic adrenalectomy reduces surgical time and has shown to result in a more rapid recovery in comparison to an open laparotomy. Laparoscopic adrenalectomy is contraindicated in masses greater than 5 cm in diameter and when vascular invasion into the caudal vena cava is present.[3,4] Independent of the approach, the adrenal gland should be located via the phrenicoabdominal vein which should be subsequently isolated and ligated, unless a tumor thrombus is present. The adrenal gland is then sharply and bluntly dissected from the surrounding tissue with meticulous hemostasis via hemostatic clips or electrocautery.[3,11] Extraction of a tumor thrombus may be required as caudal vena cava invasion occurs in 50% of patients with pheochromocytomas.[5,11] Cavotomy is performed by placing Rummel tourniquets cranial to the renal veins and caudal to the liver.[11]

While tumor thrombus is not directly associated with survival rates, vascular invasion extending beyond the hepatic hilus is associated with higher post-operative mortality rates.[4]

Once the pheochromocytoma is removed, subsequent hypotension due to the decrease in vascular tone may occur. If severe, treatment with norepinephrine (1-2 mcg/kg/min IV as constant rate infusion) may be warranted. Norepinephrine stimulates alpha-1 and beta-1 receptors causing vasoconstriction and cardiac stimulation. Blood pressure should normalize within 24-48 hours following removal of the entire tumor. The most common post-operative complication is pulmonary thromboembolism. Heparin therapy, aspirin, clopidogrel, or other anticoagulant options can be used to prevent thrombus formation in combination with cage rest and oxygen therapy.[11]

The prognosis for dogs with pheochromocytoma remains poor to guarded; however, when complete tumor resection is achieved, long-term survival can be expected with a median survival time of 15 months.[1,11] If surgery is non-emergent, and patients have been appropriately pretreated with phenoxybenzamine, mortality rates of 6-15% have been reported. Positive prognostic factors include: complete tumor resection, absence of metastatic disease, tumor size (<3 cm), absence of comorbidities, pretreatment with phenoxybenzamine, and no or limited invasion into adjacent organs.[2] While adrenalectomy is the only method to reverse the clinical signs and symptoms associated with excessive catecholamine release by the tumor, constant administration of phenoxybenzamine may be used as medical treatment alone when surgery is not an option.[2,4]

Conclusion

This case report describes the diagnosis, medical management, and surgical treatment of a 13-year-old, neutered male Cavalier King Charles Spaniel diagnosed with pheochromocytoma.

While clinical signs may be intermittent and vague, hypertension is a common clinical finding if observed. Multiple imaging modalities exist to identify adrenal masses; however, computed tomography remains the gold standard as it provides information regarding the tumor's size, shape, and the extent of vascular invasion. Definitive diagnosis of pheochromocytoma is via a urine metanephrine fractionation test. Treatment of choice includes adrenalectomy following a two-week administration of phenoxybenzamine to minimize the potentially life-threatening complications associated with massive catecholamine releases during surgery. Provided the patient survives surgery and complete tumor resection is achieved, a median survival time of 1-2 years can be expected.

References

1. Barthez PY, Marks SL, Woo J, et al. "Pheochromocytoma in Dogs: 61 Cases (1984-1995)." *Journal of Veterinary Internal Medicine.* 1997; 11(5):272-278.
2. Desmas I, et al. "Canine pheochromocytoma." *Veterinary Ireland Journal.* 7(5):268-271.
3. Fossum TW. Surgery of the Endocrine System. In: Small Animal Surgery 4th ed. St. Louis: Elsevier Mosby, 2013: 633-646.
4. Galac S, Korpershoek E. "Pheochromocytomas and paragangliomas in humans and dogs." *Veterinary and Comparative Oncology*. 2017; 15(4):1158-1170.
5. Gostelow R, Bridger N, Syme HM. "Plasma-Free Metanephrine and Free Normetanephrine Measurement for the Diagnosis of Pheochromocytoma in Dogs." *Journal of Veterinary Internal Medicine.* 2013; 27:83-90.
6. Locke-Bohannon LG, Mauldin GE. "Canine Pheochromocytoma: Diagnosis and Management." *Compendium on Continuing Education for the Practicing Veterinarian.* 2015; 23(9):807-815
7. Maher ER. "Pheochromocytoma in the dog and cat: Diagnosis and management." *Seminar of Veterinary Medicine and Surgery.* 1994; 9(3):158-166
8. Rosenstein DS. "Diagnostic Imaging in Canine Pheochromocytoma." *Veterinary Radiology and Ultrasound.* 2000; 41(6):499-506.
9. Salesov E, Boretti FS, Sieber-Ruckstuhl NS, et al. "Urinary and Plasma Catecholamines and Metanephrines in Dogs with Pheochromocytoma, Hypercortisolism, Nonadrenal Disease and in Healthy Dogs." *Journal of Veterinary Internal Medicine.* 2015; 5(29):597-602.
10. Santamarina G, Espino L, Vila, M, et al. "Aortic Thromboembolism and Retroperitoneal Hemorrhage Associated with Pheochromocytoma in a Dog." *Journal of Veterinary Internal Medicine.* 2003; 17:917-922.
11. Veterinary Society of Surgical Oncology website. Adrenal Pheochromocytoma. Available at: www.vsso.org/index.php/education-new/cancer-information-new/cancer-in-dogs-by-tumor-type-new/9-education/286-adrenal-pheochromocytoma. Accessed June 16, 2018.