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Surgical Management of a Pheochromocytoma with Caval Invasion

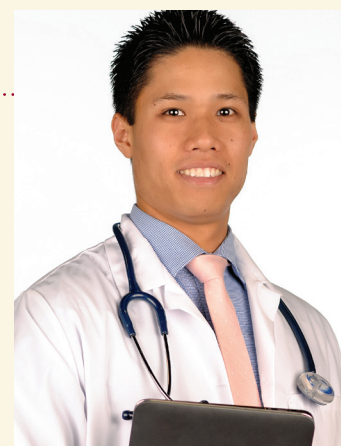
Jed Sung, DVM, Staff Surgeon

Case report:

An eight year old neutered male Wire Fox Terrier was originally presented to the local veterinarian for a two month history of polyuria and polydipsia. At the time of the examination, bloodwork did not yield significant findings, however, the patient was noted to be persistently hypertensive with measured systolic pressure ranging from 210-270mmHg. An angiotensin converting enzyme inhibitor, followed by a calcium channel blocker, was instituted but were unable to significantly improve systemic hypertension. Bicavitary ultrasonography was eventually performed which indicated the presence of a large left adrenal mass (2 x 3.5cm) that was invading

Generally speaking, the larger an adrenal mass, the more likely it is malignant.

the vena cava and causing it to be distended. He was referred to a specialty hospital in the metropolitan area for a surgical and internal medicine consult. A urine normetanephrine/metanephrine panel was submitted, which was supportive of a pheochromocytoma. At the owner's request, a CT scan was performed which confirmed the presence of a left adrenal mass and indicated that caval invasion extended 10cm cranially within the caudal vena cava. The owners elected to present to the surgery department at LIVS for a second opinion.



Background:

The adrenal glands are located in the retroperitoneal space just cranial to their respective kidneys. Intraoperatively, the glands can be identified by their beige appearance and the presence of the phrenicoabdominal vein that crosses ventral to them. Arterial blood supply consists of multiple small branches from the aorta, phrenicoabdominal, renal and abdominal arteries. Venous blood drains into a single adrenal vein which empties directly into either the vena cava (right adrenal) or renal vein (left adrenal).

The adrenal gland is divided into the cortex and medulla. The cortex is further divided into three zones: glomerulosa, fasciculata, and reticularis. These zones secrete mineralocorticoids, glucocorticoids, and sex steroids, respectively. These steroid hormones are lipids and are transported in the plasma by either transcortin, albumen, or are unbound. The mineralocorticoid aldosterone is responsible

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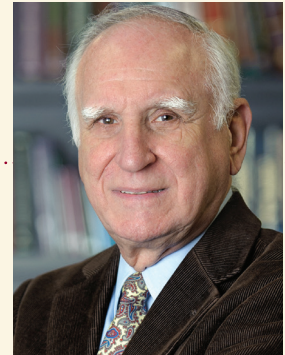
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A Note from the Editor



The events of this November, especially our elections have set our country on a new, hopefully positive path. Lots will change, it's been promised, and we look forward to a bright future with new ideas on how to deal with those who hold concepts different from our own while maintaining civility and our status in the world as a leader for peace and stability.

Major achievements have been made by drug companies and three or more vaccines, extraordinarily effective, are to be released under the "Warp Speed" program, rescuing us from COVID-19, which has changed life in some ways for all of us. "Eating out" now really means eating outside as social distancing rules are followed in restaurants, houses of worship, stores, LIVS and wherever people contact one another.

Hugging, no, being replaced by fist pumping but at least we can hug our pets! A few cases of feline infection

and suspected mink reservoirs have been discovered but none of that has been a cause of human spread.

The protocol for cases brought to LIVS has kept our facility from being adversely affected by the virus and the renovations are continuing as a brisk pace. The front parking area will be paved and will be functioning for patient use shortly.

Once again we are into a mild winter on Long Island so far, while fires and tornados have been hitting the southern and western states. Unfortunately, we can expect some inadvertent ingestion of food and treat leftovers which will adversely affect our pets; chocolate being the most common but grapes and the xylitol found in sugarfree gum are toxic. Tinsel, lilies, mistletoe and holly can be seriously harmful especially to cats. LIVS is always open for any eventual needs.

Preparations for the coming holiday season are visible all over and our pets will feel the freezing ground on their paws. We need be aware that pavement deicers contain chemicals that need to be washed off on returning home after being outside. Pets kept outside need a heated dog house with a mattress to lie on and a bucket of water that is kept warmed to a few degrees above freezing.

I recently came across an article about mysterious dogs, deep in the Amazon rainforest, with short ears, pointy noses, and bushy tails that roam the undergrowth. Officially, they're



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A Note from the Editor

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called short-eared dogs, but they're so elusive that they're often referred to by the much cooler moniker of "ghost dogs." As scientists have attempted to better understand these elusive creatures, one of the most significant findings about them has been about the size of their gonads—seriously.

Veterinarian Renata Leite Pitman, an affiliated scholar at Duke University, has devoted years of her life to studying ghost dogs which hunt solo or in groups of two or three rather than in large packs.

One of the first things she noticed when she saw a short-eared dog in person was, weirdly, how small its testicles were. Bizarrely, that fact would turn out to be important for her research.

Around the time they turn three, previously undescended testicles "drop"—weird, but a key piece of information, suggesting that a major reason that the dogs are so rarely spotted is that they don't reach sexual maturity until they're three years old, which is really late for canines. Most dogs can reproduce at just one year of age. This puts ghost dogs at a huge disadvantage for survival because many of them die before they are old enough to reproduce.

Dr. Leite Pitman has continued to study the rare species and she thinks there are fewer than 15,000 of them left. In addition to the challenges they face due to reaching sexual maturity at a relatively late age, the animals are also put at risk by hunters'

domestic dogs, which can spread deadly viruses the ghost dogs have no natural defenses against. Sounds like something we humans are experiencing too!

In the future, they'll face even more danger as 30% of the area they inhabit is threatened by Amazon deforestation for farming, logging, and mining. Further ecosystem destruction and fragmentation could lead ghost dogs to extinction. Since they're still not widely studied or understood, it's hard to know what effect their extinction could have on other species in their ecosystems. To protect these good canines, we need to protect the Amazon. That might give the ghost dogs a chance so they don't become extinct, becoming actual ghosts that haunt the forest.

— And so we wish everyone a peaceful holiday season and hope that all share with loved ones, even while socially distancing, the promises of life and a much brighter 2021.

We are pleased to continue the extended hours for consultation in all our departments to serve our clients more efficiently. Appointments can be made through our telephone receptionists at 516-501-1700.

Again, we welcome your observations e-mailed to lmario@livs.org

Leonard J. Marino, MD, FAAP, LVT



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for blood pressure and electrolyte regulation. Decreased renal blood flow activates the renin-angiotensin-aldosterone system and leads to stimulation of peripheral vasoconstriction as well as the secretion of aldosterone. Aldosterone promotes sodium, chloride, and water retention and potassium excretion. Glucocorticoids have a myriad of systemic effects that include gluconeogenesis, protein catabolism, peripheral glucose uptake, vasopressin inhibition and suppression of inflammation and the immune system. Androgens and estrogens are synthesized by the adrenal glands but typically only a small amount. The adrenal medulla contains chromaffin cells that produce catecholamines in response to stress. Catecholamines produce systemic sympathetic effects through α and β adrenergic receptors.

Diagnostics:

Adrenal masses are typically identified during an abdominal ultrasound exam or advanced imaging such as computed tomography, magnetic resonance imaging, or nuclear scintigraphy. Some adrenal masses are considered incidentalomas since they were an unexpected discovery. Once an adrenal mass is identified, it is important to determine the significance of the finding since it will dictate the appropriate therapy. Surgical management is indicated for adrenal masses that are malignant, hormonally-active or hemorrhaging. Surgery may not be indicated for small or benign masses. Since the nature of an adrenal mass can only be identified after histopathologic evaluation, there are certain guidelines and additional diagnostics that may be helpful to the clinician.

From an imaging standpoint, an adrenal gland that exceed 1.5cm in width, loses its kidney bean shape, and is asymmetric in shape and size compared to the contralateral gland should be regarded as an adrenal mass. Generally speaking, the larger an adrenal mass, the more likely it is malignant. Invasion into the surrounding vasculature or organs as well as the presence of other masses within a patient are highly suggestive of malignancy. Patients with non-cortisol secreting adrenal tumors such as a pheochromocytoma tend to have a normal contralateral adrenal gland.

A low-dose dexamethasone suppression test can be helpful in determining the location of an adrenal mass. Cortisol is regulated by a negative feedback loop between the pituitary and adrenal glands. In many patients with pituitary-dependent hyperadrenocorticism (Cushing disease), the administration of dexamethasone can suppress cortisol levels. In a patient that has an adrenal mass with clinical signs of hyperadrenocorticism, suppression of cortisol levels after administration of dexamethasone is strongly suggestive of a non-cortisol secreting adrenal tumor (eg. pheochromocytoma). In a patient with a cortisol secreting tumor, administration of dexamethasone will most likely not suppress cortisol levels.

While there are no routine urine or blood tests that confirm the diagnosis of a pheochromocytoma, significantly higher urinary normetanephrine and metanephrine/ creatinine ratios are supportive of a pheochromocytoma. Additionally, persistent hypertension secondary to sympathetic stimulation can be suggestive of a pheochromocytoma.

Pre-operative and peri-operative considerations:

Patient with cortisol secreting tumors are at a higher risk of immunosuppression, impaired wound healing, systemic hypertension, coagulopathy and thromboembolic events. Some patients are pre-treated for 3-4 weeks prior to surgery to minimize some of these risks. Some surgeons will also initiate anticoagulant therapy (heparinized plasma) immediately post-operatively to reduce the risk of pulmonary throm-

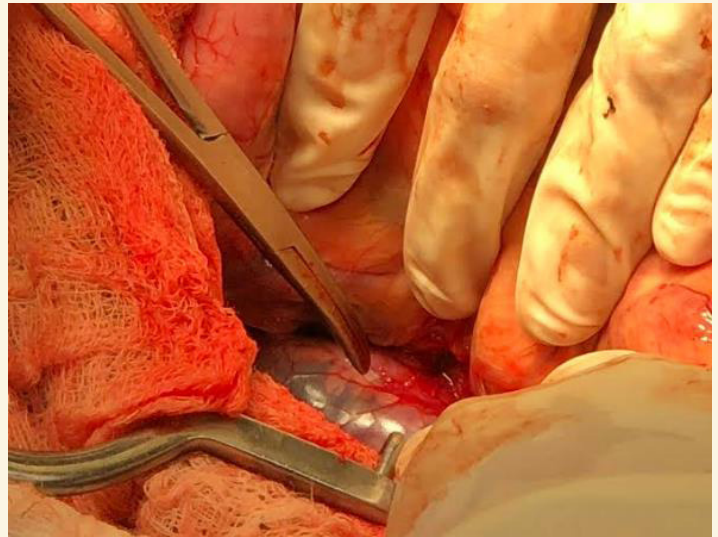


Figure 1. Visualization of the distended caudal vena cava (pointed to by the curved hemostat) and tumor thrombus



Figure 2. The left adrenal tumor (black arrow) and caudal vena cava (white arrow)

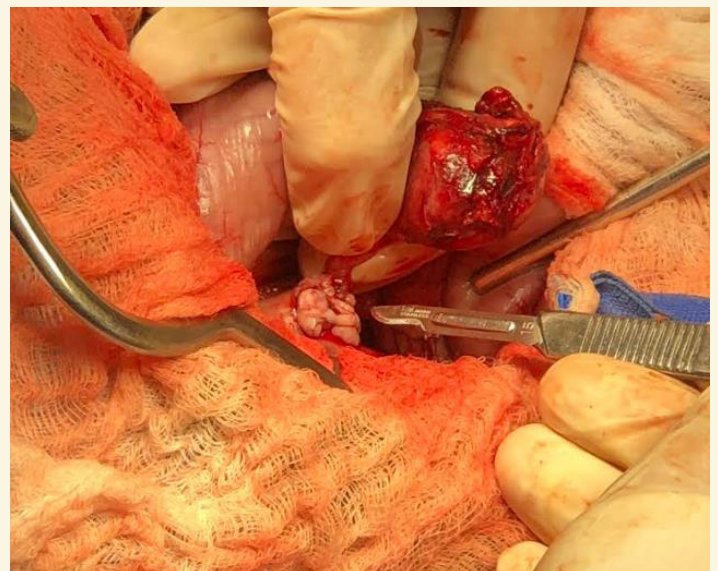
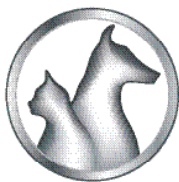


Figure 3. Caudal vena cavotomy (venotomy) with the emergence of the tumor thrombus

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boembolism. To prevent acute hypocortisolism, glucocorticoid supplementation is initiated post-operatively and continued at a physiologic level for several months until the contralateral adrenal gland has compensated. For patients with severe or persistent hyponatremia and hyperkalemia, deoxycorticosterone pivalate is recommended.

For patients with a suspected pheochromocytoma, the excess catecholamine causes generalized vasoconstriction and are at a higher risk of intraoperative hypertension, arrhythmia, and cardiac arrest. Phenoxybenzamine is an α -adrenergic receptor blocker and is generally instituted 2-3 weeks prior to surgery. This has been shown to significantly improve mortality rate (13% vs 48% without phenoxybenzamine).

Surgery:

There are multiple approaches for an uncomplicated adrenalectomy. The most common one is the ventral midline approach but flank and laparoscopic approaches can be performed as well. Due to the significant caval invasion of this presenting patient, a ventral midline approach was elected. During the abdominal exploratory part of the procedure, the caudal vena cava was noted to be significantly distended and the tumor thrombus could be directly visualized through the caval wall. The left adrenal gland was significantly enlarged, contained multiple dilated tortuous vessels, and locally invaded the surrounding soft tissue structures. Meticulous tissue dissection was performed using a combination of blunt dissection, cotton-tipped applicators, and bipolar electrocautery device. The renal artery and vein were noted to be within the caudal extent of the affected adrenal gland. A left nephrectomy and ureterectomy was performed. After undermining all of the surrounding soft tissue, a venotomy of the caudal vena cava was performed. Due to the significant space that the tumor thrombus was occupying, minimal hemorrhage was initially noted. With gentle



Figure 4. Adrenal tumor (top) with tumor thrombus (bottom)

Historically, the mortality risk of adrenalectomies was reported as high as 60%, however, more recent studies have indicated significantly better results.

traction of the left adrenal gland, the tumor thrombus was able to be moved with minimal resistance. As the cranial and caudal extents of the thrombus were visualized in the surgical field, digital occlusion of the vena cava was performed. The gland and its tumor thrombus were removed without significant hemorrhage. A Satinsky vascular clamp was used to partially occlude the vena cava and the venotomy was able to be closed without complication. The patient was hospitalized for several days for post-operative monitoring and then discharged to the charge of his owners. The histopathologic report confirmed the diagnosis of pheochromocytoma.

Prognosis:

Historically, the mortality risk of adrenalectomies was reported as high as 60%, however, more recent studies have indicated significantly better results, which may be associated with better pre-anesthetic treatment and anesthetic technique. In 2019, Mayhew et al. reported that in a cohort of 45 patient-owned dogs that had an adrenalectomy with cavotomy, the mortality rate was approximately 25% of patients. The median overall survival was 547 days (18 months). The study noted that the tumor type and size of the caval thrombus did not affect survival to discharge, however, thrombi that extended cranially past the diaphragm were at a higher risk of mortality (~70%).

Consideration:

Adrenal tumors with vena caval invasions were historically thought of as either inoperable procedures or carried significant risk. Due to the improvement of veterinary knowledge, medication and technique, a majority of these patients can be surgically managed successfully.

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When to Refer a Glaucoma Case?

John S. Sapienza, DVM, Diplomate, w ACVO

I recently received a call from a referral veterinarian, and the question that he posed to me was "What other glaucoma medications can I prescribe to this patient? Dorzolamide does not seem to be lowering the intraocular pressure enough?" Many veterinary ophthalmologists, including me would simply respond that surgery is the key to intraocular pressure (IOP) control, and the time to refer this case is NOW. Glaucoma is rarely a medically manageable disorder, especially primary glaucoma in dogs. The goal for glaucoma therapy in our small animal patients is to decrease the IOP as soon as the patient presents to you (the referring veterinarian). Surgery must be part of the early treatment plan for every glaucoma case. Vision is our primary goal, but if already lost, IOP control is then the most important therapy goal.

I often see animals referred to me with maximal medications for weeks: latanoprost TID, dorzolamide QID as well as additional topical and oral anti-glaucoma medications. There is no advantage to using these topical medications more than their recommended prescribed frequency (latanoprost 1-2X per day and dorzolamide every 8 hours). One must remember that rarely will the IOP be controlled on medical therapy alone, there-

Glaucoma is rarely a medically manageable disorder, especially primary glaucoma in dogs.

fore, surgery in the form of a gonioimplant (or glaucoma shunt), laser therapy or combination shunt-laser procedures will always be advised in almost all cases of primary canine glaucoma. The advantage of gonioimplants are the relatively low vision-threatening complications as compared to laser-induced complications. Long term success of the currently available gonioimplants, however, is poor: average of IOP control for 2-12 months. We are presenting our work on a new gonioimplant that delivers aqueous humor to the ocular surface thus bypassing any fibrotic capsule formation around the shunt reservoir. One such patient is now visual and off all medications 4 years post-glaucoma shunt to the ocular surface. (**Figure 1**).

Laser therapy, namely transscleral, micropulse or endocyclophotocoagulation (or endolaser), is readily available and has its advantages and disadvantages like any surgical procedure. Control of IOP is between 70-90% dependent on whether one performs a transscleral (TSCP) or endolaser (ECP). Major risks are recurrence of the glaucoma and secondary complications such as uveitis, cataract formation, and intraocular bleeding. A major disadvantage is the first 1-2 weeks post-laser ablation of the ciliary body, the IOP remains



elevated and if markedly elevated can cause permanent vision loss. The micropulse laser has not been a reliable and predictable surgical laser in small animals. We recently did a 1 year review of all canine cases treated over the last 3-4 years and have presented this information at the 2020 annual ACVO virtual congress that the micropulse laser therapy resulted in long term control of IOP and retention of vision in 54% and 31%, respectively.

In summary, surgical options exist for glaucoma cases in the form of gonioimplants, laser or combination therapies, but the key to success is early referral to the ophthalmologist and early surgical intervention. Any questions or concerns, please do not hesitate to contact us. □

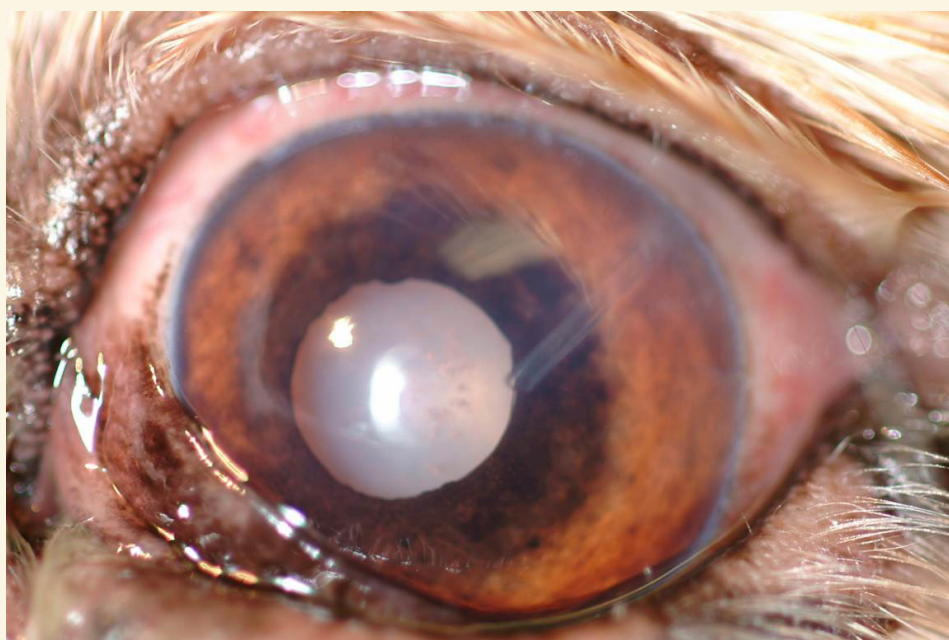


Figure 1: One such patient is now visual and off all medications 4 years post-glaucoma shunt to the ocular surface.



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