PERIOPERATIVE MEDICAL MANAGEMENT OF ADRENAL NEOPLASIA
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Veterinarians are often presented with complex adrenal neoplasia cases that have significant intraoperative challenges, which require the skills of an experienced surgeon. Perioperative evaluation and treatment of these patients can be equally challenging, and successful outcomes require a thorough understanding of the tumor types that affect the adrenal glands, as well as an understanding of appropriate preoperative and postoperative management of these cases. Even when a clinician has a thorough understanding of adrenal neoplasia, definitive preoperative diagnosis can be difficult. Further difficulty can arise when a patient with no obvious outward signs of adrenal disease is diagnosed with an adrenal tumor during abdominal ultrasound for an unrelated condition. These are some of the many factors that make adrenal gland neoplasia a complex but often times rewarding condition to treat.

A basic understanding of adrenal gland anatomy and physiology is critical for successful diagnosis and management of adrenal tumors. The adrenal gland is composed of an outer cortex and inner medulla. The cortex consists of the zona glomerulosa, zona fasciculate and zona reticularis, which produce mineralocorticoids (primarily aldosterone), glucocorticoids (primarily cortisol) and sex hormones, respectively. Catecholamines (primarily epinephrine and norepinephrine) are produced by the medulla. Based on the above, the major tumors that are encountered in companion animals include benign and malignant tumors of the cortex that can be cortisol secreting, aldosterone secreting or non-functional. The primary tumor of the adrenal medulla is pheochromocytoma, which leads to excessive circulating levels of catecholamines.

Preoperative Diagnosis: Patients with adrenal tumors can display a wide array of clinical signs, ranging from significant polyuria, polydipsia and polyphagia, typical of hyperadrenocorticism (HAC) to anorexia that might occur secondary to acute kidney injury induced by severe hypertension. In other patients, in which adrenal tumors are found incidentally during abdominal ultrasound, there may be no obvious outward clinical signs.

Obtaining a thorough history and performing a complete physical examination are both essential and can give insights into the type of adrenal tumor that is present. For instance, dogs with cortisol-secreting tumors will often have a history of polyuria/polydipsia/polyphagia, weight gain, and pyoderma, while dogs with pheochromocytoma may experience collapse episodes or periods of anxiety secondary to spikes in systemic blood pressure. The absence of polyuria/polydipsia makes a diagnosis of a cortisol-secreting tumor unlikely. Dogs with cortisol-secreting tumors may also demonstrate characteristic physical examination findings seen with HAC, such as a potbelly appearance, poor hair coat and muscle wasting. Obtaining a blood pressure and performing ocular and fundic examinations are essential components in patients suspected to have adrenal tumors. Due to sporadic secretion of excessive catecholamines by pheochromocytomas, fluctuations in blood pressure are common, and hypertension may not be present at the time of evaluation; fundic examination may allow for
evaluation of retinal changes consistent with previous episodes of hypertension. Blood pressures elevations may also be present in dogs with adrenal cortical tumors, but the accompanying tachycardia that can be seen with pheochromocytomas is not typically seen with adrenal dependent HAC.

Screening laboratory testing, including complete blood count, serum chemistry screen, urinalysis and urine culture should be performed. Patients with adrenal dependent HAC may have elevated alkaline phosphatase and cholesterol levels, while patient with aldosterone-secreting tumors may have elevated or high normal sodium levels and low or low normal potassium levels. Patients with pheochromocytomas often have unremarkable chemistry panels, and may also show changes consistent with end-organ damage secondary to hypertension. Persistently isosthenuric or dilute urine is common in patients with HAC, but can be seen with all adrenal tumor types. Patients with urine concentrations persistently greater than 1.035, are unlikely to have a cortisol secreting tumor.

Preoperative diagnosis and treatment of cortisol-secreting adrenal tumors is imperative prior to surgery, to prevent development of thromboembolism and iatrogenic hypoadrenocorticism perioperatively. There are multiple tests that can be used to aid in the diagnosis of cortisol-secreting tumors and these are discussed briefly below. Interpretation of these tests must be made in conjunction with history, clinical signs and physical examination findings.

1. Urine cortisol-creatinine ratio (UCCR): The UCCR test is a screening test that is performed on free catch urine collected at home by an owner. This is a sensitive but non-specific test, which can have false positive results, especially if the sample is collected during a time of stress. While a negative UCCR test does not definitively rule out HAC, it makes it a much less likely diagnosis, as most patients with HAC have a positive test. A negative UCCR test in a patient without obvious polyuria/polydipsia and/or with concentrated urine, generally rules out a cortisol-secreting tumor.

2. Low dose dexamethasone suppression (LDDS) test: This screening and differentiating (differentiating between adrenal dependent and pituitary dependent HAC) test, involves the collection of three blood samples over an 8-hour period, and is one of the most useful tests for ruling out the presence of a cortisol-secreting tumor. Suppression of cortisol in response to administration of dexamethasone rules out the presence of an adrenal-secreting tumor.

3. Endogenous ACTH: Dogs with cortisol-secreting tumors typically have low circulating levels of endogenous ACTH, due to the negative feedback of excessive cortisol levels on the pituitary. While this differentiating test can be useful when used in COMBINATION with other tests, it is an insensitive test that is difficult to perform. For these reasons, it is not commonly performed.

4. Abdominal ultrasound: When a cortisol-secreting adrenal tumor is present, the contralateral adrenal gland is often small, due to negative feedback from excessive cortisol levels. The absence of a small contralateral gland does not rule out the presence of adrenal dependent HAC.

If results of the above tests (in conjunction with history and physical examination findings) demonstrate that an adrenal tumor is not cortisol-secreting, the assumption then becomes that the adrenal tumor is non-functional or an adrenal tumor of the adrenal medulla. Diagnosis of a pheochromocytoma is typically based on the presence of
physical examination and/or a history consistent with a pheochromocytoma (as discussed above), in addition to ruling out the presence of a cortisol secreting tumor. Extremely rarely, a patient could have more than one tumor type. Below is a brief discussion of the available testing for more definitive diagnosis of a catecholamine secreting adrenal tumor.

5. Urine/Serum catecholamine concentrations: In veterinary medicine, measurement of urine catecholamine levels is rarely performed in the clinical setting. The rapid metabolism of epinephrine and norepinephrine makes it difficult to obtain accurate measurements. In addition, release of these hormones can occur in normal patients during times of stress, making false positive results possible. In humans, 24-hour urine collection methods are used, but this can be difficult in our veterinary patients. Recent studies have evaluated the use of urine catecholamine metabolites normalized to creatinine for differentiation of adrenal tumors. While results of these assays have been promising, the assays are expensive and are not widely available at this time.

Several imaging modalities are utilized when evaluating a patient with an adrenal tumor. Radiographs can demonstrate mineralization of the adrenal gland, and this finding has been documented in 50% of adrenocortical tumors. Ultrasound often provides an excellent screening tool for adrenal tumors and can provide some information about tumor size, location and vascular involvement. At our clinic, we generally recommend computed tomography scans prior to all planned adrenalectomy procedures, and the results with this approach have been excellent as this allows the surgeon to appropriately plan the procedure. The use of magnetic resonance imaging in the evaluation of adrenal tumors in humans has been well documented, however, the use of this modality for adrenal tumors in veterinary medicine is still developing.

Medical Management: The results of the diagnostic workup will help to guide preoperative therapies. If a cortisol-secreting tumor has been diagnosed, it is critical to manage the HAC prior to initiation of surgery. It seems intuitive that Lysodren, which destroys adrenal cortical tissue (specifically the zona fasiculata), would be useful for treatment of adrenal dependent HAC, however, effective control of adrenal dependent HAC is not typically achieved with Lysodren. Instead, trilostane has been used successfully.

Patients suspected of having a pheochromocytoma should be treated with an alpha-antagonist (phenoxybenzamine or prazosin) prior to surgery. Beta-blockers are less commonly indicated; however, tachycardia may necessitate the use of these medications. The use of these drugs helps to normalize patient blood volume and decrease the risk for development of fatal hypertension and arrhythmias during anesthesia and during manipulation of tumors.

Intraoperative

Several intraoperative medical management options exist for patients with adrenal tumors. Patients with adrenal tumors frequently develop blood pressure alterations secondary to anesthesia and surgical manipulation of tumors. A full description of the anesthetic and blood pressure medications used intraoperatively is beyond the scope of
these proceedings, but a skilled anesthetic team is crucial for maximal success during adrenalectomy.

Postoperative

Patients undergoing adrenalectomy are in a dynamic state postoperatively. Major concerns include bleeding, thromboembolic disease, and the development of pancreatitis and hypoadrenocorticism. Physical examination and blood pressure monitoring are used to evaluate for significant postoperative bleeding, and if concern arises, abdominal ultrasound and abdominocentesis can be performed.

An ACTH stimulation test should be considered postoperatively, especially in patients with a suspected cortisol-secreting tumor. Proactive evaluation for hypoadrenocorticism will allow for initiation of therapy before development of life-threatening complications.

Thrombus formation has been a major source of morbidity and mortality in patients undergoing adrenalectomy, especially in patients with cortisol-secreting tumors and patients with tumoral vascular invasion. Medical management of coagulation can include perioperative administration of heparin, low molecular weight heparin and drugs to reduce platelet aggregation (low dose aspirin and clopidrogel). Careful use of these medications is critical to prevent hemorrhage.

Surgical retraction of the pancreas has been another major cause for patient decompensation postoperatively. Feeding of low fat diets, ensuring adequate hydration and volume status and careful monitoring for pancreatitis are critical in these patients. In the experience of our clinic, the use of laparoscopy has led to decreased incidences of pancreatitis postoperatively.

Adrenal tumors in veterinary patients can be challenging to diagnose and to treat effectively. A thorough understanding of the perioperative management is crucial for success. Additionally, collaboration with internists, surgeons, anesthesiologists and criticalists can further optimize outcomes in our patients.