When does thyroid and parathyroid disease become surgical?

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Objectives:

1. Review the pathophysiology of primary hyperparathyroidism.
2. Understand methods of diagnosis and treatment of primary hyperparathyroidism.
3. Review thyroid neoplasia pathophysiology and presentation.
4. Understand staging and treatment options for thyroid neoplasia.

Parathyroid disease

Pathophysiology: One cause of hypercalcemia in middle aged to older dogs is primary hyperparathyroidism (PHP). This is usually the result of a hyperfunctional nodule located on one or more of the parathyroid glands. The clinical signs may be insidious and usually manifest relating to the hypercalcemia. Determining a diagnosis of PHP is based on the presence of hypercalcemia in the face of a normal or elevated parathyroid hormone (PTH) concentration. Once diagnosed with PHP, a dog has an excellent prognosis following treatment which includes either surgical excision or ablation of the hyperfunctional tissue.

Background information: Most dogs have four parathyroid glands, although the actual number of glands can vary. The parathyroid glands are associated with the thyroid gland in that they are located either external to the thyroid capsule or internal, within the thyroid capsule. Parathyroid glands may be ectopic, located in an abnormal position due to their development. The thymus develops alongside the internal parathyroid glands and islets of parathyroid tissue may break off and continue descending into the mediastinum with the thymus resulting in additional and ectopic parathyroid glands. Parathyroid glands are normally very small ranging in size from 2-4 mm and may be difficult to detect or can be easily mistaken for a thyroid cyst or nodule.

The parathyroid glands function to generate, store, and secrete PTH. Parathyroid hormone is made autonomously and stored within the cells of the gland. The hormone is secreted in response to low extracellular calcium concentrations. Special calcium sensing receptors reside within the chief cells of the parathyroid glands that send signals to either increase or decrease PTH synthesis and release. Parathyroid hormone acts directly on the kidneys to increase calcium reabsorption, phosphorus excretion, and biosynthesis of calcitriol. Calcitriol and PTH act synergistically to increase calcium and phosphate release from bones. Calcitriol will also increase calcium reabsorption in the intestines.
Hypercalcemia: Differentials for dogs presenting with hypercalcemia include primary hyperparathyroidism, hypercalcemia of malignancy (lymphosarcoma, anal sac apocrine gland adenocarcinoma, thymoma, and others), Addison’s disease, vitamin D toxicosis, renal disease, skeletal lesions, and spurious lab errors. Hypercalcemia of malignancy, Addison’s disease and renal failure seem to be the most common causes of hypercalcemia in dogs. Recent studies have determined that up to 1/3 of dogs with PHP may be asymptomatic and that the elevations in calcium may also be mild. Therefore the incidence of primary hyperparathyroidism may actually be higher and the disease more common among middle aged to older dogs.

Primary Hyperparathyroidism: Clinical signs of PHP are classified as being gastrointestinal (vomiting, anorexia), urinary (stranguria, hematuria, polyuria, polydypsia), or musculoskeletal (weakness, tremors). The urinary tract signs seem to be the most common with up to 50% of patients having urinary tract infections or bladder stones. Renal insufficiency or failure may be correlated to total calcium concentration and prolonged hypercalcemia.

Hypercalcemia in dogs with PHP may be noted incidentally on routine geriatric blood work. Since the true incidence of PHP may be underestimated it is a good idea to work up any dog with a slightly elevated calcium level. A standard work-up for dogs with hypercalcemia includes a full physical examination with thorough lymph node evaluation and rectal examination to assess the anal sacs. If a full chemistry panel, complete blood count, and urinalysis have not already been submitted, these tests should be assessed. Next, the ionized calcium needs to be evaluated as this is the most accurate way of assessing the true calcium status of the patient. A PTH and PTHrP can usually be submitted at the same time to help keep costs down and prevent the owner from having to bring the patient back to the hospital several times. Given the high incidence of urinary tracts infections, a urine culture should also be considered as dictated by the clinical signs. If the patient is displaying urinary tracts signs an abdominal radiograph to assess for bladder stones would be prudent. Lastly, three view thoracic radiographs can be useful to assess cardiothoracic structures. An ultrasound can be used to detect the parathyroid nodule pre-operatively, but this is user dependent due to the small size of the parathyroid glands.

The finding of an elevated ionized calcium level with a concurrent normal or elevated PTH level is consistent with a diagnosis of PHP. A common misconception is that the PTH must be above the reference range; this is not true in fact the PTH can be in the middle of the reference range. Because elevated calcium levels provide a negative feedback loop to the parathyroid glands, a dog with hypercalcemia should have very low PTH concentrations. Therefore a dog with a PTH that is normal in the face of hypercalcemia has an inappropriate PTH concentration.

Once the diagnosis of PHP has been established, treatment should be recommended to prevent the effects of prolonged hypercalcemia. The most common and effective method of treatment is surgical excision of the hyperfunctional parathyroid nodules(s). The surgical cure rate is 95% if all hyperfunctional tissue has been removed. The success of surgery can be dependent on the experience level of the surgeon. A less invasive way of treatment is by glandular ablation. An
ultrasound probe is used to detect the enlarged gland(s) and heat is used to ablate the tissue. The cure rate is ~90% but the patient may require multiple treatments. A common misconception for owners is that their pet is too old for anesthesia and treatment. If the surgery is being performed by an experienced surgeon the anesthetic time and risks are low and the success rate is very high.

In conclusion, PHP may be more common than originally described and all dogs with any elevation in calcium concentration should be worked-up. Ionized calcium is the best determinate of the calcium status in dogs. Dogs with PHP may have a PTH concentration that falls within the reference range. Treatment is highly effective and should be strongly recommend in all patients, even old dogs.

Thyroid disease

Pathophysiology: Thyroid tumors are rare, but are the most common endocrine tumor in dogs. The majority of thyroid tumors in dogs are malignant and around half of patients will have metastasis at the time of diagnosis. These tumors have local regional metastasis to the submandibular, retropharyngeal and parotid lymph nodes. They can also have distant metastasis to adrenal glands, brain, kidney, heart, liver, lungs and bone. Most dogs have a single thyroid lobe tumor, but up to 25% have both lobes affected. Unlike cats, thyroid tumors in dogs are usually non-functional with reports of functional tumors being less than 25%.

Background information: The median age at presentation is 9 years, but reported ranges are 5-18 years. The Boxer, beagle, Siberian husky and golden retriever are breed overrepresented in retrospective studies. In some cases there is only a palpable mass noted on physical exam and no clinical signs, which highlights the need to always perform cervical palpation during a routine physical exam. Differentials for a cervical mass include abscess, granuloma, salivary gland disease, carotid body tumors, lymph node disease and other skin/ subcutaneous neoplasia. Clinical signs include cough, gag, retching, regurgitation, dysphonia, Horners, or cranial vena cava syndrome. Functional tumors secrete thyroid hormone and can lead to clinical signs consistent with hyperthyroidism such as weight loss, polyphagia, polydipsia, or change in behavior. Interestingly, dogs with thyroid cancer are significantly more likely to have an additional distinct tumor type so a thorough physical exam is important as well. Staging for these patients includes examination of palpable head and neck lymph nodes, thoracic radiographs and abdominal ultrasound due to the risk of metastasis at the time of diagnosis. Thyroid tumors may ectopic (~10%) located from the base of the tongue along the cervical region, mediastinum, to the heart tissue.

Thyroid carcinoma: When a patient is presented and a thyroid nodule is noted on exam, the mass should be characterized with palpation and a fine needle aspirate obtained. Tumors of the thyroid can be characterized by their size and mobility with smaller tumors and mobile tumors being more amenable to surgery. It is very common for these tumors to bleed
significantly with a fine needle aspirate due to the highly vascular nature of the tumor and paraneoplastic effects of the tumor leading to local coagulopathies. Because of these features as well as the potential for local invasion, incisional and excisional biopsies prior to diagnosis and full work-up are not recommended. Using a 25 gauge needle for fine needle aspirates may reduce some of the bleeding. After cytology full staging is performed and thyroid imaging is typically recommended. When comparing imaging modalities, ultrasound had the least ability to predict capsule integrity and tumor size while MRI and CT was considered superior. Imaging is beneficial for evaluating the head and neck lymph nodes that aren’t palpable, evaluating local invasion, and vascularity.

Treatment: Patients with a thyroid mass and no metastasis or just local regional metastasis and a tumor with minimal invasion are candidates for surgery. Surgery is the preferred modality for treatment of thyroid tumors with multiple studies demonstrating improved survival times. Surgery can be complicated by local anatomy including the trachea, esophagus, large blood vessels including the carotid, recurrent laryngeal nerve, vagosympathetic nerves and musculature. Hemorrhage during and after surgery can occur from the highly vascular and tortuous blood supply of the tumors, fragile blood vessels, local coagulopathies and aneurysmal vascular dilations within the tumor. Many surgeons will perform a blood type and coagulation profile prior to surgery in preparation of potential complications. Dogs with bilateral thyroid lobe tumors are candidates for surgery, but a thorough discussion with the owner prior to surgery about the potential for management of hypothyroidism and hypoparathyroidism following surgery is important. Postoperative chemotherapy may be recommended in patients that have local regional metastasis, larger tumors, those with vascular invasion, and bilateral disease. Patients that don’t have metastasis and are not good surgical candidates can undergo full course radiation therapy and have good survival times. Radioiodine therapy is another option for nonresectable thyroid tumors, but there are very few locations around the United States that perform this treatment option due to the safety concerns of the radioactive iodine that is administered. Those patients that have metastasis can elect for palliative treatments which include radiation and chemotherapy.

In conclusion, thyroid tumors are highly malignant but with early detection and surgery the survival times can be very good. Performing cervical palpation on routine physical exams is beneficial to locate small thyroid nodules. Any mass in the cervical region warrants a work-up beginning with a fine needle aspirate.