Hemithyroidectomy in a horse with confirmed hyperthyroidism

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- Clinical signs of hyperthyroidism in horses may include emaciation, hyperexcitability, polyphagia, tachycardia, polydipsia, enophthalmos, and unilateral thyroid gland enlargement.
- Hyperthyroidism in horses can be substantiated by endocrine testing, histologic examination of the affected portion of the thyroid gland, and response to hemithyroidectomy.
- Health of horses with hyperthyroidism may be restored by hemithyroidectomy.

A 23-year-old Quarter Horse gelding was referred to the Boren Veterinary Medical Teaching Hospital for evaluation of cachexia and hyperactive behavior of 1 year's duration. The hyperactive behavior was characterized by excessive pacing in a paddock and circling in a stall. The horse had received routine dental care, vaccinations, and an antihelmintic before admission to the hospital. At the time of admission the horse appeared severely emaciated, weighed 391 kg (860 lb) compared with an estimated typical weight of 476 kg (1,050 lb), was tachycardic (68 beats/min) with a grade V/VI diastolic murmur ausculted over the left base of the heart, and was pyrexic (38.4 C [101.2 F]), polydipsic, and enophthalmic. A subcutaneous mass (8 cm × 6 cm) was detected on the right side of the cervical portion of the neck, caudal to the angle of the mandible. The neck, dorsal surface of the shoulder (withers), and gluteal regions had multiple patches of alopecia. The horse was considered hyperexcitable because it overreacted to the normal sights and sounds of the environment and it struggled excessively during the passage of a nasogastric tube. The horse had a ravenous appetite because it consumed 2 to 3 times the expected daily ration. Initial diagnostic tests included a CBC, serum biochemical analysis, and urine analysis. Test results were within reference range except for a slightly low serum albumin concentration (2.3 g/dl [reference range, 2.5 to 3.8 g/dl]) and high γ-glutamyltransferase activity (51 U/L [reference range, 12 to 46 U/L]). Initial differential diagnoses included oral disease, parasitism, cardiac disease, neoplasia, gastrointestinal tract malabsorption, and endocrinopathy.

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A complete oral examination failed to identify any abnormalities. The horse was also observed to eat without difficulty. Results of fecal examination for parasites were negative. Abnormalities of the heart were not detected, using M-mode and B-mode echocardiography with a 2.5-MHz sector scanner. Variables measured on a lead-I base apex electrocardiogram were within reference range. On the basis of echocardiographic and electrocardiographic findings and those of auscultation, the diastolic murmur was determined to be physiologic, aortic in origin, and artificially intensified as the result of the horse's severe emaciation. A neoplastic process affecting the thoracic or abdominal cavities was considered possible because such neoplasia can induce cachexia. Lateral radiographic views of the thorax were obtained from left and right sides of the horse and were normal in appearance. Results of abdominal palpation per rectum and transabdominal ultrasonography by use of a 3.5-MHz sector scanner were unremarkable. Results of peritoneal fluid analysis to determine WBC count and total protein concentration were within reference range values and were not indicative of abdominal neoplasia or other abdominal disorder.

A malabsorption syndrome caused by chronic gastrointestinal tract irritation as the result of sand ingestion was considered. To detect sand in the gastrointestinal tract, fecal samples were placed in a container, thoroughly mixed with water and evaluated for sand. None was found. To further evaluate the possibility of a malabsorption syndrome, an oral glucose tolerance test was performed. Food was withheld for 12 hours before a 10% dextrose solution was administered via a nasogastric tube at a dosage of 1 g/kg (0.45 g/lb) of body weight. Blood samples (5 ml) were collected by jugular venipuncture in 5 ml glass tubes containing 10 mg sodium fluoride and 12.5 mg potassium oxalate at 1 minute before and 30, 60, 90, 120, 180, and 240 minutes after dextrose administration.[1] Glucose concentrations in plasma were quantified using a chemistry analyzer. Glucose concentration increased rapidly during the first 60 minutes of testing from an initial value of 78 mg/dl to 110 mg/dl, then declined to baseline values by 240 minutes. Interpretation of glucose tolerance test results was difficult because of concerns over physiologic factors affecting glucose uptake and metabolism. A d-xylose absorption test was attempted, but the horse's hyperexcitable behavior progressed to a point that prevented safe passage of a nasogastric tube. On the basis of clinical signs and results of diagnostic testing, primary oral, infectious, cardiac, malignant neoplastic, or intestinal disease processes were considered unlikely.

Hyperadrenocorticism or an endocrinopathy involving thyroid function was believed to be the likely cause of disease. A dexamethasone-suppression test was done to determine whether the horse had hypera-

drenocorticism. Blood (5 ml) was collected by jugular venipuncture into chilled glass tubes containing 7.5 mg of EDTA. Samples were obtained immediately before (baseline) and 20 hours after IM administration of 40 µg/kg (18.18 µg/lb) dexamethasone.[a] Tubes were centrifuged (4 C) at 1,500 × g for 20 minutes. Plasma was recovered and stored frozen (–18 C).

Plasma concentration of cortisol was quantified by a validated radioimmunoassay.[b] Sensitivity in the cortisol assay was 0.2 ng/ml. Mean interassay coefficient of variation was 6.8% for plasma cortisol concentration of 29.3 ng/ml. After withholding food, the horse had a plasma cortisol concentration (51.5 mg/ml) that was within the reference range (15 to 90 ng/ml) established by the laboratory.[b] Plasma cortisol concentrations in clinically normal horses undergoing a dexamethasone-suppression test should be < 10 ng/ml at approximately 16 to 24 hours after dexamethasone administration.[2] Plasma cortisol was 0.9 ng/ml in the affected horse 20 hours after dexamethasone administration, which is a result indicating that the horse's adrenal glands were functioning normally.

Ultrasonographic evaluation of the mass in the neck by use of a 3.5-MHz curvilinear transducer revealed a well-encapsulated mass with a homogenous and mildly hyperechoic parenchyma. These findings in addition to the anatomic location of the mass were consistent with thyroid tissue. A biopsy specimen of the mass was obtained percutaneously, and the tissue was fixed in formalin. Fixed tissue was embedded, sectioned, and stained with H&E. Histologically, the mass appeared to consist of thyroid parenchyma with multiple thyroid follicles of relatively typical size. Interspersed among the follicles were numerous smaller follicular-like structures with a small amount of colloid located centrally. Cellular structure appeared mature and invasive characteristics, such as mitotic figures, were not seen in the tissue sections. The mass was identified as a thyroid adenoma, a histopathologic diagnosis that was not unexpected, because these tumors are reported to be common in aged horses.[3]

Clinical signs in this horse were suggestive of an endocrinologically active thyroid tumor. Plasma concentrations of thyroxine (T_4) and triiodothyronine (T_3) were quantified by validated radioimmunoassays.[b] Sensitivities in the T_4 and T_3 assays were 0.2 and 0.05 ng/ml, respectively. Mean interassay coefficients of variation were 5 and 7.8% for plasma concentrations of 9.9 and 1 ng/ml in the T_4 and T_3 radioimmunoassays, respectively.

Concentrations of plasma T_4 and T_3 were quantified initially in the horse at 8:30 AM on 2 successive days. For a T_3-suppression test, plasma concentrations of T_4 and T_3 were measured over a 22-day period in the affected horse and in 3 clinically normal horses. Horses received doses of 3,5,3′-triiodothyro-L-thyronine[c] (2.5 mg diluted in 5 ml sterile saline solution [0.15 M NaCl]) IM at 8:30 AM and 6:00 PM on days 1, 2, and 3, and at 8:30 AM on day 4 of the 22-day period. Plasma T_4 and T_3 concentrations were determined at 30 and 5 minutes before the first dose of T_3 and at 5 minutes before each successive dose of T_3. Additional blood samples were collected at 6:00 PM on day 4 and at 8:30 AM on days 6, 7, 9, 17, 20, and 22. Blood samples (5 ml) were collected by jugular venipuncture into glass tubes containing EDTA. After tubes were centrifuged, plasma was recovered and stored frozen.

Initial concentrations of T_4 (46.5 ng/ml) and T_3 (1.15 ng/ml) in the affected horse exceeded the upper limit of the reference range values (T_4, 24 ng/ml; T_3, 1.05 ng/ml) established by the laboratory.[b] Administration of T_3 resulted in an increase in plasma T_3 concentrations of 10 to 20 fold in the 3 clinically normal horses and approximately only twofold in the affected horse (**Fig 1**). Plasma T_3 concentration remained high throughout the 4 days of T_3 administration in the affected and clinically normal horses. Mean (± SE) plasma T_3 concentrations in the affected and clinically normal horses were 2.17 ± 0.9 ng/ml and 4.14 ± 0.49 ng/ml, respectively, from approximately 10 hours after the first dose of T_3 to 10 hours after the last dose of T_3. Concentrations of plasma T_3 returned to baseline in the affected and clinically normal horses at approximately 72 to 120 hours after the last dose of T_3.

Mean plasma concentrations of T_4 in clinically normal horses were suppressed from a baseline of 12.2 ± 3.3 ng/ml to values of 9.9 ± 2.2 ng/ml at 6:00 PM on day 1 and 6.2 ± 1.8, 2.3 ± 0.9, 1.1 ± 0.7, 0.5 ± 0.2, 0.7 ± 0.3, 0.2 ± 0.1, and 0.7 ± 0.2 ng/ml at 8:30 AM on days 2, 3, 4, 6, 7, 8, and 9, respectively (Fig 1). Plasma T_4 concentrations in clinically normal horses were suppressed for at least 5 days after the last dose of T_3. In contrast, plasma T_4 in the affected horse was unaffect-

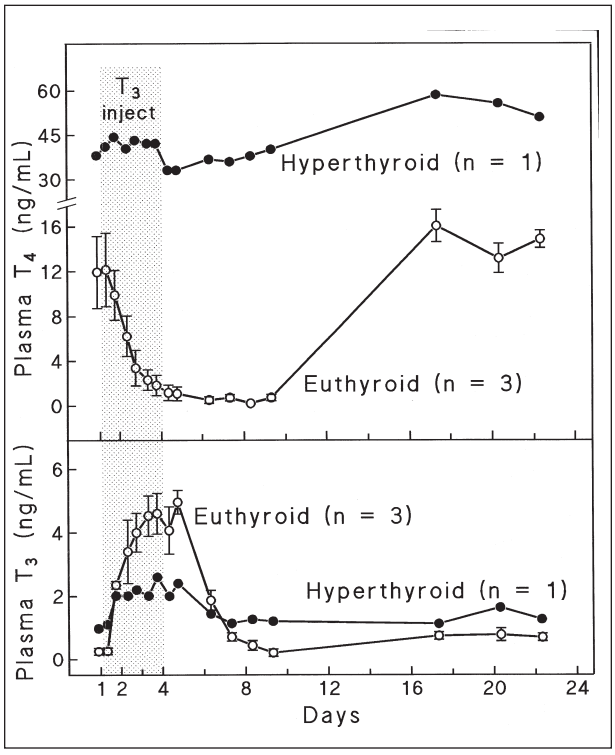

Figure 1—Mean (± SE) plasma concentrations of thyroxine (T_4) and triiodothyronine (T_3) before, during, and after a T_3-suppression test in 3 euthyroid horses and a horse with hyperthyroidism. Horses received 7 doses of T_3. Each dose contained 2.5 mg of T_3. Doses were administered IM at 8:30 AM and 6:00 PM on days 1, 2, and 3, and at 8:30 AM on day 4 (shaded area). Notice the axis break for plasma concentrations of T_4.

ed by T_3 administration, and plasma T_4 remained high at concentrations of 33 to 44 ng/ml during the period of T_3 administration. Results of the T_3-suppression test confirmed that the thyroid gland in the affected horse was autonomously hypersecreting thyroid hormones.

The affected portion of the thyroid gland was removed. The adenomatous portion of the thyroid gland measured 8 cm × 6 cm × 6 cm and was encapsulated and smooth. The size of the adenomatous gland was approximately 2 to 3 times the size of a typical thyroid gland in horses, which measures approximately 5 cm in length, 2.7 cm in height, and 1.5 to 2 cm at its greatest width.[4] Sections of the removed tissue were preserved in formalin and stained with H&E for histologic evaluation. Evaluation of the tissue sections revealed thyroid tissue similar to that seen on the initial biopsy specimen. Extremely compressed and severely atrophied follicular and interstitial thyroid tissue was situated at the edge of the tissue section. The atrophied thyroid tissue was located between the thyroid capsule and the adenomatous tissue. Follicles in the adenomatous tissue were widely divergent in size. Evidence of mitotic activity was not seen. The tissue was again described as a thyroid adenoma (**Fig 2**).

Removal of the thyroid tumor resulted in a large, rapid, and sustained decrease in plasma thyroid hormone concentrations, indicating that the unilateral adenoma had been the source of excessive thyroid hormone production. Plasma T_4 decreased from a presurgical value of 48.5 ng/ml to values of 20.5, 4.1, and 0.7 ng/ml on days 1, 4, and 7 after surgery, respectively. However, plasma T_4 and T_3 concentrations increased to values within reference range approximately 35 days after the hemithyroidectomy. This suggested that the atrophied lobe of the thyroid gland and the hypofunctioning pituitary thyrotrophs returned to normal function approximately 35 days after removal of the excessive negative feedback effects of the elevated plasma concentrations of thyroid hormones.

Reevaluation 81 days after the hemithyroidectomy revealed complete resolution of polyphagia, polydipsia, alopecia, tachycardia, enophthalmia, hyperexcitability, and hyperactivity. The horse also was no longer cachectic and its body weight had increased by 68 kg (150 lb). The cardiac murmur identified on initial examination was still detectable, however the intensity of the murmur had decreased from a grade V/VI to a grade III/VI.

Hyperthyroidism is a well-documented disease in humans,[5] cats, and dogs.[6] Signs of hyperthyroidism in humans include a high state of excitability, intolerance to heat, increased sweating, mild-to-extreme weight loss, diarrhea, muscle weakness, nervousness or other psychic disorders, extreme fatigue with insomnia, exophthalmus, and tremors of the hands.[5] Signs of hyperthyroidism in cats include weight loss, goiter, hyperactivity, weakness, fatigue, polyphagia, polyuria and polydipsia, dyspnea, panting, hyperventilation, tachycardia, systolic murmurs, gallop rhythms, and other cardia arrhythmias.[6] Hyperthyroidism in dogs results in similar signs including goiter, polyuria and polydipsia, weight loss, weakness and fatigue, polyphagia, heat intolerance, nervousness, diarrhea, and tremors.[6]

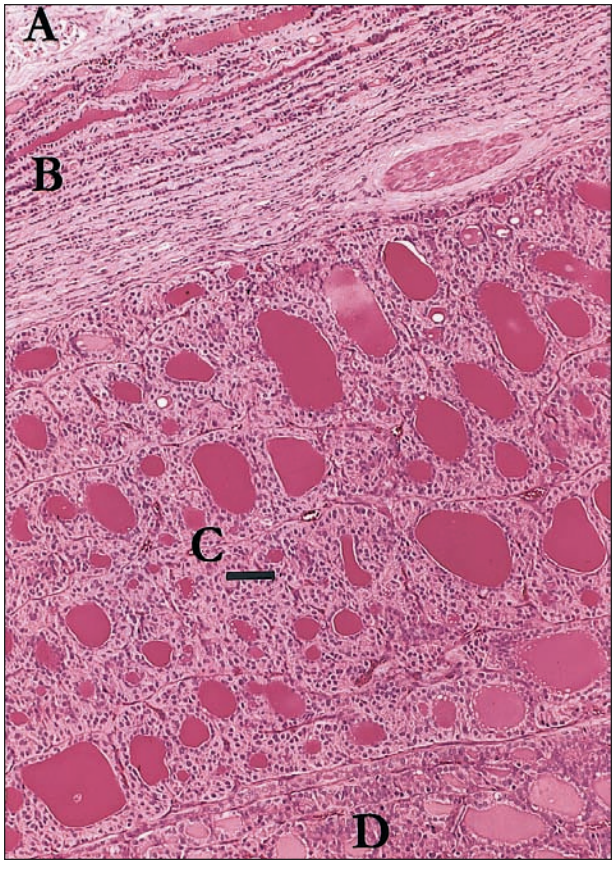

Figure 2—Photomicrograph of a section of thyroid tissue obtained from a horse with hyperthyroidism. Notice the irregular appearance of follicles. Connective tissue of thyroid capsule (A) is apparent. Notice that the degree of the compression atrophy of thyroid tissue (B) increases as proximity to adenomatous thyroid tissue increases. Adenomatous thyroid tissue has 2 morphologic zones (C and D). Examination of the complete histologic sections revealed that zone C was narrow and located peripherally around the much larger zone D. Regardless of zone, the neoplasm was composed largely of well-differentiated follicular cells, often forming thyroid follicles of variable size. Follicular cells were cuboidal to low cuboidal. Colloid content was moderately-to-densely eosinophilic. H&E stain; bar = 40 µm.

To our knowledge, hyperthyroidism in horses has not been investigated systematically. Despite the lack of documentation, anecdotes of the hyperthyroid state in the horse are encountered. Recently, Ramirez et al[7] reported clinical signs of hyperthyroidism in a 21-year-old Arabian gelding with a thyroid adenocarcinoma that may have been endocrinologically active and autonomously secreting excessive amounts of thyroid hormone. We report here definitive evidence for the existence of hyperthyroidism in a horse. Initial evaluation revealed markedly high plasma concentrations of T_3 and T_4 in this horse, a finding consistent with hyperthyroidism. The diagnosis was substantiated by the lack of suppression of plasma T_4 concentrations in the affected horse as compared with clinically normal horses when both were challenged with a T_3-suppression test. Obliteration of the high plasma T_3 and T_4 concentrations following hemithyroidectomy further confirmed hyperthyroidism. Additionally, histologic findings of the affected portion of the thyroid gland confirmed that the mass was a thyroid adenoma.

Because the horse of this report did not have bilateral hypertrophy of thyroid gland, and because it did have resolution of clinical signs of disease following hemithyroidectomy, we believe that the horse had primary and not secondary hyperthyroidism.

Disease processes that were initially ruled out included oral disease, parasitism, cardiac disease, neoplasia, and an intestinal malabsorption syndrome. Clinical cardiac disease, other than hyperthyroid-associated tachycardia, was not identified historically, on physical examination, or via echocardiography and electrocardiography. An oral glucose absorption test was completed to determine whether the horse had a malabsorption syndrome, but the results were not considered diagnostically reliable because of the confounding effects of hyperthyroidism on the absorption, distribution, and metabolism of glucose.[1,8-11] The response of the horse to the hemithyroidectomy retrospectively supports our assessment of the lack of a primary malabsorption syndrome. Evidence was not found for another disease condition that could account for the clinical signs of the horse.

Interestingly, humans that have hyperthyroidism are usually exophthalmic, secondary to swelling of the retro-orbital tissues,[5] whereas this horse with hyperthyroidism was severely enophthalmic. An immune-mediated disease process is considered the cause of the exophthalmus in humans with hyperthyroidism, but this pathologic component may be lacking in horses with hyperthyroidism. Dogs and cats with hyperthyroidism, are commonly polyuric and polydipsic.[6] The horse described here was polydipsic but not polyuric. The excessive ingestion of water may have been secondary to the large volume of dry matter (hay) consumed by this horse. Water requirements were probably high to maintain normal hydration status and gastrointestinal tract function. Aside from these exceptions, the admitting signs of hyperthyroidism in this horse were similar to those seen in humans, dogs, and cats with hyperthyroidism.

[a]Azium, Schering-Plough Animal Health Corp, Kenilworth, NJ.
[b]McCann JP, Clinical Hormone Laboratory, Department of Physiological Sciences, College of Veterinary Medicine, Oklahoma State University, Stillwater, Okla.
[c]T_3, Sigma Chemical Co, St Louis, Mo.

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