HYPOTHYROID DIAGNOSTIC CHALLENGE IN A GALAH

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INTRODUCTION

Hypothyroidism is a controversial topic in avian medicine. Thyroid abnormalities are frequently implicated in disease, yet very little support for diagnosis is made. Stress, feather damaging behaviour, nutritional deficiencies and unrelated medical conditions are suggested to be associated with decreased thyroid function in caged birds (Clubb, 2007: Fudge, 2001). A plasma T_4 evaluation is often unrewarding because normal basal plasma T_4 concentrations have not yet been established for most psittacine bird species. Assessment of thyroid function is more valuable if it is incorporated with the TSH (thyroid stimulating hormone) response test (Schmidt, 2002).

In the following case report, plasma thyroid hormone concentrations were determined before and after administration of TSH in a galah (*Eolophus roseicapilla*) with suspected hypothyroidism and compared the results from 5 clinically healthy galahs. In addition, results of physical examination, hematological evaluation, skin and thyroid biopsies were performed to establish evidence of the disease.

CLINICAL REPORT

History: A male aviary galah of unknown age from a large mixed collection presented to Wattle grove Veterinary Hospital (WGVH) for assessment. It had been paired and was breeding successfully for many years. The past two clutches were infertile and the owner noted feather changes. It was on an all seed diet, with no other past medical problems. On physical examination the bird was quiet, alert and responsive, in moderate body condition with poor quality feathering; affected outer primary feathers had elongated shafts with thickened, hyperkeratotic sheaths. Powder-down feathers were elongated with excess plumulaceous barbs, giving the appearance of "dreadlocks". There was feather discolouration with replacement of normally grey feathers with red feathers (Figures 1 and 2).

A diffuse, erosive, oval shaped, epidermal skin lesion was observed over the right pectoralis major muscle that incorporated the axillary region. Whole body radiographs showed no signs of skeletal abnormalities. Psittacine circovirus disease (PBFD) profile (polymerase chain reaction, haemagglutination inhibition, and haemagglutination tests) was negative. The bird had a mild,

nonregenerative anaemia (PCV 44%; normal 49-66). Plasma serum biochemical profile was unremarkable. Presumptive diagnosis of hypothyroidism was made and the owner subsequently surrendered the bird to WGVH as future breeding prospects were unlikely. Further investigation of possible hypothyroidism was pursued.

Figure 1 Presumptive hypothyroid galah. Note: elongation of powder down feathers with excessive plumulaceous barbs. 10 January 2008.

Figure 2 Presumptive hypothyroid galah. Note: feather colour changes. 10 January 2008.

THYROID TESTING T4

Blood was collected from the suspect hypothyroid bird for plasma thyroid hormone concentration. To approximate standard plasma thyroid hormone concentrations, blood was collected from 5 clinically healthy galahs with normal plumage housed outdoors at Murdoch University, Perth, Western Australia. These birds were microchipped and regularly tested negative for psittacine circovirus

disease (PBFD), using polymerase chain reaction, hemagglutination inhibition and hemagglutination. Each bird was captured, restrained manually and scanned for identification. One milliliter of blood was collected from either the jugular vein or cutaneous ulnar vein within one minute of capture. Blood samples were inserted into lithium heparin plasma separator tubes and immediately placed in on ice. Plasma was separated by centrifugation within 30 minutes of blood collection. All samples were analyzed at VETPATH laboratory services (Perth, Western Australia) using solid-phase competitive chemiluminescent enzyme immunoassay specific for T_4. All sampling occurred during the same period (9:00–10:00 am) on the same day.

Results: March 26, 2008

Test	Radar	Galah 1	Galah 2	Galah 3	Galah 4	Galah 5
T_4 nmol/L	**< 13**	16.9	15.4	18.3	17.4	25.5

Documentation of a low T_4 assay is suggestive of primary hypothyroidism but to rule out other causes for low plasma T_4 concentration, thyrotropin stimulating hormone administration was performed on all six birds. Base line blood samples were taken as previously described. Thyroid-stimulating hormone (TSH) from porcine pituitary tissue (0.5 IU; Sigma) was administered into the pectoral muscle immediately after blood collection. A second blood sample was collected 6 hours after the TSH injection. All sampling occurred during the same time period on the same day (pre TSH 9:00-10:00am, post 3:00-4:00pm).

Results: May 7, 2008

Test	Radar	Galah 1	Galah 2	Galah 3	Galah 4	Galah 5
Pre TSH T_4 nmol/L	**14.3**	Insufficient sample	22.4	32	26	28
Post TSH T_4 nmol/L	**13.2**	25	24.8	42.2	30.7	30

THYROID AND SKIN BIOPSY; PROCEDURE (PERFORMED BY DR. TIM OLDFIELD; WGVH)

The bird was premedicated with 1mg butorphanol by intramuscular injection. 30 minutes later it was mask induced using 5% isoflurane®and intubated with a 3mm uncuffed endotracheal tube and maintained on 2.5% isoflurane®and 2 litres per minute oxygen. The bird was placed in dorsal recumbency on pre-warmed heat packs with the cranial end elevated by 30 degrees and the head and neck dorso-flexed. Meloxicam 0.2mg was given by intramuscular injection and a Doppler sensor placed over the cutaneous ulnar vein.

The skin over the thoracic inlet was plucked and cleaned with alcohol. A skin incision was made at the midline 0.5 cm cranial to the cranial end of the sternum. The crop was deflected to the right and the incision was extended into the clavicular air sac. A 2.7 mm endoscope was inserted into the air sac and the left thyroid gland identified closely adherent to the left jugular vein and left internal carotid artery. A 9 Fr rigid cup biopsy forcep was then introduced through the same incision site and 'walked' down the endoscope until it was at the level of the thyroid. The left thyroid was then grasped in the forcep and the forcep withdrawn. The intention had been to remove approximately 50% of the thyroid but after removal no thyroid tissue could be reliably visualized. There was no post biopsy

hemorrhage. The endoscope was withdrawn and the clavicular air sac and skin were closed separately with continuous suture pattern using 5/0 PDS. A skin biopsy was taken from the epidermal skin lesion over the right pectoralis major muscle that included damaged tissue, its margin and normal appearing epidermis. A second biopsy was taken from a region in the left shoulder that appeared clinically normal and included a feather follicle. Post-anesthetic recovery was unremarkable.

In the skin there was moderate diffuse orthokeratotic hyperkeratosis and follicular hyperkeratosis. One feather follicle had a focal infiltration of lymphocytes into the follicular pulp and nodular focus of epithelial dysplasia adjacent to the epidermal collar. In the section of thyroid gland there was moderate to marked epithelial hyperplasia and hypertrophy along with a deficit of colloidal material and undersized follicles. Many follicles contained mineralising pale colloid material.

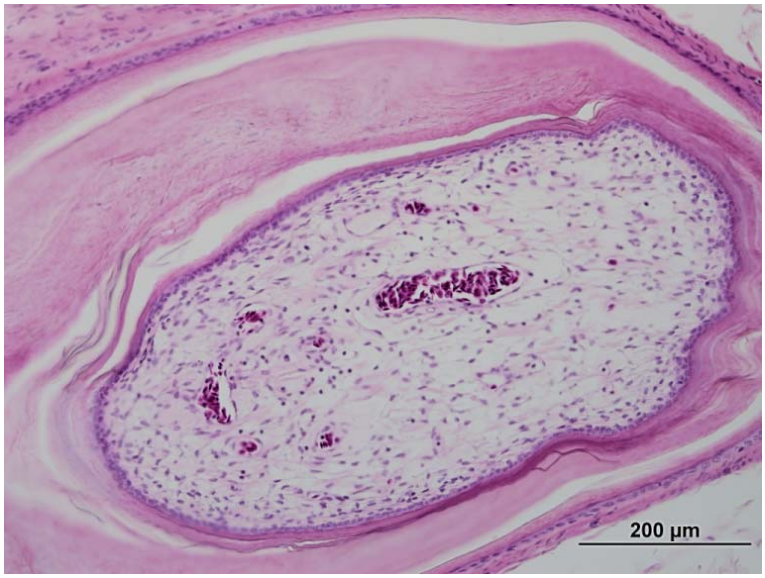

Figure 3 Histological section of skin demonstrating severe intrafollicular orthokeratotic hyperkeratosis.

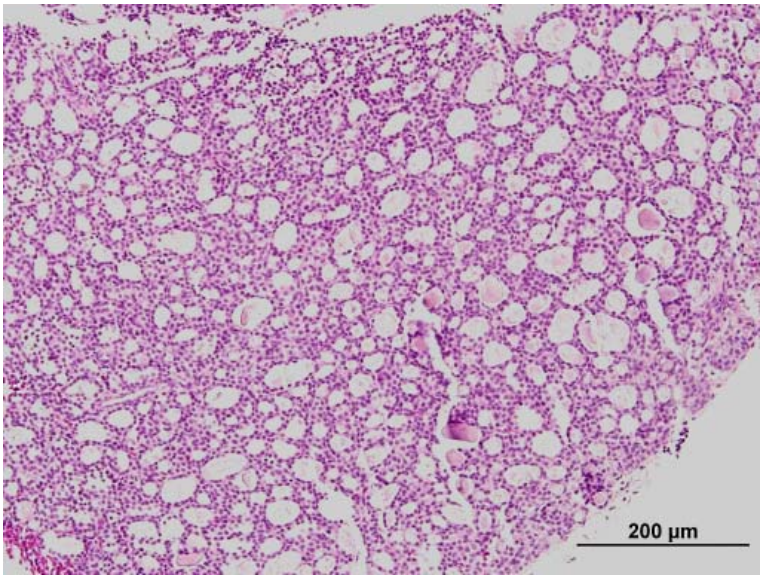

Figure 4. Histological section of thyroid gland demonstrating moderate to marked epithelial hyperplasia and hypertrophy along with a deficit of colloidal material and undersized follicles. Many follicles also contained mineralising pale colloid material.

TREATMENT

Blood was collected for pretreatment plasma T_4 assay (13.8 nmol/L) and complete blood count. The bird continued to be mild to moderately anemic (PCV 38%). Supplementary L-thyroxine (Oroxine® 200 µg tablets – Sigma Pharmaceuticals (Australia) PTY LTD) was administered by dissolving one quarter of a 200 µg tablet in 15ml of water and dosed at 0.5 ml/kg orally once daily. Plasma T4 assay at four weeks post L-thyroxine administration was 17.3 nmol/L. An induction of moult was observed within two weeks of L-thyroxine supplementation. The bird did not show any aggressive behaviour. Six weeks post L-thyroxine administration, the bird displayed seizure like activity that appeared to be induced by excitement. Ionized calcium levels 24hrs post seizure activity was1.15 mmol/L (reference range 1.45-2.20mml/L). Subsequent Plasma T4 levels 10 weeks post L-thyroxine administration was19.1 nmol/L. Ionized calcium levels had improved to within reference range (1.88mmol/L). Treatment resulted in a vast improvement in feather colouration and regrowth (Figure 5). The erosive skin lesion in the right axillary region continues to be significant. Second intention healing was observed but re-injury occurred when the right wing was elevated. This is more likely attributed to the location rather than endocrine causes.

Figure 5: 10 weeks post oral L-Thyroxine administration. December 2008.

Over the next 6 months, treatment with oral L-Thyroxine was given by dissolving one quarter of a 200 µg tablet in 300 ml of drinking water for ease of compliance. Water intake was measured to extrapolate a dosage. On average, 6µg was consumed every 24hrs. In addition, the galahs T_4 concentration was monitored to ensure that adequate therapeutic levels were being maintained. Blood was also collected at the same time from the control galahs as previously described.

Results: June 17, 2009

Test	Radar*	Galah 1	Galah 2	Galah 3	Galah 4	Galah 5
T_4 nmol/L	<6	26	22.4	14.5	23.6	25.2

* 10 months post L-thyroxine treatment

DISCUSSION

Hypothyroidism is a well-recognized clinical disease in dogs that is most often the result of primary lesions in the thyroid gland. Many functional disturbances are caused by a reduction in basal metabolic rate including body weight gains, hyperpigmentation of the skin and thinning of the hair coat (McGavin and Zachary, 2007). In birds, thyroid hormones are synthesized as they are in mammals (Schmidt 2002). For this reason, hypothyroidism is often implicated as the cause similar conditions in birds. Experimentally, hypothyroid induced in birds has resulted in growth retardation, reduced gonadal function and modifications in feather structure that include; elongation of feathers with loss of barbules, colour changes and delayed moult (Rae, 1995).

There are several similarities between the signs of hypothyroidism reported experimentally and those observed in the galah in this report. However, in the clinical setting confirmation of primary hypothyroidism diagnosis is difficult. To date, only one well documented case of hypothyroidism has been reported in a psittacine bird (an adult scarlet macaw [*Ara macao*] (Olgesbee, 1992).

Limited information regarding normal thyroxine levels in psittacine birds makes diagnosis difficult. Basal T_4 concentration values are considered unreliable because T_4 levels can be influenced by environmental temperature, time of day, season, nutritional status and non-thyroidal illness (Ritchie et al., 1994). An additional method of testing thyroid function is through the administration of thyroid stimulation hormone. Further evidence of hypothyroidism was established by using thyroid-stimulating testing (TSH). For comparison, testing was completed in galahs with presumed normal thyroid function on the same day and time period. The suspect hypothyroid galah T_4 concentration failed to respond to thyrotropin stimulation. A minimal T_4 concentration increase was seen in the clinically healthy galahs. Past research demonstrates a significant rise in T_4 levels after TSH stimulation in healthy psittacine birds (Lothrop, 1985; Oglesbee, 1992; Clubb et al., 2007). The minimal increase observed in this report may be attributed to the type of pituitary tissue administered; this study used porcine tissue while bovine tissue has been previously described. In addition, a dose of 0.5IU TSH per galah was administered as reported by Clubb et al., 2007. Similar studies performed on clinically normal psittacine birds used a higher dose (1-2IU) of TSH to evaluate thyroid function (Lothrop, 1985; Oglesbee, 1992).

Confirmation of hypothyroidism can also result from finding appropriate endocrine gland lesions. The thyroid tissue revealed epithelial hyperplasia and hypertrophy along with a deficit of colloidal material and undersized follicles consistent with thyroid hyperplasia. The major pathogenic mechanisms for the type of thyroid hyperplasia are iodine-deficient diets, goitrogenic compounds that interfere with thyroxinogenesis, dietary iodine excess, and genetic enzyme defects in biosynthesis of thyroid hormones.

Hypothyroidism is often mentioned as a cause of dermatological conditions in psittacine birds. Histologic lesions revealed diffuse orthokeratotic, hyperkeratotic dermatosis. A feather follicle had focal infiltration of lymphocytes into the follicular pulp and nodular focus of epithelial dysplasia. These morphologic changes in the skin and feather follicles are similar to those described by Oglesbee (1992) in the diagnosis of hypothyroidism in a male scarlet macaw.

Diagnosis of hypothyroidism was made based on poor reproductive performance, characteristic feather changes, histologic, dermatological and thyroid lesions and evidence of a poor TSH stimulation response test. In addition, the bird responded well to L-thyroxine therapy. Within six weeks of initiating treatment the bird molted, the feathering had improved and T_4 concentration increased to within the range of the clinically normal birds.

Surprisingly, within the same time period transient seizure activity was observed. Subsequent ionized

calcium levels were low. Differential diagnosis for hypocalcaemia includes dietary deficiency, hypovitaminosis D, secondary renal hyperparathyroidism, renal disease, primary hypoparathyroidism, intestinal malabsorption, and severe rhabdomyolysis (Johnston and Ivey, 2002). In African grey parrots (*Psittacus erithacus*) with hypocalcaemic-induced seizures no definitive etiology has been identified. They usually have normal skeletal density, suggesting that the problem be one of calcium metabolism (Johnston and Ivey, 2002). In this case, it is hypothesized that the removal of the left thyroid gland may have resulted in a low ionized calcium level (1.15mmol/L). The parathyroid tissue consists of two pairs of small yellow-tan glands that lie caudal to the thyroid glands on either side of the thoracic inlet (Johnston and Ivey, 2002). Parathyroidectomy has been shown to cause fatal hypocalcaemia in birds and it is reasonable to assume that some tissue was inadvertently removed with the left thyroid gland during the biopsy procedure. As a consequence, parathyroid hormone concentrations may have been disrupted until replenishment and the presence of a steady state occurred. With time, ionized calcium levels returned to within normal range (1.88mmol/L) reported for psittacine bird species.

Suggested regimens for thyroid replacement therapy include drinking water–based treatment and by placing medication in a favourite food. In this case report, the dose was more effective when administered by use of an oral suspension. A poor response was shown when thyroid replacement therapy was changed to a drinking water-based method. These findings suggest that the T_4 concentration should be monitored during long-term therapy to ensure adequate therapeutic levels are being maintained.

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