CASE STUDIES

Nutritional Support for a Case of Canine Hypoadrenocorticism

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Canine hypoadrenocorticism (Addison’s disease) is described as the “great pretender” because the clinical signs resemble those seen with many other disorders (Podell, 1990). It is a disorder that is seen more frequently in breeds such as the Great Dane, Portuguese water dog, standard poodle, Rottweiler, Leonbergers, West Highland white terrier, and wheaten terrier (Auge, 1985; Shaker et al., 1988; Smallwood and Barsanti, 1995). The average age of most of these dogs is seven years or less, but may range from four months to 14 years (Willard et al., 1982; Reimers et al., 1990; Kintzer and Peterson, 1997). Female dogs comprise about 70% of cases.

The clinical presentation can be grouped into one of two categories:

- Acute or end-stage adrenal insufficiency
- Subacute or chronic adrenal insufficiency

Acute or end-stage adrenal insufficiencies are characterized by depression and weakness that progresses to collapse, bradycardia, hypovolemia, and shock. Subacute or chronic adrenal insufficiencies are characterized by depression, muscle weakness, and intermittent anorexia, vomiting, and diarrhea. These clinical signs respond transiently to fluid therapy and corticosteroids. Stress often worsens these clinical signs.

Atrophy or destruction of all layers of the adrenal cortex results in primary adrenocortical insufficiency. An autoimmune or idiopathic disturbance is thought to be the most common cause. Bilateral atrophy of the adrenal cortices with mononuclear cell infiltration and fibrosis of the capsule has been reported (Schaer et al., 1985; Boujon et al., 1994). Fungal infections, viral diseases, and neoplasias have also been implicated as factors in the development of primary adrenocortical insufficiency. Secondary adrenocorticism can be the result of pituitary or hypothalamic lesions caused by neoplasias, inflammation, or trauma. Another important cause is abrupt withdrawal of long-term or high-dose corticosteroid therapy.

Generally, primary hypoadrenocorticism results in both glucocorticoid and mineralocorticoid deficiency. Glucocorticoid deficiency causes decreased gluconeogenesis and glycogenolysis, reduced stress tolerance, impaired renal function, and decreased vascular sensitivity to catecholamines. Mineralocorticoid deficiency results in renal retention of potassium and hydrogen, and renal loss of sodium, chloride, and water.

Hypoadrenocorticism patients can have lymphocytosis and an absolute eosinophilia. Dehydration may create an increased hematocrit and total solids. Most cases of primary hypoadrenocorticism have hyperkalemia and hyponatremia although the electrolytes may be normal in early phases. However, serum electrolytes are generally normal in secondary hypoadrenocorticism.
Azotemia may develop from prerenal or renal causes. Approximately 30% of patients have hypercalcemia that may be related to decreased renal function. Interestingly, a mild hypoalbuminemia is occasionally seen. Urine specific gravity is usually <1.030, in spite of the prerenal azotemia (Peterson et al., 1996), and is felt to be a result of medullary washout secondary to sodium wasting in the kidney. Electrocardiographic abnormalities may exist dependent on the level of hyperkalemia, acid-base balance, and serum sodium and calcium concentrations. An ACTH stimulation test is essential for diagnosis of hypoadrenocorticism.

Effective nutritional support is based on a broad understanding of the entire hypoadrenocorticism clinical picture. This nutritional support should focus primarily on the adrenal gland and its physiology, but it should also recognize the etiological factors that contribute to reduced adrenal function. Considerations include:

• Addressing the autoimmune components with an adrenal Protomorphogen™ extract
• Broad adrenal support with adrenal Cytosol™ concentrates and other whole food nutritional factors

Important nutritional factors include vitamin C, vitamin E, vitamin B6, bioflavonoids, and chelated minerals. Additional support should be provided to the liver and kidneys to facilitate adaptation to the deranged metabolism created by the adrenal dysfunction and accompanying pharmaceutical therapies.

One of the significant benefits of nutritional support, even when the diseased tissue cannot be rehabilitated, is the ability to improve case management. Patients with appropriate nutritional support appear to maintain a more positive health level with less intensive pharmaceutical management and are easier to maintain at a more optimal state of health. This translates into fewer adjustments in medication over the course of the disease, improved longevity, and a reduced number of problematic episodes.

**Clinical Case**

Inga: An eleven year old, spayed, female husky mix

Inga was brought to me for a nutritional consultation on 2/5/98. She had an 18-month history of hypoadrenocorticism. Her previous veterinarian had performed the initial ACTH stimulation test at the time of diagnosis on 5/3/96:

- Resting cortisol: 0.1 mg/dL (normal: 1.0-5.0 mg/dL)
- Cortisol at one hour post-Cortrosyn (Organon, West Orange, NJ): 0.1 mg/dL (normal: 8.0-17.0 mg/dL)

Treatment with fludrocortisone acetate 0.4 mg SID and prednisone 5 mg SID was initiated at that time.

Seven months prior to her visit to my practice, Inga had been taken to an emergency facility for restlessness, hyperpnea, and drooling. The attending veterinarian suspected an “early pancreatitis.” However, a clear diagnosis was not obtained and insufficient information was included in the record for adequate interpretation of the episode. Symptomatic treatment was given and the dog was released. Recovery was uneventful. An ACTH stimulation test was repeated on 5/29/97 with the following results:

- Resting cortisol: 8.2 mg/dL (normal: 1.0-5.0 mg/dL)
- Cortisol at one hour post-Cortrosyn: 11.6 mg/dL (normal: 8.0-17.0 mg/dL)

At that time, the patient was still receiving prednisone, 5 mg SID and fludrocortisone acetate, 0.4 mg SID, as well as carprofen, 75 mg SID to BID. When presented to me for nutritional consultation, Inga was also receiving Proanthozone (Animal Health Options, Golden, CO) 50 mg SID.

Inga was being fed Science Diet Canine Maintenance (Hill’s Pet Nutrition Inc., Kansas City, MO) and her body weight was 70.8 lbs, considerably higher than her previous long-term average weight of 56 lbs. She showed reduced mobility in the right shoulder.

A complete blood count and serum chemistry profile were requested. Abnormal serum chemistry results are summarized as follows:

- Alkaline phosphatase: 630 IU/L (normal: 8-76 IU/L)
- ALT: 132 IU/L (normal: 6-70 IU/L)
- Sodium: 141 mEq/L (normal: 142-150 mEq/L)
- Chloride: 104 mEq/L (normal: 105-117 mEq/L).
Based on these findings and Inga’s history, I recommended initial nutritional support consisting of the following:

- Drenamin® (Standard Process Inc., Palmyra, WI): three tablets SID
- Hepatrophin PMG® (Standard Process Inc., Palmyra, WI): one tablet BID
- Lipotrophic Complex (Integrative Therapeutics Inc. Wilsonville, OR): one capsule BID.

Drenamin® was utilized for its supportive adrenal effects, and Lipotrophic Complex and Hepatrophin PMG® were used for their liver supporting effects.

On 3/12/98, B6-Niacinamide (Standard Process Inc., Palmyra, WI) two tablets SID, was prescribed and carprofen was decreased and then eliminated. The B6-Niacinamide was utilized for its action as an adrenal hormone precursor. In May of that year, the fludrocortisone acetate dose was adjusted to 0.3 mg BID and salt was added to the food, based on an internal medicine consultation, in an attempt to maintain appropriate serum sodium. In November, the Lipotrophic Complex was replaced with an experimental canine liver formula (Standard Process Inc., Palmyra, WI) ¼ teaspoon SID.

The patient did well on the above routine with only occasional episodes of shoulder soreness after long walks. Her body weight slowly decreased to 61.4 lbs in September 1999. At that time, it was noted that the patient’s hair coat was becoming thin and rough. She had become lethargic and was urinating frequently. Routine serum chemistries showed a continuing increase in alkaline phosphatase to 1769 IU/L (normal: 5-131 IU/L), and an elevation in ALT (162 IU/L; normal: 12-118 IU/L) and total bilirubin (0.4 mg/dL; normal: 0.1-0.3 mg/dL). A fasting and post-prandial bile acids test was performed on 9/30/99 with the following results:

- Fasting: 8.5 µmol/L (normal: 1.9-7.0 µmol/L)
- Post-prandial: 9.3 µmol/L (normal: 6-20 µmol/L)

The dosage of the experimental canine liver formula was increased to ¼ teaspoon BID.
Research

A urinary tract infection was noted on routine urinalysis and standard antibiotic therapy with amoxicillin 400 mg BID for 21 days was administered with complete resolution. The probiotic, Enterogenic Concentrate (Integrative Therapeutics Inc., Wilsonville, OR) was also given at one capsule BID and continued for seven weeks. Beginning on 10/1/99, prednisone was decreased to 3.75 mg SID. By 10/19/99, Inga’s coat was improved and continued to improve throughout 1999. The prednisone was decreased again to 2.5 mg SID, but it was noted that joint discomfort was increasing. Traumeel (Heel Inc., Albuquerque, NM), a homeopathic anti-inflammatory and analgesic, was prescribed at a dose of one tablet BID. See Figure 1 for blood results showing the progression of change in ALT, alkaline phosphatase, and total bilirubin from May 1997 to January 2002. Striking is the progressive decline in alkaline phosphatase, ALT, and bilirubin to normal levels beginning November 1999.

The patient currently is in excellent condition with a body weight of 56.4 lbs. Joint discomfort is being adequately controlled with Traumeel tablets. The prednisone dose is down to 0.75 mg SID and the fludrocortisone acetate dose is 0.3 mg BID. The owner considers Inga’s hair coat to be the “best it has ever been.” However, ACTH stimulation testing on 3/7/01 showed no adrenal response:

- Resting cortisol: 0.2 mg/dL (1.0-5.0)
- Cortisol at one hour post-Cortrosyn: 0.2 mg/dL (8.0-17.0)

Discussion

This patient was diagnosed with hypoadrenocorticism based on her initial ACTH stimulation response. Management of this case has been reasonably uneventful over the course of the last six years. The only notable concerns were the occurrence of the thin, coarse hair coat, pollakiuria, lethargy, and the progressive increase in serum liver enzymes. Clinical signs at the time were consistent with hyperadrenocorticism. A urinary tract infection was found and appropriately treated. The prednisone dose was progressively decreased and an experimental liver whole food nutritional supplement was utilized resulting in resolution of the clinical signs that were reminiscent of hyperadrenocorticism.

Complete elimination of the prednisone was not attempted based on the clinical status of the patient and ACTH stimulation test results. While it is known that fludrocortisone acetate does have some glucocorticoid effects, the owner has elected to move slowly with medication changes. This is an ongoing clinical case with the goal of reducing the fludrocortisone acetate and continuing to decrease the prednisone based on patient clinical status.

At the present time, the patient is stable in terms of the clinical picture and the serum chemistry testing. However, complete evaluation of the liver has not been done. It can be surmised from the total bilirubin, albumin, and most recent bile acids test that the liver is functioning adequately. Ultrasound and biopsy of the liver has not been performed to further assess liver status. The assumption is that the physical examination findings are consistent with adequate hepatic function especially when these findings are correlated with the serum chemistry results. Ongoing monitoring is indicated in this patient and adjustments in supportive care are warranted as the patient continues to age.

This case illustrates the application of whole food based nutritional supplementation and support in conjunction with pharmaceutical management. The adjunctive nutritional support was utilized in an attempt to rehabilitate the adrenal gland and compensate for the known side effects of the pharmaceuticals. A review of the patient’s history reveals a relatively problem free course over the last four years. While it is difficult to state with certainty that nutritional support of this nature will solve all issues in canine hypoadrenocorticism cases, it does point out the potential for improved case management when sound, whole food nutritional support is provided.

It does not appear that one of our primary goals, complete withdrawal of all pharmaceuticals, will be achieved. The most recent ACTH stimulation testing did not reveal any adrenal response, which is unfortunate. Likely, this lack of adrenal response is due to a lack of functional adrenocortical tissue. Autoimmune destruction is the most probable explanation since this is known to be a common cause of canine hypoadrenocorticism (Smallwood and Barsanti, 1995). However, adrenal suppression from chronic exogenous glucocorticoid administration cannot be ruled out as a component. It should be noted that without the presence of functional adrenal cells, nutritional rehabilitation cannot occur to the point of full glandular function.
If we can assume that functional adrenocortical tissue is not present, then the episode of apparent hyperadrenocorticism must be explained. Not all facets of that episode can be adequately explained at this time. However, some causative factors can be evaluated.

First, the dose of fludrocortisone acetate was increased in the early phases of the initial nutritional support. Additionally, the patient’s body weight declined from 70 lbs. to 56.4 lbs. Changes in receptor sensitivity must also be considered. These factors combined with the prednisone may have contributed to the development over time of the mild Cushingoid signs. Also, the functional status of the liver must be considered relative to its ability to effectively eliminate the steroid compounds from the body. Note that the liver serum values had already started rising. There was a progressive increase in alkaline phosphatase and the previously normal ALT and total bilirubin began to rise above the normal range. When the experimental canine liver formula was initiated, the serum liver values declined but then began to rise again. It is clear that the resolution of the clinical signs and relative normalization of the alkaline phosphatase, ALT, and total bilirubin coincided with the reduction of the prednisone dose. However, it should be noted that the experimental canine liver formula dose was doubled 9/20/99. Studies indicate that nutritional therapies of this type can require 4-6 weeks for a clinical response. This corresponds to the time that the serum alkaline phosphatase values began to decline toward normal following their peak on 11/9/99. The ALT and total bilirubin declined into the normal range 12/99 and 1/00, respectively. Further studies are needed to completely ascertain the true relationship.

It is interesting to speculate on the results of the ACTH stimulation test performed on 5/29/96. The results were normal. It is unclear from the medical record if prednisone was withheld prior to ACTH stimulation testing. Regardless of any cross-reactivity with the prednisone, there was an adrenal response: resting cortisol 8.2 mg/dL (1.0-5.0) and one-hour post-Cortrosyn 11.2 mg/dL (8.0-17.0) (Kemppainen and Behrend, 2000). At that point in time, sufficiently viable adrenocortical tissue may have been present that would have responded to the nutritional support and adrenal Protomorphogen™ therapy. The important point is that early nutritional intervention is critical for optimal tissue response and rehabilitation. Additional, in-depth, controlled studies are needed to fully define the benefits of the integrated medical approach advocated here.

References