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Adrenocortical insufficiency can result from the following causes: idiopathic adrenal atrophy, immune-mediated adrenocortical destruction, glucocorticoid administration, o,p'-DDD treatment, hemorrhage or infarction, mycotic or other granulomatous disease, neoplastic involvement, surgical adrenalectomy, and anterior pituitary gland insufficiency.

Typical primary Addison’s disease and atypical Addison’s disease will be discussed first. Secondary Addison’s and iatrogenic hypoadrenocorticism will be covered at the end of this paper.

History, physical examination, findings and diagnosis

The dog with typical Addison’s disease commonly presents with an acute or a chronic history. The acute presentation is heralded by a rather sudden onset of mental dullness, muscle weakness, vomiting, and eventually collapse. The physical examination findings include mental depression, weak pulses, bradycardia, and varying degrees of dehydration. Oliguria can also occur. The typical clinicopathologic findings include hyponatremia, hyperkalemia (Na/K <20:1), hypochloremia, azotemia, hypobicarbonatremia, and mild hypercalcemia. Other less common laboratory features are lymphocytosis, eosinophilia, and hypoglycemia.

The dog with chronic Addison’s has a less dramatic clinical picture with signs consisting of periodic lethargy, poor appetite, weight loss or an inability to gain weight, and occasional episodes of vomiting and/or diarrhea. The clinical findings include mild to moderate evidence of weight loss, hyponatremia, hyperkalemia, and mild to moderate anemia and azotemia. The sodium and potassium concentrations do not necessarily have to occur in a proportional manner allowing for one parameter to be pathologically disproportionate to the other. In both the acute and chronic forms, the adrenocortical response to ACTH injection is absent to minimal.

The electrocardiogram (ECG) can be used to detect hyperkalemia. The most common ECG abnormalities include flattened P-waves, increased PR interval, increased positive or negative deflected T-waves, broadened QRS complexes, bradycardia, sinoventricular complexes, and atrial standstill. The earlier changes are the most frequently overlooked. Some patients will surprisingly lack ECG changes despite the presence of serum potassium levels exceeding 7.5 mmol/l.

The atypical Addisonian shows signs that usually resemble the chronic form as illustrated with lethargy, decreased appetite, and poor weight gain. ‘Atypical’ refers to clinical pathological findings that differ from the more familiar features. These can include: 1) Hyponatremia with normokalemia, 2) Eunatremia with hyperkalemia, 3) Eunatremia with normokalemia, 4) Normal serum electrolytes with or without eosinophilia and lymphocytosis, 5) Hypoglycemia with or without any of the findings in 1-4. The causes can theoretically include selective adrenocortical autoimmune destruction, adrenocortical enzyme deficiency, or anterior pituitary pathology. Atypical serum electrolyte shifts can be due to asynchronous changes between sodium and potassium because of separate endogenous compensatory mechanisms. The diagnosis of hypoadrenocorticisit should not be made ONLY on the basis of the serum electrolyte abnormalities because several other clinical conditions can cause similar changes.

Diagnostic confirmation depends on the demonstration of absent or minimal adrenocortical response to an injection of corticotropin (ACTH). In order to avoid any unnecessary delay in therapy, the following procedure is recommended soon after the patient’s admission: (1) draw blood for hemogram, serum biochemistry and basal plasma or serum cortisol determinations, (2) begin intravenous fluids (0.9% saline) and give 2-5 mg/kg of dexamethasone phosphate intravenously (prednisolone, hydrocortisone, prednisone, and fludrocortisone acetate will interfere with cortisol assays), (3) administer 0.25 mg of alpha 1-24 corticotropin (Cortrosyn, Organon) intramuscularly or intravenously, and (4) one hour later obtain a second blood sample for plasma or serum cortisol determination. If ACTH gel is used, the second cortisol sample is taken at 2 hours. Typical hypoadrenocorticisit is present when the post-ACTH serum cortisol level is ≤1 μg/dl (<27.59 nmol/L). Those with post-stimulation levels ranging from 1.5 μg/dl (<27.59-1379 nmol/L) can have hypoadrenocortical function.

Treatment

If the patient is eating and drinking and has normal serum electrolytes, only oral replacement glucocorticoid treatment as an out-patient will be necessary. The therapeutic objectives for the clinically ill patient include: (1) intravascular volume repletion, (2) reversal of any hyponatremia and hyperkalemia, (3) providing glucocorticoid replacement, and (4) recognizing and reversing any life-threatening cardiac arrhythmias.

Sodium chloride 0.9% is the fluid of choice and should be administered intravenously. It should be infused in
the dog at a rate of 10 to 15 ml/kg body weight (5-10 ml/kg for a cat) during the first 15 minutes of treatment and given as needed in the same amounts every 15 minutes over the first hour of treatment. The saline should be continuously infused at a maintenance dose of approximately 60-90 ml/kg body weight for the remainder of the 24-hour period. Central venous pressure monitoring may be useful in helping prevent excessive iatrogenic fluid overload, but this complication should be avoided with the lower volume loading doses described above. The intravenous fluids are discontinued when hydration, urine output, serum electrolytes, and the serum creatinine levels are restored to normal (usually after 48 to 72 hours of treatment) and the patient can eat and drink in the absence of vomiting.

Mineralocorticoid hormone supplementation is also necessary to enhance renal distal tubular sodium reabsorption and potassium excretion if the animal shows either hyponatremia or hyperkalemia. DOCP (desoxycorticosterone pivivate, Novartis) 1.5-2.0 mg/kg givenintramuscularlyor subcutaneously every three weeks and Florinef (fludeforcortisone, Squibb-Bristol Myers) 0.1 mg/5 kg once daily orally are presently available for this need. Re-assessment of the serum electrolyte levels will serve as a helpful treatment guide. Some patients will require DOCP every 3-5 weeks depending on each individual’s response to the medication. It is important to remember that DOCP provides only mineralocorticoid activity while fludrohydrocortisone (Florinef) provides mineralocorticoid PLUS glucocorticoid activities.

The glucocorticoid deficiency during a crisis is corrected with rapid-acting drugs such as prednisolone sodium succinate (Solu-Delta-Cortef, Upjohn), dexamethasone phosphate, or hydrocortisone. Prednisone and hydrocortisone should not be given until the ACTH stimulation test is completed. The initial intravenous doses of prednisolone sodium succinate, dexamethasone, and hydrocortisone hemisuccinate are 5-10 mg/kg, 2.5 mg/kg, and 50 mg/kg body weight, respectively. Subsequent glucocorticoid requirements are fulfilled by administering 1 mg/kg body weight of prednisolone orally, intramuscularly, or intravenously every 12 hours for 48 hours. The dose is then reduced to 0.25 to 0.5 mg/kg body weight every 12 hours for the remaining duration of hospitalization. Cortisone acetate (0.5 mg/kg/day divided) can theoretically be substituted for prednisone for added mineralocorticoid effect; however, the actual benefit is clinically insignificant. Prednisone at 0.25 mg/kg/day is usually required when DOCP is used as the mineralocorticoid of choice or when the glucocorticoid effects of Florinef are inadequate. Prednisone is given at 0.25 mg/kg/day for those addisonians that are only primarily glucocorticoid deficient. The response to treatment should be immediate as shown by return of normal appetite, weight gain and improved overall vitality. It is important to remember that larger doses will be needed to accommodate periods of physical or medical stress.

Serum potassium concentrations greater than 7.0 mmol/liter can cause progressive depressions of the excitability and conduction velocity of the myocardium. Treatment entails the administration of drugs that will either antagonize the effects of potassium at the myocardial cell membrane (calcium gluconate) or lower its serum level by displacing it intracellularly (insulin-dextrose and sodium bicarbonate).

**Iatrogenic and secondary Addison’s disease**

Iatrogenic hypoadrenocortical response to ACTH caused by prior glucocorticoid treatment is a result of negative inhibition of the hypothalamo-pituitary-adrenal axis. These patients will have normal serum electrolytes because adrenal aldosterone production is not critically affected by ACTH production. The ACTH stimulation test on these patients will show abnormally low cortisol blood levels, but if the patient is asymptomatic, no treatment is necessary unless decreased appetite and lethargy ensue. Providing prednisone at 0.2-0.25 mg/kg/day or every other day should restore an improved sense of well being.

Secondary Addison’s disease is the result of the anterior pituitary gland’s failure to produce ACTH. These patients will have normal serum plasma levels of ACTH. This is very similar to iatrogenic hypoadrenocorticism, except that the history provides for no glucocorticoid administration. These patients will require supplemental doses of prednisone treatment.