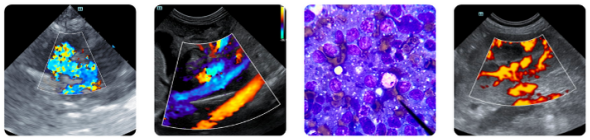


PATIENT

Medic Swett

SPECIES

Canine

BREED

Long Hair Chihuahua

SEX

Neutered male

AGE

11 years

WEIGHT

11 lbs

INTERPRETED BY

Remo Lobetti, BVSc, MMedVet (Med), PhD, Dipl. ECVIM

IMAGING PERFORMED BY

Karen Ebersole DVM, DABVP

HOSPITAL NAME

Scanvet

REFERRING VET

Dr. Kutcher

INVOICE

69311

DATE

12/4/25

Signalment

11-year-old neutered male long-haired Chihuahua.

History

Poorly controlled diabetes mellitus and pituitary-dependent Cushing's disease.

Therapy

- 3.5 IU Vetinsulin BID with an initial starting dose of 1.5 IU BID.
- 20 mg trilostane SID
- Denamarin.

Serum Biochemistry

Elevated liver enzyme activity and fructosamine.
Hyperlipidemia.
Hyperglycemia.

Survey Radiographs

No abnormalities on either the thorax or the abdomen evident.

Abdominal Ultrasound

- Bilateral adrenomegaly.
- Vacuolar hepatopathy.
- Pancreatitis, low-grade.
- Mild small intestinal thickening with mucosal speckling.

Interpretation

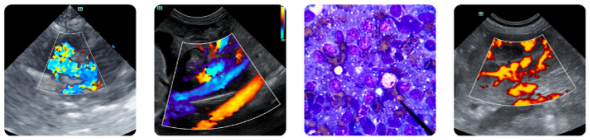
The persistent hyperglycemia, elevated liver enzyme activity and fructosamine, hyperlipidemia, and high dose of insulin (1.4IU/kg) is consistent with poorly controlled diabetes mellitus because of possible insulin resistance. Elevated liver enzyme activity in diabetes is associated with lipidosis and/or glycogen accumulation secondary to the insulin deficiency as well as to cholestasis from hepatocellular swelling and/or lipidosis.

The bilateral adrenomegaly is consistent with pituitary-dependent hyperadrenocorticism as well as the Trilostane therapy.

The hepatopathy would be consistent with an endocrine hepatopathy and ascribed to the diabetes mellitus and Cushing's disease.

Although the pancreatitis evident on ultrasound may be incidental early fibrosis, it may be contributing to the poor glycemic control.

As there are no report clinical signs of GI tract disease, the enteropathy evident on ultrasound can be considered an incidental finding and most likely associated with a recent meal.



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Further Assessment

- Urinalysis and urine culture to rule out bacterial cystitis.
- cPL/PSL assay to rule in/out concurrent active pancreatitis.
- ACTH stimulation test to assess control of the Cushing's disease.
- Serial blood glucose curve or ideally placement of a continuous glucose monitor (FreeStyle Libre).

TROUBLESHOOTING PERSISTENT HYPERGLYCEMIA IN TREATED DIABETICS

Persistent hyperglycemia is a frustrating and all too common problem in diabetic dogs treated with insulin with numerous factors contributing to poor glucose regulation. Some of these factors are related to management, such as improper insulin administration, while others have a physiological basis, such as biologic variability of insulin action.

Identifying persistent hyperglycemia

Diabetic dogs with persistent hyperglycemia are typically classified as poorly regulated diabetics. Owners may report that clinical signs of diabetes persist and that the recommended at-home treatment is not working as well as expected. Clinical examination may reveal findings compatible with diabetes, such as hepatomegaly, cataracts, and poor body condition. Poor glycemic control is reflected in the laboratory evaluation as elevated fructosamine levels and abnormal glucose curves.

Once a diabetic patient is identified as having persistent hyperglycemia, careful review of the history, clinical examination, and current therapeutic protocol may reveal possible causes or suggest a possible diagnostic work-up. A sequential approach to evaluating persistent hyperglycemia patients is warranted bearing in mind that problems related to diabetes management are the most frequent causes of persistent hyperglycemia. For this reason, it is important to completely rule out problems with the management protocol before beginning an extensive investigation to search for additional medical problems.

Patient history

It is important to determine whether some factor(s) related to the pet's home environment or daily habits might be responsible for the poor diabetes control. In people, glycemic control can be upset by stress or emotional strain as well as seemingly innocuous departures from the patient's ordinary routine, such as unusual exposure to sunlight or increased physical activity. Presumably, similar factors could affect diabetic control in dogs; so careful questioning of the pet's owner is warranted. Hunting or service dogs, for example, might experience increased insulin needs when working. Similarly, it is conceivable that a cat with a preference for a particular windowsill might absorb insulin more rapidly on sunny days. In addition to routine questions about appetite, water consumption, urinary and defaecation habits, and general attitude, the owner should be questioned about the diet, administration of non-prescribed medications or supplements, changes in the home environment or any unusual events. Owners often do not realize the importance of these factors and will not offer the information unless specifically asked.

Non-prescribed dietary changes, feeding excessive amounts of treats or table scraps, and some dietary supplements all have the potential to alter daily caloric intake. Some herbal medications have been associated with glycemic dysregulation in people and might have the same effects in animals. Self-

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prescribed medications or medications provided by another veterinarian, especially topical preparations, may not be seen as problematic by owners. Topical ocular or otic medications containing steroids may produce systemic effects in some dogs and antagonize diabetes regulation. Changes in the home environment or daily routine might also disrupt glucose control. Some events are clearly stressors on the patient, such as new pets or people in the household, a recent move to a new home, recent illness, or surgery. While it is important to consider any change in the patient's environment as potentially contributing to persistent hyperglycemia, it is equally important to resist placing too much emphasis on relatively minor changes unless all other causes of persistent hyperglycemia have been thoroughly investigated and ruled out.

Treatment protocol

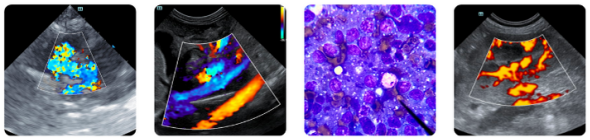
This entails evaluation of all aspects of therapy including the insulin protocol, diet therapy, and management of any concurrent illness. When evaluating the insulin protocol, it is important to establish that the animal is receiving insulin at the prescribed dose and that the injection is performed properly. The first step is to confirm that the insulin and syringes being used are the prescribed products. Mismatch between the insulin product and the syringe used to administer it (e.g. using 100 IU syringes to administer 40 IU insulin) is a relatively common error that can lead to profound problems with diabetes regulation. Use of non-prescribed, degraded or out-dated insulin can be potential causes for poor glycemic control and easily remedied. Once insulin type and syringes are ruled out as possible sources of errors, the owner's insulin handling and injection techniques should be evaluated. This can be accomplished by observing the owner draw up and inject the insulin dose. This can eliminate gross errors in insulin dosage, improper injection site selection (e.g., into adipose tissue), poor patient restraint, and related errors.

Glucose curve

If at this point, a cause for the persistent hyperglycemia has not been found, a metabolic basis for persistent hyperglycemia should be considered. Investigation of metabolic causes of persistent hyperglycemia begins with glucose curve, which will document the magnitude and duration of hyperglycemia over the course of the day. The traditional serial glucose curve is useful for monitoring blood glucose concentrations over time but recent studies have highlighted the low reproducibility of this technique, even when performed under ideal conditions. As the technique can yield vastly different results even when performed only 12-hrs apart under the exact same conditions, care must be taken not to place too much weight on a single glucose curve result. Glucose curves are usually performed in the hospital. However, techniques for teaching owners to generate at-home glucose curves in dogs have also been described. Blood samples should be obtained every 1-2 hours so that rapid changes in glucose will not go undetected. In most circumstances a portable glucometer is adequate, as several models have been shown to be accurate in dogs.

Insulin absorption

Delayed insulin absorption may lead to persistent hyperglycemia. Insulin absorption from a subcutaneous site in humans can vary as much as 50% from day-to-day, even if the same insulin, dose, and injection site are used. As alluded to earlier, insulin absorption and action in humans can also be affected by variations in countless factors associated with daily life, including physical exercise, body temperature, and emotional state. While there are few studies in dogs examining variables that alter insulin absorption and action, it is likely that there is a high degree of true day-to-day biologic variability as in humans. Biologic variability is distinct from the variability introduced by human error and the technology used for insulin administration and glucose measurement. Other potential causes of delayed



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insulin absorption include interference by insulin antibodies, which develop in response to exogenous insulin, and poor blood flow at the site of injection, which can occur when the injection is administered in adipose tissue. Anti-insulin antibodies have been detected in diabetic dogs but there is not convincing evidence that these antibodies interfere with insulin absorption.

Somogyi reaction

This is characterized as post-hypoglycemic hyperglycemia and is caused by excessive insulin dosage. The patient typically has an early hypoglycemic reaction followed by hyperglycemia the following morning. Factors playing a role in this are the insulin dose and the patient's counter-regulatory hormones. The solution entails insulin dosage reduction by 25-50% and administering insulin twice a day.

Insulin resistance

Insulin resistance is probably the most common metabolic cause of persistent hyperglycemia in dogs but is not a specific diagnosis. By its simplest definition, insulin resistance is an inadequate biologic response to either endogenous or exogenous insulin. Insulin resistance is usually a clinical diagnosis made on the basis of persistent hyperglycemia, an unusually high insulin requirement, and the presence of a condition associated with insulin resistance. Insulin resistance should be considered if persistent hyperglycemia exists despite an insulin dose >2.2 IU/kg is needed to control hyperglycemia. Common causes of insulin resistance include obesity, bacterial/fungal infection, and concurrent endocrinopathies. Additionally, ketosis, hyperlipidaemia, cardiac insufficiency, chronic pancreatitis, renal disease, hepatic insufficiency, and neoplasia can potentially lead to insulin resistance and poor glycemic control. Any condition that activates counter-regulatory hormones (cortisol, catecholamines, and glucagon), such as stress, trauma, major surgery, oestrus, and pregnancy, can induce an insulin resistant state. Insulin resistance is best treated by specific treatment of the underlying disorders.

Obesity

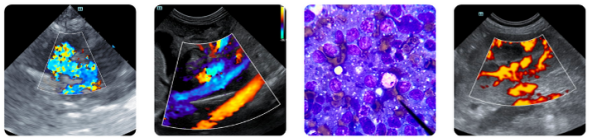
Obesity is probably the most common cause of mild to severe insulin resistance in dogs and has been shown to be associated with glucose intolerance. Obesity, hypertension, and insulin resistance commonly occur together in people with type 2 diabetes mellitus, but this metabolic complex is not well defined in veterinary patients. Insulin resistance due to obesity is reversible with sufficient weight loss and exercise.

Microbial infection

Secondary bacterial and fungal infections may cause persistent hyperglycemia in diabetic dogs. Infection may occur in any tissue but infections of the urinary tract, skin, intervertebral disc, cardiac valves, lungs, abdominal organs (especially the liver), and reproductive tract are most common in diabetic animals. Whenever possible, the organism should be identified by bacterial or fungal culture. Treatment with broad-spectrum antibiotics or antifungals should be initiated when an infection is suspected and treatment adjusted based on culture and sensitivity. Surgery may be required when an abscess has formed.

Hyperadrenocorticism

Hyperadrenocorticism is a common cause of persistent hyperglycemia in dogs. Glucocorticoids can exacerbate hyperglycemia and impair glucose control in diabetic dogs via the induction of insulin resistance in target tissues. Dogs with hyperadrenocorticism often require very large amounts of insulin to maintain reasonable control of glycaemia. The diagnosis is made using adrenal testing (ACTH



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stimulation test, low-dose-dexamethasone suppression test) with treatment options as for non-complicated hyperadrenocorticism.

Thyroid disorders

Hypothyroidism has been reported to be associated with insulin resistance. The pathophysiology underlying insulin resistance in hypothyroidism may result from the obesity that develops in affected dogs but elevated growth hormone secretion is also known to occur in hypothyroid dogs. Treatment involves normalizing thyroid function.

The information and recommendations provided are based on the images presented by the referring veterinarian/sonographer. No evaluation can be communicated regarding pathology that was not visible in the image/video clips provided.

Thank you for this referral. If the clinical or image interpretation does not parallel your findings or if I can be of any further assistance please contact me.

Remo Lobetti, BVSc, MMedVet (Med), PhD, Dipl. ECVIM (Internal Medicine)

info@sonopath.com