Case Summary

- Gidget is just one of those dogs, currently on the second medical records folder
- First seen when 8 months old, up to date on vaccines
- Previous episodes of going “floppy”
- Other veterinarian had suspected low blood sugar, recommended oral honey which worked
Case Summary

- Had some signs today, owner gave honey, this worked initially but then Gidget got worse
- Signs at presentation
  - Couldn't walk
  - Shaking
  - Gastroenteritis with bloody diarrhea
- Neuro exam normal, physical relatively normal as well
- Glucometer reading of 25 mg/dL

Case Summary

- Lab work shows hypoalbuminemia
- Leukon is unremarkable, no indications of significant inflammation or infection
- Cells are microcytic

Case Summary

- Liver values are mildly elevated, probably not significant
- Hypoalbuminemia could be from decreased production, increased loss or third spacing
- Microcytosis could indicate problems with iron usage
- Of the findings the most significant is marked, symptomatic hypoglycemia
Hypoglycemia

- First thing to rule out is lab error, though this is less likely in Gidget since the clinical signs fit
- In older animals neoplasia (insulinoma or non-pancreatic tumors) would be a major consideration
- In younger animals differentials such as liver dysfunction, Addison's or severe infections (sepsis) would be more likely.
- In toy breeds hypoglycemia is not uncommon
- Rare causes are metabolic disorders (GSD)

If hypoglycemia is found, a battery of tests is indicated to search for an underlying reason
- CBC, chemistry panel, UA
- Possibly imaging
- Possibly liver function assessment
- Possible ACTH stimulation test
- Toy breed hypoglycemia is a diagnosis of exclusion

Porto-Systemic Shunting

- Shunts can be single (congenital) or multiple (acquired)
- Shunting can also occur with portal vein hypoplasia (microvascular dysplasia)
- Valid differential in this patient
Porto-Systemic Shunting

• With Porto Systemic Vascular Anomalies, shunts can be intra- or extrahepatic

Images courtesy Dr. Cindy Shmon

Portal vein
Vena cava

Images courtesy Dr. Cindy Shmon
Porto-Systemic Shunting

- Shunts can present with various clinical signs
  - Runt of the litter
  - Neurologic signs
  - Urinary tract signs
  - Lab work abnormalities

Case Summary

- Hypoglycemia, hypoalbuminemia and microcytosis could all point to a liver problem, especially a porto-systemic shunt
- Bile acid testing was normal, both pre and post-prandial

Case Summary

- In real life, although testing did not point to a shunt, the clinicians did not believe it and decided to run an ammonia tolerance test as well
Major Teaching Point

• Allow reality to dispel your preconceived notions
  – Bile acids are very sensitive and specific, running an ammonia tolerance test was unnecessary

Testing Liver Function

• Bile Acids
  – High sensitivity for hepatic disease
  – Cannot differentiate between the various hepatic issues present
  – With shunts, bile acid values tend to be very high, especially post prandial
  – Values can be high in Maltese that are normal

Testing Liver Function

• Ammonia testing
  – Sample handling an issue
  – In house analyzers can run this value
  – Fasting ammonia more sensitive than fasting bile acids
  – Elevations are associated with significant shunting
  – False positives in some young Wolfhounds
Case Summary

• Generally doing well after hypoglycemia incident
• Developed bilateral cataracts with uveitis
• Treated with topical prednisolone drops 1%

Minor Teaching Point

• Topical meds can be absorbed very effectively
• Pred eye drops are usually 1%, that is 10mg/ml, with 20 drops per bottle that means 0.5 mg/drop.
• In small patients a significant amount of drug can be absorbed

Case Summary

• Gidget next presents for ADR
• Not eating well for 3 days
• In heat 4 weeks ago
• Went to ER where they found that she was febrile and dehydrate
Case Summary

- Stabilized on fluids and antibiotics
- Seizures later on, at that time glucose severely decreased
- Major differential is sepsis
- Treated symptomatically with dextrose infusions
- Lab tests are interesting

Case Summary

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<td>NRBC /100 WBC's</td>
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<table>
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<td>Monos</td>
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Major Teaching Point

- Normal is only in “normal” animals
- In this case the CBC is normal, but it shouldn’t be, animal is hypoglycemic and has a severe uterine infection
- Issue arises with other situations, i.e. calcium and PTH values in hypercalcemic dogs
Case Summary

- ACTH stimulation test run, < 20 nmol/L pre and post.
- Diagnostic for hypoadrenocorticism
- However Na, K normal so it is an “atypical” case or also called secondary Addison's

Normal HPA Axis

**Hypothalamus**

CRH → **Anterior Pituitary**

ACTH → **Adrenal Gland**

Adrenal Gland Structure

- **Cortex**
  - Zona Glomerulosa (mineralocorticoid)
  - Zona Fasciculata (corticosteroid)
  - Zona Reticularis (androgens)
  - Medulla
- Catecholamines
Hypoadrenocorticism

- Usually caused by an autoimmune destruction of the adrenal glands, primary form
- Can also be caused by insufficient CRH or ACTH production, in that case only glucocorticoid deficient
- Breed and gender related differences in incidence of the disease
  - Increased risk in females
  - Standard Poodles, Portuguese Water Dogs, West Highland White Terriers are some of the breeds predisposed

Hypoadrenocorticism

- Clinical signs are varied
  - Glucocorticoid deficiency
    - Can cause many of the GI signs including hemorrhage
    - Weakness can develop as well as neurologic signs from low blood sugar (decreased glucose production of the liver and insulin receptors are unopposed)
    - General apathy
    - Hyponatremia because of unopposed ADH release
    - Hypotension because of decreased vascular catecholamine receptors and therefore ability to respond to sympathetic nervous system stimulation

“Atypical” Hypoadrenocorticism

- Nothing on lab work says “Addison’s”, except possibly a lack of stress response on the CBC
- Sometimes only vague non-specific problems
“Atypical” Hypoadrenocorticism

• Duke:
  – 3 year old male Labrador Retriever
  – Ear cleaning and shot of methylprednisolone (very rambunctious when cleaning, quite an ordeal for everyone)
  – After injection dog collapses, blood vomiting and diarrhea, drug reaction suspected
  – On lab work no stress leukogram, blood sugar low, no response to ACTH

“Atypical” Hypoadrenocorticism

• Dolly
  – 4 year old female toy poodle
  – Had all teeth removed because she was a land shark
  – Came in for seizing
  – On lab work low blood sugar and no stress leukogram
  – No response to ACTH

Hypoadrenocorticism

• Mineralocorticoid deficiency = “Typical” Addison’s
  – Without aldosterone less potassium is excreted and sodium is wasted
  – Sodium makes water loss increase as well
Mineralocorticoid deficiency
- Hyperkalemia
  - Typical EKG changes
  - Causes bradycardia
  - As extracellular potassium increases the cell no longer is excitable (resting membrane potential reaches threshold potential)

Mineralocorticoid deficiency
- Hyponatremia
  - Hypovolemia
  - Hypoperfusion
  - Prerenal azotemia that can progress to renal failure if left untreated
  - Shock with bradycardia, should make you suspicious of Addison’s disease
Hypoadrenocorticism: Common Clinical Signs

- Lethargy, weakness
- Vomiting, diarrhea, melena
- Hypoperfusion
- Hypotension
- Hypothermia
- Shock with inappropriate bradycardia
- Dehydration

Hypoadrenocorticism: Uncommon Clinical Signs

- Neurologic dysfunction: can be related to hypoglycemia including seizures
- Megaesophagus: rare, can be significant problem
Hypoadrenocorticism: Routine Lab Results

• Anemia
  – Decreased EPO without ACTH
  – Increased loss into GI tract
  – Anemia of chronic disease

• Hypoalbuminemia
  – Hemorrhage
  – PLE
  – Decreased hepatic synthesis

Hypoadrenocorticism: Routine Lab Results

• Hyperkalemia and hyponatremia and/or decreases sodium potassium ratio
  – Not specific for Addison’s
  – Can be seen with
    • Pseudoaddisons (Whipworm associated diarrhea)
    • Renal disease
    • Effusions
Hypoadrenocorticism: Routine Lab Results

- Liver enzyme elevations
  - Poor perfusion
  - Poor GI barrier function?
- Pre-renal azotemia, however no concentrating ability, can mimic renal failure
- Hypercalcemia

Hypoadrenocorticism: Imaging

- Radiographs
  - Microcardia
  - Small liver
- Ultrasound
  - Small adrenal glands

Hypoadrenocorticism: Diagnosis

- ACTH stimulation test
  - Synthetic preferable to gel
  - Use 5 μg/kg i.v. or one 0.25 mg vial per dog, repeat sample in 1 hour
Hypoadrenocorticism: Treatment

- **Emergency**
  - Fluids, fluids, fluids
    - 0.9% NaCl preferable, however other fluids such as Ringers Lactate also work, though they contain some potassium
    - If patient unstable give shock doses (40-80 ml/kg/hour) initially, also if hyperkalemia is present or suspected

- **Emergency**
  - Hyperkalemia Tx
    - Fluids, fluids, fluids
    - Sodium bicarbonate 1-2 mEq/kg slow i.v.
    - Insulin/dextrose (0.5 units/kg of regular insulin i.v. together with dextrose bolus)
    - Calcium i.v. in severe cases (calcium gluconate 10% solution, 0.5 to 1.0 ml/kg given i.v. over at least 10 minutes with ECG monitoring
    - Atropine???

- **Emergency**
  - Glucocorticoid supplementation
    - Dexamethasone ideal, does not interfere with ACTH stimulation test and acts fast
    - 0.2 to 0.4 mg/kg i.v.
    - After ACTH stimulation test done other products including hydrocortisone (has glucocorticoid and strong mineralocorticoid activity) can be used
      - 2 mg/kg i.v. q 6 hours or 0.3 mg/kg/hour as CRI
Hypoadrenocorticism: Treatment

• Chronic management
  – Glucocorticoid supplementation
    • May not be necessary if fludrocortisone is used
    • Generally use prednisone
    • Increase dose if stress or illness is occurring (0.5 mg/kg/day), otherwise physiologic doses of 0.2 mg/kg/day should be adequate

• Chronic management
  – Mineralocorticoid supplementation
    – Fludrocortisone
      • 0.01 to 0.02 mg/kg initial dose
      • Check electrolytes every 7 to 14 days till stabilized
      • With time dose may need to be increased

• Chronic management
  – Mineralocorticoid supplementation
    – DOCP
      • Injections every 25 days initially
      • Start with 2.2 mg/kg
      • Check electrolytes 12 and 25 days after injection
        – If abnormal day 12 increase dose 5 to 10%
        – If normal at 12, but abnormal at 25 decrease time between injections
        – If normal at 25 repeatedly may be able to decrease dosing frequency
Hypoadrenocorticism: Prognosis

- Generally good, survival time of around 5 years
- Expense associated with therapy and frequent monitoring
- If the patients survive the initial episode they usually do well
  - Myelinolysis can occur with depression, weakness, ataxia, and spastic quadraparesis because of too rapid correction of hyponatremia by fluid therapy.
  - The recommendation is to correct hyponatremia <12 mEq/L/day

Thank You!

To complete the evaluation, please go to the following website:
http://www.keysurvey.com/survey/416584/1a3f/
Thank you for your participation!