The Geriatric Collapsed Ferret: More than Insulinoma

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Abstract

Clinicians are often presented older ferrets that are ataxic with intermittent collapsing episodes, exercise intolerance, changes in appetite, and muscle mass loss. The immediate jump to a diagnosis of insulinoma unfortunately happens as a quick test with a glucometer measures a blood glucose under 70-90. Although there has been more testing of these glucometers to show that they are often not accurate, and no consideration is made towards when, what and how much the ferret ate, the ferret is placed on prednisone and sent home. Sometimes bloodwork is sent out, which may yield a more accurate glucose if it was processed quickly, and radiographs were taken which were inconclusive other than noting splenomegaly and possibly cardiomegaly. The ferret does not respond to the prednisone and signs may even worsen.

This lecture will explore the differentials for a collapsing ferret which include further diagnostics and imaging. Dental, cardiac, renal, musculoskeletal diseases and other types of neoplasia may be the root cause of the clinical signs. Islet cell disease can be correctly diagnosed, but not on one glucometer reading as normal ferret physiology fluctuates blood glucose differently than dogs and cats. Case reports illustrating more common reasons for a geriatric, collapsing ferret will be discussed.

Outline

I. Learning objectives

A. Understanding basic ferret anatomy and physiology as relates to metabolism and disease
B. Develop an appropriate differential diagnoses list
C. Identify and obtain appropriate diagnostics, including imaging
D. Immediate treatment of the ferret
E. Develop a diagnosis-based treatment plan, including client education

II. Important anatomy and physiology

A. Species considerations

1. Domesticated species (*Mustela putorius furo*)
2. Single global blood type
3. No true wild "fitch" ferrets

B. General characteristics of the gastrointestinal tract

1. Simple, relatively short gastrointestinal tract.
2. No cecum
3. Rapid transit time – 1.75-3 hours

C. Nutrition

1. High protein, high fat diet

    - 40–45% protein
    - 30–40% fat

2. Limited fiber digestion (<4%)
3. Avoid carbohydrate-rich diets
4. Feeding considerations

    - Feed diets supported by feeding trials (avoid boutique diets)
    - Raw diets: risk of pathogens (e.g., Campylobacter, Salmonella)
    - Whole prey: domestic prey higher in fat/carbohydrates than wild prey

D. Gastrointestinal tract

1. Gastric physiology

    a. Spontaneous acid and proteolytic enzyme secretion
    b. Stimulated by histamine and vagal input
    c. Innervation
        i. Parasympathetic fibers of vagus
        ii. Sympathetic via celiacomesenteric plexus
    d. Histamine effects
        i. Stimulates acid secretion
        ii. Low endogenous histamine levels
        iii. Limited histamine-forming enzyme activity (L-histidine decarboxylase)
        iv. Histamine H2 receptor antagonists abolish acid secretion response to exogenous histamine (pentagastrin)
        v. Atropine only reduces response 30%

2. Intestinal anatomy and function
    1. Small intestine
        a. Duodenum (3 sections)
        b. Major duodenal papilla (~3 cm from pylorus)
        c. Minor papilla may be absent
        d. Jejunum and ileum indistinguishable (jejunoileum)
    2. Innervation
        a. Vagus nerve
        b. Sympathetic trunk (celiac, cranial mesenteric plexus)

3. Colon

    a. Tubular glands and goblet cells
    b. Sulfated mucosubstances (similar to humans)

4. Motility

    a. Similar to canine ileum
    b. Vagus-dependent
    c. Mediated by cholinergic and noncholinergic pathways
    d. Sacral innervation is excitatory
        a. Retroperistalsis contributes to vomiting
        b. Ferrets are used as emetic models

5. Pancreas

6. Gallbladder and GI integration
        a. Cholecystokinin (CCK) function
            1. Stimulates gallbladder contraction
            2. Inhibits gastric emptying

3. Increases intestinal and colonic motility

b. Overall GI function
    1. Highly motile, secretory system
    2. Designed for rapid transit
    3. Requires highly digestible food

III. Differentials for a collapsed ferret

A. Hypoglycemia

1. Islet cell endocrinopathy (insulinoma)
2. Inappetence/anorexia
    a. Systemic illness
    b. Dental disease
    c. Pain
    d. GI disease (gastroenteritis, malabsorption, inflammatory bowel disease, etc.
    e. Neoplasia
3. Poor diet or feeding practices

    a. I inappropriate diet
    b. Feeding irregularities, competition, stress at the food bowl

B. Cardiac disease

1. Cardiomyopathy (dilated, hypertrophic, restrictive)
2. Arrhythmias
3. Heart block
4. Congestive heart failure

C. Other causes

1. L-carnitine deficiency
2. Pain
    1. Orthopedic
        1. Spinal
        2. Osteoarthritis
    2. GI
    3. Dental
    4. Neoplasia

IV. Clinical evaluation: symptoms versus etiology

A. Key history questions

1. Diet and feeding schedule
    1. What diet is the ferret eating?
    2. When was the last meal?
2. Access to food?
    1. Is food always available?
    2. Can the ferret get to the food easily?
3. Clinical signs?
    1. Does the ferret paw at its mouth?
    2. Hypersalivate?
    3. Show hindquarter weakness prior to going "flat ferret/speed bump"?
    4. Show any signs of nausea or pain?
    5. Show inactivity, lack of playing, other limitations?

B. Measuring blood glucose

1. One low blood sugar result on a collapsed ferret in the exam room should not be a definitive reason to diagnose "insulinoma"
2. Ferret normal can be 66-69 mg/dL. Lower than dog/cat

3. In clinic blood glucose analyzers – immediate reading
4. Greenacre: AEMV 2011

- Considered most ferrets 66-69 mg/dL on regular lab
- Every human glucometer indicated severe hypoglycemia
- Alpha Trac C overestimated by 15% but was closest
- Alpha Trac F, PBGM One Touch, and AccuChek poor correlation
  C. Alpha Trak 2 – on C was fairly good, at least for trends
  D. Alpha Trak 3 – so far hard to correlate
  E. Send out: need to spin immediately, separate serum

V. Islet cell endocrinopathy

A. Referrals
B. Signalment: most are older ferrets
C. History

1. Collapsing episodes
    a. Most not directly related to meals

b. Many have pattern, often connected to sleeping or inactivity

2. Many have concurrent diseases and medical treatments
3. Collapsed or lays around (flat ferret, speed bump, pelt)
4. May walk a little, play a little then collapses again
5. Sometimes hypersalivation
6. Sometimes pawing at the mouth, bruxism
7. Sometimes gagging or tremors
8. May/may not be progressive - frequency

D. True testing

1. Feed the ferret
2. Time 2 hours, 3 hours, 4 hours
3. Glucose and insulin draws
4. When glucose drops below 60 mg/dL, use serum for insulin -University of Tennessee Endocrinology Laboratory -Validated ferret insulin assay
5. *NOTE*: If the blood glucose is below 50 mg/dL at 2 hrs: high suspicion
6. If blood glucose is below 40 mg/dL at 3 hrs – likely
7. If blood glucose is over 70 mg/dL at 4 hours – unlikely
8. Interpretation
    1. Insulin
        a. Elevated or "within normal limits"
        b. Compare with low blood glucose.
    2. Normal blood glucose at 2 or 3 hours, but insulin elevated – suspicious
    3. If BG less than 50 mg/dL at 2 hrs and high insulin – likely

E. Full workup: assess other organs

1. Many have concurrent GI, liver, kidney, other endocrinopathies
2. Most have some degree of adrenal disease, should have deslorelin implant
3. CBC, chemistries, radiographs, abdominal ultrasound (may find tumors)
4. Imaging: large nodules may be seen with ultrasound, sometimes evidence of gastritis/gastroenteritis, gallstones, changes in liver.

F. Surgery: If ferret good candidate, remove neoplastic islet cell masses
    1. Usually peel out unless adherent adjacent organs, invagination, neovascularization, metastasis
    2. May not be able to find actual nodules
    3. Removal of part of the pancreas? Diffuse changes can metastasize into the liver.
        a. Create diabetes mellitus, exocrine pancreas insufficiency
    4. IV fluids during/post surgery should contain glucose
    5. A rebound insulin surge may occur so monitor for several days post-op. May use dexamethasone in fluids post op

G. Chemotherapy?

1. Doxorubicin 1 mg/kg IV two to three treatments, 2-3 weeks apart has helped slow progression
2. In some, virtual elimination of symptoms for months
3. May have cardiotoxic effects: closely monitor with ECG and echocardiography. Do not use if there is concurrent cardiac disease

H. Supportive care

1. Recognize nausea, pain
2. Famotidine at 1-2 mg/ferret q 24h
3. Maropitant helps with gut pain (?): 1 mg/kg PO q 24h
4. Buprenorphine: Ethiqa: 0.6 mg/kg SC q 72h
5. Gabapentin: 3-10 mg/kg PO q8-12h prn
6. Make sure eats every 4-6 hours
7. SC fluids prn

I. Medical therapy

1. Diazoxide PO

   a. Published doses seem too low for efficacy in my experience
   b. Start at 10 mg/kg PO q 12h
   c. Can increase to 30 mg/kg PO q 12h
   d. Depends on compounding formulation for absorption?

2. Corticosteroid PO

   a. Dexamethasone 0.5-1 mg/kg PO q12h
   b. Prednisone 0.25-2 mg/kg PO q12h
      i. Can be used with diazoxide up to 2 mg/kg/day
   c. Side effects: fatty liver, iatrogenic Cushing's disease, GI bleeding, hyperactivity, hypertension, alopecia
   d. Contraindicated with cardiomyopathy, renal and preexisting liver disease.
   e. Monitor: CBC, Chems, Imaging, fecal occult blood, cytology, BP, UA with specific gravity

3. Apocaps® (large dog size)
   a. Nutraceutical
   b. One-half capsule per day per ferret
   c. Anecdotal action against solid tumors
   d. Can't hurt – inhibits neovascularization
   e. Contains antioxidants
   f. Available on Amazon

VI. Cardiac insufficiency

A. Cardiac conditions

1. Cardiomyopathy: dilated, hypertrophic, restrictive
2. Cardiomegaly
3. Hypotension/poor perfusion
4. Pulmonary edema
5. Ascites
6. Arrhythmias – Grade 2 or 3 heart block, atrial fibrillation, etc.

B. Cardiomyopathy

1. Clinical signs

    a. Weakness, collapse
    b. Arrhythmias
    c. Dyspnea
    d. Poor perfusion

2. Diagnostics

    a. ECG
    b. Echocardiography
    c. Radiographs
    d. Blood pressure measurement

3. Treatment

    a. Pimobendan
    b. ACE inhibitors (enalapril, benazepril)
    c. Diuretics (furosemide)
    d. Terbutaline for heart block
    e. Pacemaker for complete heart block

4. Emergency cardiac management

    a. Acute cardiac arrest (CPR may be effective)

    b. Stabilize before major diagnostics

        - Heat
        - Oxygen
        - Get IV access as soon as possible
        - Can do SC fluids while getting IV

c. Dobutamine

- 0.01 mg/kg slow bolus IV to increase HR, stabilize rhythm
- May need constant rate infusion for 24-72 hours

VII. Additional differentials

A. L-carnitine deficiency
   a. Older ferrets
   b. Metabolism abnormality liked to skeletal muscle weakness
   c. Hindquarters paresis, collapse
   d. Supplement with L-carnitine
B. Pain
   a. Orthopedic
      i. Spinal
      ii. Osteoarthritis
   b. Dental disease, especially fractured canines, periodontal
   c. Neoplasia
      i. GI
      ii. Spleen, splenomegaly
      iii. Chordoma
   d. GI disease
   e. Urolithiasis
   f. Gallstones
   g. Urolithiasis

VIII. Case-based applications

A. Case 1: Misdiagnosed insulinoma → cardiac disease
B. Case 2: Dilated cardiomyopathy with arrhythmia
C. Case 3: Severe arrhythmia with cardiomyopathy
D. Case 4: Cardiac disease misdiagnosed as insulinoma

IX. Conclusion

A. Perform thorough diagnostic evaluations
B. Islet Cell Endocrinopathy
   a. Confirm with controlled testing
   b. Recognize limitations of glucometers
   c. Address concurrent disease

C. Consider major differentials
    a. Insulinoma
    b. Cardiac disease
    c. L-carnitine metabolism disruption
    d. Pain

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C. Reference text

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