Pathology of the Domestic Ferret

Matti Kiupel
Islet Cell Tumor

- Most common ferret tumor
- Clinical signs: hypoglycemia, lethargy, stupor, ptyalism, ataxia, hindlimb paresis, salivation, seizures, coma, death
- Inappropriate secretion of insulin resulting in “trances”
Islet Cell Tumor

- Most tumors secret insulin
- Non-functional islet cell tumors common in old ferrets
- Benign progression, metastasis is rare in contrast to dogs
• Diagnosis: history, clinical signs, blood glucose test
  - 60-80 g/dl – questionable, <60 positive
• Insulin testing generally not necessary
• Histology does not correlate with behavior
• Watch out for pancreatic nodular hyperplasia!
Islet Cell Tumor
Diabetes mellitus

- Most commonly seen following insulinoma surgery
- May be seen concomitantly with insulinoma
- May follow long-term prednisone administration
- Very difficult to regulate, require insulin 4x day
- Insulin levels over 600 = poor prognosis
Adrenal-associated Endocrinopathy

- Extremely common
- Due to hyperestrogenism, not Cushings!!!
- Proliferative lesions have identical clinical signs

- hyperplasia
- adenoma
- carcinoma
Adrenal-associated Endocrinopathy

On the adrenal cortical cells are LH receptors that are activated after neutering by high LH levels.
Adrenal-associated Endocrinopathy

Non-gonadectomized

Gonadectomized

Hypothalamus

CRH

GnRH

Pituitary

Inhibit

ACTH

LH

Adrenal

Gonads

Sex steroids

Glucocorticoids
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy

Normal adrenal gland

Enlarged adrenal gland
Adrenal-associated Endocrinopathy

- Clinical signs
  - Bilateral symmetrical truncal alopecia
  - Vulvar swelling in spayed females
  - Return to intact sexual behavior
  - Dysuria in males
Adrenal-associated Endocrinopathy

bilateral symmetric alopecia
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy
Adrenal-associated Endocrinopathy

- Surgical treatment of choice
  - Adrenalectomy
  - Cryosurgery
  - Medical treatment
Adrenalcortical Carcinoma with Myxoid Differentiation

- origin of myxoid cells: unknown, most likely adrenal cortex, zona reticularis, differentiation into mucin producing cells
  - degeneration of neoplastic cells, stroma?, ectopic rests of gonadal stromal granulosa or Sertoli cells?!
Adrenalcortical Carcinoma with Myxoid Differentiation

- Surgical treatment of choice
  - Adrenalectomy
  - Cryosurgery
  - Medical treatment
Other Adrenal Neoplasms

Adrenal Teratoma
Subcutaneous Tumors of the Ventral Abdomen with Histologic Features of Adrenocortical Tumors

Islands of polygonal cells, interlacing streams of spindle cells
Granular to microvacuolated cytoplasm, low mitotic index
Subcutaneous Tumors of the Ventral Abdomen with Histologic Features of Adrenocortical Tumors

- Inhibin
- GFAP
- Smooth muscle actin
Subcutaneous Tumors of the Ventral Abdomen with Histologic Features of Adrenocortical Tumors

intermediate filaments

clear vacuoles
• Commonly seen, especially in older ferrets
• Stereotypical response to chronic smoldering inflammation
• Enlarged up to 10 cm, prone to rupture
• Mostly diffusely enlarged, sometimes nodular (neoplasm)
Splenomegaly

- Less than 5% are neoplastic, 95% are benign EMH
- Marked variation in cell size and populations
- Sometimes coagulative necrosis
- Splenectomy is treatment of choice
Malignant Lymphoma (Lymphosarcoma)

- Most common malignancy in ferrets:
  - 1-2 years - Juvenile (Lymphoblastic) - visceral distribution
  - 2-7 years - Lymphocytic - lymph node distribution
  - 2-7 years - Immunoblastic polymorphous
**Malignant Lymphoma**

- **Juvenile (Lymphoblastic) Lymphoma**

- Most commonly seen in ferrets under 2 years
- Primarily viscera: thymus, liver, spleen
- Neoplastic cells immature
- Rapid progression time
Malignant Lymphoma

- Juvenile (Lymphoblastic) Lymphoma
Malignant Lymphoma

- Adult (Lymphocytic) Lymphoma

- Most commonly seen in ferrets older than 2 years
- Primarily affects lymph nodes
- Neoplastic cells mature well-differentiated
- Long progression time, lethargy, weight loss, anorexia
Malignant Lymphoma

- Adult (Lymphocytic) Lymphoma
Malignant Lymphoma

• Adult (Immunoblastic polymorphous) Lymphoma

• Clinical signs and clinico-pathologic changes most commonly reflect the organs affected (but not always!)
Cutaneous Lymphoma

- May be seen in any age, most commonly affects feet
- Slow progression
- Surgical excision of cutaneous lesion prolongs lifespan
- No apparent response to topical or systemic chemotherapy
Malignant Lymphoma

Treatment

• Poor prognosis except in primary cutaneous cases
• Chemotherapy available, but less than 10% respond
Malignant Lymphoma

Cytology and Immunophenotyping
Actinomycosis

- Very uncommon chronic infection
- Probably traumatically induced
- Refractory to antibiotic treatment
Aleutian Disease

- Primarily a disease of mink
- Identified in mink in 1940’s, ferrets in 1960’s
- Identified as a parvovirus in 1980
- Wide range of mustelid hosts
- Receives its name from color-diluted Aleutian mink
Aleutian Disease

- Resurgent disease in ferrets – new strain?
- New outbreaks have almost 100% morbidity and mortality
- Insidious disease with long latency, death in 2-3 years
- Classic Disease: glomerulonephritis, disseminated vasculitis, splenomegaly, coagulation defects, hematuria, hypergammaglobulinemia, cachexia, gastric ulcers
Aleutian Disease

- Transmission
  - Horizontal
  - Vertical
- Factors impacting transmission
  - Genetic makeup
  - Environmental factors
  - Age
  - Viral strain
    - ADV-F
    - ADV-Utah
    - ADV-G
Laboratory Findings
- Gammaglobulin >20% TP
- (TP >7.5 suspicious)
- Anemia
- Variable leukocytosis
  - Lymphocytosis
- Thrombocytopenia

Clinical Signs
- Three types of infection
  - Progressive AD
  - Persistent Non-Progressive
  - Non-Progressive
- Clinical signs only seen in progressive infections
Aleutian Disease

Pathogenesis

• Innocuous parvovirus resulting in deranged immune response
• Antiviral response results in formation of abundant non-neutralizing antibodies
• Persistence of viral antigen in body results in hyperfunction of immune system with resulting hypergammaglobulinemia and “lack of focus” when dealing with other viral/bacterial infections
Aleutian Disease

- Antigen antibody complexes are formed in large numbers which are deposited in vascular basement membranes throughout body
- Widespread vasculitis
- Glomerulonephritis
- Interstitial pneumonia
Aleutian Disease

- Histopathology the most definitive diagnosis of progressive infection
- Plasmacytic infiltrates in multiple organs
- Look at kidneys, liver, and spinal cord in paretic ferrets
Aleutian Disease
Aleutian Disease
Testing

- Serologic tests are most commonly used
- Cost-effective
- Knowledge of antibody response is important in interpreting tests
- Counter-immuno-electrophoresis (CIEP)
- ELISA
- Polymerase chain reaction (PCR)
- IFA, IHC
- Histology

Aleutian Disease
Aleutian Disease

“Antibody timeline”

- IgM – 6-60d, peak 12-15
- IgG – 12d+
- IgA – 60d+

IgG represents the majority of detectable Ab
Aleutian Disease

ELISA testing

- Available for last 24 months
- Blood or saliva testing
- Saliva tests measures IgA – miss early infections?
- Blood testing has fewer false negatives
- Data not published for review
Aleutian Disease

PCR Testing

- Polymerase chain reaction
- Tests for viral-specific DNA in tissue, feces, serum, etc.
- Limited availability, but very specific
Aleutian Disease

Prevention

• Prolonged survival in moist conditions
• Parvoviruses are susceptible to a number of cleaning agents
• Require negative CIEP tests 3-4 weeks prior to shows and gatherings