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A 1-year-old female ferret was presented with an acute history of severe respiratory distress. Abnormal clinical signs noted during the initial physical examination were hypothermia, dehydration, pale mucous membranes, tachypnea, and severe dyspnea. Thoracic radiographs revealed pleural effusion, an enlarged cardiac silhouette, and areas of lung consolidation. Both blood and thoracic fluid were hyperproteinemic and hypergammaglobulinemic. Antibiotic, corticosteroid, and diuretic supportive treatment provided temporary improvement. After the initial positive response to treatment, the ferret’s condition progressively deteriorated until the owners decided to euthanize the patient 15 days after initial presentation. Gross necropsy results revealed 5 mL of serosanguinous fluid within the thoracic cavity, cardiomegaly, and consolidated lungs that had a patchy, pale golden tissue pattern. The histologic diagnosis was endogenous lipid pneumonia. Findings suggest that endogenous lipid pneumonia can be associated with severe respiratory disease in ferrets. Copyright 2011 Elsevier Inc. All rights reserved.

Key words: disease; endogenous lipid pneumonia; ferret; Mustela putorius furo; respiratory

Lipid pneumonia is a pulmonary disease characterized by the accumulation of foamy macrophages in the pulmonary parenchyma; it is classified into 2 major groups depending on whether the oil/fat found in the respiratory tract has an endogenous (idiopathic, with accumulation of lipid material within the alveoli) or exogenous (aspiration, with accumulation of lipid material within alveolar spaces and interstitium) source. Endogenous lipid pneumonia has been reported in rats, mice, cats, dogs, raccoons, and opossums, with single reports in a llama, brown bear, genet, and a black-footed ferret. In most cases the underlying etiologic cause of endogenous lipid pneumonia has been classified as idiopathic, but can be associated with bacterial or parasitic infections, or the result of airway obstruction by exudative fluid/cellular debris, bronchoconstriction, tumors, or anomalous bronchi. Endogenous lipid pneumonia has been rarely reported in domestic ferrets (Mustela putorius furo), but appears to be a minor and common histologic finding at necropsy for many conditions that contribute to these animal’s deaths (Carles Juan-Sallés, DVM, Dip. ACVP, July 2007, personal communication).
Lipid pneumonia is considered a rare pulmonary disease in humans; this is in part because there is no classical radiographic appearance or clinical signs associated with the disease and it is therefore able to imitate other lung diseases. In domestic ferrets, as in other animal species, most cases of endogenous lipid pneumonia do not appear to have any clinical significance.

**Case Report**

A 1-year-old, female domestic ferret weighing 693 g was presented depressed, weak, and with an acute onset of respiratory distress. The respiratory condition was first noticed by the owners 12 to 18 hours before presentation, and they were not sure if the animal had been eating or drinking at that time.

The ferret was kept in a house along with other ferrets, cats, dogs, raccoons, prairie dogs, gerbils, rabbits, and birds. It had been purchased at 4 months of age with another 4-month-old male ferret. Both were surgically sterilized, born in The Netherlands, and vaccinated against rabies. The young male died at the age of 6.5 months and was diagnosed through a postmortem examination with ferret systemic coronaviral disease. The young female had a history of multiple illnesses post purchase, including coccidiosis, giardiasis, nematodiasis, chronic cough, and mesenteric lymphadenopathy. A serologic test for Aleutian disease (Quickcheck ADV; Avecon Diagnostics, Bath, PA USA), performed when the animal was 7 months of age, was negative. The cough started at the time of purchase and improved only after treatment that included corticosteroid, antibiotic, and bronchodilator therapy. According to the owner, this ferret had a poor appetite and was never healthy compared with the rest of the colony.

On physical examination the patient was tachypneic (75 breaths/minute) and exhibited a rapid shallow breathing pattern. Mild dehydration (6%-8%) and pale mucous membranes were also noted. Rectal temperature was 36.5°C (97.7°F) (reference range, 37.8°C-40°C; 100.0°F-104.0°F), and thoracic auscultation revealed increased respiratory noises and muffled heart sounds. The remainder of the physical examination was unremarkable. A lateral thoracic radiograph taken without the use of anesthesia or sedation revealed retraction of lung borders from the spine and diaphragm, pleural effusion, enlarged heart silhouette, and areas of pulmonary consolidation (Fig 1). The ferret was placed in an oxygen cage for stabilization before further diagnostic tests were performed. After 10 minutes, a plane of light anesthesia was induced with isoflurane in combination with oxygen to facilitate diagnostic sample collection. Blood was collected from the jugular vein and submitted for a complete blood count and plasma chemistry panel. Thoracocentesis was performed, and 1.5 mL of serosanguinous fluid was collected. The ferret recovered uneventfully and was subsequently treated with furosemide (2 mg/kg, intramuscular, Furosemida 20 mg/2 mL solution injectable; CDM Lavoisier, Paris, France) and amoxicillin/clavulanate (15 mg/kg, subcutaneous, Clamoxyl injectable; Pfizer Animal Health, Madrid, Spain). The animal remained in an oxygenated critical care unit overnight.

The following morning the ferret had improved, with a respiratory rate that had been reduced to 50 breaths/minute. A serologic test for Aleutian disease was negative (Quickcheck ADV). Abnormal results of the complete blood count and plasma chemistry panel were an increased total protein (8.5 g/dL; reference range, 5.3-7.2 g/dL), increased urea nitrogen (54 mg/dL; reference range, 12-43 mg/dL), decreased glucose (51 mg/dL; reference range, 64-136 mg/dL), and increased white blood cell count (14,500/mL; reference range, 5,100-12,600/mL). Protein electrophoresis showed increased globulins (6.5 g/dL; reference range, 2.2-3.2 g/dL), with γ-globulins representing 41.4% of total proteins and an albumin:globulin ratio of 0.23 (reference range, 1.0-1.6). Microscopic analysis of the thoracic fluid revealed mainly erythrocytes; total protein 3.8 g/dL and protein electrophoresis showed the same pattern obtained for serum proteins (γ-globulins represented 42.3% of total proteins). Based on clinical signs, hypergammaglobulinemia, and history, a prelimi-

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**Figure 1.** Right lateral radiograph of a ferret with severe dyspnea due to endogenous lipid pneumonia. Note the enlarged cardiac silhouette, pleural effusion, and retraction of lung borders.
nary diagnosis of ferret systemic coronaviral disease was made and the ferret was discharged on a treat-
ment protocol of amoxicillin/clavulanate (15 mg/
kilogram, orally, twice a day), furosemide (2 mg/
kilogram, orally, twice a day, Seguril comprimidos; Aventis Pharma, Madrid, Spain), and prednisolone (2 mg/
kilogram, orally, twice a day, Estilona gotas; Sonphar SL, Barcelona, Spain). Instructions to keep the animal isolated from the rest of the colony were declined by the owners.

Seven days later the ferret represented with mild lethargy, but otherwise showed significant clinical improvement. On physical examination and auscultation, no abnormalities were noted with the heart and lungs and the patient’s respiratory rate was 35 breaths/minute. The furosemide dose was reduced to 1 mg/kg orally, twice a day, and the rest of the medication continued at previously prescribed doses. The ferret remained stable for 6 more days, after which its respiratory condition worsened. Furo-
semide was increased to 3 mg/kg, orally, twice a day, but the patient did not improve and 2 days later, 15 days after initial presentation, the owners elected to euthanize the ferret.

At necropsy, 5 mL of serosanguinous fluid was recovered from the thoracic cavity. Mild cardiomeg-
aly and pericardial effusion were also noted. The lungs were consolidated with a patchy, pale golden pattern of nodular areas that penetrated deep into the parenchyma (Figs 2 and 3). Histologically, the nodular areas within the lung tissue contained foamy macrophages and giant cells associated with cholesterol crystals that filled the alveolar lumen. The al-
veolar septa were thickened by mononuclear cells and mild fibrosis. In some areas the pulmonary tis-
sue was completely replaced by cholesterol crystals and histiocytic inflammatory reaction (Fig 4). In addition, the liver was congested. No histologic changes were observed in the heart.

Further questioning of the owner failed to indi-
cate any oil or fat ingestion or inhalation, and the diagnosis was determined as endogenous lipid pneu-
monia. Tissues were negative for group 1 coronavi-
rus antigen and canine distemper by immunohisto-
chemistry. Tissues conserved in paraffin were tested for Aleutian disease virus by polymerase chain reaction and the samples were negative.
Discussion

The ferret described in this case presented with a history of chronic cough, which has been reported in humans with lipid pneumonia.2,17 We hypothesize that this chronic course of disease was responsible for the hypergammaglobulinemia observed in both the blood and the pleural effusion. The progression of the lipid pneumonia may have led to pathologic changes in the lung tissue that increased the intrapleural negative pressure, thereby producing fluid accumulation due to an increase in the hydrostatic pressure gradient.18 In addition, those pulmonary changes may have induced cardiac enlargement and insufficiency, contributing to the pleural effusion. Pathologic changes in the heart associated with lipid pneumonia have been described in humans.19 In this case, lipid pneumonia was believed to be the major cause of respiratory failure. Although pleural effusion was noted, it has been reported in dogs and cats that 30 to 60 mL/kg of pleural effusion are required to produce respiratory compromise in the absence of parenchymal disease.20 In the present case, less than 8 mL/kg of fluid were recovered from the thoracic cavity at necropsy. Furthermore, dyspnea did not improve immediately after thoracocentesis or after increasing doses of furosemide.

Lung aspiration or bronchoalveolar lavage might have provided an antemortem diagnosis, although lung biopsy is necessary for a definitive diagnosis.2 Successful treatment of lipid pneumonia has been achieved in humans using prednisolone21; however, in this case it only appeared to provide temporary improvement. Although not successful in this case, corticosteroid therapy should be considered in the therapeutic protocol of ferrets in which lipid pneumonia may have led to pathologic changes in the lung tissue that increased the intrapleural negative pressure, thereby producing fluid accumulation due to an increase in the hydrostatic pressure gradient.18 In addition, those pulmonary changes may have induced cardiac enlargement and insufficiency, contributing to the pleural effusion. Pathologic changes in the heart associated with lipid pneumonia have been described in humans.19 In this case, lipid pneumonia was believed to be the major cause of respiratory failure. Although pleural effusion was noted, it has been reported in dogs and cats that 30 to 60 mL/kg of pleural effusion are required to produce respiratory compromise in the absence of parenchymal disease.20 In the present case, less than 8 mL/kg of fluid were recovered from the thoracic cavity at necropsy. Furthermore, dyspnea did not improve immediately after thoracocentesis or after increasing doses of furosemide.

Endogenous lipid pneumonia is a common incidental and subclinical disease affecting the lung tissue of domestic ferrets. However, this report supports the hypothesis that this condition can be a very serious disease condition in domestic ferrets. A primary underlying etiology for endogenous lipid pneumonia could not be found in this ferret, but the possibility of an initiating cause should not be ruled out. Interestingly, idiopathic endogenous lipid pneumonia associated with death has been reported in a black-footed ferret,5 and therefore lipid pneumonia should be included in the differential diagnosis of domestic ferrets that present with respiratory disease.

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