Feline Hemothrophic Mycoplasmosis
A case of *Mycoplasma haemofelis* in a domestic short hair

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Abstract

A 4 year old male castrated domestic short hair presented to Cornell University Hospital for Animals for severe anemia caused by *Mycoplasma haemofelis. M. haemofelis* is one of the hemotrophic mycoplasmas that affect the cat. The hemotrophic mycoplasmas were formerly known as Hemobartonella and were considered to be rickettsial organisms. Recent PCR findings show that it is closely related to mycoplasma organisms rather than rickettsial organisms. Although the disease caused by this organism has been recognized in the US since 1953 there are still several aspects that remain unclear. The exact mode of transmission along with the exact pathogenesis of the anemia has still not been completely worked out. What is known about *M. haemofelis* is that it is an epierythocytic parasite that can cause a severe hemolytic anemia in cats.

Case History and Clinical findings

A 4 year old 6.2 kg castrated male domestic short hair presented to the triage service at the Cornell University Hospital for Animals (CUHA) in August of 2004 for lethargy, inappetence and pale mucous membranes. He was adopted from a local shelter at one year of age and two months prior to presentation at CUHA he had become an indoor-outdoor cat. He was not vaccinated for FeLV. Prior to this time, the cat had been in good health and did not have any previous medical problems

On physical exam the cat was quiet, alert and responsive to occasionally obtunded. He was in good body condition (body condition score of 6 out of 9), afebrile (100.6° F) and his heart rate was within normal limits (200 b.p.m.). He was tachypneic (54 b.p.m.) and had pale as well as slightly icteric mucus membranes. Due to the degree of pallor, the capillary refill time was unable to be assessed. He was approximately 5% dehydrated and had a II out of VI systolic

murmur. His femoral pulses were fair and there was no evidence of peripheral lymphadenopathy.

Initial diagnostics included determination of packed cell volume (PCV), total solids (TS), blood glucose, sodium, potassium, chloride, total carbon dioxide, blood urea nitrogen, blood pH, partial pressure of carbon dioxide, bicarbonate, base excess, anion gap, in house blood typing, and an in house FeLV/FIV snap test. Abnormalities included anemia (PCV = 13%), hyperglycemia (281 mg/dL; reference range 65 - 140), partial pressure of carbon dioxide was slightly decreased at 25.2 mm/Hg (reference range is 28 - 34), and a decreased base excess at -11 mmol/L (reference range is -5 to +2). The blood typing was inconclusive due to the degree of autoagglutination present. The FeLV/FIV snap test was negative for both retroviruses. Initial treatment included one unit of type A packed red blood cells and intravenous fluids (plasmalyte A).

Initial Problem list and Differential diagnoses

The initial problem list consisted of anemia, pale and mildly icteric mucus membranes, a II out of VI systolic murmur, tachypnea, mild dehydration and hyperglycemia. The hyperglycemia was most likely due to stress, but the rest of the problems can be explained by the severity of the anemia. The loss of red blood cells causes a decrease in the oxygen carrying capacity which leads to pale mucus membranes, tachypnea, depression, inappetence and mild dehydration.

There are three general causes of anemia. These are decreased hematopoiesis, blood loss and hemolysis. Causes of decreased hematopoiesis include immune mediated disease directed at precursors in the bone marrow, infectious causes like FeLV that can directly suppress the bone

marrow, chronic disease through the sequestration of iron in macrophages, chronic renal failure through the decrease in production of erythropoietin, nutritional deficiencies (i.e. cobalamin, folate and iron), certain neoplasias (i.e. lymphoma or leukemia), certain drugs (i.e. chloramphenical, trimethylprim sulfa, and chemotherapy drugs) and other bone marrow disorders.

Causes of blood loss anemia can be inherited or acquired. Inherited causes include hemophilia A and B, vitamin K dependent coagulopathy, platelet disorders and von Willebrand's disease. All of the inherited causes of blood loss are rare in domestic short hairs. More commonly the cause of blood loss in acquired. Acquired causes of blood loss include trauma, certain drugs (i.e. aspirin and other NSAIDs), thrombocytopenia, anticoagulant rodenticides, liver disease, renal failure, parasites, certain neoplasias (i.e. lymphoma, leukemia, myeloma), disseminated intravascular coagulation and vasculitis.

The last major cause of anemia is hemolysis. There are inherited, immune mediated, infectious, chemical as well as other miscellaneous causes of hemolytic anemia. Inherited causes include pyruvate kinase deficiency, cytochrome-b5 reductase deficiency, porphyria, increased osmotic fragility and poikilocytosis. Like the inherited causes of blood loss anemia, the inherited causes of hemolytic anemia are rare in the domestic short hair. There can be immune mediated destruction of red blood cells. Primary immune mediated hemolytic anemia (IMHA) is rare in the cat. Secondary IMHA is more common. Secondary IMHA can be caused by several infectious agents as well as certain drugs (i.e. sulfonamides, cephalosporins, heparin and methimazole). Infectious causes of hemolytic anemia include *Mycoplasma haemofelis* (formerly known as *Hemobartonella felis*), *Cytoxzoon*, *Babesia* and FeLV (subtype A). *Cytoxzoon* is rare, restricted to the South Central and SouthEastern United States, and is usually fatal with in one

week of the onset of clinical signs. *Babesia* is another red blood cell parasite, but it is very rare in domestic cats in the United States. There are numerous drugs and foods that contain chemicals that cause hemolytic anemia due to oxidative damage. Some of these include acetominophen, propofol, zinc, propylene glycol, onions and garlic. There are also other miscellaneous causes of hemolytic anemia such as hypophosphatemia, microangiopathic diseases and hepatopathy.[1]

Profound anemia can also cause a low grade mid-systolic murmur. Severe anemia decreases the viscosity of the blood and the body tries to compensate for the anemia by increasing the stroke volume. This decrease in viscosity along with the increase in velocity leads to an innocent or physiological murmur. Other causes of a systolic murmur include many possible cardiomyopathies or valvular disorders, of which hypertrophic cardiomyopathies are common in cats.[2]

Further Diagnostics and Diagnosis

Further diagnostic tests included a complete blood count (CBC), chemistry panel, urinalysis and abdominal ultrasound. The results of the CBC showed an anemia (HCT = 9%; refernce range = 32 – 52%) with a total solids within normal limits (TS = 7.1 g/dL; refernce range = 5.9 7.5). The corrected reticulocyte count was 4.2% and the absolute reticulocyte count was 208.8 thou/uL showing a strong regenerative response. There were nucleated red blood cells (41/100 white blood cells), which is also suggestive of a strong regenerative response. There was a macrocytic, normochromic regenerative anemia. On the blood smear there were spherocytes and basophilic stippled red blood cells as well as polychromasia and hypochromasia.

Epicellular red blood cell parasites that were suspected to be *Mycoplasma haemofelis* were observed as well.

Abnormalities on the chemistry pattern included hyperglobulinemia (6.1 g/dL; reference range is 3.1 – 5.1), hyperbilirubinemia (1.6 mg/dL; reference range is 0 – 0.2) and an increased iron (386 ug/dL; reference range is 57 – 156). The results of the urinalysis were unremarkable. Abdominal ultrasound showed a slightly enlarged liver with a mottled echogenicity, consistent with extravascular hemolysis. All of the findings are consistent with a strongly regenerative hemolytic anemia caused by *Mycoplasma haemofelis*. In order to obtain a definitive diagnosis, blood was sent to the University of Illinois for PCR analysis looking for *Mycoplasma haemofelis*, the results of which were positive.

Mycoplasma haemofelis

Mycoplasma haemofelis was originally referred to as feline infectious anemia when it was first recognized in the United States in 1953. It was originally proposed to be a virus due to its small size. It was subsequently named *Hemobartonella felis* and classified in the family *Anaplasmatacea*, order *Rickettsiales* due to the fact that it lacked an outer membrane, was unculturable and was parasitic to erythrocytes.[3] As more studies were performed on the organism, researchers started noticing more similarities to *Mycoplasma* species such as lack of a cell wall, lack of intracellular parasitism, lack of flagella, resistance to penicillins and sensitivity to tetracyclines. Recently PCR DNA analysis was able to show more genetic similarities to *Mycoplasma* species and the organism was renamed.[4]

Mycoplasma haemofelis is a small gram negative obligate red blood cell parasite. It is unable to be grown in culture which has made this organism difficult to study. It is

epierythrocytic, found in depressions in the red blood cell membrane and attaches to the red blood cell membrane with small fibrils. It occurs in three different forms: cocci, rings and rods.

The disease caused by *Mycoplasma haemofelis* can be divided into different stages: preparasitemic, acute, recovery and carrier. Once an animal has been inoculated it can take between 2-34 days to achieve parasitemia.[5] This parasitemia is cyclic in nature, which can make diagnosis difficult. In one study, over 90% of the red blood cells were parasitized with multiple organisms and within less than one hour there were no detectable organisms.[4] As the degree of parasitemia increases the animal's PCV decreases. The resulting anemia may be mild and go unnoticed or can be fatal. The anemia is regenerative, given enough time and is often Coomb's positive.

Several mechanisms have been suggested to try to explain the pathogenicity of *Mycoplasma haemofelis.* The main cause of the anemia appears to be extravascular erythrophagocytosis by macrophages in the spleen liver and bone marrow. Occasionally there is partial phagocytosis, also called "pitting" in which only the portion of the red blood cell with the parasite is phagocytosed. It has also been proposed that once red blood cells become parasitized they lose their normal biconcave shape, which causes them to become sequestered in small vessels. Attachment of the organism to the red blood cell membrane may cause alterations in the red blood cell membrane exposing foreign antigen and inciting a secondary immune mediated hemolytic anemia. The parasite may directly damage the red blood cell, although most of the anemia is thought to be the result of extravascular erythrophagocytosis. It has also been suggested that the red blood cell may be an innocent bystander of complement fixation.[3,4,6]

The exact prevalence of the *Mycoplasma haemofelis* has not been determined, but recent research has estimated it between 5-23% in the United States. The exact mode of transmission is

still not exactly known. Experimentally it can be transmitted intravenously, intraperitoneally, and orally. It can be transmitted vertically from queens to kittens, although it is not known if they are infected in utero or while nursing. There can be iatrogenic infections from contaminated transfusions. Biting insects have been proposed as a potential vector for the disease. It is also thought to be potentially transmitted through cat bites.[3,5] Risk factors include male cats, less than 4 years of age, access to the outdoors, present during the spring and summer months, history of a cat bite abscess, not up to date on vaccines and FeLV infection.[7]

A definitive diagnosis can now be made with PCR techniques recently developed. PCR can also distinguish between the two types of hemotrophic mycoplasmas, *Mycoplasma haemofelis* and *Mycoplasma haemominutum*. *Mycoplasma haemominutum* has not been shown to cause overt disease on its own, although it can exacerbate the clinical signs of other diseases like FeLV and FIP.

Treatment and Outcome

Appoximately 1/3 of cats die without treatment.[8] Blood transfusions may be necessary depending on how rapidly the anemia developed and its severity. *Mycoplasma haemofelis* is susceptible to tetracycline antibiotics. For this reason doxycycline should be given orally for three weeks since it has fewer side effects than other tetracycline antibiotics. Doxycycline has occasionally been associated with esophageal strictures, so it should be followed by administration of water. Some researchers have recently suggested the efficacy of enrofloxacin in treating *Mycoplasma haemofelis*.[9] Antibiotic treatment does not completely eliminate the organism. The cat will always be a carrier at risk of recurrent parasitemia. Prednisone treatment has also been recommended since there is also an immune mediated aspect to the anemia.

In our case, the cat was given a unit of type A packed red blood cells and started on IV fluids (plasmalyte A). His PCV then increased to 15%. He was also started on oral doxycycline and prednisone. Due to his rapid recovery he was discharges after 2 days in the hospital when his PCV was upto 22%. In a week after discharge, his PCV was upto 27% and both his systolic murmur and icterus had resolved.

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