Severe Anemia in a Cat

Leah A. Cohn, DVM, PhD, Diplomate ACVIM, University of Missouri

A 5-year-old, castrated male domestic shorthair presented for severe, nonregenerative anemia.

History. The cat was an exclusively indoor pet with no exposure to other cats, and he was current on vaccinations, including FeLV vaccine. He was adopted from an animal shelter at approximately 2 months of age, and had negative results for FeLV and FIV on ELISA at that time. The cat had two bouts of anemia—one at 1 year of age and another at 3 years of age—that responded well to blood transfusion, tetracycline, and immunosuppressive drug therapy. No specific diagnosis was made with either episode, and in both episodes, the cat was given a 6-month course of cyclophosphamide.* He remained normal until 1 month before presentation. Clinical signs were nonspecific and included lethargy, anorexia, recent weight loss, and scant but normal stools. Severe anemia was identified, and treatment was initiated with prednisone (7.5 mg PO Q 12 H), cyclophosphamide (12 mg PO 4 days out of 7), doxycycline (25 mg PO Q 12 H), and vitamin/iron supplementation. The cat did not respond after 1 month of therapy and was referred for more detailed evaluation.

Physical Examination. The cat (body weight 3.2 kg) was quiet but alert; temperature and respiratory rate were unremarkable. Tachycardia (230 bpm), grade III/VI left parasternal systolic heart murmur, and marked pallor were the major abnormalities identified.

Diagnostics. FeLV/FIV combination ELISA and polymerase chain reaction testing for *Mycoplasma haemofelis* were normal. Other initial diagnostics included CBC, chemistry profile, and urinalysis. Mild polychromasia was noted; other abnormal results are shown in the **Table**.

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Diagnostic Testing

Variable	*Result*	*Reference Range*
Red blood cells ($\times 10^6$/µl)	1.47	5.0–10.0
Packed cell volume (%)	7	24–45
Mean corpuscular hemoglobin concentration (%)	37.9	30–36
Lymphocytes ($\times 10^3$/µl)	0.850	1.5–7.0
Nucleated red blood cells (/µl)	212	—
Reticulocytes ($\times 10^4$/µl)	60,000	—
BUN (mg/dl)	35	15–29
Globulin (g/dl)	4.1	2.3–3.8
Alanine transaminase (U/L)	236	20–170
Urine specific gravity	1.039	—

ASK YOURSELF…

- What are some possible causes for profound anemia in this cat?
- Do the negative FeLV ELISA results rule out FeLV as a potential cause of anemia?
- How do the prior episodes of anemia relate to the present illness?
- What diagnostic tests are indicated next? Should any treatment be started before the diagnostic workup is continued?

*The use of cyclophosphamide for immune-mediated anemia is controversial. Its use certainly cannot be recommended in the absence of a diagnosis of either neoplastic or immune-mediated disease.

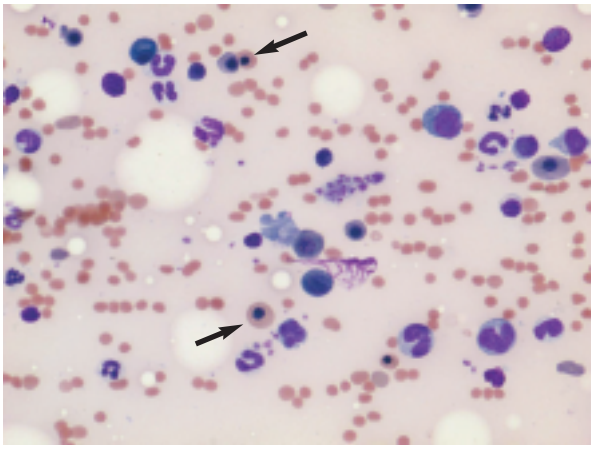
ELISA = enzyme-linked immunosorbent assay; FeLV = feline leukemia virus; FIV = feline immunodeficiency virus

Diagnosis: Megaloblastic anemia related to FeLV virus infection

After stabilization, a bone marrow aspirate was collected for cytologic evaluation, and IFA testing for FeLV was done. The marrow aspirate was hypocellular overall, and megakaryocytes were rare despite the estimate of normal peripheral platelet numbers. Myeloid-to-erythroid ratio was increased at 10:1. While myeloid progression to maturity was normal, there were numerous megaloblastic changes associated with the erythroid cell line (**Figure**). The IFA testing of the marrow for FeLV was positive.

Interpretation. Megaloblasts suggest asynchronous nuclear and cytoplasmic maturation; in cats, these cells are most often associated with FeLV infection. FeLV can cause transient viremia, persistent infection, or latent infection. Since this is an indoor cat, the patient was probably infected as a young kitten before it was adopted.

The cat tested negative for FeLV by routine ELISA on three separate occasions. Although detection of viral antigen is the diagnostic test of choice for FeLV infection and the commonly used ELISA assay for p27 core antigen is quite sensitive, ELISA from peripheral samples will be negative if the infection is confined to the bone marrow (latent infection). Although illness associated with FeLV infection is generally associated with viremia, the disease occasionally manifests only in the bone marrow. In these cases, diagnosis depends on identification of virus in the marrow and such identification typically relies on IFA testing of a marrow sample.



Courtesy Dr. Charles Wiedmeyer (UMC-VMDL)

Aspirated bone marrow stained with Wright-Giemsa. This hypocellular sample contains rare megakaryocytes. The myeloid-to-erythroid ratio is 10:1. While the myeloid series seems to be maturing normally, there are numerous megaloblastic changes associated with the erythroid cell line. Megaloblasts (*arrows*) are large, red blood cell precursors. They have immature, bizarre, pale-staining nuclei that contain irregular chromatin clumps, suggesting asynchronous nuclear and cytoplasmic maturation (original magnification, 500×).

Anemia is a common complication of FeLV infection and occurs via any of several mechanisms. Depending on the mechanism, FeLV-related anemia may be regenerative or nonregenerative and may be associated with a variety of morphologic characteristics of red blood cells. Immunosuppressed, FeLV-positive cats are more likely to be infected with a variety of other viral, bacterial, protozoal, or fungal organisms. These concurrent infections may result in anemia directly (e.g., *M. haemofelis*) or indirectly (e.g., anemia of inflammatory disease). Lymphoproliferative and myeloproliferative disorders are additional causes of anemia associated with FeLV infection, as is bone marrow fibrosis. FeLV may also cause anemia by selective marrow depletion of blast-forming erythroid units or by inhibition of differentiation blast-forming units.

See Aids & Resources, back page, for references, contacts, and appendices.

DID YOU ANSWER …

- **Blood loss (unlikely in light of normal total protein and no identifiable source of bleeding), hemolysis (primary immune-mediated hemolytic anemia is rare in cats, but secondary forms and hemolysis related to infection are more common. Other causes of hemolysis include congenital RBC defects, toxins, and fragmentation of RBCs), or decreased erythropoiesis (supported by the nonregenerative nature of the anemia). Decreased erythropoiesis can result from inflammatory disease; lack of erythropoietin; endocrine disease; maturation defects; myelophthisis; or marrow fibrosis, necrosis, or hypoplasia.**
- **The ELISA is sensitive for detection of transient or persistent viremia. However, latent, or sequestered, infection of bone marrow will not produce the FeLV core antigen p27 in the peripheral blood, resulting in negative results.**
- **Prior episodes at ages 1 and 3 years responded well to treatment with tetracycline antibiotics and immunosuppression, while this episode did not. It is impossible to say what caused those prior episodes, but hemolysis seems likely (note that spherocytosis is absent in cats with immune-mediated hemolysis). It is extremely unlikely that the megaloblastic anemia identified during this episode caused the prior episodes, because FeLV-related megaloblastic anemia is very likely to be fatal.**
- **Bone marrow aspirate for cytologic evaluation and FeLV IFA were indicated for this cat because of the nonregenerative anemia, which is probably not attributable to inflammatory disease, endocrine disease, or renal failure. Before being sedated and anesthetized for the marrow biopsy, this profoundly anemic cat should be stabilized with hemoglobin. This cat was incompatible by cross-match with two type-specific donor cats and was therefore treated with Oxyglobin (Biopure) solution.**

IFA = immunofluorescent assay