DEADLY DISEASE
The veterinary team turned to bone marrow aspiration to diagnose a 12-year-old cat with multiple myeloma in this case report.

Who Will Win the Grand Prize? A panel of judges will choose 4 finalists whose case reports will be published in Today’s Veterinary Nurse in 2021. TVN’s Facebook community will then select the Grand Prize winner from among the 4 finalists; the winner gets free registration for VMX 2022.
CASE REPORT: ONCOLOGY

Multiple Myeloma in a Cat

Darcy is an RVT/CVT with a master’s degree in education. Prior to obtaining her AA in Veterinary Technology, she worked as a 6th-12th grade math teacher and contributed to a long-term research study led by the Bill and Melinda Gates Foundation on teaching effectiveness. She has enjoyed combining her education background with her veterinary medical career and has worked in shelter medicine, feline-only practice, and specialty/emergency care. She discovered a passion for veterinary oncology after accepting a position with BluePearl Specialty Hospital in Maryland in 2018. She has since relocated to Portland, Oregon, with her husband and 2 college-aged children and is preparing for her next adventure with the support of her Corgi-mix, Bailey, and her German Shepherd, Jenga.

Myeloma-related disorders are caused by neoplastic plasma cells and include multiple myeloma, extramedullary plasmacytoma, and, more rarely, Waldenström’s macroglobulinemia. The most clinically significant myeloma-related disorder is multiple myeloma, which is rare in cats, accounting for only 0.9% of all malignancies and 1.9% of hematologic malignancies. Diagnosis of multiple myeloma is based on finding bone marrow plasmacytosis (increased percentage of plasma cells in the bone marrow) concurrent with osteolytic bone lesions and/or increased M component (immunoglobulin). However, because bone lesions are uncommon in cats, the diagnosis may instead be based on visceral organ involvement with associated bone marrow plasmacytosis. Bone marrow involvement differentiates multiple myeloma from extramedullary plasmacytoma and is responsible for many of the nonspecific clinical signs of multiple myeloma, including lethargy, weakness, and anorexia. In this case report, the author will describe a case of multiple myeloma in a cat, diagnosed by bone marrow aspiration.

INITIAL PRESENTATION

Sara was a 5.8-kg spayed female domestic shorthair cat that was 12 years and 2 months of age on her initial visit. On February 1, 2019, she was brought to her primary veterinarian due to progressive weakness, difficulty walking, and lethargy. She had been receiving gabapentin (9 mg/kg PO q12h) intermittently since an injury in September 2018, but it did not seem to be
alleviating the current clinical signs. A new heart murmur (grade 1 to 2 out of 6 left parasternal) was detected at this visit.

The veterinarian performed a complete blood count (CBC), which revealed pancytopenia (a decrease in white blood cells [WBCs, primarily neutrophils], red blood cells [RBCs], and platelets) (TABLE 1). The veterinarian was concerned that the sample may have clotted during collection and thus collected another sample, which corroborated the original results. In addition, a chemistry screen revealed elevated total protein (>12.0 g/dL; reference 5.2 to 8.8 g/dL). Previous bloodwork from 2 years earlier had revealed no abnormalities. Sara’s owners elected to monitor her at this point and continue symptomatic treatment with gabapentin.

During February and March, Sara returned to her primary care veterinarian several times for repeat bloodwork with little to no improvement of her persistent pancytopenia. She remained generally active with a good appetite, although she continued to lose weight and demonstrated intermittent lethargy and lameness. In March, abdominal ultrasonography revealed mild splenomegaly, bilateral chronic degenerative changes to the kidneys, and a mottled hypoechoic pancreas.

Her blood values led to suspicion of a cancerous process (i.e., lymphoma, leukemia, multiple myeloma) because hematologic cancers can interfere with the bone marrow’s ability to produce healthy blood cells. A definitive diagnosis, based on histopathologic/cytologic classification, would require additional sampling. Sara’s owners were informed of further diagnostics to consider, including bone marrow aspiration (for cytologic examination) and biopsy (for histopathologic examination), Bence-Jones urine precipitation, survey radiography, and computed tomography. They elected the testing most likely to lead to a diagnosis and treatment plan, which was collection of bone marrow aspirates and a core biopsy sample along with a concurrent CBC.

REFERRAL PRESENTATION
Sara was referred to the oncology department at BluePearl Pet Hospital, where her initial presentation was unremarkable. She was bright, alert, and responsive with pink mucous membranes and a capillary refill time under 2 seconds. She was euthermic (rectal temperature 101.3°F [38.5°C]). Her heart rate was 196 beats per minute (reference 140 to 220 beats/min), and her femoral pulses were strong and synchronous. Her respiratory rate was 42 breaths per minute (reference 16 to 40 breaths/min) with no increased effort. Auscultation of the heart and lungs revealed no abnormalities. Peripheral lymph nodes were soft, small, and symmetrical.

Sara was admitted to the hospital. CBC and chemistry profile indicated continued anemia and neutropenia along with severely increased globulin levels (12.8 g/dL; reference 2.3 to 5.3 g/dL). The decision was made to proceed with bone marrow aspirates and core biopsy for diagnostic purposes.

DIAGNOSTIC WORKUP
A 22-gauge intravenous catheter was placed in the left cephalic vein, and butorphanol (0.2 mg/kg IV) was administered as premedication. Anesthesia was then induced with propofol given to effect (2.8 mg/kg) and

<table>
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<th>DATE</th>
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<th>NEUTROPHILS/µL (REF 2300–10 290)</th>
<th>RBCs, x 10^12/µL (REF 6.54–12.20)</th>
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RBCs=red blood cells; WBCs=white blood cells.
then titrated throughout the procedure for a total dose of 5.2 mg/kg. Lidocaine (0.175 mg/kg) was infused at the site for local pain control, and flow-by oxygen was provided. The right shoulder was shaved and aseptically prepared for the bone marrow sampling.

Throughout the procedure, the author monitored Sara’s vital signs, including pulse oximetry (96% to 100% oxygen saturation), continuous lead II electrocardiography (heart rate 162 to 212 beats/min), oscillometric blood pressure (mean 62 to 102 mm Hg), respiratory rate (30 to 36 breaths/min), and temperature (99° to 101°F). Sara recovered smoothly and was discharged to her owners’ care within 2 hours, with buprenorphine (0.015 mg/kg PO as needed) for pain control.

For financial reasons, only the bone marrow aspirates (17 slides) were submitted to an outside specialty laboratory. An American College of Veterinary Pathologists–certified pathologist diagnosed myelophthisic plasma cell tumor (definitive) highly suspicious for multiple myeloma. After definitive diagnosis was made via the bone marrow aspirates, the core biopsy sample was discarded.

**NURSING CARE PLAN**

Sara’s owners considered the treatment options and elected to proceed with concurrent prednisolone and the chemotherapy drug cyclophosphamide. For dosing purposes, Sara’s weight was converted to a body surface area (BSA) by using the formula: 

\[
\text{BSA (m}^2\text{)} = K \times \frac{W^{2/3}}{100}
\]

where \(K = 0.100\) for cats and \(W\) is body weight in kg.

Sara’s BSA (m²) = 0.100 × (5.79 kg)²/³ = 0.322 m²

Cyclophosphamide was prescribed at a dose of 200 mg/m² (64 mg) to be given orally once every other week (q14d). A specialty pharmacy was able to compound the exact dose into capsules. Prednisolone was also prescribed at 5 mg PO q24h. The owners were counseled that prednisolone is a steroid and can cause increased thirst, urination, appetite, and panting and that to discontinue prednisolone, the dosage should always be tapered and never stopped abruptly. They were also given a handout and verbal instructions about chemotherapy safety and protocols for administering oral chemotherapy at home.

Sara returned 1 week after beginning cyclophosphamide treatment at home. The owners had struggled to administer the medication, so Sara probably only received a partial first dose. A blood sample, obtained by using a 22-gauge butterfly catheter in the medial saphenous vein, indicated continued pancytopenia (WBCs 2300/µL, RBCs 4.45 × 10⁶/µL, platelets 66 000/µL). Her neutrophil count (1127/µL) was below the typical cutoff point for chemotherapy (should be >1500/µL), but because her bone marrow disorder would probably continue to suppress neutrophil production in the absence of treatment and because Sara had not received the full (if any) chemotherapy the previous week, the veterinary team administered the next dose of oral cyclophosphamide in the clinic by using a pill popper and noted no immediate reactions or complications.

Sara returned 2 weeks later for a recheck examination, including blood sample collection and cyclophosphamide administration. The clients reported that she had been bright and happy at home with a good appetite, although she was experiencing slight polyuria/polydipsia (probably from the prednisolone). The blood sample indicated persistent but slightly improved pancytopenia (WBCs 2800/µL, RBCs 5.36 × 10⁶/µL, platelets 120 000/µL) and a still significantly elevated globulin level (11.8 g/dL). Because Sara had received only 1 full dose of cyclophosphamide at this point, was feeling well at home, and her neutrophil count was appropriate for treatment (2184/µL), the decision was made to continue cyclophosphamide chemotherapy. The veterinary team again administered the next dose of cyclophosphamide (64 mg PO) in the clinic by using a pill popper and noted no immediate reactions or complications.

Three days after receiving her third dose of cyclophosphamide in the hospital, Sara was brought to the 24-hour emergency department because she was...
M component is an abnormal antibody (immunoglobulin), or a fragment thereof, that is produced in excess by an abnormal proliferation of plasma cells, typically in patients with multiple myeloma.

anorexic, hiding, vomiting, and seemed slightly dazed. Examination revealed elevated temperature (105.5°F) and weight loss (decreased by 0.20 kg). A venous blood sample indicated persistent pancytopenia (WBCs 1570/µL [1100 neutrophils/µL], RBCs 5.21 x 10^6/µL, platelets 64 000/µL). Because of concerns for secondary infection, the veterinary team gave her cefovecin sodium (Convenia; Zoetis, zoetisus.com) at 8 mg/kg SC. To help alleviate any nausea that may have caused the anorexia, she was also given maropitant citrate (Cerenia; Zoetis, zoetisus.com) at 1 mg/kg SC. The client reported that Sara improved quickly after receiving these supportive medications.

Sara's fourth dose of cyclophosphamide was reduced by 15% to 170 mg/m^2 (53 mg). A venous blood sample indicated slightly improved pancytopenia (WBCs 2800/µL [1963 neutrophils/µL], RBCs 5.25 x 10^6/µL, platelets 140 000/µL).

Sara's owners brought her back every 2 weeks for cyclophosphamide administration (at the reduced dose of 53 mg) and periodic bloodwork. She seemed to be tolerating the reduced dose well, but her globulin and total protein levels remained elevated, at 11.8 g/dL and 14.8 g/dL, respectively. Because Sara was feeling well at home and had a good appetite, her owners elected to continue cyclophosphamide therapy rather than change to another chemotherapy agent such as melphalan.

OUTCOME

When Sara returned for what should have been her eighth cyclophosphamide dose, a blood sample indicated grade 3 neutropenia (975 cells/µL), progressive anemia (hematocrit 16.2% [reference 29% to 48%]; RBCs 3.52 x 10^6/µL), and markedly decreased platelets (22 000/µL). Her globulin (10.4 g/dL) and total protein (12.6 g/dL) levels remained significantly elevated and her weight had decreased. Because bone marrow suppression is part of the disease process, the veterinary team was concerned that these values indicated continued progression of Sara's disease and decided to discontinue chemotherapy. And because further bone marrow suppression could be serious and potentially life-threatening, Sara's owners elected to continue monitoring her at home and enjoy what time they had left with her. They requested and were given information on palliative care and a handout listing mobile veterinarians who perform hospice and end-of-life care. Four weeks after her last oncology visit to our hospital, Sara was euthanized by her primary veterinarian.

MULTIPLE MYELOMA

Multiple myeloma results from proliferation of malignant plasma cells. Plasma cells, or B cells, are WBCs that originate in the bone marrow and produce antibodies to specific antigens. Myeloma cells are neoplastically transformed plasma cells that produce an excess of M component (also called myeloma protein, M protein, M spike, spike protein, or paraprotein). M component is an abnormal antibody (immunoglobulin), or a fragment thereof, that is produced in excess by an abnormal proliferation of plasma cells, typically in patients with multiple myeloma. This high level of circulating M component is responsible for much of the pathology of multiple myeloma, including impaired immune function, abnormally high blood viscosity, and organ damage. Most cats with multiple myeloma have concurrent organomegaly of the liver, kidney, or spleen, as did Sara, resulting from infiltration of the visceral organs by neoplastic cells. Clinical signs may be nonspecific (e.g., lethargy, weakness, lameness, hind limb paresis/paralysis, anorexia) and may be present up to a year before diagnosis.

These nonspecific symptoms combined with systemic involvement make diagnosing multiple myeloma challenging, especially in a general practice setting. Minimally invasive screening can be performed by testing for Bence-Jones protein in the urine, which cannot be performed with a commercial urine dipstick. Bence-Jones proteinuria is suggestive of multiple myeloma but may provide false-negative results. Serum electrophoresis may indicate presence of an M component spike, also suggestive of multiple
myeloma, but this test also may provide false-negative results. Definitive diagnosis of multiple myeloma is therefore usually made by collecting a bone marrow core biopsy sample or multiple bone marrow aspirations to obtain a representative sample to meet the threshold of 10% to 20% plasmacytosis. This sampling typically requires a visit to a specialty hospital with an internal medicine department to obtain the samples and submit them to a diagnostic laboratory for evaluation.

Treatment for multiple myeloma is aimed at reducing tumor cell burden and minimizing clinical signs. The mainstay of treatment for multiple myeloma in dogs is concurrent melphalan (0.05 mg/kg/q24h) and prednisone (0.5 mg/kg/q48h). Although this protocol can be used in cats, it can be very myelosuppressive and must be carefully monitored. An alternative alkylating agent, cyclophosphamide (200 mg/m²), with concurrent prednisolone has been shown to be equally effective in cats, particularly in those with widespread systemic involvement.²

As a hematopoietic disease, multiple myeloma enables us to observe the interconnectedness of all body systems. The infiltration of neoplastic cells into bone can cause bone lesions and pathologic fractures, especially in bones engaged in active hematopoiesis, such as the vertebral and long bones. For patients with multiple myeloma, interference in the coagulation process by the M components can lead to bleeding diathesis. Tumor infiltration or diminished perfusion caused by the higher molecular weight of the immunoglobulin in the blood (hyperviscosity syndrome) can lead to renal disease. Hyperviscosity syndrome can also cause excessive cardiac workload and cardiac disease. Perhaps most deadly, leukopenia secondary to myelophthisis can make the patient susceptible to infection and severe immunodeficiency.

The typical presentation of multiple myeloma (pancytopenia and elevated total protein [globulin]) also represents the correlation of hematologic abnormalities with disruptions in the normal functioning of many body systems. The main component of globulin is antibodies, which are produced by plasma cells. In patients with multiple myeloma, the malignant plasma cells produce an overabundance of antibodies, resulting in excess protein (globulin) circulation in the blood, affecting kidney filtration. Anemia in multiple myeloma patients is also concerning because low RBC counts can affect healthy oxygenation of cells. The thrombocytopenia of multiple myeloma can lead to an inability to clot after injury. Leukopenia can make the patient susceptible to other opportunistic diseases.

Although the veterinary team all hoped for successful treatment of Sara’s multiple myeloma, several signs indicated that her disease was aggressive. Her serum protein levels remained elevated after 12 weeks of treatment, indicating that malignant plasma cells were still producing an overabundance of immunoglobulin (most commonly M component). These same M components were also interfering with coagulation, resulting in low blood calcium levels, a key component of the coagulation cascade. Typically, cats with multiple myeloma succumb to the disease within 4 months.³

References