Corticosteroid-responsive thrombocytopenia in two beef cows

Phillip G. Hoyt, DVM; Marjorie S. Gill, DVM, MS, DABVP; Kenneth L. Angel, DVM, MS, DABVP, DACVIM; Stephen D. Gaunt, DVM, PhD, DACVP; Sharon M. Dial, DVM, PhD, DACVP; Ricky M. Landreneau, DVM

Thrombocytopenia in cattle may have various causes or may be idiopathic. Treatment of thrombocytopenia by administration of corticosteroids may be effective in some cows.

A 5-year-old 454-kg (999-lb) purebred Brangus cow with a body condition score of 4/9 was admitted and donated to the teaching hospital for evaluation of recurrent hematoma formation of 4 months' duration. The cow had calved 8 months previously and was not pregnant at the time of admission. The cow had been kept on an improved Bermuda grass pasture that did not contain timber, brushy areas, or bracken fern. In addition to grazing, the cow received a daily ration of grass hay and oats. There was no history of vaccination, deworming, administration of medication, or diet change associated with the onset of initial clinical signs. The owner had not attempted treatment, and all other cows in the herd appeared to be clinically normal.

At the time of admission the cow appeared nervous and excited. Rectal temperature was 38.3°C (100.9°F), heart rate was 92 beats/min, and respiratory rate was 40 breaths/min. Mucous membranes were pale and petechiated. Two firm, subcutaneous masses, in the same locations as originally observed by the owner, were noticed. One bilaterally symmetrical mass extended from the ventral commissure of the vulva and posterior to the sternum had substantially decreased myeloid to erythroid ratio, with megakaryocytic and erythroid hyperplasia, consistent with regenerative anemia and regenerative thrombocytopenia. Prothrombin time was 17 seconds (control, 18.8 seconds) and partial thromboplastin time was 49.1 seconds (control, 69.3 seconds). Because coagulation times were within reference ranges, a clotting factor disorder was discounted as the cause of anemia. Because BVD virus and BLV have been associated with thrombocytopenia and BVD vaccination history was not available for the cow, serum was submitted for determination of BVD and BLV titers, and blood was submitted for BVD virus isolation from the buffy coat. The BVD titer (< 1:10) was considered clinically unimportant, antibodies against BLV were not detected, and BVD virus isolation results were negative.

Results of a CBC performed on a specimen obtained at the time of admission revealed PCV of 17% (reference range, 24 to 48%), RBC concentration of 2.31 × 10¹² cells/µl (reference range, 3 to 10 × 10¹² cells/µl), mean corpuscular volume of 78.4 fl (reference range, 40 to 60 fl), mean corpuscular hemoglobin concentration of 31.5 g/dl (reference range, 30 to 36 g/dl), 2% reticulocytes, 3 nucleted RBC (NRBC)/100 WBC, basophilic stippling, WBC concentration of 8,900 cells/µl (reference range, 4 to 12,000 cells/µl), and 12,000 platelets/µl (reference range, 1 to 8 × 10⁹ platelets/µl). Serum biochemical analyses revealed mild increase in creatine kinase (CK) activity (1,380 U/L [reference range, 0 to 300 U/L]). Problems identified by results of CBC were regenerative anemia and thrombocytopenia. Increased serum CK activity was attributed to increased muscular activity associated with trailer transport as well as muscle damage that may have occurred secondary to the dissecting hematomas. Possible causes for thrombocytopenia included acute bovine viral diarrhea (BVD) virus infection, disseminated intravascular coagulation (DIC), bracken fern toxicosis, endotoxiaemia secondary to sepsis, and bovine leukemia virus (BLV) infection, although these causes (except BLV infection) were unlikely because of their typically acute nature.

Clotting factor analyses followed by a bone marrow aspiration and analysis were performed to further characterize the anemia and thrombocytopenia. Wright's-stained smears of bone marrow aspirated from the sternum had substantially decreased myeloid to erythroid ratio, with megakaryocytic and erythroid hyperplasia, consistent with regenerative anemia and regenerative thrombocytopenia. BVD virus was not available for the cow, although these causes (except BLV infection) were unlikely because of their typically acute nature.
which was performed to help evaluate the possibility of autoimmune thrombocytopenia, revealed more pronounced erythroid and megakaryocytic hyperplasia. Marrow smears were tested for megakaryocyte-associated antibody by use of fluorescein isothiocyanate-conjugated goat anti-bovine IgG; megakaryocyte fluorescence was not observed at 1:10 or 1:100 dilutions of the conjugate. In retrospect, it would have been more appropriate to have acquired adequate bone marrow initially for performing this diagnostic test, thereby avoiding potential complications or risk associated with a second bone marrow aspiration.

Corticosteroid treatment was initiated by administration of dexamethasone (0.2 mg/kg [0.09 mg/lb] of body weight, IM, q 24 h). Platelet concentration (14,300 platelets/µl) improved 2 days after initiation of treatment; however, PCV (18.6%) remained relatively unchanged. Dosage of dexamethasone was gradually decreased to 0.02 mg/kg (0.009 mg/lb) administered IM every 48 hours during the following 48 days, at which time treatment was discontinued, and the cow was moved to a Bermuda grass pasture on university property. During the course of treatment, the hematomas regressed, and new hematomas did not develop. Results of repeated CBC during treatment revealed incremental increases in PCV and platelet concentration. Two days after the final treatment, PCV was 36.3%, and platelet concentration was 305,000 platelets/µl. When reexamined 60 days after movement to pasture, the cow's body condition score was unchanged, and platelet concentration was again decreased (43,000 platelets/µl). Because of recurrence of the condition, further treatment was not performed, and the cow was sold for slaughter.

A 5-year-old 545-kg (1,199-lb) purebred Brahman cow with a body condition score of 6/9 was admitted for emergency evaluation with a history of unilateral epistaxis of 36 hours' duration. The cow was reported thinner than other cows in the herd and had ceased nursing a calf 3 weeks prior to evaluation. The cow had been kept on a Bermuda grass pasture and received a protein supplement. There was no history of recent diet change, vaccination, deworming or other routine management practices.

Rectal temperature was 39.1°C (102.4°F), heart rate was 64 beats/min, and respiratory rate was 36 breaths/min. Right unilateral epistaxis was evident, and petechiae on the nasal mucosa of the right nostril were detected approximately 5.5 cm caudal to the naris; petechiae were not apparent on other mucous membranes. The cow was approximately 4 months pregnant. Visual examination and digital palpation of both nasal cavities revealed no other abnormalities.

Results of CBC for a blood sample obtained at admission revealed PCV of 23%, 38,000 platelets/µl, and plasma protein concentration of 5.5 g/dl. Clotting factor analyses and determination of activated clotting time were not available after regular hospital hours; therefore, a clotting disorder or vitamin K deficiency could not be ruled out. Because allergic rhinitis was also a consideration at that time as the cause of epistaxis, initial treatment included administration of triamcinolone acetonide (1 mg/kg [0.43 mg/lb], IM, q 12 h), vitamin K1 (1 mg/kg, IM, q 24 h), and topical application of 5 ml of epinephrine (dilution, 1:1,000) in the affected nostril.

On the morning of the second day after admission the PCV, plasma protein concentration, and platelet concentration were substantially decreased (PCV, 20%; plasma protein concentration, 4.9 g/dl; platelet concentration, 17,000 platelets/µl) and epistaxis was still evident. By that afternoon, the PCV was 18% and platelet concentration was 12,000 platelets/µl. Because of similarities to findings in the other cow, lack of availability of further diagnostic tests at that time, and continued decline in PCV and platelet concentration, administration of prednisone (0.22 mg/kg [0.10 mg/lb], IM, q 24 h) was added to the treatment regimen. Treatment with prednisone was chosen for this cow because of decreased risk of abortion associated with its use, compared with dexamethasone. Results of a coagulation profile and determination of fibrinogen degradation products on the following day revealed values within reference ranges.

By day 3 after admission, epistaxis was apparent only when the cow was stressed by handling. On day 4, epistaxis was not evident, and a regenerative hematologic response was noticed, because the platelet concentration increased to 115,000 platelets/µl. Blood was obtained, serum was submitted for evaluation of titers against BVD virus and BLV, and blood was submitted for BVD virus isolation from the bloody coat. The BVD titer was < 1:10, the cow was seronegative for BLV antibodies, and BVD virus isolation results were negative. Attempts to aspirate bone marrow from the ilium were unsuccessful. Treatment with epinephrine, vitamin K1, and antihistamine was discontinued.

On the following day, bone marrow collection attempts from the sternum were unrewarding. The dosage of prednisone was decreased (0.11 mg/kg [0.05 mg/lb], IM, q 24 h).

The cow's clinical appearance, PCV, and platelet concentration continued. The cow improved during the following 3-day period, at which time administration of prednisone was discontinued, and the cow was released from the hospital. The cow's PCV was 23% and platelet count was 857,000 platelets/µl at the time of discharge. Thirteen days after discharge, the cow was reevaluated on the farm. Results of physical examination, PCV (24%), and platelet count (677,000 platelets/µl) were within reference ranges, and a live fetus was detected by use of transrectal palpation. Approximately 5 months after discharge from the hospital, the cow delivered a live, healthy calf and was reportedly doing well 1 year later.

Thrombocytopenia is uncommonly diagnosed in cattle and may be caused by decreased production of platelets as a result of bone marrow hypoplasia, increased destruction or removal of platelets resulting from immunologic or nonimmunologic mechanisms, or splenic sequestration of platelets. Commonly reported causes of thrombocytopenia in ruminants include acute BVD infection, DIC,27-29 bracken fern toxicosis,23 and endotoxemia secondary to septic mastitis.
or metritis. Less common causes are chronic furazolidone toxicosis, trichloroethylene-extracted soybean meal toxicosis, lymphosarcoma, immune-mediated thrombocytopenia (IMTP), sarcocystosis, stachybotryotoxicosis, salmonellosis, gram-negative sepsis, plasma cell myeloma, and myelofibrosis (in Pygmy goats). Sporadic cases of apparent idiopathic thrombocytopenia in cattle have also been reported. Immune-mediated thrombocytopenia is usually responsive to administration of corticosteroids in horses, and this treatment was beneficial in 1 case of idiopathic thrombocytopenia in a young dairy bull.

A disorder characterized by abnormal platelet function with platelet concentration within reference range has been reported in Simmental cattle, for the 2 cows reported here, this diagnosis was excluded because thrombocytopenia was persistent and the cows were of other breeds. Other causes of bleeding disorders in cattle, such as moldy sweet clover toxicosis, warfarin toxicosis, hepatotoxins, congenital factor XI deficiency, and chronic hepatic fibrosis were eliminated on the basis of prothrombin and partial thromboplastin times within reference ranges.

Thrombocytopenia associated with BVD has been observed in experimental and naturally occurring acute BVD; the exact mechanism is unknown but may be attributable to a direct viral effect on platelets. Although the virus may be carried by platelets, surface-bound immunoglobulin has not been detected; therefore, a nonimmune-mediated mechanism of thrombocytopenia after BVD infection has been proposed. Neither of cows reported here had clinical signs compatible with acute BVD. Lack of substantial BVD titers in either cow. Infectious diseases can cause thrombocytopenia by decreasing the thrombocyte lifespan, the rate of thrombopoiesis, or both. Absence of fever, results of careful physical examination, and clinical pathology findings allowed the exclusion of an underlying infectious disease.

Disseminated intravascular coagulopathy was considered unlikely, because results of clotting factor analyses and determination of fibrinogen concentration were unremarkable in both cows, and concentration of fibrin degradation products was within reference range in the second cow. In addition, clinical evidence of a predisposing cause of DIC was not detected in either cow. Infectious diseases can cause thrombocytopenia by decreasing the thrombocyte lifespan, the rate of thrombopoiesis, or both. Absence of fever, results of careful physical examination, and clinical pathology findings allowed the exclusion of an underlying infectious disease.

Bracken fern toxicosis, stachybotryotoxicosis, trichloroethylene-extracted soybean meal toxicosis, furazolidone toxicosis and myelofibrosis cause bone marrow depression or aplasia. Hyperplastic bone marrow in the first cow eliminated these as possible causes of thrombocytopenia and historical lack of exposure to harmful substances in both cows lowered the likelihood of a toxicosis. The finding of serum globulin concentration within reference range and hyperplastic bone marrow without evidence of neoplastic cells made plasma cell myeloma unlikely in the first cow. The long-term survival and apparently healthy condition of the second cow made neoplastic disease in this cow unlikely as well.

Sarcocystis cruzi reportedly causes thrombocytopenia, anemia, prolonged clotting times, decreased fibrinogen concentrations, and erythroid hypoplasia in calves. With the exception of anemia, all the other hematologic values were within reference ranges in the cows reported here.

Drug-induced IMTP occurs in horses, but the cows of our report had no history of receiving drugs or biologics prior to development of clinical signs. Diagnosis of IMTP is challenging in large animals. In horses, a diagnosis of IMTP is assumed when coagulation factors are within reference ranges and there is no clinical evidence of consumptive coagulopathy or other diseases. Response to corticosteroid treatment is supportive of the diagnosis. The platelet factor 3 test, used in dogs to detect antplatelet antibody, is often less sensitive in other species and gives negative or inconclusive results in horses and cattle. Fluorescent antibody and ELISA techniques have been used to measure platelet-bound antibody in humans and dogs. These products are not commercially available for their use in horses, and their use in cattle has not been reported, to the authors' knowledge.

The 2 cases of thrombocytopenia of this report appeared to be idiopathic and corticosteroid-responsive. The most striking laboratory finding in both cows was persistent thrombocytopenia. Neither cow required blood transfusions during treatment. Although the cause of thrombocytopenia was not determined, resolution of the thrombocytopenia after 48 days of corticosteroid treatment and reoccurrence of clinical signs 60 days after treatment was discontinued occurred in the first cow. Clinical signs resolved in the second cow of this report after administration of corticosteroids for 8 days, a finding that was similar to another case of idiopathic thrombocytopenia.

References