Management of hemodynamic changes associated with removal of a large abdominal myofibroblastic tumor in a pony

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- A myofibroblastic tumor should be considered as a differential diagnosis for a large abdominal mass in horses.
- Surgical removal of large abdominal tumors may be feasible and extend the life span of affected horses.
- With removal of a large mass from the abdomen, there is the potential for large fluid shifts and hemorrhagic losses; these events may result in a combination of distributive shock and hemorrhagic shock, both which can be treated via administration of crystalloid or colloid solutions.

A 339-kg (746-lb) 22-year-old female Welsh-cross pony was evaluated at the University of California at Davis **Veterinary Medical Teaching Hospital (VMTH)** because of intermittent colic, signs of depression, pyrexia, anorexia, muscle wasting with abdominal distention, and weight gain over the past 12 months. Historically, laboratory findings indicated that the pony had regenerative, macrocytic, hypochromic, mild anemia (Hct, 30% [reference range, 30% to 46%]; and mean corpuscular volume, 55.1 fL [reference range, 37 to 53 fL]; mean corpuscular hemoglobin concentration, 34.6 g/dL [reference range, 36 to 39 g/dL]). The pony had neutrophilia (11,371 cells/µL; reference range, 2,600 to 6,800 cells/µL) with signs of slight toxic changes, hyperglobulinemia (5.5 g/dL; reference range, 1.7 to 4.7 g/dL) with concurrent hypoalbuminemia (2.0 g/dL; reference range, 2.3 to 3.6 g/dL), and hyperfibrinogenemia (700 mg/dL; reference range, 100 to 400 mg/dL).

Via transrectal palpation, a large firm mass was detected in the caudal portion of the abdomen. A transabdominal ultrasonographic examination[a] revealed a large loculated mass with multiple cystic structures filled with fluid (hypoechoic appearance). At a depth of 40 cm, the diameter and origin of the mass could not be determined ultrasonographically. Abdominocentesis revealed a reddish-brown hemorrhagic effusion with total protein concentration of 4.3 g/dL, nucleated cell concentration of 11,400 cells/µL (comprised of 93% well-preserved neutrophils, 5% small mononuclear cells, and 2% large mononuclear cells), and RBC concentration of 640,000 cells/µL. The clinicopathologic evaluation was acute, marked hemorrhage or hematoma formation with mild suppurative inflammation of unknown origin. On cytologic evaluation of an ultrasound-guided aspirate of the mass, findings were consistent with cystic fluid of unknown etiology because a low number of cells were obtained. Neoplastic cells were not detected in either the effusion or aspiration sample. Bacteriologic culture and antimicrobial susceptibility testing were not performed because of limited quantity of sample material.

Further diagnostic testing at that time included detection of *Corynebacterium pseudotuberculosis* via a synergistic hemolysin inhibition test, serum immunodiffusion identification of *Coccidioides immitis*, and evaluation of serum progesterone, testosterone, and inhibin concentrations to rule out a granulosa cell tumor; results of all assessments were negative. An ELISA was performed to detect *Streptococcus equi* and revealed a high titer of *S equi*-specific antibody. At that time, differential diagnoses included neoplasia, hematoma, ovarian cyst, and internal abscess (most likely caused by *S equi*). The stable Hct value made a developing hematoma less likely. Percutaneous, ultrasound-guided biopsy specimens of the mass were obtained, but examination of these samples did not provide a diagnosis. The pony was administered trimethoprim sulfadiazine (24 mg/kg [10.9 mg/lb], PO, q 12 h) for 6 weeks.

On examination at the VMTH, the pony had marked abdominal distention and muscle wasting. Over the past 12 months, the pony had gained approximately 50 kg (110 lb). Results of another CBC and serum biochemical panel were within normal limits. The owner elected surgical exploration of the abdominal mass.

Preoperatively, ampicillin (21 mg/kg [9.5 mg/lb], IV, q 8 h) and gentamicin (6.6 mg/kg [3 mg/lb], IV, q 24 h) were administered to the pony. The pony was anesthetized, placed in dorsal recumbency, and the skin of the abdomen was aseptically prepared for ventral midline celiotomy. A ventral midline incision was made that extended from the xiphoid process to the pubis. Flunixin meglumine (0.6 mg/kg [0.27 mg/lb], IV, q 8 h) was administered intraoperatively. Lactated Ringer's solution was administered IV via a constant rate infusion (10 mL/kg/h [4.5 mL/lb/h]) intraoperatively for the first half hour. The rate of administration of lactated Ringer's solution was increased (15 mL/kg/h [6.8

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mL/lb/h], IV) for the following 2 hours and 45 minutes via placement of a second IV catheter. A cystic mass was observed within the abdomen, and a trocar with suction was used to drain 3 to 4 L of mucoid yellowish fluid from the mass. Multiple adhesions were identified and reduced, including 1 attachment to the cecum, 1 attachment to the small colon, and multiple adhesions to the omentum. The solitary, multilobulated, pedunculated abdominal mass had a 15 × 60-mm-wide stalk that attached it to the right side of the abdominal wall at a position 10 cm caudal and 15 cm ventral to the caudal edge of the right lobe of the liver. The stalk, which could be isolated but not exteriorized, was stapled and excised with a thoracoabdominal stapler.[b] There was no evidence of carcinomatosis on abdominal exploration. An enterotomy tray placed in the left flank area was used to facilitate mass removal. On removal from the abdominal cavity, the mass weighed 64.5 kg (141.9 lb; **Figure 1**). As the abdomen was lavaged, it appeared that minor hemorrhage was occurring diffusely throughout the abdomen. The hemorrhage was likely associated with small omental vessels that were severed when the multiple omental adhesions were reduced. Hyaluronate sodium (0.24 mg/kg [0.11 mg/lb]) diluted in 1 L of sterile physiologic saline (0.9% NaCl) solution was added to the abdomen to help limit further adhesion formation.[1] The linea alba was closed routinely with size 3 polyglactin 910 suture[c] in a simple continuous pattern, the subcutaneous tissues were closed with 2-0 polydioxanone suture[d] in a simple continuous pattern, and the skin was closed with skin staples.[e] The pony recovered from anesthesia without incident. The patient's greatest complications that developed during anesthesia were hypoproteinemia and apparent hemorrhage; the pony had a plasma total protein concentration of 2.6 mg/dL (reference range, 5.5 to 7.7 mg/dL) and an Hct of 25% during anesthesia. The pony was administered hydroxyethyl starch solution (3 mL/kg [1.4 mL/lb], IV) to increase the presumably low **colloid oncotic pressure (COP)** immediately after recovery. The pony was not transfused with plasma at that time because of the owner's financial constraints. Administration of hydroxyethyl starch solution was discontinued because of concerns regarding alteration of hemostasis and cost.

Figure 1—Photograph of the cross-sectional cut surface of a 64.5-kg (141.9-lb) multilobulated mass removed from the abdomen of a pony. Notice that the surface is shiny, smooth, and mottled yellow and dark red; there are variable amounts of solid, yellow soft tissues between which are numerous variably sized cystic structures filled with either clear yellow fluid or blood. Bar = 30 cm.

After surgery, the pony received ampicillin, gentamicin, and flunixin meglumine at the dosages administered preoperatively. In addition, omeprazole (3.9 mg/kg [1.8 mg/lb], PO, q 24 h) and lactated Ringer's solution (2 mL/kg/h [0.9 mL/lb/h], IV via constant rate infusion) supplemented with calcium gluconate (11.5 mg/kg/h [5.2 mg/lb/h], IV via constant rate infusion) were administered; increasing amounts of food were gradually provided. Heart rate, respiratory rate, rectal temperature, indirect blood pressure, PCV, plasma total protein and electrolyte concentrations, and venous blood gas concentrations were monitored every 4 hours. After removal of the mass, the pony's weight decreased to 257 kg (565.4 lb), which represented a loss of > 24% of its weight before surgery. At the time of recovery from anesthesia, the PCV was 30% and plasma total protein concentration was 4.0 mg/dL. Within 5 hours of recovery from anesthesia, the pony was tachycardic (heart rate, 84 beats/min) and tachypneic (respiratory rate, 36 breaths/min). After administration of flunixin meglumine, heart and respiratory rates returned to within reference limits. At this time, COP was notably low (9.2 mm Hg; reference range, 19.3 to 26.4 mm Hg). At 8 hours after recovery from anesthesia, the PCV had decreased to 24% and plasma total protein concentration was 3.7 mg/dL. The pony again became tachycardic (heart rate, 76 beats/min) but was eupneic with a respiratory rate of 20 beats/min. Via indirect oscillometric assessment, the pony's mean arterial blood pressure was low (57 mm Hg; reference range, 70 to 110 mm Hg). Abdominal ultrasonography revealed echogenic, swirling, free cellular fluid ventrally that was consistent with blood.

The pony was administered a loading dosage of aminocaproic acid (40 mg/kg [18.2 mg/lb] as a 1% solution, IV, once) followed by a maintenance dosage (20 mg/kg [9.1 mg/lb] as a 0.5% solution, IV, q 6 h). By 24 hours after surgery, the PCV had decreased to 15% and remained stable from 12 to 24 hours postoperatively; the plasma total protein concentration remained at 3.9 mg/dL. The pony continued to be tachycardic (heart rate, 60 beats/min) and to have low indirect arterial pressure (65 mm Hg). The amount of free abdominal fluid appeared unchanged ultrasonographically, and a sample obtained via abdominocentesis had a PCV of 8%. Blood transfusion was declined by the owner. Fluid administration to the pony was reduced (1 mL/kg/h [0.45 mL/lb/h], IV via constant rate infusion) to prevent excess hemodilution, development of pulmonary edema (as a result of low COP), and an excessive increase in blood pressure that could potentiate internal hemorrhage.[2] At 40 hours after surgery, the pony's PCV had decreased to 11%; it had persistent tachycardia (heart rate, 65 beats/min), low mean indi-

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rect arterial blood pressure (60 mm Hg), white mucous membranes, undetectable capillary refill time, weak peripheral pulse, and signs of depression. Because of the emotional investment, financial constraints were obviated and the decision was made to provide the pony with a blood transfusion. The patient received 3.5 L of fresh whole blood from a cross-matched donor (13 mL/kg [5.9 mL/lb] at a rate of 2 mL/kg/h, IV, via constant rate infusion) and had mild transfusion reactions, including muscle fasciculations and a slight increase in heart rate. This transfusion increased the PCV to only 14% and plasma total protein concentration to 5.2 mg/dL. The pony continued to have signs of depression and was anorexic, pale, and tachycardic (heart rate, 62 beats/min). However, the mean arterial blood pressure had improved to 95 mm Hg. Prothrombin time and activated partial thromboplastin time were within reference limits. To promote clotting, a formalin solution (0.06 mL/kg [0.027 mL/lb] diluted to 0.3% in lactated Ringer's solution) was administered IV to the pony. Because of the inadequate response to the first transfusion, an additional 4.5 L of whole blood (1 mL/kg/h, IV via constant rate infusion) from the same donor was administered starting at 58 hours after surgery. In addition, the pony received tripelennamine hydrochloride (1 mg/kg [0.5 mg/lb], IM, once) prior to the second transfusion to help minimize reactions to the donor blood. After the second blood transfusion, the pony began to improve clinically. Its attitude was bright and appetite was excellent; heart rate decreased to 40 beats/min, and mean indirect arterial blood pressure increased to 105 mm Hg. At completion of the second blood transfusion (72 hours after surgery), the PCV had increased to 20% and plasma total protein concentration was 7.0 mg/dL; furthermore, the COP was 18.6 mm Hg.

To provide precursors for RBC production, vitamin B_{12} (0.2 µg/kg [0.09 µg/lb], PO, q 24 h), vitamin B_6 (0.05 mg/kg [0.02 mg/lb], PO, q 24 h), and an iron supplement (ferric phosphate; 2.49 mg/kg [1.13 mg/lb], PO, q 24 h) were administered to the pony. Treatment with flunixin meglumine was gradually decreased until it was discontinued 6 days after surgery; administration of antimicrobials was continued until the ninth day after surgery. Values of PCV, COP, heart rate, and blood pressure had remained unchanged after the second blood transfusion. The pony was discharged from the hospital; because of the healing abdominal incision and to prevent disruption of any blood clots, the owner was instructed to provide strict stall confinement for the pony during the next month. One week later, the pony was evaluated by the local veterinarian and the PCV was unchanged. At an evaluation at the VMTH 1 year later, ultrasonographic examination of the abdomen yielded no abnormal findings and results of a hemogram were within reference limits. At 1 year after surgery, the pony was apparently healthy and used regularly for riding. On the basis of histologic and immunohistochemical assessments of the removed mass, a diagnosis of myofibroblastic tumor was made.

To the authors' knowledge, there are no other reports of the successful surgical removal of an abdominal mass that weighed as much as 19% of a pony's body weight before surgery. Nor are there any reports that describe the postoperative management that is required and the hemodynamic alterations and complications associated with the dramatic fluid losses and shifts that can occur in association with removal of a large abdominal mass. Previous reports include details of the surgical removal via midline celiotomy of an abdominal mass that was characterized as disseminated peritoneal leiomyomatosis and represented 7.8% of the horse's preoperative body weight[3] and removal via hand-assisted laparoscopic surgery of an ovarian tumor that represented 9% of a mare's preoperative body weight.[4] In the horse in the latter report, the combined loss of abdominal fluid and the ovarian mass resulted in a decrease of 29% of its preoperative weight, but there was no discussion of the postoperative management.

The pony of this report appears to be unusual in that primary neoplasms of the peritoneum are uncommon and intra-abdominal neoplasms appear to be more commonly associated with the abdominal organs.[5] The abdominal mass in the pony was a myofibroblastic tumor, which is a type of tumor that is seldom diagnosed in animals. To the authors' knowledge, only 1 other case has been reported in horses; the tumor found in the pony of this report closely resembled the description of the myofibroblastic tumor that was diagnosed at necropsy in an 18-year-old Thoroughbred gelding.[6] The major differential diagnoses for tumors arising from the mesentery and body wall are tumors of fibroblastic or lipoblastic origin. In the pony of this report, lipoblastic origin of the tumor was excluded on the basis of the absence of cytoplasmic lipid and fibroblastic origin of the tumor was excluded on the basis of the presence of smooth muscle actin. No direct connection of the tumor with the intestinal tract was identified, which made a diagnosis of gastrointestinal stromal tumor or a smooth muscle cell tumor (leiomyoma and leiomyosarcoma) unlikely.

Removal of a large space-occupying mass can result in major fluid losses and pooling of blood in splanchnic vasculature. Postsurgical vascular volume expansion can be achieved through administration of crystalloid or colloid solutions. Overhydration, especially with crystalloid solutions, should be avoided to prevent iatrogenic hemodilution with resultant decrease of the body's oxygen-carrying capacity, dilution of circulating proteins, and decrease in oncotic pressure of the blood. With a concurrent rapid decrease in oncotic pressure, overhydration with crystalloid fluids would expand the extravascular fluid compartment, thereby increasing interstitial pressure and overloading the capacity of the lymphatic system. This would result in the development of pitting edema, pulmonary edema, and further compromise in tissue perfusion.[7] The pony of this report had a plasma total protein concentration of 2.6 mg/dL during surgery, which indicated that considerable hemodilution and major reduction of COP had occurred as a result of the intra-operative fluid therapy. Intravenous administration of plasma can help restore COP by replacing albumin, but a typical 450-kg (990-lb) horse requires 7 L of

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plasma to increase the circulating concentration of albumin by 1 g/dL.[8] Therefore, the pony of this report would have required administration of a minimum of 5 L of plasma, a volume that was cost prohibitive at the time. Administration of a solution of the synthetic colloid hydroxyethyl starch was initiated to provide vascular expansion and correction of the hypoproteinemic state in this pony, but the standard dosage (10 mL/kg [4.5 mg/lb]) also proved to be too expensive.

The use of hetastarch solution in cases of hemorrhage of unknown cause is controversial in both human and animal patients. Treatment with repeated high doses of hetastarch solution (cumulative dose > 30 mL/kg [13.6 mg/lb]) can alter platelet function in humans by decreasing the activity of circulating von Willebrand factor and factor VIII coagulant.[9] Administration of high doses of hetastarch solution (20 mL/kg) in ponies has been associated with increased cutaneous bleeding times[10]; however, numbers of platelets were not decreased in these ponies, so the alteration in cutaneous bleeding time was considered attributable to alterations in von Willebrand factor and factor VIII coagulant activity levels. The pony in this report only received hetastarch solution at a dosage of 3 mL/kg, so it is unlikely that its administration had an effect on hemostasis postoperatively. The effect of hetastarch solution on oncotic pressure should be determined via direct measurement of COP versus use of a predictive nomogram to calculate COP from plasma total protein concentrations.[11] The low dosage of hetastarch solution used in the pony of this report was selected on the basis of the aforementioned hemostatic and financial concerns; this dosage probably had minimal effect on the correction of COP because the value after administration of the hetastarch solution was 9.2 mm Hg.

At the time of surgery, hemorrhage associated with removal of the mass did not appear excessive. The PCV decreased from 30% to 25% during surgery as a result of hemodilution caused by fluid administration. Postoperatively, the PCV remained stable at 30% and the pony's tachycardia was presumed to be a result of pain, which was managed with flunixin meglumine. Although the plasma protein concentration decreased from 6.3 g/dL prior to surgery to 4.0 g/dL postoperatively, the pony's clinical condition appeared to be stable. Intensive monitoring of the pony's PCV and plasma total protein concentration was continued after surgery to identify clinically important hemorrhage. An accurate assessment of the amount of hemorrhage cannot be determined by initial PCV, as a decrease in this variable will not be detected until 12 to 24 hours after the hemorrhagic event. This phenomenon is associated with loss of whole blood volume (ie, both plasma and cellular constituents) and splenic contraction.[12] Splenic contraction, caused by a release of catecholamines, can restore as much as 20% of the original blood volume and delay the hemorrhage-associated decrease in PCV.[13] To evaluate the extent of hemorrhage via changes in plasma total protein concentration, a minimum of 4 to 6 hours is required.[12] Premature administration of whole blood transfusions may have negative consequences, such as suppression of the normal erythropoietin response that stimulates the bone marrow to produce more RBCs, hypersensitization of the recipient to future blood transfusions through production of antibodies, and potential overload of the cardiovascular system.[14]

In the pony of this report, both the PCV and the plasma total protein concentration were decreased from preoperative values at 8 hours after recovery from anesthesia. This created concerns about ongoing postsurgical hemorrhage associated with a rise in blood pressure after recovery from anesthesia. Despite treatment with an antifibrinolytic agent (aminocaproic acid), the pony's PCV decreased to 15% by 24 hours after surgery. Intraoperative losses and subsequent rehydration with a crystalloid solution also contributed to the decrease in the value of PCV. Approximately 40 hours after surgery, the pony's PCV had dropped to 11%; clinical signs were consistent with shock and included white mucous membranes, weak peripheral pulses, low mean arterial blood pressure, signs of depression, and persistent tachycardia despite treatment for pain. These factors led to the decision to provide the pony with a transfusion of whole blood. In addition, measurement of plasma lactate concentration also could have been used as a marker for tissue hypoperfusion.[15]

A blood transfusion can provide necessary oxygen-carrying capacity until the bone marrow can produce sufficient RBCs. The normal life span of an RBC is 150 days,[16] but cross-matched transfused RBCs survive for only 3 to 4 days in the recipient[17]; after loss of RBCs, an effective bone marrow response requires 4 to 7 days.[14] There are several factors to consider when making a determination regarding the volume of blood to be transfused. The total blood volume deficit can be calculated with the following formula[14]:

$$\text{Deficit} = ([\text{desired PCV} - \text{recipient PCV}]/\text{donor's PCV}) \times (0.08 \times \text{recipient's body weight in kilograms})$$

where the total blood volume of the recipient is assumed to be 8% of the body weight in kilograms (to convert pounds to kilograms, divide value by 2.2). By use of this formula, the total blood deficit calculated for the pony of this report was 13.4 L. The provision of a transfusion is intended to provide 30% to 50% of calculated deficits. To avoid circulatory overload, transfusion volumes are kept below 20% of total circulatory blood volume[14]; accordingly, 3.5 L of blood was administered to the pony of this report. A safe administration rate can be as high as 10 to 20 mL/kg/h. Because of mild transfusion reactions in this pony, this first transfusion was administered at a rate of 2 mL/kg/h. If concurrent hemorrhage had existed, the ongoing losses may have exceeded the administration rate, resulting in no improvement in the PCV.[8] A second transfusion of 4.5 L of blood from the same donor was given within 24 hours to the pony of this report because there had been neither a notable increase in PCV nor any clinical improvement. A transfusion from the same donor within 24 hours was feasible because production of alloantibodies does not begin until 48 hours after a transfusion.[14]

The lack of improvement in PCV and deteriorating clinical signs after administration of the first transfusion and antifibrinolytic treatment increased suspicion

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of ongoing hemorrhage in the pony of this report. Therefore, despite its controversy, formaldehyde was administered IV prior to the second blood transfusion to promote primary hemostasis. In 1943, Roberts[18] reported results of uncontrolled studies in horses that suggested that administration of formaldehyde was associated with a decrease of coagulation time by 75.2%. A more recent study[19]determined that healthy control horses had no alterations in coagulation profiles when they received tolerated concentrations (without clinical side effects) of 0.37% formaldehyde; to our knowledge, no similar controlled studies in horses with hemorrhage have been performed.

This report highlights that a myofibroblastomic tumor should be considered in the differential diagnoses of large abdominal masses in horses and ponies. Surgical removal of large intra-abdominal masses may be feasible and may extend the patient's life if metastasis has not occurred. With intensive postoperative monitoring and care, the hemodynamic alterations associated with removal of such large masses may be successfully managed with a favorable outcome.

[a]Ausonics Impact, Universal Medical Systems, Bedford Hills, NY.
[b]TA 90, United State Surgical Corp, Norwalk, Conn.
[c]Vicryl, Ethicon, Johnson & Johnson Co, Somerville, NJ.
[d]PDS, Ethicon, Johnson & Johnson Co, Somerville, NJ.
[e]USS DG, Appose ULC, Tyco Healthcare, Norwalk, Conn.

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