Pure Red Cell Aplasia in the Canine

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INTRODUCTION

Anemia is a common clinical presentation in both referral and general practice. Anemia is defined as a decrease in the red blood cell mass and can further be defined as a decrease in the packed cell volume (PCV), hematocrit (HCT), or hemoglobin concentration, all of which indicate the same clinical finding.[1] There are a number of differential diagnoses for anemia which include: hemorrhage, hemolysis, infectious agents, drug and toxin administration, bone marrow disorders, radiation therapy, iron deficiency, and endocrine disorders.[2] The most common classification of an anemia is a regenerative anemia.

With the exception of anemia of chronic disease, non-regenerative anemias are not commonly recognized in canine patients. The opposite is true in feline patients, and is generally associated with non-hematologic disease.[1]

There are few reported cases of primary Pure Red Cell Aplasia in dogs, and as such, there are limited resources on the management and prognoses of these patients. Most data is extrapolated from the clinical manifestations, treatments, and prognosis of immune mediate hemolytic anemia. Pure red cell aplasia is defined as the presence of a severe non-regenerative anemia in the blood and a granulocyte:erythrocyte ration of >75:1 in bone marrow.[8]

CASE HISTORY AND PRESENTATION

The case presented is an approximately six-year-old female, spayed, Rottweiler, Trina. She presented to the Internal Medicine Service at the Mississippi State University College of Veterinary Medicine for a history of lethargy of two months duration, anorexia of one week duration, and a recently diagnosed non-regenerative anemia on September 16, 2016. The patient presented to the referring veterinarian the day prior (September 15, 2016) for anorexia and

lethargy. The veterinarian performed blood work including a complete blood count and a blood chemistry which revealed a non-regenerative anemia. The complete blood count revealed a Packed Cell Volume of 17% with a corrected reticulocyte count of 0.08%. The patient was administered mirtazapine for appetite stimulation, metronidazole, and glucosamine (all with unknown dosages) for previously diagnosed osteoarthritis. The patient then presented to the Mississippi State Internal Medicine Service the next day as an emergency patient.

Upon presentation to the College of Veterinary Medicine, Trina was triaged and was quiet, alert, and responsive. Completion of the physical exam revealed a body condition score of 2.5/5, with adequate hydration. Her temperature was elevated at 102.9 degrees Fahrenheit, her heart rate was elevated at 126 beats per minutes, and her respiratory rate was within normal limits at 24 breaths per minute. Mucus membranes were pink with a capillary refill time of less than two seconds. A left sided systolic murmur (grade III/VI) was auscultated with normal lung sounds. The murmur was likely a hemic murmur associated with the level of the anemia. Her abdomen palpated normally. Rectal examination was unremarkable. Pain was elicited when the left stifle was manipulated. A further orthopedic exam was performed, but revealed no abnormalities.

At this time, an anemia was evident but needed further evaluation. A CBC was performed revealing a hematocrit of 18% with rare auto-agglutination, the platelet estimate was 256,000 (which was adequate), and the white blood cell count was normal at 8.4 K/uL. A reticulocyte count was also performed and was corrected to 0.05%. A corrected reticulocyte count of 0.05% is considered a non-regenerative anemia. A blood chemistry was performed revealing a hypoalbuminemia of 2.3 g/dL. To rule out a coagulopathy associated anemia, PT and PTT's were performed which were within normal limits. Initial treatment options were discussed with

the owners including hospitalization for IV fluid administration and close monitoring of the hematocrit and total solids. Pain control was also discussed for Trina's previously diagnosed osteoarthritis and stifle pain found on physical examination.

PATHOPHYSIOLOGY

Anemic patients should first be determined as either regenerative or non-regenerative, as this helps to determine likely etiologies. The regenerative status of the anemia is determined based on a circulating reticulocyte count. A reticulocyte is an immature red blood cell that is produced by the bone marrow in response to a decreased circulating red blood cell count. A non-regenerative anemia is characterized by an absence or an inappropriate response of circulating reticulocyte count.

Regenerative anemias stem from extra-marrow etiologies because of the presence of reticulocytes that are being produced by functional marrow. Extra-marrow causes are restricted to blood loss or hemolysis and are usually acute in nature. The two can be differentiated based on the presence of free blood being lost externally or blood loss internally noted on physical exam. Blood loss anemia is also associated with a decreased total solids as evidenced on the serum chemistry. Hemolysis is either categorized as intravascular or extravascular. Intravascular hemolysis can occur as a consequence of direct red blood cell lysis caused by antibodies that activate complement.[2] In extravascular hemolysis, the red blood cells are destroyed by the spleen, liver, or bone marrow via phagocytosis. The most common causes of hemolysis in the dog include immune-mediated hemolysis, infectious causes (*Mycoplasma, Ehrlichia, Babesia,* cytauxzoonosis, FeLV, and septicemia), fragmentation/physical damage to RBC membrane, as well as drugs, toxins, and chemical damage.[2] Immune mediated hemolysis can be diagnosed via

the presence of spherocytes or auto-agglutination on a blood smear as well as a positive Coomb's test.

In cases of non-regenerative anemia, there is a marked depletion of erythroid progenitor cells[4] or decreased/ineffective erythropoiesis.[5] A lack of regeneration can be caused by early blood loss or hemolysis (in cases so acute, the bone marrow has not had adequate time to mount a regenerative response), infiltrative bone marrow disease (such as myelophthisis, myelofibrosis, or myelonecrosis), neoplasia, bone marrow suppression from underlying disease (anemia of chronic disease, viral diseases, or endocrine diseases), inadequate nutrients (such as iron deficiency anemia, cobalamine, folate, or copper deficiency), and immune-mediated destruction of red blood cell progenitor cells.[2,6]

Pure red cell aplasia (PRCA) is considered to stem from a bone marrow abnormality where there is a specific lack of erythropoiesis and no other cell lines affected. The mechanism is hypothesized to be similar to that of immune mediated hemolytic anemia however, serum antibodies are against erythroid cell formation, categorizing PRCA as a non-regenerative form of immune-mediate hemolytic anemia occurring in dogs and cats at the level of the bone marrow.[1,7]

Bone marrow aspirates in dogs with PRCA reveal erythroid hypoplasia or hyperplasia of erythroid precursors and an arrest of maturation at the rubricyte or metarubricyte stage. Most clinical pathologists classify bone marrow aspirates that are hypoplastic as PRCA, and classify aspirates with hyperplastic marrow and maturation arrest as non-regenerative immune mediated hemolytic anemia.[1]

CLINICAL PRESENTATION

Clinical features of dogs with PRCA include a median age of 6.5 years (ranging from 10 months to 12 years), with spayed females being over-represented. The most common breeds

affected include Golden Retrievers, Rottweilers, Dachshunds, Beagles, Boston Terriers, Cocker Spaniels, and Bull Terriers among others. The most commonly reported breed is the Labrador Retriever.[4,6]

Most dogs presenting with PRCA had a five day to three-month history of lethargy, anorexia, pallor, weakness, weight loss, collapse, exercise intolerance, vomiting, fever, syncope, coughing, seizures, and signs of depression.[4,6] Pica is also noted to be a common presenting complaint in dogs diagnosed with PRCA.[1] On physical exam, the dogs ranged from bright and alert to depressed and listless. Examinations included: mucus membrane pallor, systolic cardiac murmur ranging from grade I/VI to IV/VI, tachycardia and tachypnea, and hepato-splenomegaly.[4,6] Most dogs are clinically stable and appear well adapted to the anemia.

Laboratory results include severe anemia (with a median hematocrit of 11%) and an absolute reticulocyte count of less than 60 x 10^3/uL (with a median reticulocyte count being 1.5 x 10^3). The anemia is categorized as being normocytic and normochromic or normocytic and hypochromic. The most common biochemical abnormality is elevated liver enzyme activity (likely due to corticosteroid administrations), low bicarbonate concentration and hyperferremia.[4,6] Approximately 50% of dogs have a positive Coomb's test indicating an immune mediated process.[1]

DIAGNOSTIC APPROACH:

Pure Red Cell Aplasia is a relatively rare clinical abnormality. A thorough history should be obtained to rule out several causes of non-regenerative anemia including drug induced anemia, vaccine associated hemolytic anemia, anemias associated with infectious disease while traveling[1] as well as exposure to toxins or metals. A thorough physical exam should also be

performed. Evaluation of mucus membrane color/pallor, abdominal palpation for organomegaly, palpation of all limbs (to rule out a primary bone tumor), as well as heart auscultation can help rule out other causes of anemia. Serologic testing for rickettsial diseases should also be performed.[4]

Routine blood work is the first diagnostic step in diagnosing the anemia. A red blood cell count of <20% is a hallmark of PRCA.[4,6] Typically, animals with PRCA have a lower mean hematocrit than animals with non-regenerative immune-mediated hemolytic anemia.[7]

A blood smear should be made to evaluate reticulocyte counts and blood cell morphology. Once the reticulocyte count is performed, it should be corrected. This is to determine if the bone marrow response is appropriate compared to the degree of decrease in red blood cells. The formula for a corrected reticulocyte is:

$$\text{reported reticulocyte count} \times \frac{\text{patient's HCT}}{\text{normal HCT}}$$

Generally, a non-regenerative anemia is classified as a reticulocyte count as <1 %. Blood cell morphology can also indicate whether there is an immune mediated component of the disease process and indicates that there is destruction of mature red blood cells. Most dogs with non-regenerative anemia are classified as being normocytic and normochromic.[4,6]

Further diagnostics include a slide agglutination test and a Coomb's test. Positive agglutination and Coomb's tests are indicative of an immune mediated process.

Once the patient is determined to have a non-regenerative anemia, the bone marrow should be investigated. The animal should be placed under general anesthesia and a bone marrow aspirate and core biopsy should be obtained for pathology review. Most dogs with PRCA have high cellularity present in the bone marrow,[4] myeloid to erythroid ratios are usually > 99:1, and

no erythroid precursors are present in the marrow.[6] Erythroid hypoplasia is defined as a granulocyte:erythroid ratio of >2:1, and in pure red cell aplasia the granulocyte to erythroid ratio is > 75:1.[8] In dogs with bicytopenias or pancytopenias (absence of more than one blood cell line), there is destruction of all blood cell progenitors in the marrow and this is usually caused by diffuse bone marrow disease such as myelophthisis, myelofibrosis, and myelodysplastic syndromes. However, less diffuse progression of these diseases can account for selective aplasia of red cells only.[1] Dysmyelopoiesis, myelonecrosis, increased vascular permeability, hemophagocytic syndrome, lymphocytic hyperplasia, and lymphoid aggregates have all been associated with non-regenerative anemia but are all typical of non-regenerative IMHA as opposed to PRCA. None of these marrow disorders are generally used to categorize pathologic findings associated with PRCA.[7]

To summarize, once the anemia has been confirmed as a non-regenerative anemia, a bone marrow biopsy and analysis are critical for a definitive diagnosis of PRCA. The most common clinical finding in the bone marrow analysis is bone marrow (erythroid) aplasia or hypoplasia.

TREATMENT AND MANAGEMENT:

The goal of treatment in these patients is to increase the circulating red blood cell mass and to treat the underlying disease. Treating the underlying disease is achieved by stopping the destruction of the red cell progenitor cells. Symptomatic treatment is also of paramount importance to stabilize the dog in order to get a diagnosis.[9]

When a PRCA patient first presents, the severity of anemia and clinical signs should be assessed to determine if the patient is in need of a blood transfusion. With PRCA, the anemia is more chronic in nature and the patients are well adapted to the decreased circulating red blood

cells. It is at the clinician's discretion to decide if the patient needs to be transfused. Packed red cells are often preferred over whole blood[9] in cases of PRCA.

In cases where response to treatment is prolonged, multiple transfusions may be indicated. In patients that have received more than one transfusion or patients of unknown history, cross matching should be performed to decrease the risk of transfusion reaction. Dogs do not have naturally occurring antibodies against blood group antigens, so the first transfusion is generally safe. Beyond one transfusion, the animal should be cross matched to decrease the likelihood of an adverse reaction. Cross-matching can be performed in house. It can help decrease the likelihood of a reaction, however does not guarantee that the donor red cells are compatible.[1]

The recommended rate of administrations should not exceed 22 ml/kg/day. In order to increase the PCV of the recipient by 1%, a volume 2.2 ml/kg of whole blood should be administered. During transfusion administration, the patient should constantly be monitored for evidence of a transfusion reaction. These are more likely to occur at the beginning of the transfusion, and the patient's heart rate, respiratory rate, and temperature should be evaluated regularly. The blood product should also be periodically monitored for evidence of hemolysis before administration to the patient. If there is evidence of a reaction occurring, the transfusion should be stopped immediately.[1]

Due to the immune mediated nature of PRCA, immunosuppressive therapy is the hallmark of treatment. Treatments are usually very similar to that of immune-mediate hemolytic anemia and most clinical decisions are extrapolated from that data. The most commonly used drugs include prednisone/prednisolone, dexamethasone sodium phosphate, cyclophosphamide, azathioprine, cyclosporine, mycophenolate mofetil, leflunomide, danazol, and high-dose human

immunoglobulin, either used alone or in combination.[6,10]

The most commonly used drug in PRCA is glucocorticoids. The reasons for using glucocorticoids as the first line of therapy include rapid onset of action, low risk of toxicity, and low cost. Intermediate-acting steroids such as prednisone, prednisolone, methylprednisolone and triamcinolone have a biologic half life of 12 to 36 hours, whereas dexamethasone has a biological half life of 48 hours or longer. The early effects of corticosteroids are believed to result from a rapid decrease in the phagocytic activity of splenic and hepatic macrophages, whereas the long-term effects result from suppression of cell mediated immunity. Effects on B-lymphocytes likely occur from suppression of T-helper cells that are required for full antibody response to an antigen.[1] The recommended dose for prednisone is 2.2- 4.4 mg/kg PO as a single or divided dose every twenty-four hours.[11] The most ideal route of administration is oral, however in cases where the animal is not able to be administered pills or is not eating, parenteral dexamethasone may be administered. The dose of dexamethsone is based on the comparative potency of prednisone (approximately eight times less than the dose of prednisone). Long term adverse effects of glucocorticoids can cause significant problems in the pet and can cause great stress to the owners. These effects include polyuria, polydipsia, panting, weakness, dermatologic changes, predisposition to infection, and muscle atrophy. The goal of treatment is to taper the drug to the lowest effective dose without relapse of the disease in order to minimize adverse side effects. Also, other immune-modulating drugs can be added to the treatment protocol to further decrease the steroid dose.[1]

Corticosteroids are commonly used as a single agent and are the mainstay as treatment. Some dogs respond favorably to corticosteroids alone however, in many cases corticosteroids alone may not be sufficient enough treatment. Use of other immunosuppressive agents has been

proven to improve the acute and long term survival of the disease.[6,10] Azathioprine is a commonly used drug in addition to glucocorticoids. Azathioprine is a purine-analogue antimetabolite, that preferentially affects T-cells function and inhibits cell-mediated immunity and T-cell-dependent antibody synthesis. It also has minimal short term effects on immunoglobulin production. It influences lymphocyte blastogenesis in as early as seven days.[1,10] Typically, the starting dose for azathioprine is 2 mg/kg PO once daily.[1] Adverse effects of azathioprine include pancreatitis, cholestatic hepatopathy, myelosuppression, vomiting, anorexia, and diarrhea. These affects are infrequently encountered, however.[10] The bone marrow suppression that is caused by azathioprine is rare and life-threatening. It can cause a thrombocytopenia, a leukopenia, and anemia predisposing the dog to bleeding disorders and secondary infections. Bone marrow suppression usually occurs within the first one week to four months of treatment and is reversible within seven to fourteen days after the drug is discontinued. Because of the potentially severe consequences of this drug (bone marrow suppression and hepatotoxicity), a CBC and liver panel should be performed every one to two weeks for the first month of treatment, and then every one to three months throughout duration of treatment. Once a positive response is noted, the prednisone that is used in conjunction with azathioprine should be tapered to the lowest effective dose over a period of two to four months. If there are still no clinical signs once the prednisone has completely been weaned away, the azathioprine dose can then be tapered. Azathioprine should not be used in cats due to severe neutropenia and thrombocytopenia that have been reported even at very low doses.[1]

Cyclophosphamide is a common secondary drug that is used, however cyclophosphamide in conjunction with prednisone may not be superior to prednisone treatment alone.[11] It has been suggested that use of azathioprine and prednisone or prednisone alone may be more effective for

the disease than for cyclophosphamide.[11] Cyclophosphamide is an alkylating agent that decreases cell division of B and T lymphocytes, whose main effects are bone marrow suppression and lymphoid atrophy.[1,11] Cyclophosphamide affects both cell mediated and humoral immunity, with the effects of the humoral immunity being more pronounced. Adverse effects for this drug include bone marrow suppression, gastrointestinal upset, poor hair growth, alopecia, and sterile hemorrhagic cystitis from the toxic effects on the bladder.[1] Cyclophosphamide is not as used as frequently as azathioprine due to the more significant adverse affects and due to recent studies that show the superior activity of azathioprine and cyclosporine.[6]

Cyclosporine is a potent immune-modulating agent and is a cyclic polypeptide extracted from fungi. The major mode of action is by inhibition of the initial activation phase of CD4 T lymphocytes, and blocks the transcription of genes encoding IL-2, preventing activation and proliferation of T lymphocytes. Cyclosporine does not affect the humoral immune system. The recommended dose for cyclosporine ranges based on the product being used and the disease being treated, but generally the range is between 5 mg/kg PO once daily to 10 mg/kg PO twice daily. Adverse effects of cyclosporine include gastrointestinal disturbance, predisposition to infection, gingival hyperplasia, papillomatosis and increased shedding of the haircoat. There is increased risk of infection when cyclosporine is used in conjunction with other immunosuppressive drugs.[1] Cyclosporine is deemed an expensive drug, and as such cost can limit its use in clinical practice, especially in larger patients.

Supportive care is indicated in the treatment of PRCA and can include gastroprotectants, such as famotidine at 0.5 mg/kg PO q24 or sucralfate at 1 g PO q8 to q12. Antibiotics are often indicated and include tetracycline at 5 mg/kg PO q24, enrofloxacin at 2.5 mg/kg PO q12, or amoxicillin at 20 mg/kg PO q12.[6]

Response to treatment can be prolonged ranging from one to ten weeks with the median time being two weeks.[6] One study on pure red cell aplasia reports that 55% of the dogs evaluated had a complete response, 18% had a partial response and 27% had no response to therapy. Relapse can occur in dogs, once the medications are tapered, and generally responds to an increased dose or frequency of the drug. Variables such as median hematocrit, white blood cell count, platelet count, serum ALP, and serum bilirubin are not associated with poorer prognosis. Similarly, myelofibrosis or erythroid hypoplasia or aplasia is not associated with poorer prognosis.[6] Prognosis for PRCA seems to be equivalent to or better than that for regenerative and non-regenerative immune mediate anemias, therefore, lack of reticulocytosis should not be considered a poor prognostic indicator.[4]

CASE OUTCOME

The patient was hospitalized in the ICU for close monitoring. An intravenous catheter was placed and intravenous fluids were administered, which consisted of Lactated Ringers Solution at 80 mL/hour (maintenance fluid therapy). Additional medications started on Day 1 of hospitalization included dexamethasone sodium phosphate at a prednisone equivalent dose of 2 mg/kg intravenously every 24 hours as well as hydromorphone at 0.1 mg/kg intravenously every 6 hours. Serial packed cell volumes were monitored throughout the night and revealed a PCV of 20% at 4 pm, 25% at 8 pm, and 35% at 8 am.

The morning following admission to the hospital, the patient was evaluated to be stable with a normal temperature and respiration rate, but with an elevated heart rate. Thoracic and abdominal radiographs were performed. Thoracic radiographs revealed numerous, round, sharply marginated, soft tissue to mineral opaque nodules throughout the lung fields. The differentials

for these nodules were benign mineral opacities, however metastatic nodules could not be ruled out. The thoracic radiographs also revealed a mild left atrial bulge, which may have been associated with mitral valve insufficiency, however a definitive diagnosis was never obtained. After further questioning of the owners, it was revealed that Trina was adopted at 3 years of age and had previously been diagnosed with heartworm disease that had been treated, possibly leading to the bronchial pattern in the lungs. Abdominal radiographs revealed no evidence of a primary neoplastic mass however, the radiographs revealed evidence of spondylosis and osteoarthritis in the lumbar spine and hips.

Abdominal ultrasound was performed to rule out a primary neoplasia accounting for the nodular lung pattern. The ultrasound revealed some gall bladder sludge, irregular margins of the kidneys that was attributable to age related changes, and a small amount of free fluid. The fluid was sampled which revealed a modified transudate with no abnormal cell population.

Blood work on day 2 consisted of serial PCVs that revealed a HCT of 25% at 12 pm, 17% at 8 pm, 16% at 12 am and 24% at 8 am. It was discovered that the patient was inadvertently administered a quarter shock bolus of fluids leading to the decrease in hematocrit. During the second night of hospitalization, the patient broke with loose, watery diarrhea. The anorexia and lethargy had not resolved, and the patient was discontinued on hydromorphone. If the patient appeared painful (as indicated by a pain score of >= 6/24 on the Glasgow pain scale), the hydromorphone could then be administered.

After stabilization and close examination of two days duration, a bone marrow aspirate and biopsy were performed under general anesthesia. While under anesthesia, an endotracheal wash was performed to further evaluate the pulmonary pattern detected on thoracic radiographs. The endotracheal wash revealed a non diagnostic sample, and no bacteria were cultured. The

bone marrow aspirate revealed a large amount of blood with a large cluster of platelets and neutrophils, and moderate to large numbers of normal adipocyte clusters. There were rare clusters of normal appearing spindle stromal cells, with no atypical cell population or etiologic agents present. This suggested that there was granulocytic and megakaryocytic activity in the bone marrow. The bone marrow biopsy was also evaluated that revealed erythroid lineage atrophy with myelofibrosis. The changes in the marrow were consistent with red cell aplasia. There was appropriate myeloid cellularity in the face of very low erythroid series numbers. The only erythroid cells seen were meta-rubricyte-type cells, which is diagnostic for PRCA.

Following the biopsy, the patient was started on gabapentin at 10 mg/kg PO q8 hours and tramadol at 5 mg/kg PO q8 for pain. Mirtazapine was started at 1 tablet every 24 hours for appetite stimulation, and metronidazole was started at 10 mg/kg PO q12h due to the presence of a large bowel diarrhea, likely associated with a stress colitis. Her IV fluids were discontinued, and her intravenous catheter was removed. A PCV was measured and was a HCT of 22%.

The patient was discharged on the fifth day. At the time of discharge, she was bright, alert, and responsive with a PCV of 22% and a TP of 8.2 g/dL. She was discharged on prednisone at 2 mg/kg PO q24, gabapentin at 10 mg/kg PO q8 (for pain relief associated with arthritis and lumbosacral pain), 4 days of ondansetron at 1 mg/kg PO q12 (to alleviate any nausea and to help increase her appetite), one week of metronidazole at 10 mg/kg PO q12 (due to the large bowel diarrhea), and mirtazapine at one tablet every 24 hours as needed for appetite stimulation.

On October 3, 2016, Trina presented to the MSU CVM internal medicine service after a recheck examination with her referring veterinarian. At that visit, the veterinarian diagnosed a worsening anemia with a PCV of 11%. A blood transfusion could not be performed at that clinic,

so Trina was sent to MSU for a transfusion. On presentation, Trina was bright and alert. Her vital parameters were within normal limits aside from an elevated heart rate of 120 beats per minute. A PCV and total protein was performed that revealed a PCV of 14% and a serum protein of 7.4 g/dL. At that time, she was cross matched with a blood donor with which she was compatible. Trina received a blood transfusion of one unit of packed red blood cells over the course of 6 hours. Trina was discharged the next morning (October 4th) with a PCV of 24% and a serum protein of 7.0 g/dL. She was also prescribed azathioprine to be administered in conjunction with prednisone at 2 mg/kg q24. She was instructed to receive a recheck examination with her referring veterinarian in 7-14 days to have a serum chemistry and complete blood count performed to monitor for any adverse reactions of the azathioprine and to measure the packed cell volume.

On October 18, 2016, the patient presented again on referral from her primary veterinarian for a decreased hematocrit and thrombocytopenia. On presentation, Trina was bright, alert, and responsive, with all vital parameters within normal limits. A PCV was performed that revealed a PCV of 20%, and a total solids of 8.0 g/dL. A CBC was performed that revealed a hematocrit of 25% and an adequate platelet count of 320 K/uL with occasional clumping. The patient was discharged without a transfusion. She was instructed to continue on the prednisone, gabapentin, and azathioprine as previously prescribed. She was also instructed to continue with CBC and blood chemistry rechecks every two weeks to monitor for side effects associated with azathioprine administration.

On November 4, 2016, Trina presented for a recheck examination. The patient presented bright, alert, and responsive with all vital parameters within normal limits. A CBC was performed that revealed a HCT of 22.5%, a reticulocyte count of 1.6% which revealed that her

anemia was regenerative, and a normal chemistry panel revealing no hepatic damage that can be associated with azathioprine administration. The patient was continued on all medications as previously prescribed and was directed to have a follow-up exam performed in four weeks (December 2, 2016) to evaluate the CBC and blood chemistry. On December 5, 2016, the patient had a recheck examination with her regular veterinarian. He expressed that Trina was doing well, that her HCT had improved to 33%, and the reticulocyte count was corrected to 0.7%. At that time, he was asked to perform a CBC and chemistry due to the risk of hepatotoxic and myelotoxic adverse effects with azathioprine. The patient was instructed to continue on the current medications (prednisone, azathioprine, and gabapentin) for one more month, and then the immunosuppressive drugs could begin to be tapered. The patient is scheduled for another recheck with MSU-CVM Small Animal Internal Medicine service on January 13, 2017 for another evaluation of a complete blood count and blood chemistry so the patient could begin a taper of her immunosuppressive drugs.

REFERENCES:

1. Couto C. Anemia. In: Couto C, Nelson R. Small Animal Internal Medicine. 5th ed. St Louis: Saunders Elsevier, 2009; 1209-1224.

2. Fleischman W. Anemia: Determining the Cause. Hematology Compendium 2012; 34.

3. Weiss D. A Retrospective Study of the Incidence and the Classification of Bone Marrow Disorders in the Dog at a Veterinary Teaching Hospital (1996-2004). J Vet Intern Med 2006; 20:955-961.

4. Weiss D. Primary Pure Red Cell Aplasia in Dogs: 13 Cases (1996-200). JAVMA 2002; 221:93-95.

5. Fry M, Gimes C. Nonregenerative Anemia: Mechanisms of Decreased or Ineffective Erythropoiesis. Vet Path 2015; 52: 298-311.

6. Blue J, French T, Stokol T. Idiopathic Pure Red Cell Aplasia and Nonregeneratie Immune Mediated Anemia in Dogs: 43 Cases (1988-199). JAVMA 2000; 216: 1492-1436.

7. Weiss D. Bone Marrow Pathology in Dogs and Cats with Non-Regenerative Immune-Mediated Haemolytic Anaemia and Pure Red Cell Aplasia. J. Comp. Path. 2008; 138:46-53.

8. Weiss, D. A Retrospective study of the Incidence and the Classification of Bone Marrow Disorders in the Dog at a Veterinary Teaching Hospital (1996-2004). J Vet Intern Med 2006; 20:955-961.

9. Abrams-Ogg, A. Nonregenerative Anemia. In: Textbook of Veterinary Internal Medicine. 7th ed. St Louis: Saunders Elsevier, 2010; 788-797.

10. Barr S, Center S, Erb H, Randolph J, Warner K, Weinkle T. Evaluation of Prognostic Factors, Survival Rates, and Treatment Protocols for Immune-Mediated Hemolytic Anemia in Dogs: 151 Cases (1993-2002). JAVMA 2005; 226: 1869-1880.

11. Burgess K, Cotter S, Moore A, Rand W. Treatment of Immune-Mediated Hemolytic Anemia in Dogs with Cyclophosphamide. J Vet Intern Med 2000; 14:456-462.