Polycythemia in a llama

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- Polycythemia can develop in many species and is characterized by high serum erythropoietin concentrations.
- Affected animals may remain clinically normal unless stressed. Clinical signs, which may include tachypnea, dyspnea, and harsh bronchovesicular sounds, can be mistaken for signs of pneumonia.
- Polycythemia can result from dehydration, excessive bone marrow proliferation, hypoxia caused by pulmonary or cardiac disease or living at high altitudes, renal disease, or neoplasia.

A 38-month-old female llama (Lama glama) was admitted for evaluation of tachypnea, open-mouthed breathing, and extreme distress during breeding. The llama had been treated successfully for pneumonia at 6 days old, and had been treated successfully for metritis at 31 months old. Hematologic results at the time the metritis was diagnosed revealed neutropenia (1,530 cells/μl; reference range, 4,600 to 16,000 cells/μl);1 and evidence of erythrocytosis (PCV, 50.8%; reference range, 24 to 39%);1 high erythrocyte count (24.6 × 10⁶ cells/μl; reference range, 11.3 to 17.5 × 10⁶ cells/μl);2 and high hemoglobin concentration (21.8 g/dl; reference range, 12.8 to 17.6 g/dl).2 The referring veterinarian diagnosed pneumonia after auscultation of harsh bronchovesicular sounds over both lung fields. Hematologic results at that time again indicated erythrocytosis (PCV, 62%; erythrocyte count, 20.48 × 10⁶ cells/μl). After 5 days of treatment with ceftriaxone sodium (2 mg/kg of body weight, IM, q 12 h), the PCV was 60%, hemoglobin concentration was 25.2 g/dl, and WBC count was 28,900 cells/μl (16,762 neutrophils/μl; reference range, 4,600 to 16,000 cells/μl); 10,404 lymphocytes/μl; reference range, 1,000 to 7,500 cells/μl). Antibiotic treatment was continued for 30 days, after which hematologic results revealed leukocyte numbers decreased to within reference limits, but the PCV, erythrocyte count, and hemoglobin concentration remained virtually unchanged.

Although the llama was clinically normal at rest, tachypnea and open-mouthed breathing developed when it became stressed. The llama was referred to the Oregon State University Veterinary Teaching Hospital for evaluation of the erythrocytosis. Differential diagnoses for the erythrocytosis included dehydration (relative polycythemia), bone marrow proliferation despite normal erythropoietin concentrations (primary absolute polycythemia or polycythemia vera), and high serum erythropoietin concentrations attributable to hypoxia (secondary to pulmonary disease, cardiac disease, or high altitude), renal disease, or neoplasia.2,4

The llama weighed 130 kg. The only abnormality detected on physical examination was open-mouthed breathing after the slightest exertion. Results of thoracic and cardiac auscultation were unremarkable. Abnormal hematologic results included high PCV (66%), high erythrocyte count (22.24 × 10⁶ cells/μl), and high hemoglobin concentration (22.4 g/dl). Evaluation of a blood smear revealed mild anisocytosis, polychromasia, and a few nucleated RBC. Serum biochemical analysis revealed high values for BUN (48.6 mg/dl; reference range, 12 to 39 mg/dl);5 creatinine (4.0 mg/dl; reference range, 1.5 to 3.3 mg/dl);5 and albumin (3.0 g/dl; reference range, 3.4 to 4.4 g/dl).5 Although the llama was not clinically dehydrated, the hyperalbuminemia was indicative of dehydration. On the basis of these results, we believed the azotemia was not of renal origin, and homoconcentration was contributing to the polycythemia.

Thoracic radiography revealed a diffuse interstitial pattern and focal pulmonary mineralization, consistent with fibrosis after recurrent episodes of pneumonia. The PaO₂ (110.7 torr) and hemoglobin saturation (98%) were within reference ranges. Electrocardiography, echocardiography, and renal ultrasonography did not reveal abnormalities. Bone marrow biopsy results were suggestive of mild ery-

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The authors thank Drs. Joan Eegie and Peter Dukes for technical assistance.

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JAVMA, Vol 204, No. 9, May 1, 1994

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thyroid hyperplasia, with a myeloid/erythroid ratio of 0.85. There was no evidence of neoplasia. Reference values for myeloid/erythroid ratios have not been established for llamas, but in other clinically normal animals is reported to be approximately 1:1.6

Serum from this llama and 2 clinically normal llamas were submitted to a private laboratory for erythropoietin analysis.4 The samples were compared by radioimmunoassay, using an antirecombinant human erythropoietin antibody and recombinant human erythropoietin as the standard. The erythropoietin concentration of 104.0 ± 6.0 mU/ml in the polycythemic llama was 2.6 and 5.3 times the results for the 2 clinically normal llamas (39.8 ± 3.5 and 19.6 ± 2.7 mU/ml, respectively). A second private laboratory performed an erythropoietin assay on serum from the polycythemic llama, using the hypoxic polycythemic mouse assay, and reported the serum concentration was about 10 times the values reported for human beings, mice, rabbits, or sheep. These data supported a tentative diagnosis of absolute secondary polycythemia.

Hemodilution treatment was initiated. Approximately 1 L of blood was removed from the llama via a 14-gauge catheter and replaced with 1 L of 0.9% NaCl solution. On the basis of a blood volume of 80 ml/kg, it was calculated that 9.6% of the llama's blood was removed. The PCV before phlebotomy was 64%, and 24 hours after fluid exchange, the PCV had decreased to 58%, although clinical improvement in the llama was not apparent. The PCV increased to 60% by 72 hours after the hemodilution treatment.

Despite a guarded prognosis, the llama was discharged at the owner's request without further attempts at diagnosis. The llama remained clinically normal for several months, unless it became stressful, but it was euthanized 8 months after discharge because it was discovered recumbent, severely dyspneic, and unable to stand. At the time of euthanasia, the PCV was 74%, the erythrocyte count was 20 × 10^6 cells/μl, and the hemoglobin concentration was 31.9 g/dl. Serum biochemical analysis revealed renal and hepatic insufficiency.

The major finding on necropsy was congestion of the lungs and liver. Both organs appeared slightly swollen, and excess accumulation of blood was evident on examination of cut surfaces. Histologic examination revealed severe congestion of the spleen, kidneys, liver, and lungs. Renal tissue contained thrombosed blood vessels and hemosiderin droplets in the cytoplasm of convoluted tubular epithelial cells. Hepatic tissue contained dilated centriflobular sinusoids and fibrosis surrounding central veins. Bile stasis was prominent in hepatocytes. Pulmonary vessels were thick-walled and hemosiderosis of pulmonary parenchyma was detected. The history, lesions, and laboratory data of this llama were consistent with secondary absolute polycythemia.

Polycythemia develops infrequently in dogs,8 and rarely in cats,9 horses,10,11 and cattle.12,13 To our knowledge, this is the first report of polycythemia in a llama. The llama of this report resembled a group of Jersey calves with high hemoglobin, PCV, and erythrocyte counts,14 in which tachypnea and dyspnea with bronchovesicular sounds over both lung fields resulted in the clinical diagnosis of pneumonia. In retrospect, the respiratory signs were probably attributable to pulmonary congestion. The PaO2 of the calves was normal and abnormalities were not detected at necropsy that could explain the polycythemia.

Erythropoietin assays have not been validated for llamas; however, the peptide sequence of 166 amino acids and structure of erythropoietin is highly consistent among all species studied thus far.14 Erythropoietin from animals cross-reacts with antiserum to human recombinant erythropoietin.11 Increases in serum erythropoietin concentration are a physiological response to hypoxia caused by either pulmonary or cardiac disorders or living at high altitudes. Cardiopulmonary abnormalities were not detected on clinical or postmortem examination, and this llama lived its entire life at only 950 M above sea level.

Erythropoietin is synthesized primarily in the kidneys, and excessive production has been reported in dogs with renal carcinoma15,16 and renal lymphosarcoma.17 Erythropoietin is also synthesized in the liver,18 and excessive production was reported in a horse with hepatocellular carcinoma.11 Histologic examination did not reveal evidence of renal or hepatic neoplasia in this llama; however, it is possible that a focus of neoplastic cells capable of producing enough erythropoietin to cause polycythemia may have remained unidentified.

Secondary absolute polycythemia has been associated with nonneoplastic renal disease in dogs.8 At the time the llama was referred, the BUN and creatinine were high, although earlier serum biochemical analyses did not reveal renal dysfunction.

In polycythemia, the excessive concentration of RBC increases blood viscosity and pulmonary vascular resistance and decreases cardiac output, resulting in decreased blood flow and reduced tissue oxygenation despite normal arterial oxygen saturation.19 The chronic, passive congestion and cellular dysfunction from reduced tissue oxygenation are the probable cause of the hepatic and renal insufficiency in this llama. Similarly, dyspnea and tachypnea in this llama were the result of pulmonary congestion and poor oxygen exchange from the hyperviscous blood, and were not caused by hypoxia.

This llama may have benefited from additional phlebotomy. The PCV of a polycythemic horse, from which 2 to 4 L of blood was removed 7 times dur-

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9Dukes P, Children's Hospital, Los Angeles, Calif: Personal communication, 1993.
ing a 4-week period, decreased from 70 to 40%. In a report of 250 human beings who died of polycythemia vera, half of those not receiving treatment died within 18 months, whereas survival time doubled in those treated with phlebotomy.

References

Correction: Compendium of chlamydirosis (psittacosis) control, 1994

In “Compendium of chlamydirosis (psittacosis) control, 1994” (*JAVMA*, Dec 15, 1993, pp 1673–1680), item 3 in the Appendix should read, “A bird that is too sick to eat can be given 100 mg of nonreactive doxycycline/kg every 5 to 7 days, until the bird has a normal appetite, then switched to medicated feed to complete the 45-day treatment regimen.” Also, the last line in the Appendix should read, “Intramuscular injections of nonreactive doxycycline can be given at the rate of 100 mg/kg every 5 to 7 days, if the bird is not eating.” The authors regret the errors.