Synovial extramedullary hematopoiesis in a dog

Bryce Talsma, DVM; Rommaneeya Leela-arpon, DVM, PhD; Indira Rojas Rivera, DVM; Leah K. Sauerwein, DVM; Lindsay Elam, DVM, MPH, DACVSMR; Craig B. Webb, PhD, DVM, DACVIM*

College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO

*Corresponding author: Dr. Webb (cbwebb@colostate.edu)

OBJECTIVE
Synovial extramedullary hematopoiesis is a rarely reported condition in humans and, to date, has never been reported in canines. This case report describes the clinical presentation, diagnostic work-up, treatment, and outcome of a canine case confirmed to have hematopoietic tissue within multiple joints.

ANIMAL
A client-owned canine.

CLINICAL PRESENTATION, PROGRESSION, AND PROCEDURES
The clinical presentation was most consistent with immune-mediated polyarthritis, and arthrocentesis was performed in multiple joints for cytological evaluation and culture. Cytology revealed evidence of extramedullary hematopoiesis, and shortly thereafter the dog was diagnosed with immune-mediated hemolytic anemia and thrombocytopenia.

TREATMENT AND OUTCOME
Pregabalin, prednisolone, clopidogrel, and cyclosporine were started, and after several recheck appointments and dose adjustments, the dog’s clinical signs resolved for all conditions.

CLINICAL RELEVANCE
Unusual sites of extramedullary hematopoietic tissue may result in a clinical presentation for which more traditional etiologies and differentials are not applicable.

Keywords: extramedullary hematopoiesis, polyarthritis, synovial, arthrocentesis, immune-mediated hemolytic anemia

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left hind limb lameness with multiple effusive and painful joints, most marked in the left stifle. No stifle laxity was identified. Given the history, signalment, clinical signs, and orthopedic examination findings, the primary differential at the time was IMPA.

**Diagnostic Findings and Interpretation**

The dog's CBC revealed a strongly regenerative anemia with an Hct of 31% (reference range [RR], 40% to 55%) and a reticulocyte count of $402 \times 10^3/\mu L$, an elevated plasma protein of 9.0 g/dL (RR, 6.0 to 7.5 g/dL), a severe thrombocytopenia of $18 \times 10^3/\mu L$ (RR, 200 X $10^3$ to 500 X $10^3/\mu L$) with rare clumps and an elevated mean platelet volume at 22.0 fL (RR, 7.5 to 14.6 fL), and otherwise normal WBC counts. There was 4+ saline agglutination, consistent with immune-mediated hemolytic anemia (IMHA). The chemistry panel revealed a low creatinine of 0.32 mg/dL (RR, 0.6 to 1.6 mg/dL), elevated globulins at 5.1 g/dL (RR, 3.0 to 4.3 g/dL), and a slight hyperbilirubinemia at 0.3 mg/dL (RR, 0.0 to 0.2 mg/dL). Urinalysis was unremarkable.

The dog was sedated, and the right carpal joint, right tarsal joint, and left stifle joint were aspirated. On aspiration, the synovial fluid grossly had negligible viscosity and was homogenously dark red and opaque. Three milliliters of fluid was drawn from the left stifle. Fluid cytology of the left stifle and right tarsus revealed individual and aggregated hematopoietic precursors with myeloid, erythroid, and megakaryocytic lineages seen. All stages of all hematopoietic cell lines were found, and some of the aggregates were associated with plump spindle mesenchymal cells and scant extracellular matrix (Figure 1). This cytology is consistent with extramedullary hematopoiesis (EMH), an expected response to the significant anemia and thrombocytopenia but in a previously unreported location in canines. Cytology of the right carpus was minimally cellular and nondiagnostic. Aerobic and anaerobic culture of the pooled joint fluid showed no growth.

Additional diagnostics included a basal cortisol of 12 µg/dL; a negative 4Dx test for heartworm, *Anaplasma*, *Ehrlichia*, and *Borrelia*; and a positive Coombs (warm) test (1:64). Flow cytometry showed that 67.7% of platelets were associated with immunoglobulin, consistent with an immune process, but a positive result does not differentiate associative versus nonassociative thrombocytopenia (ITP).

Abdominal ultrasound revealed mild medial iliac lymphadenopathy and mild splenomegaly, both thought to be reactive hyperplasia and EMH, respectively. The patient’s thrombocytopenia informed the decision not to attempt fine-needle aspiration of either structure. Thoracic radiographs were normal.

Radiographs of the left stifle revealed moderate to marked osteopenia of the femur and tibia, marked diffuse muscular atrophy of that limb, and increased soft tissue opacity within the stifle joint. Joint survey radiographs revealed mild diffuse osteopenia of all osseous structures and moderate soft tissue swelling in both carpi, marked diffuse osteopenia of all osseous structures, soft tissue swelling of both tarsi, and marked diffuse muscular atrophy.

**Treatment and Outcome**

The patient was started on pregabalin (2 mg/kg, q 12 h) and prednisolone (2 mg/kg, q 24 h). Physical therapy was also recommended but was not pursued by the owner.

Ten days after starting treatment, the dog was no longer febrile and the owners reported that the dog was “doing well” at home, although showing

![Figure 1](image_url)
signs of fatigue during evening walks. The dog was still significantly underconditioned with diffuse muscle wasting, and mild effusion was appreciated in the stifle joints. The patient’s Hct had risen from 31% to 37% and was still strongly regenerative. Platelet count had increased from 18 X 10^3 to 449 X 10^3/µL with clumps. There was no saline agglutination noted on the 10-day recheck CBC. The prednisolone dose was decreased to 1.5 mg/kg every 24 hours, and cyclosporine (5 mg/kg, q 12 h) and clopidogrel (1.5 mg/kg, q 24 h) were added to the treatment regimen.

Two weeks later, the dog’s Hct was within normal limits at 43% and all other parameters were stable, although the WBCs then showed a typical steroid-induced stress leukogram. The owner reported that the dog was ambulatory on all 4 limbs, and mobility was overall much improved. Only mild left stifle discomfort was noted at this time. The treatment plan was to continue to taper the prednisolone as dictated by the continued clinical response.

**Comments**

Extramedullary hematopoiesis is demonstrated most frequently in the spleen or liver, usually in response to a reduction in intramedullary hematopoiesis. If present in an unusual location, EMH may cause clinical signs that are a diagnostic challenge. For example, case reports include refractory ascites in a dog with peritoneal EMH and a T3-L3 myelophasic secondary to extradural spinal masses of EMH tissue. This is the first known report of synovial EMH in a dog. This case differs from the previously reported cases of synovial EMH in humans in that a biopsy of the synovial tissue was not performed, only aspiration of joint fluid, and evidence of EMH was found in multiple joints.

It would appear that this dog had untreated ITP and IMHA for some period of time before seeking veterinary care for lameness. The degree of anemia was not severe and was being supported by a highly regenerative response, and although the thrombocytopenia was marked, there was no obvious clinical evidence of ITP. It is impossible to determine what degree of the reported lethargy was due to painful joints, muscle wasting, or anemia. It is unclear why the dog was stimulated to utilize joint space for EMH as a way to help maintain the Hct in the face of a chronic immune-mediated challenge. There is a case report of a dog with peritoneal EMH and IMHA. It seems likely but remains an unanswered question as to whether this dog actually suffered from immune-mediated polyarthritis. None of the joints produced fluid with cytology consistent with joint fluid, much less IMPA. One theory would be that the dog’s joints were in fact the site of an immune-mediated process around the same time as the ITP and IMHA and, under the stress of those 2 conditions, the joints in some way became available as EMH depots. The rapidity and degree of response to prednisolone therapy at multiple levels—Hct, platelet count, and clinical comfort—strongly supports a single underlying immune-mediated etiology. An alternative interpretation could be that successful treatment of the anemia and thrombocytopenia removed the stimulus for EMH in the joint, which then returned to a normal, pain-free structure and function.

One limitation of this report was the absence of repeat joint taps after the other parameters normalized and the dog became comfortable. The diagnostic work-up failed to identify a definitive trigger, and hence the patient’s immune-mediated conditions would be considered primary or nonassociative. It would be interesting to determine whether the EMH receded from the joints with successful treatment of the presumed stimulus, but this follow-up information is not available.

This case represents the first published report of EMH in the joint of a dog. The dog presented for joint pain, with a prior history of seemingly untreated IMHA and ITP. It would appear that those preexisting comorbidities impacted the dog’s joints, but the actual timing, pathologic process, and causality remains unclear. As in similar but rare reports in humans, this case highlights the importance of being open-minded and diligent when presented with multiple problems that initially appear unrelated.

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