Spinal cord compression secondary to extramedullary hematopoiesis in a dog

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Case Description—An 11-year-old spayed female Siberian Husky was evaluated because of a 2-week history of progressive paraparesis.

Clinical Findings—Results of neurologic examination were consistent with a T3-L3 myelopathy. There were no abnormalities on CBC, and hypercalcemia was noted on serum biochemical analysis. Several hypoechoic splenic nodules were evident on abdominal ultrasonography, and results of fine-needle aspiration cytology were consistent with splenic extramedullary hematopoiesis (EMH). Two compressive, extradural masses in the dorsal epidural space of the thoracolumbar region of the spinal cord were seen on MRI images.

Treatment and Outcome—A dorsal laminectomy was performed to remove the extradural spinal masses. Results of histologic examination of tissue samples were consistent with EMH. Following surgery, clinical signs of paraparesis resolved, and there was no recurrence of the masses 24 months after surgery.

Clinical Relevance—Extramedullary hematopoiesis should be considered as a differential diagnosis in dogs in which results of diagnostic imaging indicate a epidural mass. In human patients, spinal EMH usually occurs secondary to an underlying hematologic disease, but it can also occur spontaneously. Treatment options reported for humans include surgical decompression, radiation therapy, chemotherapy, and blood transfusion. The dog of this report responded favorably to surgical decompression and was clinically normal 2 years after surgery. (J Am Vet Med Assoc 2013;242:803–806)

An 11-year-old 38-kg (85-lb) spayed female Siberian Husky was referred to the Neurology Service at Carolina Veterinary Specialists with a 2-month history of progressive paraparesis. The medical history included a previous diagnosis of congenital cataracts.

Abnormal physical examination findings included immature cataracts of both eyes. On neurologic examination, the dog had moderate ambulatory paraparesis with pelvic limb ataxia. Proprioceptive placing was slightly delayed in both pelvic limbs. The spinal reflexes were normal in all limbs, and the cutaneous trunci reflex was intact. Spinal hyperesthesia was not appreciated. The lesion was localized to the T3-L3 spinal cord segments, and differential diagnoses included neoplasia, intervertebral disk herniation, degenerative myelopathy, immune-mediated or infectious myelitis, and diskospondylitis.

On a CBC, there was mild thrombocytopenia (156 x 10³ thrombocytes/μL; reference range, 175 x 10³ to 500 x 10³ thrombocytes/μL), but a manual platelet count was deemed adequate. The Hct (52%; reference range, 37% to 55%) and PCV (44%; reference range, 37% to 55%) were within reference limits. Abnormalities on serum biochemical analysis included increased alkaline phosphatase activity (525 U/L; reference range, 110 to 320 U/L), increased total calcium concentration (14.3 mg/dL; reference range, 10.0 to 12.0 mg/dL) with a concurrent increased ionized calcium concentration (1.67 mmol/L; reference range, 1.25 to 1.60 mmol/L). The patient was anesthetized, and MRI of the T3-S3 spinal cord segments was performed with a 1.5-T magnet. T1-weighted (pre- and postcontrast), T2-weighted, and STIR sequences were performed in sagittal, transverse, and dorsal planes. Two discrete masses were identified in the dorsal epidural space at the level of the L1 and L3 vertebrae. These masses were causing considerable dorsal compression of the spinal cord. Both masses were isointense to hypointense on T1-weighted, T2-weighted, and STIR images (Figure 1). Minimal lesion contrast enhancement was observed after IV administration of gadolinium. Differential diagnoses included metastatic neoplasia, multicentric primary neoplasia, and hemorrhage.

A standard dorsal laminectomy was performed from the T13-L3 spinal cord segments. Two reddish-brown epidural masses that adhered to the dorsal aspect of the dura mater were easily identified. These masses did not appear to be extensions of the dorsal laminae of the vertebrae. The masses were excised in

ABBREVIATIONS

EMH  Extramedullary hematopoiesis
STIR  Short tau inversion recovery

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pieces until only a small amount of tissue that was firmly attached to the dura mater remained. The tissue attached to the dura mater grossly contained bony spicules. A durectomy was performed, and the remaining mass was removed.

The patient was hospitalized and received standard postoperative care, including IV fluids and analgesia. Forty-eight hours after surgery, the patient was discharged. At that time, the patient was ambulatory with slightly improved paraparesis and pelvic limb ataxia, compared with results of the preoperative neurologic examination.

Impression smears of the masses were submitted for cytologic analysis. The impression smears were highly cellular, consisting of hematopoietic precursors, megakaryocytes, and iron stores. There was a normal myeloid-to-erythroid ratio and an orderly and complete sequence of maturation. Cytologic diagnosis was consistent with normal bone marrow.

Larger tissue samples were submitted for histologic analysis. Histologic examination revealed fragments of normal bone and fat and an abundant amount of hypercellular marrow tissue (Figure 2). Hematopoiesis was characterized as extensive and was associated with fragments of bone and surrounding fat. Areas of osseous ossification were also noted. The histopathologic diagnosis was spinal extramedullary hematopoiesis and areas of dural ossification. An independent slide review of the impression smears and tissue was requested at another institution. Again, a cytologic diagnosis of normal bone marrow and a histologic diagnosis of spinal extramedullary hematopoiesis were confirmed.

The owner reported a considerable improvement in the dog’s gait when examined 2 weeks after surgery. On neurologic examination, the dog had a mildly ataxic pelvic limb gait and normal postural reactions. A CBC with a differential count was performed, and all cell lines were within reference ranges, with no morphological abnormalities. Elevated total calcium concentration was seen on repeated serum biochemical analysis (13.7 mg/dL; reference range, 7.9 to 12.0 mg/dL). All other values were within expected reference ranges. It was recommended that the owner pursue further work-up of the persistent hypercalcemia with the referring veterinarian. At 4 weeks after surgery, the patient was reevaluated and results of gait and neurologic examination were normal.

One year after surgery, the patient was reevaluated, and the owner reported complete resolution of previously reported clinical signs, and findings on neurologic examination were unremarkable. A CBC and biochemistry panel were obtained, and the only abnormality was

Figure 1—Magnetic resonance images of the thoracolumbar portion of the vertebral column of an 11-year-old 38-kg (85-lb) spayed female Siberian Husky with a 2-week history of progressive paraparesis. Sagittal T2-weighted (A) and sagittal STIR (B) images show 2 hypointense dorsal epidural lesions (arrows) at the level of L1 and L3 causing substantial spinal cord compression.

Figure 2—Photomicrographs of the epidural masses obtained from the patient in Figure 1. A—Trabeculae of mature bone encompass hematopoietic marrow and sheets of hematopoietic cells mixed with a small amount of adipose tissue. H&E stain; bar = 1,000 µm. B—A mixture of myeloid and erythroid cells is observed in proper proportion in relationship to stem cell counterparts. Megakaryocytes and iron stores are present. H&E stain; bar = 50 µm.
A presumptive diagnosis of spinal EMH in human patients is made with a combination of a history of or a concurrent hematologic disorder and MRI findings. Definitive diagnosis is made via histologic analysis. Extramedullary hematopoiesis is characterized cytologically by the presence of megakaryocytic and erythrocytic precursors. Myeloid precursors may or may not be observed.7

In 1 retrospective study3 of human patients, the most common site for nonhepatosplenic EMH was in or surrounding the vertebral column. This same study3 also investigated the incidence of splenic EMH prior to diagnosis of nonhepatosplenic EMH. Twenty-two of 27 patients had evidence of splenic EMH prior to diagnosis with nonhepatosplenic EMH.3 This is consistent with the finding of splenic EMH in our patient.

Magnetic resonance imaging findings of spinal EMH in the human literature are variable depending on the composition of the mass and stage of development.5,7 The more acute, active EMH lesions have rich vasculature, whereas chronic, inactive EMH lesions have more fatty tissue or iron deposition. In 1 review2 of MRI findings in human patients, active EMH lesions showed intermediate signal intensity on T1- and T2-weighted images with minimal contrast enhancement with gadolinium. That same report2 categorized inactive lesions as either hyperintense on T1- and T2-weighted images or hypointense on T1- and T2-weighted images, reflecting mostly fat or mostly iron composition, respectively.

The MRI findings of hypointense lesions on T1-weighted, T2-weighted, and STIR images for the patient described in this report seem to be most consistent with inactive, chronic EMH with heavy iron deposition, and this is supported by the histopathologic findings. A gradient echo sequence was not performed in this patient. This sequence should be performed whenever hemorrhage is a differential diagnosis, and this may have helped to further characterize the MRI findings in this patient. Unfortunately, the variability of MRI findings reported in human patients likely indicates there are no imaging characteristics that can definitively diagnose spinal EMH, and a biopsy is necessary for definitive diagnosis.

There are no evidence-based guidelines for the treatment of spinal EMH lesions in human patients, likely because of their rarity.2 Treatment options include blood transfusion, radiation therapy, hydroxyurea, and surgical decompression. Most case reports2,11–16 reviewed described the use of a multimodal treatment approach.

Intuitively, blood transfusions are used to temporarily correct the underlying hematologic deficiency, but blood transfusions alone have also been shown to temporarily decrease the size of EMH spinal masses.2,11,17 There are also many reports of spinal EMH treated with radiation therapy. Hematopoietic tissues are typically sensitive to even small doses of radiation, and excellent results have been reported with this treatment option.2,14,15 Treatment with hydroxyurea alone or in conjunction with other treatments has also been reported.2,16 Hydroxyurea can decrease the occurrence of ineffective erythropoiesis and subsequent EMH.2,16

As described in the reports2,3,11,13,16 previously mentioned, surgical decompression was reserved for human

mild hypercalcemia (12.8 mg/dL). Magnetic resonance imaging of the thoracolumbar portion of the vertebral column was repeated, and there was no evidence of lesion recurrence (Figure 3). The patient was examined 2 years after surgery, and results of the neurologic examination remained normal.

Discussion

Extramedullary hematopoiesis is the formation and growth of blood cells outside of the bone marrow. It is typically a physiologic response to primary bone marrow failure to produce adequate amounts of blood cells (myeloproliferative disease or myelofibrosis) or due to hematologic disorders that cause an increased demand for blood cells (hemolytic anemia or polycythemia vera).3,4 The most common sites for EMH formation are the spleen and liver, and this has been well documented in dogs and cats.5,7 There are infrequent case reports3,4 in the veterinary literature of EMH formation outside of the spleen and liver, including the choroid plexus and mammary gland, termed nonhepatosplenic EMH. To our knowledge, there have been no reports in the veterinary literature of spinal EMH.

Extramedullary hematopoiesis resulting in spinal compression is recognized in human medicine, but it is considered a rare disease process.2,3,10–16 In most of these case reports, an underlying hematologic disease resulting in EMH was identified, but there are sporadic reports3,16 of spinal EMH without an identifiable underlying disease process. In human patients, the most common underlying hematologic disorders associated with nonhepatosplenic EMH include β-thalassemia and myelofibrosis.3

Figure 3—Magnetic resonance images of the patient in Figure 1 obtained 1 year after surgery. Sagittal T2-weighted (A) and sagittal STIR (B) images show resolution of the previously diagnosed L1 and L3 lesions (arrows).

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patients with rapid deterioration of neurologic symptoms or those who did not respond to other treatment modalities. The benefits of surgery are the immediate relief of spinal cord compression and the ability to obtain a definitive histologic diagnosis. Most of the human patients undergoing surgical decompression reportedly had complete neurologic recovery.3,11,13,16

Surgical decompression was elected in the patient described in this report, and this was adequate for resolution of neurologic symptoms. It is possible that hydroxyurea or radiation therapy with or without surgery may have been beneficial, and these are potential treatment options for dogs with minimal neurologic deficits or those that are not surgical candidates. However, initiation of this treatment would require confirmation of EMH via histologic examination of fine-needle aspirate or biopsy specimens. Further long-term follow-up with this patient would be ideal to monitor for recurrence of disease and, if recurrence were to be observed, to evaluate the usefulness of other treatment options.

A spinal myelolipoma and an EMH mass can have similar MRI and histopathologic findings.19–21 Myelolipoma is a rare, benign tumor, which consists of fat, myeloid elements, and erythroid marrow elements. Usually, the adipose tissue is the primary component, and the marrow elements are not typically hypercellular. In dogs and cats, these tumors are reported in the spleen, adrenal gland, and liver. Interestingly, there are case reports19–20 of an epidural spinal myelolipoma in 2 dogs. In humans, differentiation between the 2 lesions is difficult and the diagnosis may be equivocal.21 We believe that the mass identified in the patient of this report was truly an extramedullary hematopoietic mass. This conclusion was based on the extensiveness of the hematopoiesis, which was both hypercellular and orderly in progression; the minimal involvement of adipose tissue; the diffuse and multicentric nature of the mass; and the presence of EMH at another site (spleen). Also, MRI findings of a myelolipoma have been reported as T1- and T2-weighted hyperintense, which is not consistent with our imaging findings.19,22

In retrospect, a bone marrow aspiration or biopsy would have been performed to definitively exclude a bone marrow proliferative disorder or neoplasia. However, given the lack of regrowth of the mass and the continually normal CBC, an underlying hematologic disorder in this patient seems unlikely. Also, further diagnostic testing, such as a parathyroid hormone panel, would have been helpful to determine the cause of hypercalcemia. At this time, it is unclear whether this dog’s hypercalcemia is clinically or pathophysiologically related to the spinal EMH mass.

This case is clinically relevant because it adds a differential diagnosis for an epidural spinal mass identified on MRI. If a hypointense epidural mass is identified on T1-weighted, T2-weighted, and STIR sequences, there should be a clinical suspicion for EMH. Extramedullary hematopoiesis lesions are benign and may not be associated with a clinically important underlying disease process; thus, spinal EMH may carry a good prognosis with appropriate treatment. Surgical removal of the mass appears to be an excellent treatment option. More case reports are needed to further evaluate the etiology, MRI findings, treatment guidelines, and prognosis for spinal EMH in dogs.

a. Sigma LX; I.3 T; General Electric, Schenectady, NY.

References


