# Extramedullary Hematopoiesis: Imaging and Clinical Implications

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## PURPOSES

- Describe the process of hematopoiesis
- Discuss the etiology and pathophysiology of Extramedullary Hematopoiesis (EMH)
- Describe the characteristic imaging appearance of EMH
- Discuss the multiple clinical presentations of EMH
- Discuss the different types of management of this disease

## PROCESS OF HEMATOPOIESIS

Hematopoieis begins at 4-5 months in the fetal bone marrow, fetal yolk sac, liver, and spleen during human pregnancy. After birth, normal hematopoiesis should occur only in the bone marrow, a specialized tissue site for maintaining and differentiating stem and progenitor cells. It is a complex process regulated by multiple factors, including osteoblasts, CXC chemokine ligand 12 expressing reticular cells, and vascular endothelium cells. Signals from the sympathetic system and osteoclasts regulate the hematopoietic stem cell, including the Wnt pathway, calcium-sensing receptors, angiopoietin 1, Tie-2, and extracellular matrix components.[1]

## INTRODUCTION

Extramedullary Hematopoiesis is the production of blood cells outside of the normal location of the bone marrow, occurring secondary to inadequate production of blood cells. EMH may be due to inefficient blood cell production or a compromise in the quality of blood cells. In the fetus, the primary sites of hematopoiesis are the yolk sac, liver, spleen, and bone marrow. After birth, hematopoiesis should occur only in the bone marrow and any extramedullary location is considered abnormal[2]. Causes of EMH are congenital or acquired hemolytic diseases, ineffective erythropoietic states, loss of control of stem cell differentiation, or nonmyeloid neoplastic diseases[3]. Conditions causing EMH include thalassemia, sickle cell anemia, myelofibrosis, leukemia, and lymphoma[2].

## METHODS

- Four cases from Tulane University Hospital were reviewed. All patients were found to have EMH findings projected on the head and neck, spine, pelvis, and musculoskeletal system.
- These cases were evaluated using Magnetic Resonance Imaging (MRI) and Computed Tomography (CT).
- Recent literature and guidelines were reviewed, and a search for EMH was performed in PubMed. From the literature we were able to identify cases of EMH and compare these to our case series. Localized anatomical landmarks were identified and pertinent findings are presented with each case.

## PATHOPHYSIOLOGY

EMH occurs when bone marrow is no longer able to support normal hematopoiesis. EMH can occur under conditions of local production of hematopoietic factors that maintain and induce differentiation of the stem and progenitor cells, when there are supporting cells, and when there is accommodation of hematopoietic progenitors. The cascade begins with displacement and mobilization of stem and progenitor cells. Consequently, hematopoietic stem and progenitor cells occupy other locations as alternative sites of hematopoiesis[1].

## HEAD

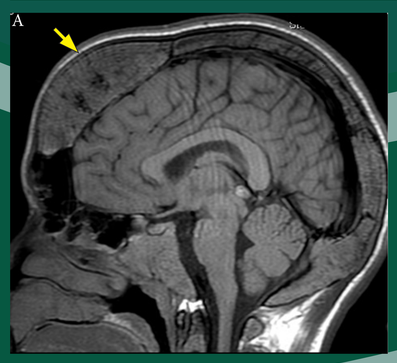


Figure 1. Magnetic Resonance Imaging (MRI) of the brain. (A) sagittal, (B-C) coronal, and (D-G) axial projections demonstrating marked diffuse expansion of diploic space and bone marrow of the calvarium, mastoid processes, and bilateral maxillary bones. Findings reflect EMH.

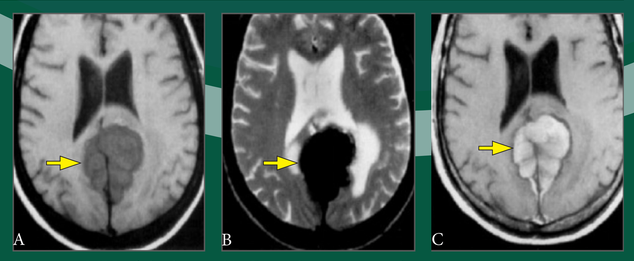


Figure 2. MRI of the brain. (A-C) axial projections demonstrating space occupying lesion arising from the posterior falx cerebri. Finding was determined to be EMH.

## SPINE

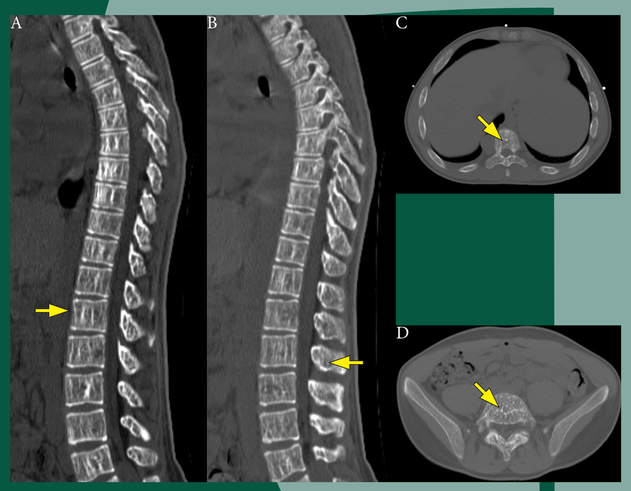


Figure 3. CT of the spine. (A-B) sagittal projections showing expansion of posterior elements and spinous processes of multiple cervical, thoracic, lumbar vertebral bodies secondary to expansion of bone marrow (arrows). Axial projections at the level of the thoracic spine (C) and pelvis (D) demonstrating expansion of bone marrow (arrow).

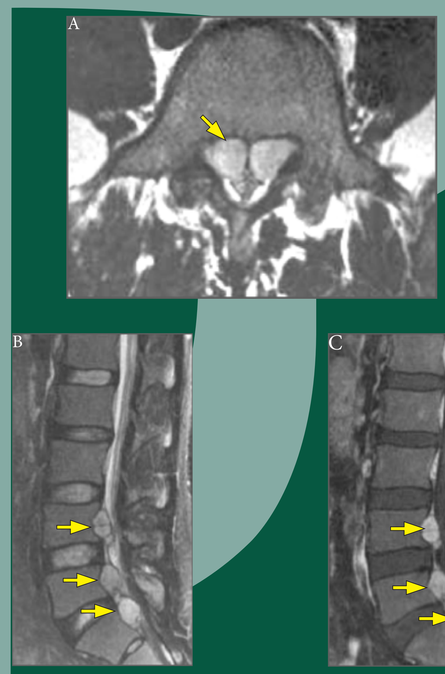


Figure 4. MRI of the spine. (A) axial and (B-C) sagittal projections demonstrating radioculopathy along with multiple small masses in the neural foramina. Findings were consistent with EMH.

## PELVIS

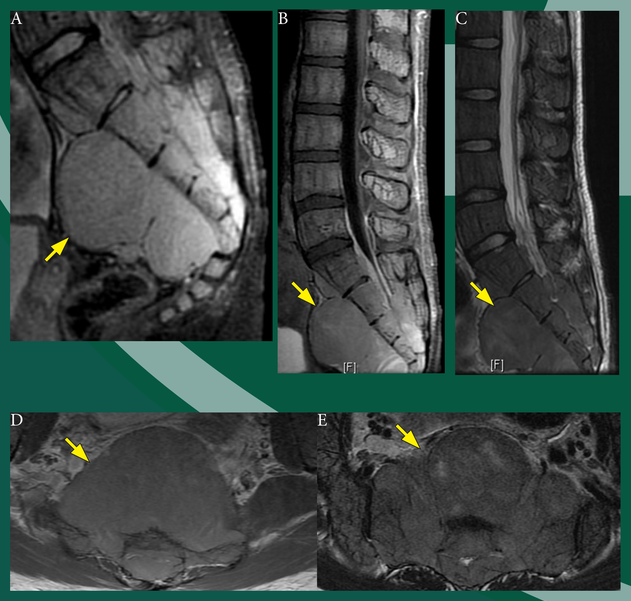


Figure 5. MRI of the lumbarsacral spine. T1 (A-B) and T2 weighted (C) sagittal projections demonstrating a presacral mass with isointense T1 and T2 signal characteristics with enhancement on postcontrast images. Axial (D-E) projections revealing enlargement of the sacral foramen and soft tissue invasion into the sacral central canal consistent with EMH.

## MUSCULOSKELETAL

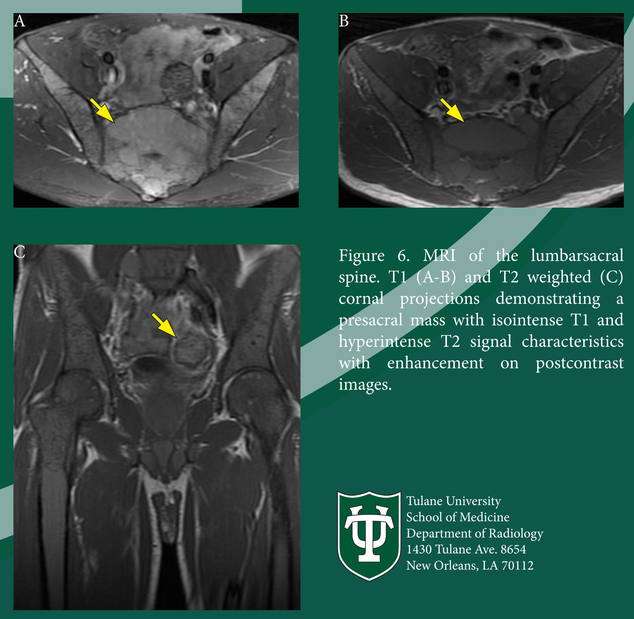


Figure 6. MRI of the lumbarsacral spine. T1 (A-B) and T2 weighted (C) cornal projections demonstrating a presacral mass with isointense T1 and hyperintense T2 signal characteristics with enhancement on postcontrast images.

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## DISCUSSION

EMH occurs in the liver and spleen for 95% of cases, with the remaining 5% of cases occurring in almost every tissue in the human body, including the adrenal gland, thymus, kidney, pleura, pulmonary interstitium, breast, skin, and gastrointestinal tract[4]. Very rarely, EMH can develop in the CNS, head and neck, and spine. After hepatosplenomegaly, bilateral heterogeneous paravertebral masses are the next most common manifestation. Symptoms for the majority of patients with non-hepatosplenic EMH (63%) will be site-specific. Patients also often present with generalized symptoms such as fatigue (15%) or are asymptomatic (22%)[5]. EMH has high risk for hemorrhage complications and paraspinal lesions may affect the spinal cord and peripheral nerves, causing symptoms such as weakness and radiculopathy[2].

## TREATMENT

The treatment approach for EMH depends on a number of factors, including the size of the mass, severity of symptoms, the clinical condition of the patient, and previous treatment methods. Excisional biopsy, radiation therapy, and frequent blood transfusions to limit hematopoietic stimulus are some treatment options[2]. Therapy may be required in cases such as EMH manifestations in the spinal canal causing spinal cord compression, and asymptomatic cases may require no therapy[2,6].

## CONCLUSION

EMH is a non-neoplastic formation of blood or blood cells outside the bone marrow found in patients suffering from various hematologic disorders. EMH usually presents as hematopoietic masses that may occur in almost all body sites, including rare manifestations in the CNS, head and neck, and spine. When imaging features suggestive of EMH are identified, ECM should be strongly considered. Knowledge of these atypical locations correlated with clinical history is needed to reach a diagnosis of EMH and to exclude other pathology. Treatment may be required if the case is symptomatic, such as when manifestation occurs within the spinal canal causing cord compression. EMH in these locations should be closely monitored with follow-up imaging.

## REFERENCE

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## ACKNOWLEDGMENT

Dr. Lorena Garza is a PGY5 radiology resident in training at Tulane University School of Medicine in New Orleans, LA. Dr. Enrique Palacios and Dr. Jeremy B. Nguyen are faculty members at the Department of Radiology at Tulane University Medical Center in New Orleans, LA. Juan Gomez is a Medical Doctor from Bogota, Colombia. Millie Yu, and Joshua Kirbens are second year medical studens. Special thanks to Donald Olivares, Digital Imaging Specialist, for assistance with poster design and printing.