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Case Report

Surgery Section

# Intrathoracic and Presacral Extramedullary Haematopoiesis in a Thalassaemia Intermedia Patient

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## ABSTRACT

Extramedullary Haematopoesis (EMH) is a normal physiologic phenomenon in inadequately transfused patients of chronic severe anaemia due to haemoglobinopathies or myelodysplasia. Although mostly asymptomatic, these haematopoetic cells rests when present along the paraspinal tissues may mimic intrathoracic and presacral masses producing pressure effects and confounding diagnoses. Intrathoracic EMH mostly develops in the posterior mediastinum. Presacral EMH is an extremely rare phenomenon with limited mention in medical literature. The precarious location leads to high risk of obtaining invasive biopsy and thus radiological and radionuclide scanning are the diagnostic modalities of choice. Intervention is only planned in symptomatic lesions. Therefore, the possibility of EMH must be kept in mind whenever diagnosing any mediastinal mass in a patient with a documented haemoglobinopathy. We present here such a case of intrathoracic and presacral EMH in a young lady with beta thalassaemia intermedia.

**Keywords:** β thalassaemia intermedia, Mediastinal mass, Spinal cord compression

## CASE REPORT

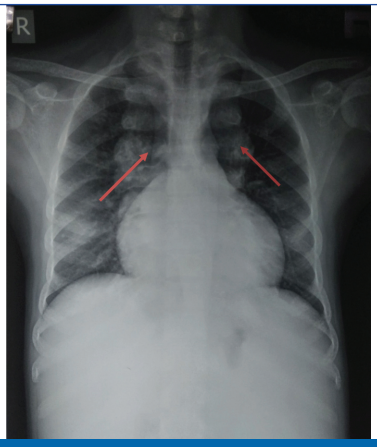
A 19-year-old lady presented to the general surgery department from the thalassaemia clinic for splenectomy with a requirement of transfusion of 2-3 units of blood every month. There was history of abdominal discomfort related to huge splenomegaly for the past two years. At initial physical examination, patient had characteristic thalassaemic facies, with pallor, mild icterus and growth stunting with delayed puberty. She had no history of exertional dyspnea, dysphagia or respiratory distress.

Examination revealed a pulse rate of 80/minute, respiratory rate of 20/minute and normal temperature. Chest was clear bilaterally. Abdomen was soft and non-tender on examination with huge hepatosplenomegaly with no evidence of free fluid.

Laboratory investigations revealed Hb: (6.7g/dL), mean corpuscular volume: 76 (fL), mean corpuscular haemoglobin concentration: (29g/dL), 81,000 reticulocytes/$mm^3$. Liver function tests showed total bilirubin of 26 mmol/L (range 4-18), direct bilirubin of 6 mmol/L (range: 0-4). Serum ferritin level was 1582 ng/mL (normal: 20-200), total protein (4.4 g/dL), albumin (3.2 g/dL), lactate dehydrogenase (519 IU/L) and international normalized ratio (2.0) and viral markers including HIV 1 and 2, Hepatitis B and C and VDRL screen were negative.

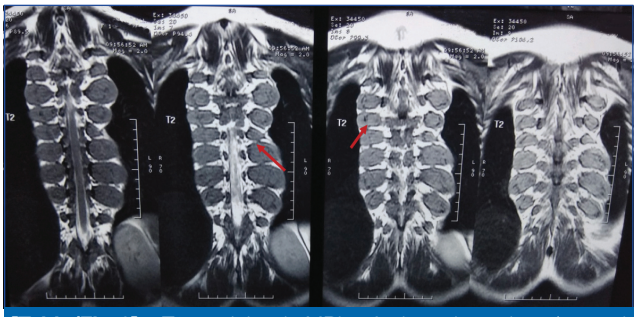
She had no siblings and no one in her family had any history of any disease requiring transfusion of blood.

Routine preoperative Electrocardiogram and 2D echocardiography were essentially normal. However, the preoperative upright chest radiogram revealed widening of the upper mediastinum, with large bilateral lobulated paraosseous opacities on either side of the thoracic spine [Table/Fig-1]. Whole spine and abdominal MRI was done purely out of academic interest to delineate the extent of EMH which was suspected by the case diagnosis. It showed

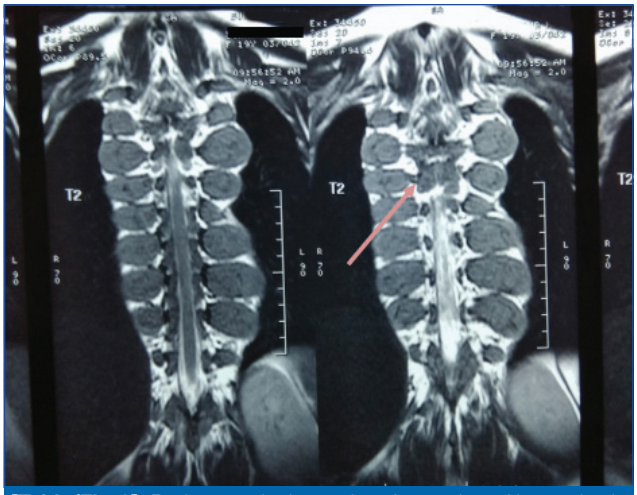


**[Table/Fig-1]:** A skiagram of chest PA view showing bilateral parasinal EMH (red arrows).

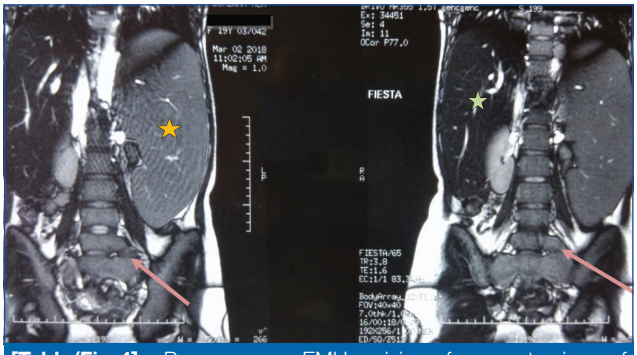
lobulated paravertebral soft tissue thickening along the whole spine with intensity changes, hyper in T2 & STIR with signal blooming in Gradient echo suggestive of EMH and huge hepatosplenomegaly with haemochromatosis. Marrow expansion and rupture through thinned out vertebral cortex with paraosseous haemopoetic deposits were noted in the both the intrathoracic and presacral areas [Table/Fig-2-6].



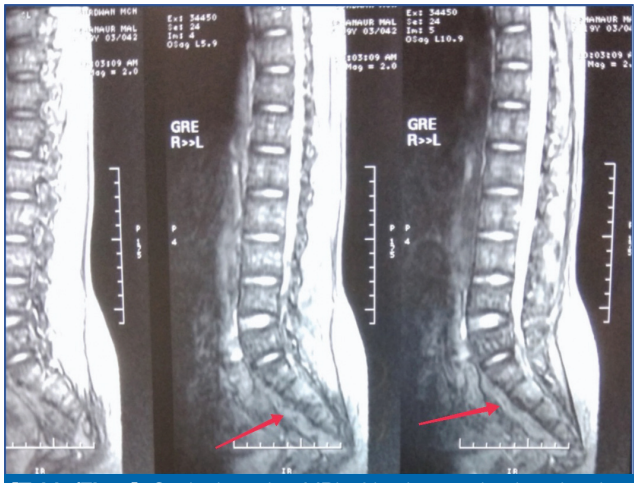

**[Table/Fig-2]:** T2 weighted MRI of thoracic spine (coronal section) showing bilateral paraspinal intrathoracic EMH in posterior mediastinum (red arrows).



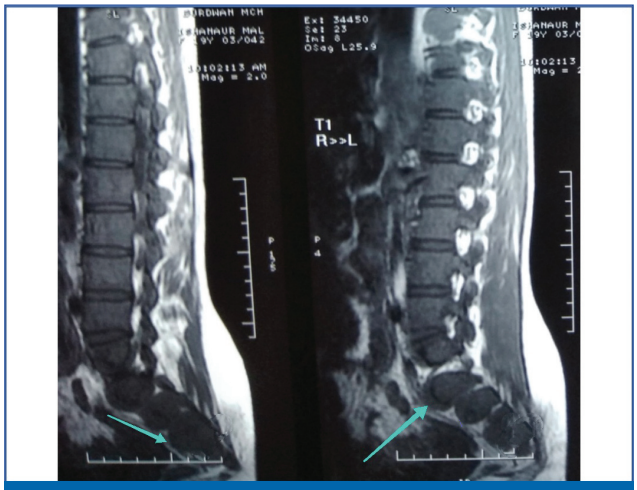

**[Table/Fig-3]:** Red arrow depicts point of extrusion of hyperplastic vertebral marrow through the thin cortex to form intrathoracic paraosseous EMH rests.




**[Table/Fig-4]:** Paraosseous EMH arising from extrusion of proliferating marrow from L1, S1 and S2 vertebral levels depicted by red arrows. Huge splenomegaly (orange star) and hepatomegaly (green star) are notable.




**[Table/Fig-5]:** Sagittal section MRI of lumbosacral spine showing thickened presacral soft tissues suggestive of presacral EMH (red arrows).




**[Table/Fig-6]:** Blue arrows depicting sites of proliferative marrow protrusion from sacral spine in a sagittal view of T1 MRI lumbosacral spine.

Ideally, further confirmatory imaging should be have been carried out with Technetium 99 m-labeled sulfur colloid scan, a noninvasive technique of detecting areas of EMH (Tc 99 is taken up by reticulo-endothelial cells) but patient refused to undergo further tests on monetary grounds. Biopsy was not undertaken taking the risk of inadvertent bleeding into account.

Patient was counseled regarding the findings and its future possibilities of spinal cord compression (SCC). She was immunized with pneumococcal, meningococcal and HiB vaccines 2 weeks prior to surgery. Adequate resuscitation was done with preoperative blood transfusion and correction of INR and serum albumin. Thereafter, planned open splenectomy through left subcostal incison was done with negligible intraoperative bleeding and no complications. Postoperative period was uneventful and patient is currently under follow-up for 8 months with no new symptoms.

A final diagnosis of extramedullary intrathoracic and presacral haematopoesis (with pending tissue diagnosis) in a case of beta thalassaemia intermedia was established.

## DISCUSSION

Thalassaemia Intermedia has been largely regarded as a mild to moderate disease with limited complications in comparison to Thalassaemia Major and the prevailing approach has been avoidance of early blood transfusions and the concomitant requirement for chelation therapy [1]. Thus, in Thalassaemia Intermedia (TI), complications related to chronic anaemia, ineffective erythropoiesis and haemolysis (mainly Extra Medullary Haematopoesis, thrombosis and Pulmonary Hypertension) dominate the clinical picture [2], unlike Thalassaemia Major (TM), in which features of iron overload predominate.

EMH is a common physiologic response noted in Chronic Haemolytic Anaemia (CHA) to compensate for bone marrow dysfunction; the male to female ratio reaches 5:1 and is frequently diagnosed between 20-40 years of age [3]. EMH is mandatorily included in the differential diagnosis of paraspinal masses especially in patients with diagnosed haemoglobinopathies like thalassaemia.

In a case series published by Wu JM et al., 79% of EMH cases were attributed to neoplastic origin, the most frequently metastatic adenocarcinomas [4]. Other differential diagnoses to be considered are nerve-sheath tumours and lymphomas, lateral meningocoele and infectious complications such as paravertebral tuberculous abscess.

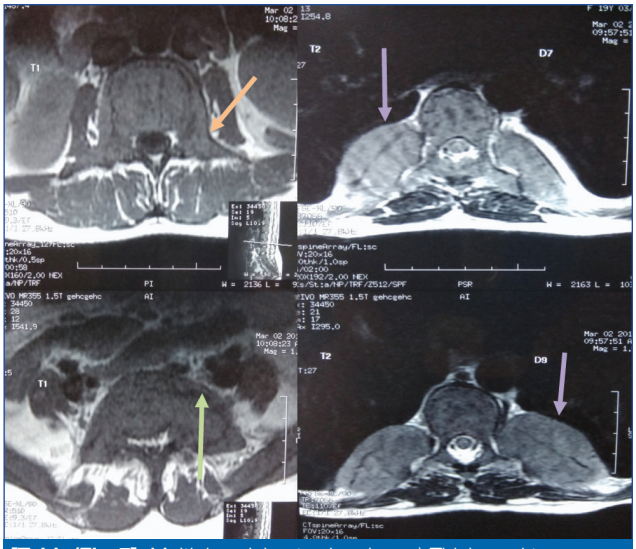
**There are two theories regarding pathogenesis of EMH:**

One theory explains its presence in a paravertebral or presacral location by supporting extrusion of a proliferating marrow through the thin cortex of the ribs and vertebral bodies into a subperiosteal location [Table/Fig-3]. This is known the paraosseous type which is more commonly seen in haemoglobinopathies [5].

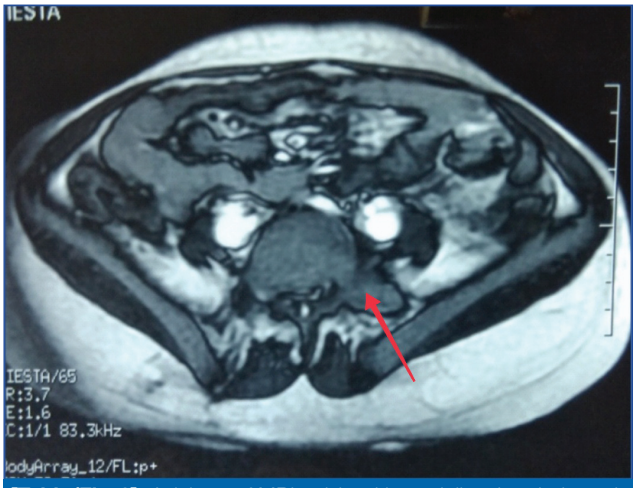
The other theory states that EMH results from transforming of embryonal cell rests into haematopoietic one under stress conditions to maintain adequate haemopoesis in visceral sites. This is the extraosseous form of EMH seen dominantly in myeloproliferative disorders [5].

Most common sites of EMH are the organs of the reticuloendothelial system- the liver, spleen and lymph nodes. The kidneys, adrenal glands, intrathoracic cavity, presacral region, peritoneum, skin, breast, central nervous system and paravertebral areas are rarely involved [6].

Intrathoracic EMH in paraspinal soft tissues is a relatively rare entity that is usually asymptomatic and treatment is unnecessary, except in the presence of complications like cord compression, cough, chest pain, massive haemothorax, respiratory distress or any symptomatic pleural effusion [7,8]. In the present case, patient was totally asymptomatic. Radiographic examinations are the initial hints towards the diagnosis in such cases.




**[Table/Fig-7]:** Multiple axial cuts showing: a) Thickened transverse process of lumbar vertebra (orange arrow); b) marrow rupture through thinned out cortex (green arrow); c) Thickened paraspinal soft tissues at D7 and D9 levels due to EMH (purple arrows).




**[Table/Fig-8]:** Axial cut of MRI pelvis with medullary break through right transverse process (red arrow)

On CT scanning, intrathoracic EMH appears as unilateral or bilateral well circumscribed, paravertebral masses, lying between vertebra T6 and T12 and having soft tissue density with homogeneous contrast enhancement. Calcification and bony erosion is characteristically absent, in contrast to neurogenic tumours which are associated with osseous destruction in about 50% cases. Rib widening and periosteal elevation are notable [7]. It may also show honeycombing of vertebral body, thickening of transverse process, and multiple breaks in the cortex with marrow protrusion [Table/Fig-7,8].

MRI is recently considered as the gold standard, allowing excellent sensitivity regarding intraspinal space invasion with superb paraspinal soft tissue delineation [9].

Radionuclide scanning with radiolabelled In-111 chloride or 99Tcm sulfur colloid is a good non invasive diagnostic test for asymptomatic cases like the present case [7]. CT guided biopsy, despite being the gold standard, should be reserved for older patients with a high probability of malignant disease and for cases in which the clinical and radiological picture is equivocal. Video-Assisted Thoracoscopic Surgery (VATS) is a novel and minimally invasive alternative for the definitive tissue diagnosis and surgical resection since it allows direct visualization and better control of haemorrhage. Nonsurgical treatment options include transfusion therapy, laminectomy, radiotherapy, hydroxyurea and the use of foetal haemoglobin inducing agents that decrease the haematopoietic drive.

Presacral EMH has been reported in only 14 cases between 1984-2009 [10]. When affecting the sacral region, the patient will mostly complain of chronic localized low back pain due to SCC or nerve root compression which may eventually lead even to paraplegia [11].

Tan T et al., reported that a history of CHA, EMH elsewhere in the body, symptoms of SCC with radiological evidence of intraspinal epidural lesion will all lead to a diagnosis of spinal EMH [12]. For screening, low cost CT scan can be used in such patients presenting with chronic backache or neurological complaints on a background of CHA.

CT scanning also detects thalassaemic osteoporosis with decreased trabecular bone density in the vertebral column noted in the vertebrae of 50.7% patients of beta TM, especially in older age by Voskaridou E et al., [13].

Significantly, a relation has been noted between high serum ferritin (above 2000ng/ml) and radiological signs of EMH in both TM and TI [14].

Ghosh A et al., reported the relationship between presence of EMH and low pre transfusion Hb levels [15]. The treatment modality of spinal EMH with blood transfusion to relieve the anaemia and suppress EMH where surgical intervention is contraindicated is based on these observations. They also found that significantly large spinal EMH that might cause SCC has an incidence of only 0.8% in thalassaemic patients. The embryonic cell rests in the epidural space may get transformed into haematopoetic tissue caused SCC [16]. EMH foci are also suspected to arise from the small penetrating veins of the vertebral body [17].

## CONCLUSION

Spinal EMH is found in inadequately transfused thalassaemia patients mostly in the second decade and is associated with low transfusion indices and high serum ferritin. When dealing with such patients, it is essential to have awareness regarding this physiological phenomenon to prevent misdiagnosis and potentially disastrous outcomes of invasive biopsy. Radiological screening with CT scans and Spinal MRI and early intervention with adequate blood transfusions and chelation therapy in high risk patients will prevent chronic neurological effects of SCC.

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