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Multiple Extramedullary Hematopoietic Foci in a Patient with Thalassemia: A Case Report

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Abstract

Background: Extramedullary hematopoiesis (EMH) is defined as hematopoiesis occurring outside the medulla of bone. It may be physiologic or occur as a complication of hematologic disorders such as thalassemia, sickle cell anemia and myelofibrosis. EMH usually involves liver, spleen, thorax, and lymph nodes. And it can involve paraspinal tissues with extension and involvement of spinal canal and could cause spinal cord compression, and present with neurological symptoms. So it is essential to be vigilant to recognize and treat such patients to prevent long-term disability. By reporting this case of EMH may help to provide imaging support for clinical diagnosis and enrich the medical cases in this field.

Case Description: The report describes a case of thalassemic patients known as β-thalassemia with multiple lesions of hematopoiesis, and analyses the imaging manifestations of EMH. In our case, the diagnosis was confirmed by the history of the patient stating underlying hematological condition and by characteristic radiographic findings showing multiple extramedullary hematopoietic foci in the multiple sites, mainly in paraspinal areas appeared as large soft tissue masses.

Conclusion: The possibility of EMH should be considered in every patient with ineffective erythropoiesis. Radiological examination is the preferred examination to detecting the EMH in early stage.

Keywords: Extramedullary hematopoiesis; Imaging manifestations; Radiological examinations; Soft tissue masses; Thalassemia

Introduction

Extramedullary hematopoeisis (EMH), which is defined as formation of blood cells outside the bone marrow, is a rare hematological disease, secondary to insufficient bone marrow function [1,2]. EMH is observed under conditions of myelofibrosis and ineffective erythropoiesis, most common in chronic hemolytic anemias, such as thalassemia and sickle cell disease [3-5]. Decreased or absent globin chain synthesis in thalassemia causes ineffective erythropoiesis [6]. Ineffective erythropoiesis causes the expansion of hematopoietic tissue outside the bone marrow and leads to hematopoietic compensatory mechanisms, mainly in the form of masses in other parts of the body. According to the clinical severity, thalassemia can be divided into non-transfusion dependent thalassemia (NTDT) and transfusion dependent thalassemia (TDT) [7]. Patients with non-transfusion dependent thalassemia (NTDT), a milder form of the condition, rarely need blood transfusions to treat their anemia. However, transfusion independence increases the incidence of EMH as the body attempts to compensate for ineffective erythropoiesis and inadequate red cell replacement. EMH is particularly common in patients with non-transfusion-dependent thalassaemia (NTDT) and rare in those with transfusion dependent thalassemia (TDT). In fact, the incidence of EMH in the former may reach up to 20% in comparison to the latter where the incidence remains less than 1.1%. EMH usually involves liver, spleen, thorax, and lymph nodes, and the paraspinal area of the thorax is the most frequently involved. The present report describes a case of thalassemic patient with common EMH locations encountered in clinical practice, including the liver, spleen, lymph nodes and the thoracic vertebra

regions. Unusual presentation as presacral and splenic masses is also discussed.

Case Presentation

A 34-year-old male patient was admitted to the hospital with gouty arthritis which caused the disformation of the left index finger as well as middle finger and swelling of the bipedal joints. He found his uric acid increased at the polyclinic for a routine examination 7 years ago. There was no family history of arthrolithiasis. The complete blood count revealed the following results: hemoglobin (Hb), 54 g/l; hematocrit value, 0.175; mean corpuscular volume, 64.5 fl; mean corpuscular Hb concentration, 308 g/l; red blood cell, $2.71x10^{12}$/l; No pathological changes were detected in erythrocyte sedimentation rate or C-reactive protein. Serum biochemical findings were as follows: total bilirubin level, 62.7 μmol/L; uric acid level, 455 μmol/L. His blood parameters were suggestive of chronic anemia due to the hematological condition. In order to make a more comprehensive assessment of his condition, a series of examination were performed. The radiological examinations findings were as shown.

Chest Radiography and Hand-Feet X-Ray

There are multiple oval soft tissue density nodules at the anterior ends of bilateral ribs, with smoothly-outlined, clear boundary and uniform density, which the long axis are consistent with the ribs. The X-ray revealed widening ribs, mass lesions superimposed on the parenchyma of both lungs and multiple smoothly-outlined masses projecting from the posterior mediastinum overlying the spine on the lateral view.

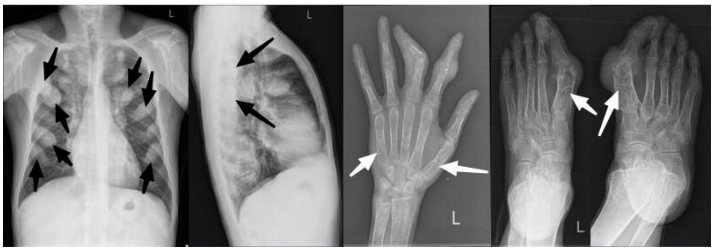

Figure 1: *On the chest radiography, expansion in the ribs forming the mass lesions superimposed on the parenchyma of both lungs (black arrow) and multiple smoothly-outlined posterior mediastinal masses overlying the spine on lateral view (black arrow) . On the hand-feet X-ray, expansion of the marrow cavity, thinning of the cortical bone and sparsely reticulated trabecula were shown on the corresponding diseased bones (white arrow).*

The corresponding diseased bones of the ribs were local expanded, which the marrow cavity was significantly widened and the trabecula was sparsely reticulated, and the cortical bone becomes thin and blurred. In the left hand and both feet, the corresponding diseased bones were severely osteoporotic, with the marrow cavity significantly widened, trabecula sparsely reticulated and bone cortex thinning. The disformation of the left index finger as well as middle finger could be seen. And several slightly high density nodules were formed in the surrounding soft tissue which pathology had been confirmed as gout nodules (Figure 1).

Computed Tomography

The diploic space in skull was widened, with cortical thinning and the myeloplasm granular. Multiple bones throughout the body were observed cortical bone thinning, marrow cavity widening and the trabecula sparsely reticulating, including the skull, sternum, ribs, scapula, vertebra and pelvic bones, etc (Figure 2).

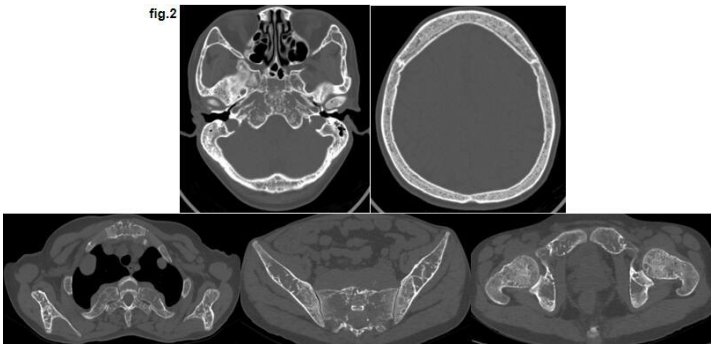

Figure 2: *The CT showed the diploic spaces in craniofacial bones widened with cortical thinning, loose bone resorption and osteopenia. The CT (bone window) demonstrated mutiple bones change with cortical bone thinning, marrow cavity widening and trabecula sparsely reticulating, which were shown in the sternum, ribs, scapula, vertebra and pelvic bones, etc.*

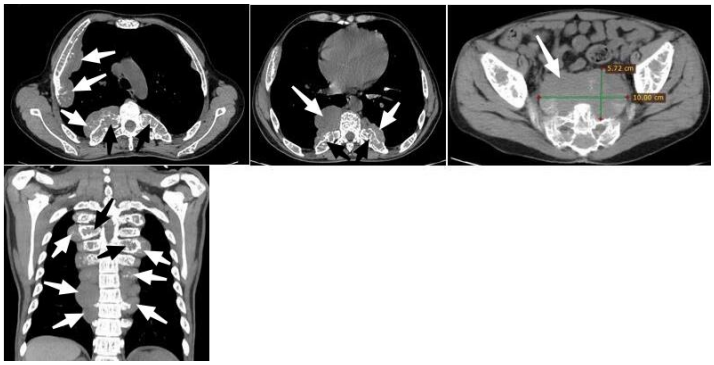

Figure 3: *CT demonstrated well-circumscribed and smoothly-outlined lobulated soft tissue masses (white arrows) bilaterally in the paracostal region, paraspinal regions of the chest and presacral spine. Generalised rib expansions (black arrows) in keeping with hyperplasia of the bone medulla were noted.*

All the bone changes were evaluated as secondary to excessive erythropoiesis [8]. As reported in the relevant literature, the typical craniofacial bones showed the widened diploic spaces in craniofacial bones with cortical thinning, outer table resorption, new bone formation and resultant classic “hair on end” appearance [9]. Multiple subpleural well-circumscribed lobulated

masses, which some of these fuse into strips, located at the Para coastal regions with clear separation from adjacent ribs and vertebras. Multiple well-circumscribed lobulated paravertebral masses were seen over the thoracic and presacral spine, with smoothly-outlined and uniform density. Especially there were large masses (Figure 3) beside the presacral vertebra, and the largest was 10.0 x 5.7cm in diameter. The adjacent posterior ribs were expanded, with the cortical bone thinning, the marrow cavity widening and the trabecula sparsely reticulating. Postcontrast images showed the masses to be heterogeneously enhancing. These scans were unfortunately not available to the patient, but the radiology report was. Axial non-contrast CT image of the abdomen showed cholelithiasis and severely enlarged siderotic liver with an average HU of 103 secondary to transfusional siderosis (normal liver attenuation should be approximately 54-60 HU) as well as splenomegaly (Figure 4). If a thalassaemia patient is proceeding to splenectomy, concomitant cholecystectomy can be considered if cholelithiasis is present.

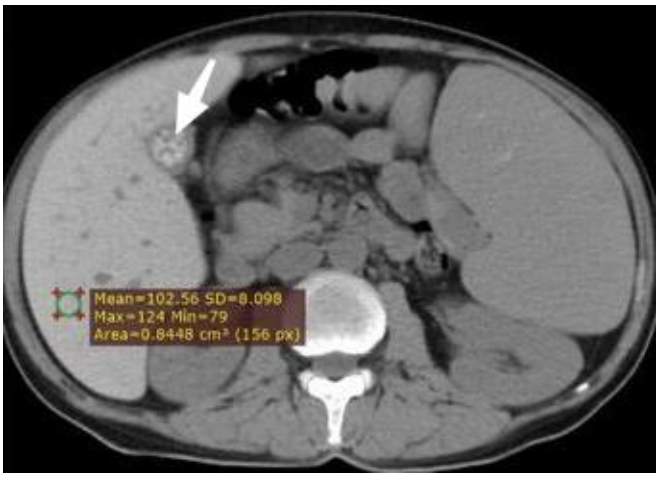

Figure 4: *Axial non-contrast CT images of the abdomen show cholelithiasis (white arrows) and severe hepatosplenomegaly as well as severely siderotic liver with an average HU of 103 secondary to transfusional siderosis (normal liver attenuation should be approximately 54–60 HU).*

Magnetic Resonance Imaging

T1WI and T2WI axial MR images of head showed thickening of the cranial diploe (Figure 5). The MRI demonstrated severe vertebral marrow hypointensity with cortical thinning and striated vertebral appearances on the sagittal whole spine MRI T1 and T2 weighted sequences (Figure 6). The striated vertebral appearances resulted from preserved primary trabecula and resorbed secondary trabecula [10]. There were multiple well-circumscribed and smoothly-outlined lobulated paraspinal masses in the whole spine, with isointensity to muscle on T1WI and hypointensity on T2WI because of excessive iron in the tissue, and the largest was 10.0 x 5.7cm in diameter beside the presacral vertebra (Figure 7 and Figure 8). The MRI showed severe hepatosplenomegaly and several well-denned heterogeneous lesions on the spleen which were considered of extramedullary hematopoiesis and appeared hypointense on both MRI T1 and T2 weighted sequences, and the largest was 2.9 x 2.6cm in diameter. The liver was markedly hypointense on all MRI sequences, in keeping with iron overload (Figure 9). Although multiorgan siderosis occurs, the liver is the main storage organ. As above-mentioned characteristic radiographic findings and the history of the patient underlying hematological condition, the possibility of EMH should be considered. Further detailed inquiry, we found that the patient was diagnosed β-thalassemia when he was 2 years old. There was no family history of anemia. On systemic examination he was found to have ochrodermia, scleral icterus and severe hepatosplenomegaly. And the patient had history of multiple previous blood transfusions.

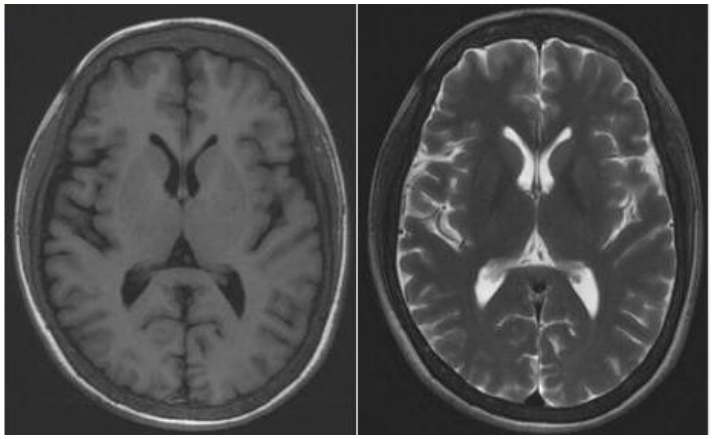

Figure 5: *T1WI and T2WI axial MR images showed thickening of cranial diploe.*

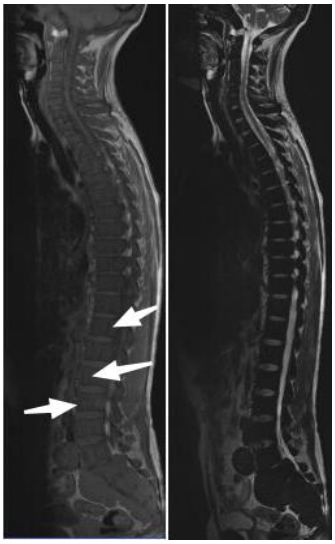

Figure 6: *The MRI demonstrated severe vertebral marrow hypointensity with cortical thinning and striated vertebral appearances (white arrows) on sagittal whole spine MRI T1 and T2 weighted sequences.*

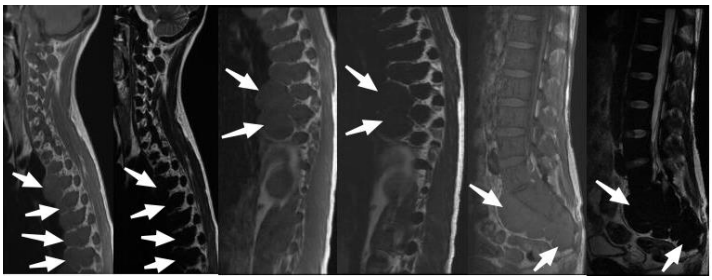

Figure 7: *MRI of the whole spine showed multiple well-circumscribed and smoothly-outlined lobulated paraspinal masses (white arrows) with isointensity to muscle on T1WI and hypointensity on T2WI.*

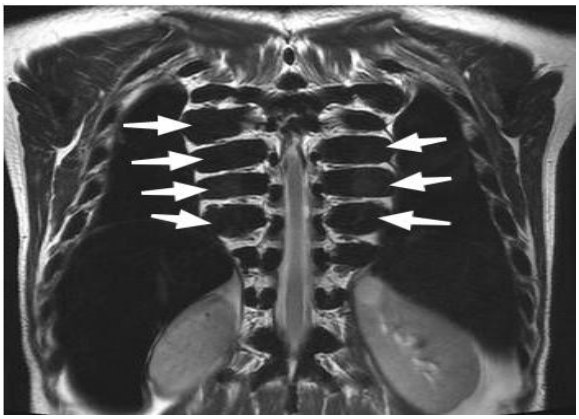

Figure 8: *Coronal T2 weighted image showed lobulated soft tissue lesion (white arrows) in paravertebral portions of dorsal spine which is suggestive of extramedullary hematopoiesis.*

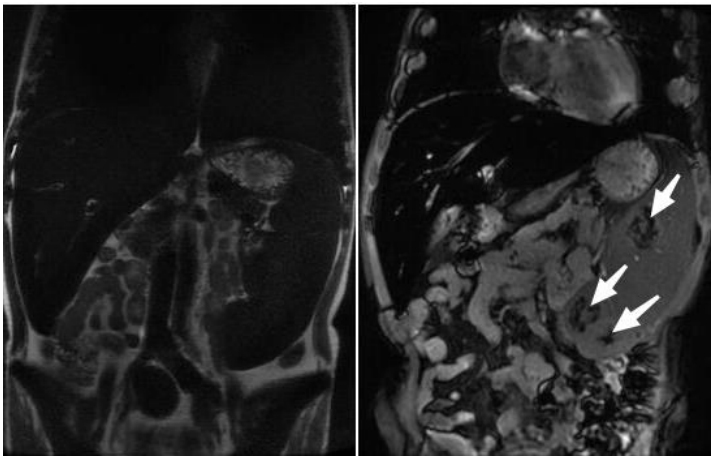

Figure 9: *The MRI showed severely hepatosplenomegaly and the liver was markedly hypointense on both MRI T1 and T2 weighted sequences, in keeping with iron overload. There were several small heterogeneous hypointense focus (white arrows) on the spleen which were suggestive of extramedullary hematopoiesis.*

Discussion

Thalassemia is a heterogeneous group of inherited blood disorders that cause ineffective erythropoiesis due to the reduction or absence of globin chain. Extramedullary hematopoeisis (EMH), which could be seen in the patients with thalassemia, occurs if the bone marrow is no longer functional, mainly in the form of masses in other parts of the body. EMH usually involves liver, spleen, thorax, and lymph nodes. Paraspinal involvement among the various body regions reported deserves special attention due to its challenges in diagnosis and management, which can be a cause of Para paresis [11,12]. Therefore, neurosurgeons must be vigilant to recognize and treat such patients to prevent long-term disability. EMH may be assorted as paraosseous or extraosseous and is more common in NTDT than in regularly transfused TDT [13]. EMH is primarily seen in untreated or inadequately treated patients with thalassemia [14]. According to the published literature, paraosseous EMH typically occurs in the thoracic region, followed by the lumbar region. This appears as well-circumscribed lobulated posterior mediastinum soft-tissue masses involving the posterior rib segments, or less often the anterior ends of ribs or presacral region [15]. In our case, EMH occurred in the multiple sites, including the thoracic and presacral region as well as the anterior and the posterior ends of ribs, mainly appearing as large soft tissue masses. The pathogenesis of EMH is still debated. Now more people agree with the theory that these paraspinal masses arise from the bone marrow of the adjacent ribs or vertebra. The expanding bone marrow due to ineffective erythropoiesis causes progressive lysis of bone, resulting in the extrusion of the marrow through the areas of bone lysis because of increased medullary marrow pressure, appearing as large soft tissue masses, and have clear separation from adjacent vertebra and ribs [16,17]. Continuity with the medullary space may be maintained or lost [18]. One or more ribs or vertebral bodies may be involved. The smooth outline of these masses suggests that a capsule is maintained by the periosteum or adjacent parietal pleura. Marrow hyperplasia secondary to chronic anemia results in medullary expansion, cortical bone thinning, cancellous bone resorption as well as osteopaenia, which may result in pathological fractures. The history and physical examination may help narrow the differential diagnosis, however, radiographic imaging is still essential to confirm the existence of hematopoietic tissue. The characteristic manifestations are mainly observed by magnetic resonance imaging (MRI) or CT scan. Paraspinal EMH appears as unique, multiple iso- or hyperintense masses, with homogeneous enhancement following contrast administration. The principle MRI imaging characteristics of paraspinal EMH includes the following: the extramedullary masses are usually lobular, well-circumscribed masses of homogenous signal intensity on T1 weighted images and hyperintense on T2 weighted images unless there is excessive iron in the tissue in which case it will be hypointense. Gadolinium enhancement has been found to be unpredictable despite the tissue being highly vascular with patterns varying from no enhancement to strong enhancement [19-21]. CT presentation is characterized by the

heterogeneous paraspinal soft-tissue masses without any adjacent bone erosion [22]. Although biopsy remains the gold standard, most authors do not favour a tissue biopsy in this situation as the lobulated mass with a history of hemoglobinopathy can be diagnosed as EMH. MRI is the gold standard for diagnosing EMH as biopsy of the vascular mass could lead to catastrophic haemorrhage [23]. Tissue biopsy can cause significant hemorrhage and is reserved for older patients with a high probability of malignancy and for cases in which the clinical picture is uncertain. Due to its rarity, there is no standard treatment for symptomatic EMH patients, and no evidence-based guidelines for EMH treatment. Therapy usually depends on the severity of the symptoms, the size of the mass, the clinical condition of the patient, and previous treatments. Management options include blood transfusion, radiotherapy, and surgical decompression by laminectomy, hydroxyurea or a combination of these modalities [24,25].

Conclusion

In conclusion, EMH is a compatible and rare disease, and should be distinguished from other neoplasms. EMH must be considered when masses with characteristic radiographic findings are detected in patients with thalassemia and it is important to recognise the foci of the paraspinal extramedullary hematopoiesis as a differential diagnosis of mediastinal and spinal masses [26]. Hence it could avoid overtreatment due to diagnostic errors, such as the misdiagnosis of these masses as tumors. Radiological examination is very helpful in seeing the above lobulated mass lesion in such hematological condition, and a follow-up study is helpful. Radiologists must be aware of the characteristic radiologic appearance of the extramedullary hematopoiesis in the patient with thalassemia. By reporting such a case of extramedullary hematopoiesis with typical imaging manifestations, this paper hopes to provide imaging support for clinical diagnosis of extrtramedullary hematopoiesis of thalassemia and enrich the medical cases in this field.

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Conflicts of Interest

There are no conflicts of interest.

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