

## Unusual Pulmonary Masses in Beta Thalassemia Major

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### Abstract

Thalassemia is common in our Mediterranean region. In severe untreated  $\beta$ -thalassemia major, extramedullary ineffective erythropoiesis is a common feature, and if patients are not correctly transfused this leads to growth retardation, multi-organ abnormalities, including hepatosplenomegaly and skeletal deformities due to overgrowth of the bone marrow.

Enlarging ribs and mass-like opacities has been described primarily in the thorax and paraspinal region.

We report a case of an unusual chest X ray in a 49 years old male, presented with multiple pulmonary masses, proved by biopsy to be an extension of ribs and vertebrae due to extramedullary erythropoietic tissue growth.

In addition, Spirometry of our patient showed combined restrictive and obstructive syndrome with small airways diseases.

Our patient present also with as reported by echocardiography: diastolic dysfunction, Aortic regurgitation grade 1 - 2, mild dilatation of right ventricle: (30 mm), Pulmonary artery pressure (50 mmHg).

He equally has hepatosplenomegaly, osteoporosis, and Secondary hypogonadism with impotence after a fully active life with 5 children.

This case illustrates the need for considering thalassemia Major as differential diagnosis in unexplained abnormalities of many systems, including intraparenchymal masses seen in pulmonary imaging.

**Keywords:** Radiography; Pulmonary Masses; Thalassemia

### Introduction

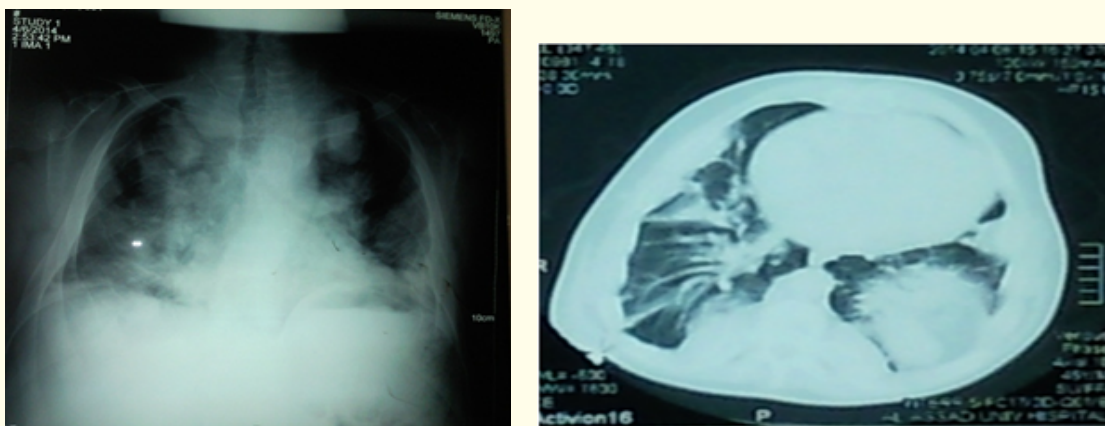
Beta thalassemia is a hereditary hemolytic anemia that is prevalent throughout the Mediterranean region [1,2]. Beta thalassemia is caused by point mutations in beta-globin genes [1-4]. More than 200 mutations have been found in beta thalassemia and deletions are usually uncommon [1- 4].

Beta thalassemia disorder affects the production of beta-globin chains, and when beta-globin chains are absent it is called beta thalassemia major (BTM) [5,6].

Beta thalassemia is usually associated with extramedullary erythropoiesis [1,3,7]. If beta thalassemia patients are inadequately transfused they develop growth retardation, and multi-organs clinical abnormalities including hepatosplenomegaly and skeletal deformities due to overgrowth of the bone marrow [1,3,7].

Enlarging ribs and vertebrae, leading in some cases to mass-like opacities has been described primarily in the thorax and paraspinal region [1,3].

We report a case of an unusual chest X-ray in a 49 years old male, presented with multiple pulmonary masses. Those pulmonary masses were proven to be an extension of ribs and vertebrae due to extramedullary erythropoietic tissue growth (Figure1).



**Figure 1:** Radiography of thorax, and computed tomography showing bone masses emanating from ribs and vertebrae.

### Case

Forty-nine-year-old male, non-smoker, married with 5 children presented to the clinic on 02-04-2015 with chest pain. No fever, no cough, no effort dyspnea, no orthopnea or paroxysmal nocturnal dyspnea were noted.

The patient was previously diagnosed with beta thalassemia major and he is under the care of the National Center for Hereditary Hemolytic Diseases.

The patient is on regular blood transfusion (1 - 2 packed red blood cell Units) and is not taking iron chelating agent regularly. The patient is also known to have osteoporosis and secondary impotence since 2003. Splenectomy was done at 10 years of age.

Family history: some of the patient siblings were treated for Thalassemia

### Clinical Examination

General condition: pale, jaundiced, conscious and oriented. Chipmunk facies (prominent frontal bossing, overgrowth of the maxillae, prominent malar eminences).

Height = 150 cm, weight = 60kgs, BMI = 26.6, Pulse = 90/min, Blood Pressure = 120/80 mmHg, Temp = 37°C, oxygen saturation = 94%.

Heart: regular, no murmurs.

Chest: tender ribs and sternum, coarse breath sounds.

Abdomen: scar of splenectomy at left hypochondrium, soft abdomen, liver palpable 6 cm below the right costal margin.

Extremities: no edema, peripheral arteries are palpable.

Neurological exam: within normal limits

Genitourinary exam: pubic hair: Tanner 4, right testis 12 ml, left testis 15 ml, penis 8x3 cm

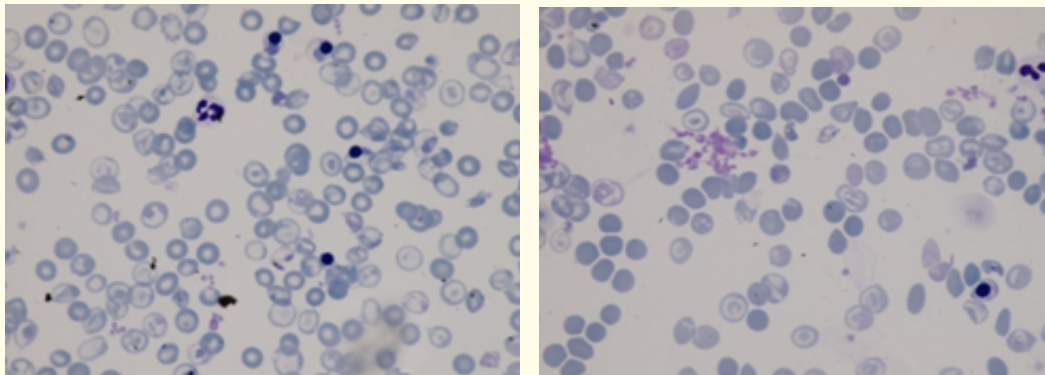
### Laboratory data (normal ranges between brackets)

Hb 8.11 (13-16 g/dl), Ht 24.3 (38-53%), WBC 22.7 (4.4 - 11x10<sup>3</sup>/μl), corrected WBC 3.678 because nucleated RBC is counted as white blood cells in automated count [8]. Platelets 657 (150 - 450x10<sup>3</sup>/μl), PT 15 (12 sec), INR 1.27 (1 - 1.3), aPTT 32 (28 - 37sec), Glucose 93 (75 - 110 mg/dl), Urea 15 (10 - 50 mg/dl), Creatinine 0.53 (0.7 - 1.36 mg/dl), ALT 54 (< 41 U/L), AST 91 (< 38 U/L), ALP 272 (90 - 270 U/L), Ferritin 3597 (16.4 - 293 ng/ml), TSH 3.3 (0.47 - 4.64 μIU/ml), FT4 1.03 (0.9 - 1.7ng/dl), FT3 2.4 (1.8 - 4.6 pg/ml), Prolactin 9.61

(1.96-16.4 ng/ml), FSH 1.13 (1.5 - 12.4 mIU/ml), Testosterone 0.215(2.27 - 10.3ng/ml), Cortisol 10.72 (6.2 - 19.4 µg/dl), ACTH 11.5 (7.2 - 63.2 pg/ml)..

### Peripheral Blood Smear

Peripheral blood smear showed anisocytosis, poikilocytosis, macrocytes, target cells, spherocytes, schistocytes, nucleated RBCs (518 /100 WBC).



**Figure 2:** Peripheral blood film.

### Hemoglobin Electrophoresis

HbA= 73.18%, HbF= 22.84%, HbA2= 3.98% (this test was performed while the patient is on blood transfusion) [8].

### Echocardiography

Left ventricle: diastolic dysfunction, aortic regurgitation grade 1-2.

Right ventricle: mild dilatation (30mm), pulmonary artery pressure (50mmHg), no pericardial effusion.

### Arterial Blood gases (ABGs)

PH = 7.44, PCO<sub>2</sub> = 36 mmHg, PO<sub>2</sub> = 73 mmHg, HCO<sub>3</sub> = 24.5, So2 = 94%

### Pulmonary Function Tests

Pulmonary function tests showed mixed syndrome: FEV1= 1.40 L/sec (53.7%), FVC=2.03 (65%), FEV1/FVC= 69% after bronchodilators. MMEF: 25 - 75% = 45%.

### Bone Densitometry

(4/2014): T-score -4.8 in lumbar spine, -3.4 in hip (Osteoporosis).

### Imaging

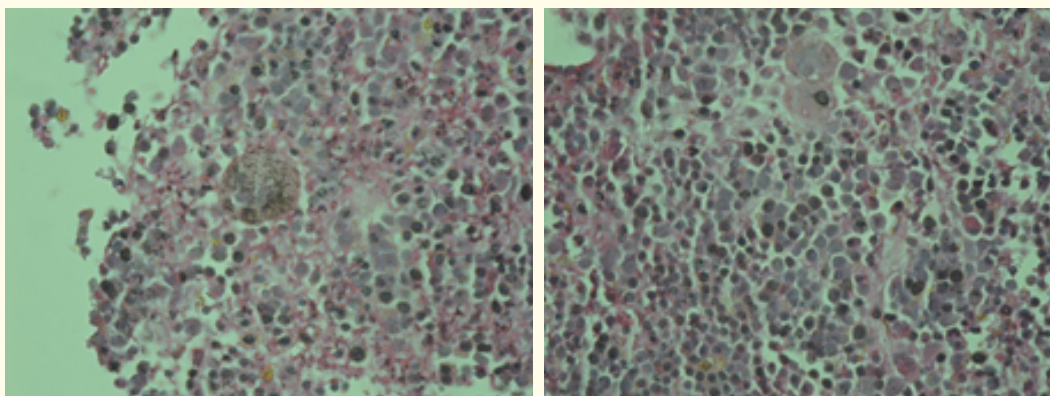
- **Plain X-ray of chest:** showed bilateral widening of ribs, bilateral masses in both lung fields, and a mild heart enlargement was observed (Figure 1).
- **MSCT:** showed severe enlargement and widening of the bone marrow in all ribs and vertebrae appearing as bilateral masses in both lungs (Figure 1).

- **Magnetic Resonance Imaging (MRI):**

- Sagittal MRI study of the dorsal spine showed decreased signal of bone marrow in all vertebrae on T1
- Coronal MR T1 study showed several widely spread low signal areas of enlarged bilateral ribs

**CT guided biopsy from intra- thoracic mass**

The biopsy showed hematopoietic proliferation in its three lineages with good maturation. No granulomas or malignant infiltration were seen. Conclusion: biopsy is consistent with myeloid metaplasia, as seen in thalassemia (Figure 3).



**Figure 3:** Biopsy of intraparenchymal mass.

*Biopsy of intraparenchymal mass: consists of hematopoietic proliferation in its three lineages consistent with myeloid metaplasia, as seen in thalassemia.*

**Discussion**

Thalassemia is a common hemolytic anemia in our region. In severe untreated beta thalassemia, major erythropoiesis may be increased by a factor of up to 10, more than 95% of which may be ineffective [6] and showing bizarre, dysfunctional marrow production [2,3].

Our patient presented with chest pain and his chest X-rays showed multiple intrathoracic masses that appeared to be as dense as the neighboring bones. Biopsy of one of the masses showed extramedullary hematopoiesis as described in BTM [9]. CT confirmed that these tumors are connected to ribs and vertebral column (Figure 1).

Previously described painful convex ribs, and enlarged vertebrae due to non-effective erythropoiesis have been reported, leading in some cases to intrapulmonary masses [3].

Our patient had abnormal lung functions. Abnormalities of pulmonary function including predominantly restrictive and small airway obstructive defects have been previously reported [10,11].

Obstructive pattern according to GOLD (FEV1/FVC < 70% after bronchodilator) is rarely present [12]. Progressive tissue iron deposition from multiple blood transfusions is common in beta thalassemia and pulmonary iron deposition may result in parenchymal damage. However, in a cohort of 27 thalassemia patients published by Tai DY, *et al.* no significant association between the restrictive pattern in lung function, interstitial lung disease and iron loading was seen [10]. In our case, we have seen a combined restrictive and obstructive syndrome with small airways diseases that is partly explained by the intrapulmonary masses. In the previously mentioned study, unlike

us, authors did not describe any abnormal skeletal pattern of the ribs [10,11]. Additionally, in our case CT did not reveal any sign of parenchymal or interstitial diseases, while others demonstrated pulmonary parenchymal disease on CT [10]. Pulmonary artery hypertension is commonly reported in BTM, we also noticed pulmonary artery hypertension (PAP = 50 mmhg) as described by others [13,14].

As described in BTM our patient presented with multiple organ dysfunction, hepatosplenomegaly, osteoporosis, and endocrinal abnormalities such as secondary hypogonadism and impotence. Notzli L., *et al.* attributed the endocrinal hormonal decrease to chronic iron overload of the endocrine glands, which led to alteration in their function [15].

Other authors noticed hemothorax in Beta Thallasemia [16], due to rupture of extramedullary hematopoietic masses.

### Conclusion

Hemolysis and ineffective erythropoiesis are common features of BTM, resulting in multiple organ abnormalities and dysfunction. In our case, our patient manifested with hepatosplenomegaly, osteoporosis, growth retardation, low testosterone and FSH. The particularity of our case is that the intraparenchymal masses seen were attributed to costal and vertebral non-efficient and exaggerated extramedullary erythropoiesis. We also noticed pulmonary hypertension and combined restrictive and obstructive lung functions.

This case illustrates the need to include extramedullary erythropoiesis in differential diagnosis of patients with beta thalassemia major presenting with pulmonary masses on X-ray.

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