

CASE REPORT

Thalassemia Intermedia and Extramedullary Hematopoiesis

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ABSTRACT:

Excessive ineffective erythropoiesis in thalassemia intermedia may cause paravertebral pseudotumors of extramedullary hematopoiesis. Due to the proximity to the spinal canal, these paravertebral masses carry the risk of severe neurological damage. Treatment strategies include hypertransfusion, radiotherapy, and laminectomy. Hydroxyurea, stimulating fetal hemoglobin synthesis, may represent an alternative therapeutic approach. This presentation reports a case of female known to have thalassemia intermedia who presented with abnormal gait with weakness of lower limbs. MRI study showed masses originate from thorax vertebra. Hypertransfusion therapy and splenectomy were followed by regular transfusion (baseline hemoglobin 10 g/dl) and chelation with desferrioxamine. With this treatment, clinical symptoms disappeared, paravertebral hematopoietic masses did not progress, Hydroxyurea therapy was initiated to reduce the required transfusion volume but suppressing concomitantly further expansion of extramedullary hematopoiesis, and finally leading to a reduction of transfusional iron load. Treatment was started with 4 mg/kg per day and stepwise increased to 20 mg/kg per day. Follow up to the patient done by clinical examination and imaging study to assess the vertebral masses.

KEYWORDS : thalassemia · extramedullary hematopoiesis · hydroxyurea · paravertebral tumor.

INTRODUCTION :

Thalassemia intermedia is a term used to define a group of patients with β thalassemia in whom the clinical severity of the disease is somewhere between the mild symptoms of the β thalassemia trait and the severe manifestations of β thalassemia major. The diagnosis is a clinical one that is based on the patient maintaining a

hemoglobin (Hb) level of at least 6-7 g/dL at the time of diagnosis without the need for regular blood transfusions ⁽¹⁾.

This initial definition of thalassemia intermedia, which was based on clinical observation alone, retained its validity even after some of the specific mutations associated with thalassemia intermedia were recognized, because severity of the clinical course remains mostly unpredictable even in known genotypes. For this reason, some patients with a β thalassemia intermedia genotype are treated as if they have thalassemia major, because they present with severe manifestations; similarly, others with a thalassemia intermedia genotype are considered to have thalassemia minor because of the mild or even asymptomatic nature of their condition. This variability is most likely related to the presence or absence of modifying genes. It has been surprisingly seen among siblings with the same genotype ⁽²⁾.

Because of the significant overlap in clinical severity among the 3 types of β thalassemia and despite the fact that several genotypes are associated with the β thalassemia intermedia picture, the diagnosis continues to be a clinical one, regardless of the genotype involved. Moreover, in an individual patient, the diagnosis may change from thalassemia intermedia to thalassemia major once the patient begins to have more severe symptoms and to require regular blood transfusions ⁽³⁾.

Corresponding to the variety of the underlying genetic defects, the clinical picture of thalassemia intermedia ranges from very mild to severe forms with typical features of thalassemia major patients, such as cardiomegaly, massive splenomegaly, and hemosiderosis due to an increased intestinal iron absorption even without additional

transfusional iron overload. Massive erythroid expansion due to ineffective erythropoiesis may lead to substantial osteoporosis with bony deformities and the risk of pathological fractures. Extensive compensatory

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extramedullary hematopoiesis may present as impressive paravertebral pseudotumors^(4,5,6). Since these pseudotumors can progress towards the spinal canal, they carry a high risk of spinal compression with severe neurological symptoms. Patients with paravertebral hematopoietic masses have been treated with hypertransfusion therapy, radiotherapy, and/or laminectomy⁽⁵⁾. An additional therapeutic approach is the use of pharmacological agents, stimulating the synthesis of HbF, thereby reducing the α -globin chain excess resulting in an increased efficacy of erythropoiesis with reduced total erythropoietic activity. An additional cytoreductive effect of these agents could contribute to the reduction of extramedullary hematopoietic masses.

Case presentation

Name: M. M. N.

Age: 21 years

Sex: Female

Chief complain: abnormal gait for last 4 years.

Known case of thalassemia intermedia since age of 4 years with irregular blood transfusion, folic acid tab and no iron chelators. The condition started in 2008 as abnormal gait and weakness of lower limbs. The family consulted doctors who suggested to do imaging study, imaging study showed mass in thoracic region.

Decision of operation to get biopsy was taken and the operation post ponded because the patient had jaundice. Treatment with steroid was started with mild improvement.

Family history of thalassemia major (one brother and one sister who died because of heart failure).

All of them diagnosed on Hb electrophoresis base (gene analysis not available).

On December, 2011 the patient presented to hemato-ocology center as case of abnormal gait, MRI of the chest was done and the result was (Figure 1)

Three right para vertebral masses, all are hypo/iso intense with vertebral bodies on T1 –T2

1- 6×4.5 mass seen at D2-3 and 4 level

2- 2×1.6 cm mass seen at D7 level

3- 3.5×2.9 cm mass seen at D9-10 level

With no extension to spinal cord and exit foramina.

All vertebra bodies show diffuse infiltration process.

Impression: regarding history, the finding are in favour of extra medullary hemopoiesis.

Treatment was started at that time with regular blood transfusion to maintain blood level more than 12 g/dl.

Hydroxyurea capsule 10 mg/kg/ per oral increasing to 20 mg/kg within 6 weeks.

Clinical evaluation for the patient revealed clinical improvement for walking and there was no neurological manifestation.

MRI study to the thoracic region done, the report was, (Figure 2)

Small right Para spinal mass (20×31 mm) in mid thoracic region (extra medullary hemopoiesis).

The whole spine shows homogenous low signal intensity in T1-T2 (red marrow infiltration).



Figure No.1

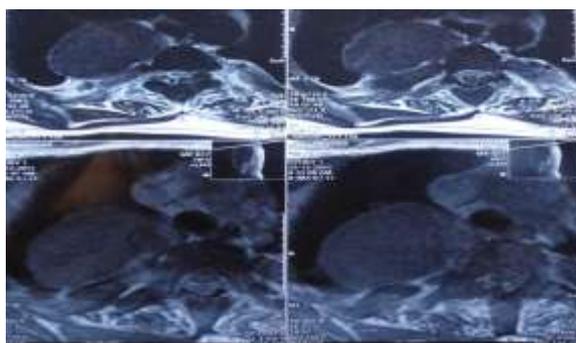


Figure No.2

DISCUSSION:

Patients with thalassemia intermedia may escape from regular medical supervision after diagnosis is made and transfusion independence is achieved. However, in the absence of transfusion therapy, severe clinical disorders due to the underlying disease may develop even in patients with apparently only minor clinical symptoms. Hypertransfusion therapy was effective in some cases^(7,8,9)

Hydroxyurea, an ribonucleotide reductase inhibitor, had been used for a long time as a cytotoxic agent in myeloproliferative disorders before it was shown to enhance HbF synthesis in anemic monkeys and in sickle cell patients⁽¹⁰⁾. Hydroxyurea proved to be effective also in some thalassemia intermedia patients, but with different hematological and clinical responses. It increases the efficacy of erythropoiesis by induction of HbF synthesis with consecutive reduction of the α -globin chain excess, leading at least transiently to higher HbF levels and, with greater variability, to an elevated total hemoglobin concentration without expansion of erythroid marrow. A decline in hemoglobin concentration and/or myelotoxicity was seen in some of the patients if a threshold hydroxyurea dose of about (10-20) mg/kg per day was exceeded, although This dose is rather low compared to that usually applied in sickle cell patients^(11,12,13). Another mode of treatment of this condition is radiotherapy as well as surgical interference if the medical failed.

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