Myelopathy Due to Spinal Cord Compression Secondary to Extramedullary Hematopoiesis in HbE/Beta Thalassemia

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CASE PRESENTATION
A 19-year-old Hmong female presented to our hospital for evaluation of a 1 month history of bilateral lower extremity paraesthesia and weakness. This was associated with difficulty walking, frequent stumbling, and falls. She denied weakness or numbness in upper extremity, difficulty with speech or swallowing, visual problems, urinary or fecal incontinence, constipation or urinary retention. She denied any trauma to her back or any febrile illness recently. No other complaints.
• **PMH**
  
  - Beta-thalassemia trait + hemoglobin E trait
    - Requiring blood transfusion every 4-6 weeks*
  - Transfusional iron overload requiring chelation therapy.

- **Medication:**
  - Deferasiroc (Exjade)
  - Folic Acid
- **FAMILY HISTORY:**
  - Elder brother had β-thalassemia major
  - Otherwise unremarkable

- **SOCIAL HISTORY:**
  - College student
  - Denied smoking, drinking alcohol or using illicit drugs

- **Review of systems:** unremarkable
Physical Examination

• **VS:** stable
• **General:** Prominent pre-maxilla, comfortable. A&O x3
• **HEENT:** PERRLA, EOMI. Conjunctival pallor and scleral jaundice present. Normal oral cavity.
• **Neck:** supple, no JVD, no thromegaly
• **Heart:** normal S1 & S2. No murmur gallops or rubs.
• **Lungs:** clear to auscultation bilaterally
• **Abdomen:** soft, NT, ND, +BS, splenomegaly
• **Lymphatic:** no cervical, supraclavicular, axillary or inguinal lymph nodes were palpable
• **Neuro:**
  
  • **GCS** = 15, **MMSE** intact,
  
  • **CN:** II-XII intact
  
  • **Motor Exam:** muscle bulk and tone were normal. Strength was 5/5 in UEs b/l, 4+ to 4- in R LE and normal in L LE.
  
  • **Sensory Exam:** diminished to light touch and pin prick from T5-T6 distally. Vibratory & proprioceptive sense is absent in toes while present at thumbs.
  
  • **Reflexes:** 2 throughout UE while 2+ to 3- in RLE at knee and ankle. Planters are up going.
  
  • **Cerebellar Function:** Intact alternating movement and heal shin test
  
  • **Gait:** Ataxic. Not able to rise up on heals or toes.
Lab Data

CBC:
- Hb: 6.7 g/dL
- Hct: 20.1
- WBC: 8.5
- Plt: 132

BMP
- Wnl except T. bili 2.0
Treatment

- Dexamethasone 10mg IV x 1, then 4mg PO every 6 hours
- 2 Units of PRBCs
- 2 fractions (of total 10) of radiotherapy to the effected area over next 48 hours.
- Patient had partial resolution of her symptoms
- Discharged on day 3 to f/u as an out patient
- Dexamethasone continued- total 3 weeks
- Radiotherapy: 10 fractions (1200 cGY)
F/U MRI @ 3 MONTHS
DISCUSSION

• Thalassemia
• HbE/ β Thalassemia
• Extramedullary Hematopoiesis (EMH)
• Treatment of EMH
Thalassemia

- Hgb A = tetramer = 2α+2β chains, ratio:1±0.05
- Two α globin gene is located at each chromosome 16.
- One β globin gene is located at each chromosome 11.
- α Thalassemia: defect in α globin gene → reduced or absent α chains.
- β Thalassemia: defect in β globin gene → reduced or absent β chain.
PATHOPHYSIOLOGY

1. Deficiency of one globin chain
2. Excess of other globin chain
3. Precipitation of remaining globin chain
4. Destruction of red cell precursors
# β Thalassemia Phenotypes

<table>
<thead>
<tr>
<th>Variant</th>
<th>Chromosome 11</th>
<th>Signs and Symptoms</th>
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<tbody>
<tr>
<td>Beta thalassemia minor (trait)</td>
<td>One gene defect</td>
<td>Asymptomatic</td>
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<tr>
<td>Beta thalassemia intermedia</td>
<td>Two genes defective (mild to moderate decrease in beta globin synthesis)</td>
<td>Variable degrees of severity of symptoms of thalassemia</td>
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<tr>
<td>Beta thalassemia major (Cooley’s Anemia)</td>
<td>Two genes defective (severe decrease in beta globin synthesis)</td>
<td>Abdominal swelling, growth retardation, irritability, jaundice, pallor, skeletal abnormalities, splenomegaly; requires lifelong blood transfusions</td>
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Hemoglobin E (HbE)

- Hb E is a β-globin chain variant resulting from substitution of glutamine by lysine at codon 26 of β-globin gene.*
- Most common Hb variant in SE Asia and 2nd most common worldwide.
- HbE activates a cryptic splice site that produces non-functional mRNAs.
HbE/ β Thalassemia (βT)

- HbE/βT results from co-inheritance (compound heterozygous)
- HbE/βT patients have extraordinary clinical heterogeneity
- HbE/βT patients represent 50% of total cases of severe βT cases worldwide
Extramedullary Hematopoiesis (EMH)

- EMH is defined as formation of blood cells outside the bone marrow

- **Cause:**
  - **Physiological response to erythropoietin** in chronic anemia in hematologic disorders, such as leukemia, myelofibrosis and hereditary hemoglobinopathies
  - **Colonal disorder of hematopoiesis** e.g. P. vera, CML

- Usual location: liver, spleen and lymph nodes
EMH in βT causing myelopathy

• Usual age: 3rd or 4th decade of life*
• Site: Lower T or L spine*
• **Mechanism:**
  ● expansion of marrow via tiny fractures associate with thalassemia
  ● Growth of hematopoietic embryonic remnants in epidural space
• **Diagnosis:** *
  • Clinical picture
  • MRI: increased signal intensity, lack of gadolinium enhancement
  • Biopsy*
Treatment*

- **Surgical Decompression:** laminectomies
  - **Advantage:** immediate decompression, histologic dx
  - **Disadvantage:** hemorrhage, spine instability, reoccurrence

- **Radiological:**
  - Alone, or in combination.
  - **Advantage:** immediate availability, rapid clinical benefit
  - **Disadvantage:** lack of histological diagnosis, radiation toxicity

- **Medical:**
  - Corticosteroids
  - **Hypertransfusion:** *alone or in combination with surgery or RTx.*
  - **Hydroxyurea:** in combination with RTx or transfusion
Take-Home Points

• Keep EMH high on differential in a patient with chronic anemia and presents with neurological symptoms & signs.

• EMH can be managed successfully by non-surgical options such as radiotherapy and corticosteroids.
References


