Diagnosis and Treatment Consideration in Thalassemia

Abstract

Thalassemia has a spectrum of varied manifestations and complications. Survival is associated with various multisystem complications primarily caused by chronic anemia, iron overload, adverse effects of chelation and transfusion associated infections. Thus, a disease that starts merely as hemolytic anemia attains the dimension of a chronic disease with multisystem involvement. The importance of thalassemia is masked by infections and nutritional deficiencies. Preventive strategies need to be developed, e.g. premarital screening, genetic counseling and antenatal diagnosis. Apart from early diagnosis, there is a need to increase the therapeutic facilities like blood transfusions, chelation therapy and bone marrow transplant. It is really a great challenge and needs an organized plan of action. This article reports the diagnosis and treatment consideration of a thalassemia patient.

Keywords: Thalassemia major, Facial deformity, LeFort I maxillary osteotomy, Orthodontics.

How to cite this article: Prakash A, Arora A, Marure P, Singh G, Agarwal A. Diagnosis and Treatment Consideration in Thalassemia. J Ind Orthod Soc 2014;48(3):184-188.

Introduction

Thalassemia is among the most widely distributed genetic disorders which causes major public health problems. β thalassemia is a severe hemolytic anemia occurring as a result of deficient or absent synthesis of β globin chain of HbA. This disorder is associated with a remarkable clinical heterogeneity with striking differences in hematological manifestations among different ethnic groups. The molecular basis of thalassemia has been studied worldwide; more than 200 different mutations in the β globin gene have been reported. It was also found that types of mutations are ethnic specific. The condition was first described by Thomas B Cooley and Pearl Lee in 1925. The term thalassemia was first used by Wipple and Bradford in 1932. Thalassemia imposes a significant intrusion in the lives of the patients and their families. The effects are many, sweeping from financial hardships and absence from school to significant issues with self-image and self esteem. There is a large increase in the number of thalassemia patients due to lack of genetic counseling and genetic screening in countries like ours.

Thalassemia patients, especially those affected by thalassemia major, may develop a skeletal Class II malocclusion subsequent to maxillary protrusion and mandibular atrophy as a direct result of early fusion of the occipital sutures. The mandibular condyles (growth center) may be involved with the early fusion of occipital sutures impeding mandibular growth relative to the anterior maxillofacial structures.5 The early fusion of occipital sutures takes place concomitantly with medullar hyperplasia of the anterior maxillofacial structures, causing maxillary skeletal protrusion, often with thalassemia major patients, the whole mandibular arch fits within the maxillary arch.

General Recommendations

• Patients should be followed at a thalassemia center every 3 to 6 months with attention to overall clinical well-being, anthropometrics as described for thalassemia major, change in exercise tolerance, complete blood count, reticulocyte count and ferritin levels.
• A baseline red blood cell phenotype should be obtained.
• Attention to changes in facial bone structure. Obtain biannual skull X-rays in growing children and facial photographs: anterior/posterior and lateral.
• Attention to growth velocity, especially in young children and in adolescents.
• Annual dental and orthodontia evaluation.
• Benefits and complications of splenectomy need to be discussed with the family and patient, particularly in cases of massive splenomegaly or hypersplenism.
• Recommend a low iron diet and drinking tea with meals to decrease absorption of iron.
• Patients should receive immunizations as outlined for thalassemia major patients.

• The general recommendations for endocrine, growth, and iron status monitoring outlined for thalassemia major should be applied to patients with thalassemia intermedia. After the initial evaluations, the frequency of monitoring can be modified based on the degree of iron loading or growth failure.

• It is recommended that orthodontic treatment be initiated as early as possible concentrating on prophylactic approaches. In other words, it is crucial that preventive and interceptive orthodontics take precedent over ‘therapeutic orthodontics’.

• Functional and extraoral appliances can be used, however, the ‘skeletal forces’ in thalassemia patients must be less than what is used with normal patients.

• The clinician should keep in mind that the cortical plates are very thin in thalassemic patients so they should be followed more closely with shorter intervals between observations.

• Radiographs at 3-month intervals can be indispensable because the thin cortical plates can complicate orthodontic treatment.

• In brief, the best forces used with thalassemic patients are low forces. The use of functional appliances during the growth period may also be helpful in lessening the side effects of this syndrome.

ORTHODONTIC DIAGNOSIS—CLINICAL CASE

A 13-year-old male reported with the chief complaint of irregularly placed upper and lower front teeth with poor esthetics. He had skeletal and dental Class II division 1 malocclusion (Table 1) with lower anterior crowding. He had a convex profile, increased lower facial height, severely retruded mandible, deep mentolabial sulcus. Model analysis revealed crowding of 0 mm in the upper arch and 7 mm in the lower arch, an overjet of 13 mm (Fig. 1). Upper and lower midlines are not coinciding and it is deviated toward right side by 1.5 mm. 4.5 mm of curve of spee present in the lower arch. Patients’ medical history revealed that he is a known case of β thalassemia major childhood, for which he has been undergoing blood transfusion and splenectomy. However, both the parents could not be traced for a detailed family history, patient has no siblings too.

On general examination, he was under-built, under-nourished with a short stature, with evident icterus, and yellow tinged finger nails. His skin was ashen grey in color. Head and neck examination revealed depressed cranial vault, frontal bossing, maxillary expansion, retracted upper lip and saddle nose (Fig. 2). Patient gives history of splenectomy 10 years back which resulted in improvement of blood count and health (Figs 3 and 4). Cephalometric analysis indicated that the patient was skeletal Class II on account of posterior
Table 1: Cephalometric findings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pretreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNA</td>
<td>84º</td>
</tr>
<tr>
<td>SNB</td>
<td>76º</td>
</tr>
<tr>
<td>ANB</td>
<td>8º</td>
</tr>
<tr>
<td>WITS</td>
<td>5 mm</td>
</tr>
<tr>
<td>FMA</td>
<td>30º</td>
</tr>
<tr>
<td>SN-Go-Gn</td>
<td>41º</td>
</tr>
<tr>
<td>U1-SN</td>
<td>123º</td>
</tr>
<tr>
<td>U1-NA</td>
<td>43º, 8 mm</td>
</tr>
<tr>
<td>L1-MP</td>
<td>91º</td>
</tr>
<tr>
<td>L1-NB</td>
<td>24º, 4 mm</td>
</tr>
</tbody>
</table>

Fig. 2: Height 4 feet 5 inch and weight 28 kg

placement of mandible and reduced size with vertical growth pattern, proclined upper incisors (Fig. 5).

**ROENTGENOGRAPHIC FEATURES**

The radiographic changes are derived from the erythroid hyperplasia of the bone marrow. The erythroid hyperplasia of the marrow results in widening of the marrow space, thinning of the cortical plates and a granular osteoporosis (see Fig. 5). In the more advanced state, partial or total atrophy of the cortical plates is seen, with ‘hair-on-end’ attachment of menisci to the cortical plate.

Fig. 3: Blood report before splenectomy showing severely decreased hemoglobin level and blood cells

Fig. 4: Blood report post-splenectomy showing improvement in hemoglobin level and blood cells
spiculation of bone. The frontal bones reveal the earliest and most severe changes, whereas the inferior bones usually remain unaltered.

**MAXILLOFACIAL STRUCTURES OF THALASSEMA MAJOR**

Marrow hyperplasia of the skull was observed. Expansion of the facial bones in infancy and early childhood inhibited the pneumatization of the maxillary sinuses (Fig. 6). Maxillary alterations laterally displace the orbits leading to hypertelorism or ‘pseudo-overgrowth of maxilla’, result in maloclusion of the jaws and displacement of the dental structures resulting in a ‘rodent’ face, ‘or chipmunk appearance’. The intercanthal space has higher than normal values, as a result of facial expansion.

**CEPHALOMETRIC FEATURES**

- Saddle angle is higher in thalassemia patients than normal patients. This is due to the early fusion of the base of skull sutures with maxillary ‘pseudo-overgrowth’s and from erythroid hyperplasia. This displaces the orbits leading to hypertelorism or ‘pseudo-overgrowth of maxilla’.
- Anterior cranial base N-S length in thalassemia patients is greater than normal (over 71.0 mm).
- Posterior cranial base S-Ar length is less than normal (less than 32.0 mm).
- PFH: AFH is less in thalassemia (under 65%).
- ACB: Mandibular body (anterior cranial base to mandibular body) is larger in thalassemic patients (over 1:1).
- UI to SN (maxillary incisor to SN) is greater than 103° in some cases of thalassemia, as thalassemia major may be one cause of Class II, division 1 development.
- UFH: LFH to UFH (lower facial height to upper facial height) is ≤45%, LFH > 55%.

**CHEST X-RAY FINDINGS**

In thalassemia, posterior mediastinal, paravertebral or presacral masses represent sites of extramedullary hematopoiesis (EMH) resulting from extrasosseous extension of medullary tissue. Expanded head and neck regions of the ribs at the sites of attachment to the vertebral column are seen in this patient (Fig. 7).

**REALISTIC TREATMENT OBJECTIVES (RTO)**

1. Correction of skeletal Class II.
2. Improvement in the smile by reducing gummy exposure.
3. Correction of Class II canine and molar relation.
4. Relieving of lower anterior crowding.
5. Closure of anterior space and derotation of premolars in the upper arch.
6. To correct the midline discrepancy.
7. Leveling of the deep curve of Spee.
8. To achieve good cusp to fossa relationship and overjet/overbite.
9. Correction of convex profile and enhancement of soft tissue esthetics.

TREATMENT PLANNING

Patient was still in growing phase (Fig. 8) and gave a history of thalassemia and splenectomy. Orthodontics with orthognathic surgery was the ideal treatment of choice which is generally considered stable and predictable. LeFort I osteotomy with maxillary impaction (7 mm) and mandibular advancement by bilateral sagittal split osteotomy (5 mm) including advancement genioplasty was the treatment option given to the patient. Soft tissue esthetics can also be improved by rhinoplasty which also helps in nasal bridge reduction. Tipoplasty procedure will sharpen the tip of the nose. After consultation with oral surgeon and physician we reached the conclusion that patient has to be kept under observation till the growth completion. Physician’s advice to not undertake any active surgical procedure at the present age was the prime factor in delaying the surgical procedure. Hemoglobin level is still quite low and is in the anemic range. If orthognathic surgery is performed now then there are chances of relapse following further growth. Thalassemia patients have thinner cortical plates and prolonged treatment with myofunctional appliance and fixed orthodontic treatment at the age of 13 years can increase the chances of root resorption.

CONCLUSION

Thalassemia is an inherited disorder; however, the earlier it is managed, the fewer the side effects. In thalassemia patients preventive and interceptive orthodontics are more important than therapeutic orthodontics. It is recommended that orthodontic treatment is started at a younger age for thalassemic patients than their normal peers. The orthodontist must keep in mind that thalassemia patients have thinner cortical plates. Finally, it is crucial that multidisciplinary team work among dental specialists, hematologists and orthopedists be coordinated to treat this syndrome efficiently and with the best results.

REFERENCES