Orthodontic Consideration in Patients with Beta-Thalassemia Major: Case Report and Literature Review

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Objective: *Beta Thalassemia (βT) patients present a unique facial appearance and specific craniofacial, jaw and dental patterns. Although this anomaly often requires orthodontic management, βT patients have received scant attention in the orthodontic and dental literature over the past 50 years. The aim of this article is to review the characteristic craniofacial and dental manifestation pattern of βT patients and to emphasize their preferred orthodontic management protocol by presenting a βT orthodontic treated patient.* ***Case report:*** *A 10 year old patient presented with a complaint of severe esthetic and functional disorders due to her diagnosis of βT. We initiated orthodontic treatment including a combined orthopedic and functional treatment modality to improve facial appearance.* ***Results:*** Maxillary restraint and increased mandibular size during treatment along with an increase in the vertical dimension were achieved. The patient presented with Angle class I *molar relationship, with reduction of the excessive overjet and deep overbite.* ***Conclusion:*** *Orthodontic treatment comprised of maxillary orthopedic treatment directed especially toward premaxilla with light forces, and mandibular modification by functional appliance along with fixed orthodontic treatment is recommended in βT patients.*

Key words: beta thalassemia, orthodontic, children

INTRODUCTION

Thalassemia diseases are a heterogeneous group of inherited anemia caused by mutations affecting hemoglobin synthesis[1]. Milder forms are among the most commonly seen genetic disorders, whereas the less frequent severe forms lead to significant morbidity and mortality worldwide. The hallmark of thalassemia syndromes is a decreased (or absent) synthesis of one or more globin chains. The designated alpha and beta thalassemia refer to deficits in alpha and beta globin production, respectively. Alpha and beta thalassemia include clinical syndromes of varying severity.

Beta thalassemia (βT) in its most severe form is often diagnosed between 6 months and 2 years of age. The clinical picture includes severe and progressive anemia, mild jaundice, pigment gallstones, cardiomyopathy, abdominal enlargement from hepato-splenomegaly, liver cirrhosis, endocrine dysfunction and impaired growth, skeletal modifications resulting from high blood iron levels, bone marrow expansion caused by extramedullary hematopoiesis and rapid blood cell turnover and bone deformities[2]. Skeletal deformities such as thinning of the cortical portions of the bones (osteoporosis), and pathologic fractures are common[3]. Radiographically, patients exhibit a widening of the diploic spaces in the skull, with thinning of the inner and outer tables. The trabecular bones are arranged in a thin vertical striation as radiating spicules, depicting the "hair-on-end" appearance described in the literature[4]. According to classic literature[5,6], the face develops typical mongoloid features caused by the prominence of the cheek bone and considerable overgrowth of the maxilla, depression of the nose and protrusion or flaring of the

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maxillary anterior teeth. Ordinarily the mandible undergoes fewer enlargements than the maxilla. In general, while the maxilla is composed of spongy bone, the mandible consists of mostly compact bone, thus the maxilla is more effected[7]. The dentition is displaced secondarily by the marrow expansion, leading to malocclusion and speech, swallowing, and eating difficulties[3]. Cephalometric evaluation has shown that patients with severe thalassemia often present with class II malocclusion, especially in males[7].

Although these craniofacial characteristics often require orthodontic management, βT patients have received scant attention in the orthodontic and dental literature over the past 50 years. According to the literature, treatment of patients with βT is under controversy, therefore, accurate diagnosis and treatment planning is crucial.

The aim of this report is to summarize the characteristic craniofacial and dental manifestation patterns of βT patients and to discuss type of orthodontic management based on the scientific literature as performed in a βT patient.

Clinical Case

A 10 year old female was referred from the Department of Pediatric Hematology to the Orthodontic and Craniofacial Department at the Rambam Health Care Campus, Haifa, Israel, seeking an orthodontic solution to severe esthetic and functional disorders due to her diagnosis of βT. She was hematologically treated by blood transfusions in intervals of two weeks.

The clinical and cephalometric evaluation (Figure 1-2) and Table 1 revealed a characteristic thalassemia facial appearance of skeletal class II relationship, grossly incompetent lips, trapped lower lip behavior and a severe convex facial profile with a normal TMJ function. Complete exposure of maxillary incisors as well as a gingival display of more than 8 mm was presented in rest position. She presented an upper jaw protrusion combined with a lower jaw retrusion relative to the cranium, (SNA=82°, SNB=67° Wits appraisal of 9 mm, A to Nasion perpendicular =+3 mm) and vertical facial growth pattern (Y Axis to SN = 81°, Y Axis to FH = 69°), with a steep mandibular plane angle (FMA=43°, GoGn to SN =54°), and clockwise rotation (posterior to anterior facial height =50%). Dentoalveolar diagnosis included Angle class II division 1 with a deep overbite of 6.0 mm and 90% overlapping of incisors. Although the skeletal discrepancy was compensated by maxillary incisors' retrusive inclination (upper incisor to SN =94°, to FH =105° to NA=12° and -0.5 mm), combined with mandibular incisors protrusive inclination (lower incisor to GoMe =98°, to NB=39° and 9 mm) an increased overjet of 15 mm was measured.

Orthodontic procedure

The pronounced skeletal discrepancy dictated a combined orthopedic and functional treatment modality to improve facial appearance. A high pull Thurow maxillary orthopedic splint was worn for the first 5 months incorporating extra oral pull traction of medium force (350 gr per side), aimed to retract and restrain maxillary and pre-maxillary growth. The force vectors were directed eccentrically (anteriorly) to the maxilla center of resistance, thereby producing a combined translatory and counterclockwise rotational movement to improve both skeletal class II maxillary relationship and the severe exposure of maxillary incisors combined with a pronounced gingival display. After 5 months of treatment, a second appliance was then inserted. Thereafter a Twin block functional appliance was used for additional 7 months to modify mandibular growth and gain full correction of the skeletal class II relations. A high pull traction was used combined with the Twin block for 16 hours a day to control the vertical growth pattern. After 12 months of combined orthopedic- functional treatment, the overjet was reduced to 2-3 mm and non-extraction orthodontic treatment with upper and lower fixed appliances was initiated. This treatment phase was successfully finished 24 months later. The 24 months retention protocol included combined maxillary and mandibular fixed retainers and vacuum former removable retainers for night time

RESULTS

The treatment objectives were fully achieved after 36 months of active orthodontic treatment. Facial profile was improved and a characteristic thalassemia facial appearance included protrusive premaxilla was eliminated (Figure 3-4). Leveling and alignment of maxillary and mandibular dental arches, stable class I molar relationship, with reduction of the excessive overjet and deep overbite, were achieved.

The pre and post treatment cephalometric analyses are presented in Table 1. Superimposition of the pre and post treatment cephalometric tracings (Figure 5) showed a maxillary restraint of 6.0 mm (A to N Perp. Initial +3.0 mm, final -3.0 mm) and an increased mandibular size of 13 mm (CoGn Initial =87 mm, final= 100 mm) during treatment along with an increase in the vertical dimension (Y Axis to SN/to FH Initial = 81°/69°, final=85°/74°). Maxillary incisor retrusive inclination of 12° and 2.0 mm was achieved combined with protrusive mandibular incisor inclination of 8°-10° and 3.0 mm. The nasolabial angle increased to 12° (initial 103°, final 115°) reflecting the combined maxillary retraction and maxillary incisor retrusive inclination.

DISCUSSION

Craniofacial morphology of βT patients

Increased red blood cell formation in βT patients affects marrow erythroid hyperplasia, which expands the medullary cavities and causes skeletal deformities of the craniofacial skeleton. The case presented displayed typical mongoloid features caused by the prominence of the frontal and parietal bones. The zygomas appear to protrude and thus the orbits are separated and the eyes have a mongoloid cant[4]. These are reflected by a vertical pattern of facial growth and maxillo-mandibular discrepancy.

Facial Growth Pattern

Our patient presented with a maxillary origin for the marked anterior-posterior (A-P) difference (CoA= 81 mm, A to N-perp.= 3.0 mm). The maxillary bone consists of large cancellous bone-containing a marrow area, therefore its role is expected to be prominent compared to the mandible[4,6]. Additionally the small mandible (SNB = 67°, Pog to N-perp.= 23mm Co-Gn=87mm) reflects mandibular component etiology for this marked A-P discrepancy. Radiographic analysis revealed that most of the patients exhibit thinned mandibular cortex and reduced ramus dimensions[8]. These findings are consistent with other studies, exhibited the same etiology[5,9-15]. Furthermore the enlarged vertical dimension growth pattern presented in our case is a characteristic growth pattern of βT. Bassimitci et al.[12] stated that maxillary marrow hyperplasia primarily influences the vertical

Figure 1: Pretreatment βT patient views: A. Facial repose. B. Facial profile. C. Intraoral Frontal. D. Intraoral lateral anteriors.

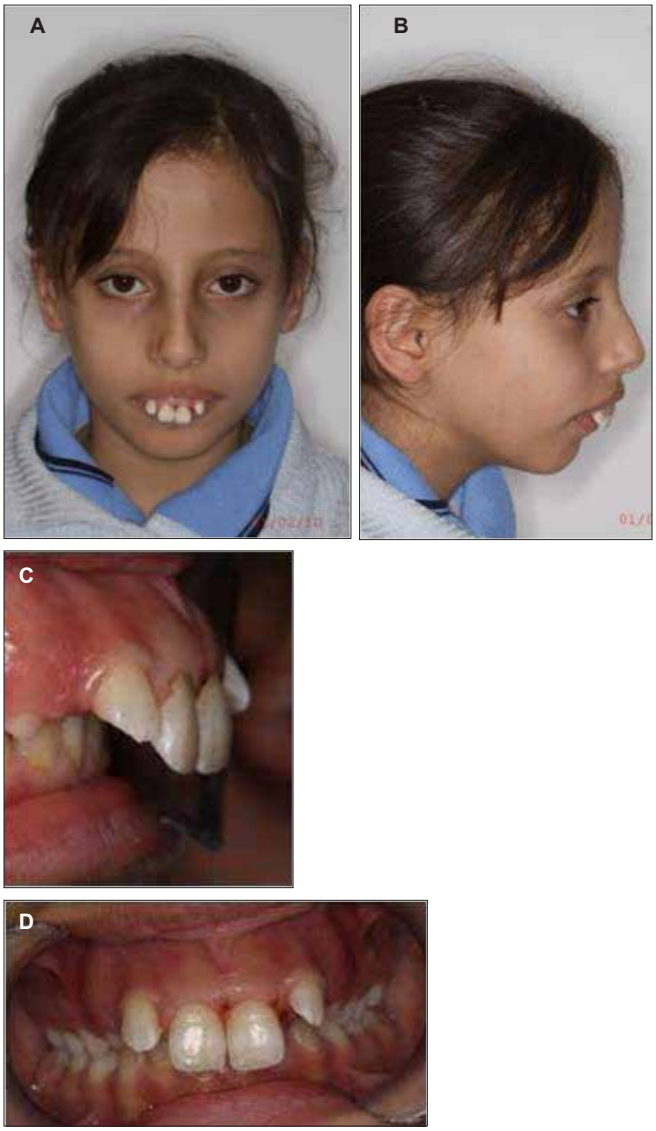


Figure 2: Pretreatment βT patient lateral cephalometric radiograph.

Figure 3: Post-treatment βT patient views: A. Facial repose. B. Facial profile. C. Intraoral Frontal. D. Intraoral lateral anteriors.

Figure 4: Post-treatment βT patient lateral cephalometric radiograph.

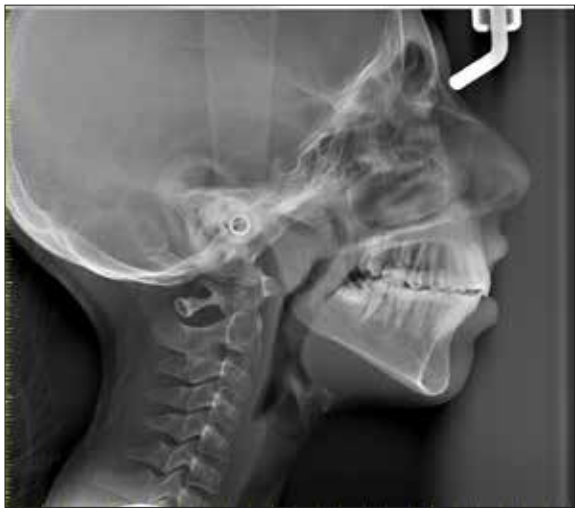
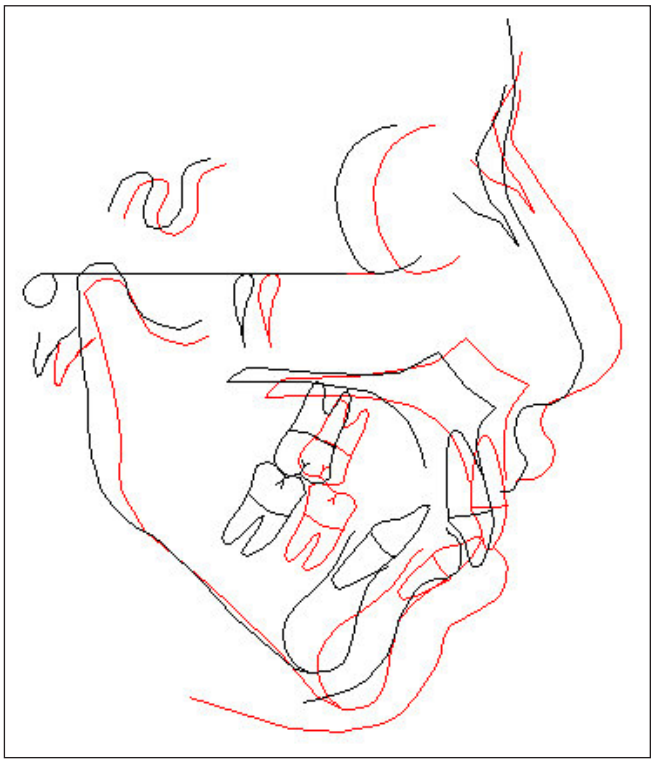


Table 1: The pre and post treatment cephalometric analyses

Measurement	Norm	Initial	Final	Diff
SNA	(82°)	82°	76°	-6°
Co-A	(84- 92 mm)	81 mm	85 mm	4 mm
A to N perp.	(0 – 1 mm)	+3.0 mm	-3.0 mm	-6.0 mm
SNB	(80°)	67°	64°	-3°
Co-Gn	(98-108 mm)	87 mm	100 mm	13 mm
Pog to N perp.	(-2 to 4 mm)	-23.0 mm	-31.0 mm	-8.0 mm
ANB	(2°)	15°	11°	-4°
WITS	(0 mm)	9.0 mm	6.0 mm	-3.0 mm
FMA	(25°)	43°	46°	3°
Go – Gn to SN	(32°)	54°	57°	3°
LFH/TFH	(55%)	53%	51%	-2%
UPH		49	58	+9
LFH		55	60	+5
Y axis (FH)	(59°)	69°	74°	5°
Y axis (SN)	(66°)	81°	85°	4°
PFH/AFH	(59-63%)	50%	50%	0%
Total 3 Angles		414°	418°	4°
Saddle Angle		132°	128°	-4°
Articulare Angle		140°	151°	11°
Gonial Angle		143°	139°	-4°
Upper 1 to FH	(110°)	105°	92°	-13°
Upper 1 to NA	(22°/4)	12°/-0.5 mm	6°/-3.0 mm	-6°/-2.5 mm
Upper 1 to SN	(104°)	94°	81°	-13°
IMPA	(90°)	98°	106°	8°
Lower 1 to NB	(25°/4)	39°/9 mm	49°/12 mm	10°/3 mm
Lower 1 to A-Pog	(1-3 mm)	5 mm	6 mm	1 mm
Interincisal	(130°)	114°	115°	1°
Nasolabial	(90°-110°)	103°	115°	12°
Soft Tissue (N Perp to Pog Perp)	-2.0 mm	-22 mm	-29 mm	-7
*E line: U Lip L Lip	-4 mm -2 mm	+2 mm +4 mm	-1 mm 5 mm	-3 mm 1 mm
*E line: L Lip L Lip	-2.0 mm	+3.0 mm	4.0 mm	1.0 mm

Figure 5: βT patient pre and post-treatment lateral cephalometric radiograph superposition.



and the transverse growth dimensions, and only to a lesser extent the sagittal plane. He referred to Bjork's compensation theory[16] which shows that maxillary prognathism might not be manifested in the anterior-posterior dimension in increased tendency towards a vertical growth mechanism due to a compensatory increased articular angle. Our patient's increased articular angle (=140°), mainly affected the vertical dimension and mainly was expressed by an increase in the mandibular plane angle (FMA=43°, Go–Gn to SN=54°) and a reduced posterior facial height (PFH/AFH=50%). These increased parameters were also found by Toman et al.[9], and the vertical jaw growth pattern was mentioned in a majority of βT patients[9-12, 15,17]. Some etiologies have been proposed for this vertical growth pattern such as an expression of condylar growth deficiency[18], mouth breathing[19] or muscular weakness[20] which is often observed in βT patients.

Dentoalveolar manifestations

The dentoalveolar class II relationships found in our patient has been frequently reported[15,17,21]. Pusaksrikit and Isarangkura [7] also found class II malocclusion among thalassemia major patients (especially in males) with no class III tendency noted, despite its high incidence of 20% among the Thai population. This has been attributed to slower mandible growth in males as it was blocked by the excessive maxillary growth. However, in a follow-up study of 88 patients with thalassemia from the same population[7], Pusaksrikit and Isarangkura noted that the patients had a tendency toward class I malocclusion with a maxillary anterior dentoalveolar protrusion. The inclination of the incisors in our patient representing dentoalveolar compensation mechanisms[22] to prevent increased overjet in such a marked maxillo-mandibular discrepancy. Most of the literature has

reported a retroclined to a normal position of maxillary incisors[9,11,12], while some case reports have described protrusive inclination[17,21] or flaring[13] of the maxillary incisors with no overjet.

The patient's increased overbite is also an expression of dentoalveolar compensation of βT typical vertical growth patterns[7,13]. Based on the limited amount of dentoalveolar extrusion reported by Solow[22], incisor vertical compensation overcomes the vertical dental discrepancy of a possible open bite malocclusion[10,12]. However, an increased overbite as exhibited in our patient has also been described in the literature[7,13] .

Soft Tissue

The reported patient's soft tissue characteristics of convex profile and upper and lower lip prominence are in accordance with the reports published in the literature [9,10,12,15,23,24], representing the typical βT patients' facial expression of severe skeletal and dental discrepancy. In general, the nasolabial angle which is considered to play an important role in facial esthetics, was larger among βT patients, but did not show any statistical difference compared to controls[24]. A smaller nasolabial angle was described in the Malian population[9], which is attributed to the depressed nose, the thicker upper lip and its elevated position. The grossly incompetent lip found in our patient has also been described in the literature[13,15] on βT patients.

Orthodontic considerations

βT manifestations increases with extramedullary hematopoiesis along the years. Consequently, early orthodontic diagnosis and management enables favorable prognosis and minimizes complications[8]. Our recommended orthodontic management is summarized in Table 2. Craniofacial malformations and dental malocclusions tend to be less intense with early medical treatment [11,25,26]. A recent study on the Malian population showed insignificant higher prevalence of craniofacial defects in thalassemia patients with signs of severe disease and less efficient treatment [27]. A marked improvement of the facial disfigurement was reported by Gotte [15], who recommended early combined hematological, orthodontic and maxillofacial surgical corrective treatment. Proper orthodontic treatment may control maxillary excessive growth in the vertical, transverse and anterior-posterior dimensions and may control and minimize early abnormal A-P and vertical skeletal growth patterns as presented in the case reported. The growth pattern of βT patients is characterized by retardation in growth rates[28] and is expressed in skeletal maturation time[29,30], mainly within the ages of 9-10 years old [31,32]. Recently, Hattab showed significant delays in dental development characterized by a mean difference between the chronologic age and the dental age of about one year among Jordanian population. In addition, less than a third percentile height was noted in 41.9% of the males and 34.8% of the females[33]. Therefore, early orthodontic intervention in balancing the facial growth pattern may improve oral functioning and reduce the malocclusion tendency.

Maxillary orthopedic appliances with an extraoral traction, such as high pull Thurow, is a superior alternative to control and redirect maxillary growth, preferably by applying medium force in shorter intervals, as cortical plates are thinner in thalassemic patients and prone to pathologic fractures[34]. In cases of pre-maxillary protrusion characteristics among βT patients, an orthopedic force vector is directed anteriorly to the maxillary center of resistance. As a result, a combined translatory and counterclockwise rotational movement is produced to maximize its orthopedic effect on the premaxilla and incisor area and frontal gingival display at rest[35]. Furthermore, as the mandible is considered to be an unambiguous etiologic factor in βT maxillo-mandibular A-P discrepancy, mandibular growth modification management should be considered as part of skeletal class II management. The Twin block with vertical control, using head gear, was selected as the preferred functional appliance in our patient, for an additional 7 months. A combination of a functional appliance and high pull head gear maximizes the enhancement of the mandibular growth in the A-P dimension towards full correction of skeletal class II. A functional appliance based on optimal muscular origin with low forces[35] and minimal side effects of anchorage loss best suits the characteristics in βT patients. In our reported case the combined

Table 2: Recommended Orthodontic Management

	RATIONAL	MEAN
1	An interceptive conservative orthodontic corrective approach in 8-10 year old	Early orthodontic diagnosis and treatment
2	Control and redirection of maxillary growth	Extraoral traction maxillary appliance
3	Continuity and thickness of the dense layer of cortical bone offered the most resistance to tooth movement	Smaller dentofacial orthopedic force
4	Rapid orthopedic response is expected due to thin layer of cortical bone	Shorter intervals between visits
5	a combined translatory and rotational movement of pre-maxillary protrusion	Force vector is directed anteriorly to the maxillary center of resistance.
6	Mandibular growth modification may redirect facial growth pattern	Functional or orthopedic appliances
7	Retardation of normal growth patterns in βT affected patients	Timing of orthodontic treatment may be synchronized with the expected general growth spurt
8	a. Maxillary growth modification by means of intra and extraoral traction b. Achieved less likely orthodontic movements to correct malocclusion	Use of TAD's (Temporary Anchorage Devices)

functional orthopedic contributed not only to skeletal balance and reduced tendency of malocclusion, but also to a significant improvement in oral functions and esthetics. It should be emphasized, that delaying skeletal treatment and considering orthogantic surgery is not recommended due to the compromise of blood transfusion required in large surgical procedures in βT patients[36].

CONCLUSION

Facial appearance of children suffering from βT is unique due to the increased formation of red blood cells caused by marrow erythroid hyperplasia. They often present a typical craniofacial and jaw growth pattern combined with grossly procumbent lower anterior teeth. Early medical care and orthodontic diagnosis are crucial in controlling the skeletal changes including improper craniofacial growth. We present a case of a young girl, a βT patient who underwent combined functional and orthopedic interceptive dentofacial treatment which controlled the skeletal changes, followed by an orthodontic treatment stage to achieve proper occlusal relationships and improved oral functions. Low force magnitude due to thinner cortical plates combined with close orthodontic follow-up was applied. Such early intervention prevents future two-jaw orthognathic surgery to control skeletal and dental malformations in all dimensions. In addition the imperative treatment contributed to reducing severe emotional trauma in the patient due to her poor facial esthetics.

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