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Osteogenesis imperfecta and rapid maxillary expansion: Report of 3 patients

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Introduction: The aim of this study was to analyze the effects of orthopedic therapy with rapid maxillary expansion (RME) in growing patients affected by osteogenesis imperfecta and treated with bisphosphonates. **Methods:** Three boys with osteogenesis imperfecta (mean age, 10.6 years) were treated with RME. They all had treatment with quarterly intravenous infusions of bisphosphonates. They were in either the early or the late mixed dentition and had indications for RME. The expansion screw was activated twice daily until correction of the transverse relationships was achieved. The retention period with the expander in place was 6 months. In 2 Class III patients, RME was associated with the use of a facemask. In all patients, occlusal radiographs were taken at the end of active RME therapy to assess the opening of the midpalatal suture and 1 year after the end of active expansion therapy to evaluate the reossification and reorganization of the midpalatal suture. **Results:** In all patients, the opening of the midpalatal suture and the healing with reorganization of the midpalatal suture were documented with the occlusal radiographs. No complications were found after a 1-year follow-up. **Conclusions:** In growing patients affected by osteogenesis imperfecta and treated with bisphosphonates, it is possible to perform RME with a standard protocol with no complications after a 1-year follow-up. (Am J Orthod Dentofacial Orthop 2015;148:130-7)

Osteogenesis imperfecta (OI), also called "brittle bone disease," is a heritable disorder of the connective tissues that can lead to multiple fractures, which in serious cases can also affect the patient's survival. This disease has an estimated incidence of about 1 in 20,000 to 50,000 births, a number that is often underestimated because less serious cases are misunderstood or diagnosed late. The male-to-female ratio is 1:1, with both dominant and recessive transmissions.[1,2] Numerous studies have established a correlation between OI and COLIA1 and COLIA2 genes that encode for either chain of type 1 collagen.[1] Since this protein is a major constituent not only of bones but also of other uncalcified tissues, this disease can involve various structures of the body, thus requiring a multispecialized medical approach.[1,3] Extraskeletal manifestations of OI are represented by blue sclerae, dentinogenesis imperfecta, muscle weakness, hearing loss, and joint laxity. Patients with OI have dentoskeletal Class III malocclusions, anterior and posterior crossbites or open bites, impacted teeth,[4-7] and craniofacial deformities (triangular face shape, protrusion of both temporal bones, and frontal bone prominence).[8] A recent study by Rizkallah et al[9] on a sample of 49 patients with OI (age range, 5-19 years) showed that malocclusions were significantly more severe in the patients with OI than in a control group with no OI. There was a higher incidence of Class III malocclusion associated with anterior and lateral open bites in patients affected by OI.

Bisphosphonates (BPs) are indicated in the treatment of OI because they inhibit bone resorption by osteoclasts, thus favoring bone formation over resorption during remodeling.[2] A systematic review by Castillo

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Fig 1. Pretreatment occlusal relationships in patient 1.

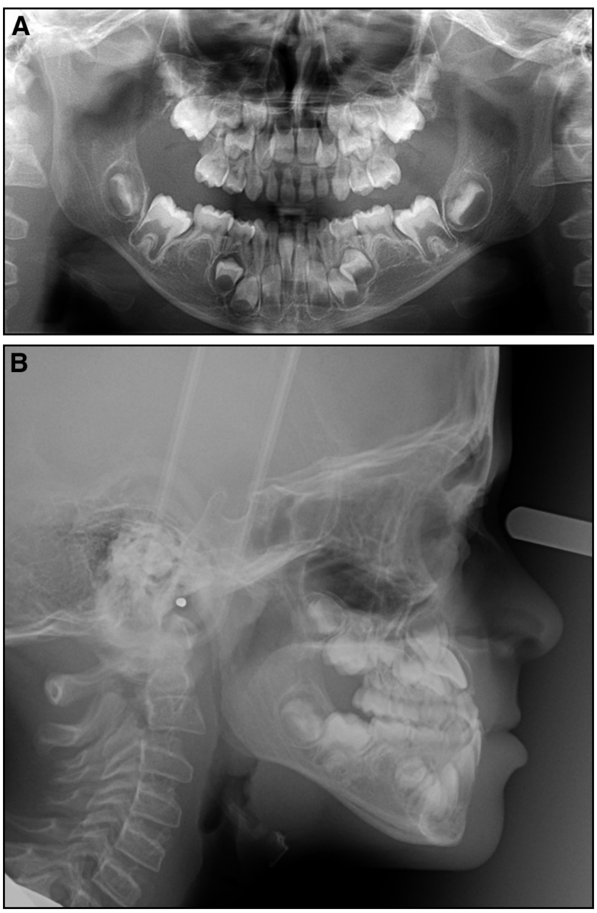

Fig 2. Pretreatment radiographic records in patient 1: **A,** panoramic radiograph; **B,** lateral cephalogram.

et al[10] showed that most studies confirmed improvements in bone density produced by BPs in patients with OI. Many but not all studies demonstrated reductions in fracture rates and enhanced growth. However, the optimal medication and dosing regimen and the duration of treatment with BPs in pediatric patients have not been elucidated yet.[10] A significant potential side effect of BPs in the adult population is the development of osteonecrosis in the mandible or the maxilla, particularly related to intravenous therapy or high-dose, long-term oral usage.[11] A recent systematic review, however, reported no evidence to support the hypothesis of a causal relationship between BPs and osteonecrosis of the jaw occurring either spontaneously or after dental surgery in children and adolescents with OI.[12]

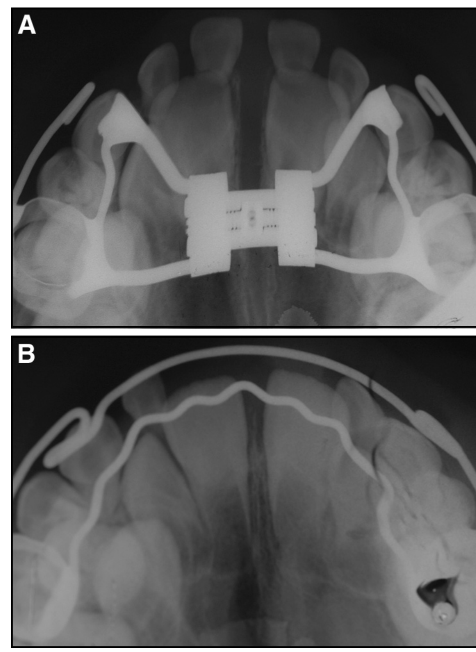

Fig 3. Occlusal radiographs in patient 1: **A,** after active RME treatment; **B,** 1 year from the end of active expansion therapy.

Quite interestingly, the orthodontic literature lacks case reports of children with OI treated with BPs who could require orthopedic treatment with rapid maxillary expansion (RME). The aim of this article, therefore, was to evaluate treatment with RME in 3 patients with OI who had received BPs.

MATERIAL AND METHODS

Three boys (mean age, 10.6 years) were treated at the Unit of Pediatric Dentistry of the Department of Oral and

Fig 4. Occlusal relationships after 1 year of treatment with a facemask in patient 1.

Fig 5. Posttreatment lateral cephalogram in patient 1.

Maxillofacial Sciences in collaboration with the Department of Pediatrics and Pediatric Neuropsychiatry of the Sapienza University of Rome in Italy. They all had a diagnosis of OI and were treated with quarterly intravenous infusions of neridronate (Nerixia, 100 mg; Abiogen Pharma, Pisa, Italy). All patients were in either the early or the late mixed dentition and had indications for RME that was performed with a banded expander with bands on the maxillary permanent first molars. The patients' parents were instructed to activate the expansion screw twice daily until the desired correction of the transverse problem was achieved. The expander was kept in place for 6 months for retention. According to the instructions of the pediatricians of the Department of Pediatrics and Pediatric Neuropsychiatry, the patients received infusions with neridronate right before starting treatment with RME. After 3 months, the next infusion of neridronate was skipped, and it was resumed after 6 months (approximately at the end of the 6-month retention period with the expander in place). For all patients, occlusal radiographs were taken at the end of active RME therapy to assess the opening of the midpalatal suture and after 1 year from the end of active expansion therapy to evaluate the reossification and reorganization of the midpalatal suture.

Table I. Cephalometric angular values (°) for patient 1

	Pretreatment	*Posttreatment*
SNA	81.5	83.4
SNB	83.0	83.0
ANB	−1.5	0.4
N-S-Ar	112.8	117.5
S-Ar-Go	147.8	143.0
Ar-Go-Me	127.5	126.6
Jarabak's sum	388.1	387.1
FH to GoMe	28.0	27.1
U1 to palatal plane	110.5	127.0
L1 to mandibular plane	71.5	90.2
Interincisal angle	154.7	120.4

FH, Frankfort horizontal; *U1*, maxillary incisor; *L1*, mandibular incisor.

CASE REPORT 1

A 7-year-old boy affected by OI with a history of multiple femur fractures, with no blue sclerae, and with mild ligamentous laxity started treatment with neridronate in 2004. At the extraoral clinical examination, the patient showed a Class III flat profile. At the intraoral clinical examination (Fig 1), he was in the early mixed dentition, with no dentinogenesis imperfecta, and had an anterior crossbite and Class III occlusal relationships.

The analysis of the panoramic radiograph (Fig 2, *A*) showed aplasia of the mandibular left and right second premolars. The pretreatment cephalometric analysis (Fig 2) showed Class III skeletal relationships associated with decreased vertical skeletal relationships. The analysis of the transverse interarch relationships showed a transverse discrepancy of −4 mm.[13] RME was indicated for this patient because a negative interarch discrepancy is often associated with a maxillary skeletal transverse

Fig 6. Pretreatment occlusal relationships in patient 2.

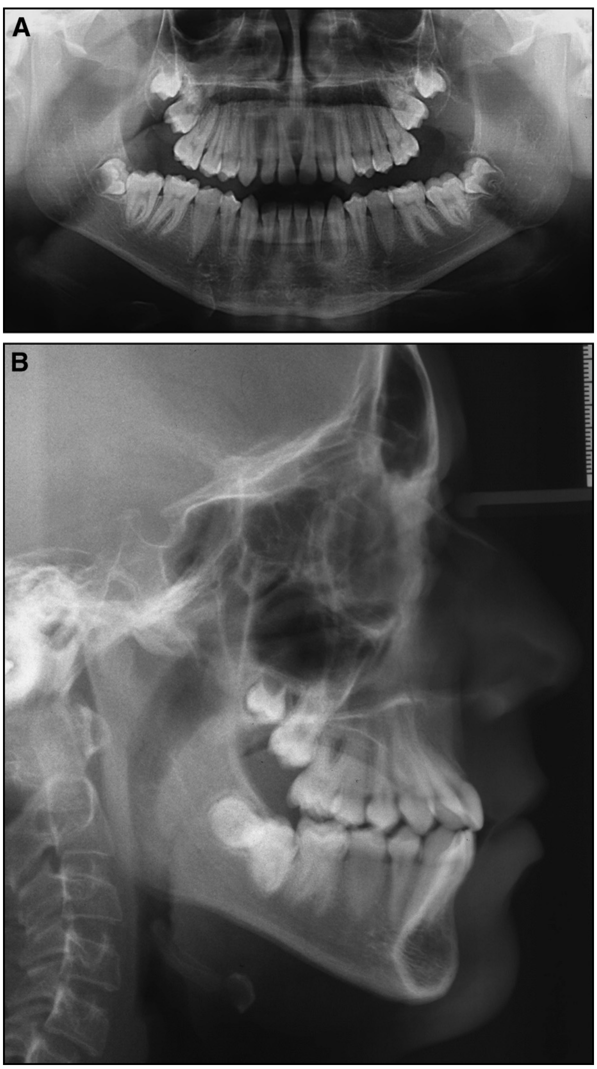

Fig 7. Pretreatment radiographic records in patient 2: **A,** panoramic radiograph; **B,** lateral cephalogram.

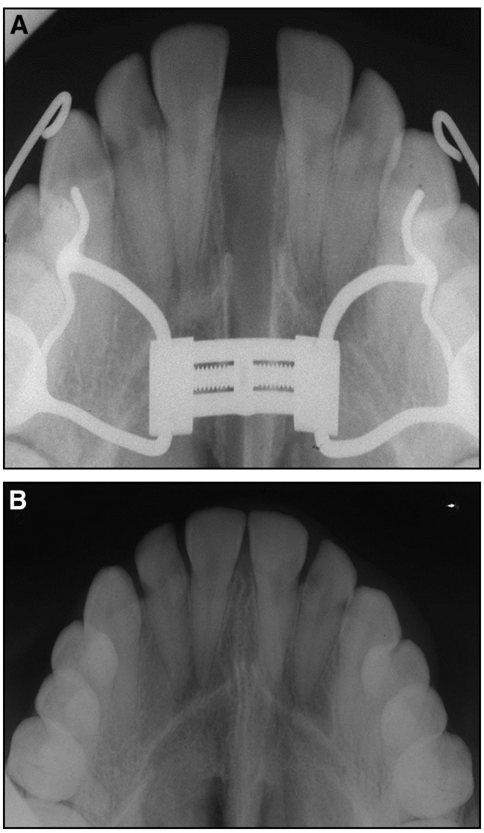

Fig 8. Occlusal radiographs in patient 2: **A,** after active RME treatment; **B,** 1 year from the end of active expansion therapy.

deficiency in Class III patients during the early developmental phases.[14]

The first phase of treatment consisted of RME with a banded expander that was activated twice daily for 15 days (Fig 3, *A*). A Delaire facemask was delivered to the patient immediately after RME, and it was applied first using the expander as anchorage and then with a double arch. The elastic traction produced forces of 14 g per side. Orthopedic treatment with the facemask lasted for 1 year. A maxillary Schwarz plate was given to the patient as a retention appliance. The treatment produced favorable changes at both the occlusal (Fig 4) and the skeletal (Fig 5) levels, with an advancement of the maxilla (SNA, +1.9°) leading to improvement in the sagittal skeletal relationships (ANB, +1.9°)

Fig 9. Occlusal relationships after 1 year of treatment with a facemask in patient 2.

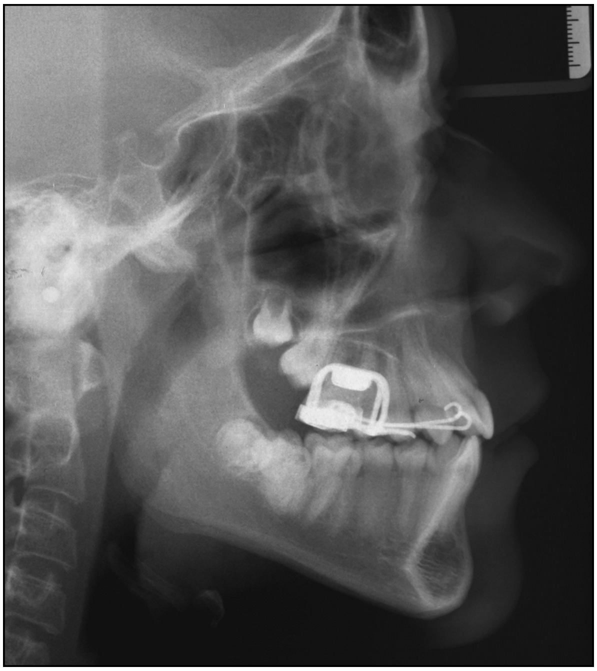

Fig 10. Posttreatment lateral cephalogram in patient 2.

(Table I). Minor changes (<1°) occurred in the vertical skeletal relationships. The postexpansion occlusal radiograph showed that the opening of the midpalatal suture was completely reossified and reorganized 1 year later (Fig 3, *B*).

CASE REPORT 2

This adolescent boy (age, 15 years) had moderate-to-severe ligamentous laxity, blue sclerae, asymmetry of approximately 4 cm in the lower limbs, a history of multiple fractures from age 1.5 years, and no dentinogenesis imperfecta (Fig 6). He had a slightly convex profile; during the intraoral clinical examination, he showed permanent dentition (without agenesis or tooth abnormalities) (Fig 7, *A*), constriction of the maxillary arch with a tendency to bilateral posterior crossbite (transverse interarch discrepancy, −3.5 mm),[13] left posterior open bite, and a tendency to Class III molar and canine relationships. The pretreatment cephalometric analysis (Fig 7, *B*) showed a tendency to Class III skeletal relationships associated with normal vertical skeletal relationships.

Table II. Cephalometric angular values (°) for patient 2

	Pretreatment	*Posttreatment*
SNA	81.5	82.4
SNB	80.4	79.6
ANB	1.1	2.8
N-S-Ar	130.8	130.6
S-Ar-Go	142.6	143.4
Ar-Go-Me	122.6	123.1
Jarabak's sum	396.0	397.1
SN to GoMe	36.1	37.2
U1 to palatal plane	118.4	114.8
L1 to mandibular plane	90.0	88.0
Interincisal angle	120.5	127.6

FH, Frankfort horizontal; *U1*, maxillary incisor; *L1*, mandibular incisor.

The patient was treated with RME (activation of the screw twice a day for 15 days) (Fig 8, *A*) followed by maxillary protraction with a Delaire facemask for about 1 year. The treatment produced favorable changes at both the occlusal (Fig 9) and the skeletal (Fig 10) levels with an advancement of the maxilla (SNA, +0.9°) and a more retruded mandible (SNB, −0.8°) leading to improvements in the sagittal skeletal relationships (ANB, +1.7°) (Table II). An increase of about 1° in the vertical skeletal relationships was observed. The postexpansion occlusal radiograph showed that the opening of the midpalatal suture was completely reossified and reorganized 1 year later (Fig 8, *B*).

CASE REPORT 3

This adolescent boy (age, 14 years) came to us with a history of multiple limb fractures, a noticeable reduction in statural height, moderate-to-severe ligamentous laxity, and dentinogenesis imperfecta (Fig 11). At the

Fig 11. Pretreatment occlusal relationships in patient 3.

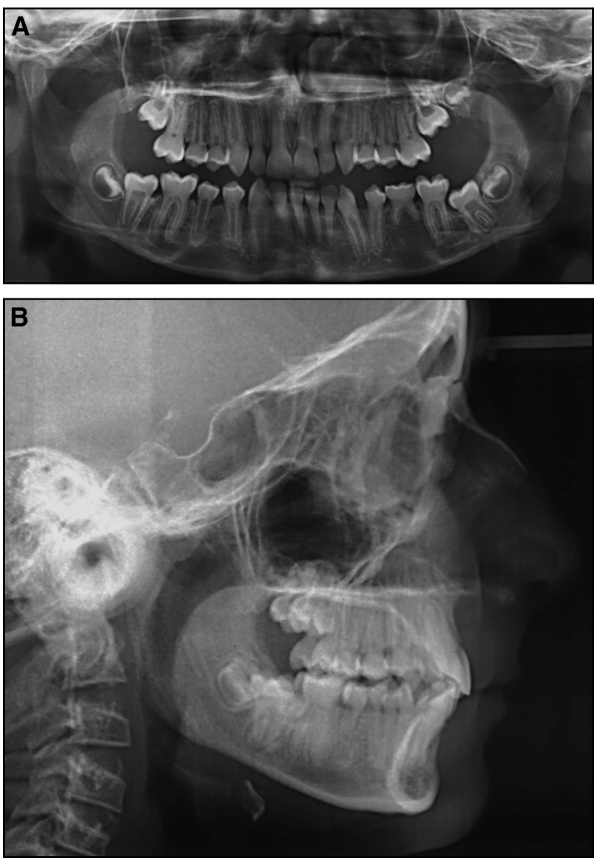

Fig 12. Pretreatment radiographic records in patient 3: **A,** panoramic radiograph; **B,** lateral cephalogram.

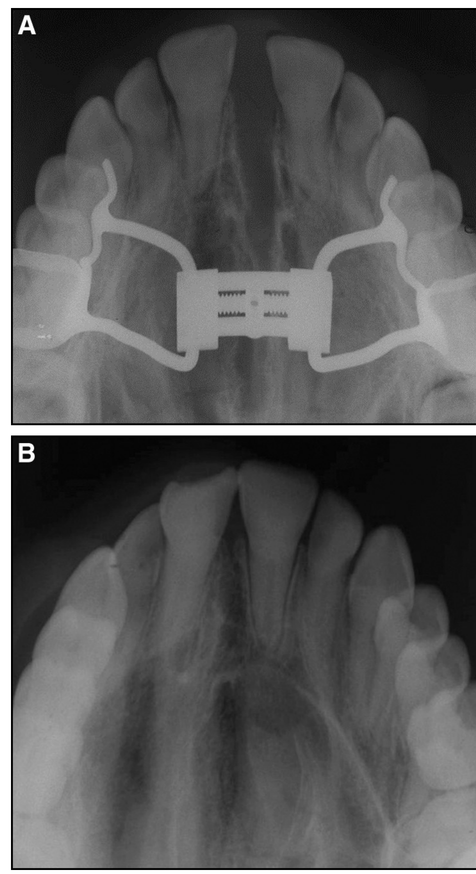

Fig 13. Occlusal radiographs in patient 3: **A,** after active RME treatment; **B,** 1 year from the end of active expansion therapy.

extraoral clinical examination, he showed a slightly convex profile. The intraoral clinical examination showed permanent dentition with an overretained mandibular left deciduous second molar, dentinogenesis imperfecta, Class I molar and canine occlusal relationships on the right side, Class II molar and canine relationships on the left side, and a unilateral posterior crossbite with a mandibular functional shift on the left side (transverse interarch discrepancy, −3.5 mm).[13] On the panoramic radiograph, agenesis of the mandibular left permanent second premolar was observed (Fig 12, *A*).

The pretreatment cephalometric analysis (Fig 12, *B*) showed Class I skeletal relationships associated with decreased vertical skeletal relationships. The expansion screw was activated twice daily for 15 days (Fig 13, *A*). The expander was kept in place for 6 months for retention. After removal of the expander, the patient showed improvements in the transverse occlusal relationships (Fig 14; Table III). Also, the postexpansion occlusal radiograph showed that the opening of the midpalatal

Fig 14. Occlusal relationships after 1 year of treatment with a facemask in patient 3.

Table III. Cephalometric angular values (°) for patient 3

	Pretreatment
SNA	77.7
SNB	75.3
ANB	2.4
N-S-Ar	119.8
S-Ar-Go	159.1
Ar-Go-Me	109.4
Jarabak's sum	388.39
FH to GoMe	28.3
U1 to palatal plane	116.5
L1 to mandibular plane	99.5
Interincisal angle	129.7

FH, Frankfort horizontal; *U1*, maxillary incisor; *L1*, mandibular incisor.

suture was completely reossified and reorganized 1 year later (Fig 13, *B*).

DISCUSSION

Three growing patients affected by OI and with constrictions of the maxillary arch were treated with RME. All were receiving treatment with BPs. Previous case reports have analyzed the effects of conventional orthodontic treatment[11,15] and combined orthodontic-surgical treatments in adult patients with OI.[15,16] No information in the literature is available on the orthopedic treatment protocols for children with OI who are receiving BP therapy. In agreement with the pediatricians, treatment with BPs was discontinued during active RME therapy to facilitate the opening of the midpalatal suture. All patients showed a positive response to the orthopedic expansion. The transverse correction was obtained with orthopedic forces similar to the standard protocols. In all patients, the occlusal radiographs showed opening of the midpalatal suture after active RME therapy. After 1 year from the end of active expansion, the occlusal radiographs documented that the midpalatal suture had a normal appearance with regular ossification and reorganization. No adverse effects associated with RME were observed in any of the OI patients treated with the expansion protocol after an observation period of 1 year.[17] All patients will be monitored in the long term to check for any complications. In the 2 patients with Class III malocclusion, RME was associated with the use of a facemask. In both patients, improvements in the sagittal skeletal relationships were observed.

Orthodontic treatment of growing patients with OI is not a routine approach, as demonstrated by the lack of case reports in the literature. According to Hartsfield et al,[15] clinical recommendations must be based on the particular characteristics and condition of each patient. Orthodontists must be aware that the extreme variability of expression seen in OI patients makes each case unique, with a potentially variable outcome regardless of the treatment plan or the management scheme.[15] Rinchuse et al,[11] in a case report of 2 orthodontic patients in treatment with BPs, emphasized that BPs can impact orthodontic treatment by impeding tooth movement caused by osteoclast destruction and decreased microcirculation, limiting bone turnover and remodeling.

The treatment protocol used in these 3 case reports cannot be considered a scientifically based rationale for pediatric OI patients affected by transverse maxillary deficiency. An interceptive orthodontic approach, as described here, can be a reference for orthodontists who must intervene in a growing patient with OI and dentoskeletal problems, without having to postpone orthodontic treatment to an older age when it can be more difficult.[11] Rosén et al,[16] in a review of the case reports described in the literature, concluded that it is possible to perform combined orthodontic and orthognathic surgery in patients with OI despite the greater risk of complications. The risk of complications is related mainly to the treatment with BPs, which can produce osteonecrosis of the jaws in patients undergoing oral surgery. Recently, the American Association of Oral and Maxillofacial Surgeons published a position paper describing the risk factors and prevention procedures for medication-related osteonecrosis of the jaws.[18] In children and adolescents with OI, however, there is no evidence to support the hypothesis of a causal relationship between BPs and osteonecrosis of the jaws.[12] In our sample of pediatric patients with OI, it was decided to interrupt the pharmacologic therapy with BPs during the active orthopedic treatment with RME. No guidelines were available in the literature in this regard. The decision to temporarily suspend treatment with BPs was based on the observations of Munns et al,[19] who found that in children with moderate-to-severe OI, treatment with BPs was associated with delayed healing after osteotomy. To minimize the chances of delayed healing in OI patients in treatment with BPs and receiving osteotomy, Munns et al suggested implementing a BP-free period around the surgical intervention. Therefore, in our study, in agreement with the pediatricians, it was decided that the patients should skip only 1 quarterly intravenous infusion with neridronate because the main priority was the systemic treatment of OI. This procedure led to a successful maxillary expansion with no complications after a 1-year follow-up in all 3 patients.

CONCLUSIONS

In growing patients affected by OI and receiving treatment with BPs, it is possible to perform RME with a standard protocol. In the 3 cases described here, the expansion screw was activated twice daily until the desired correction of the transverse relationships was achieved. The retention period with the expander in place was 6 months. In the 2 Class III patients, RME was associated with use of a facemask that produced favorable sagittal skeletal changes. No complications were found after a 1-year follow-up.

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