



Fixed-functional appliance treatment combined with growth hormone therapy

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The purpose of this study was to illustrate the effects of growth hormone (GH) therapy and fixed functional appliance treatment in a 13-year-old Class II malocclusion patient without GH deficiency. GH has been shown to effectively increase endochondral growth and induce a more prognathic skeletal pattern. Although a major concern in Class II retrognathic patients is chin deficiency, long-term studies have shown that the mandibular growth enhancement effects of functional appliances are clinically insignificant. This case report demonstrates that the mandible grew significantly during fixed functional appliance treatment combined with GH therapy, with stable results during 2 years 11 months of retention. More studies are needed to evaluate GH therapy as a supplement in Class II treatment. (*Am J Orthod Dentofacial Orthop* 2017;152:402-12)

When a Class II patient has mandibular growth deficiency, we usually hope to increase mandibular growth to improve the patient's facial esthetics. However, randomized clinical trials^{1,2} and systematic reviews^{3,4} have shown that it is not possible to effectively increase skeletal growth in children. Some researchers still argue that the effectiveness of mandibular growth treatment depends on the treatment timing,⁵ but until now, there have been no long-term studies to support this hypothesis.^{6,7} Thus far, dentoalveolar changes and short-term increases in mandibular growth are the only proven effects of functional appliance treatment.

Human growth hormone (GH) is a polypeptide chain with 188 amino acids that is produced by the anterior pituitary gland. GH deficiency can delay craniofacial growth and tooth eruption.⁸ Growth deficiency of the mandible is usually more severe than growth deficiency of the maxilla.^{9,10} GH has been shown to be effective for increasing craniofacial growth in GH-deficient patients, particularly in growth sites with endochondral ossification, such as condylar cartilage.^{11,12} In these patients, GH induced a more prognathic growth pattern.^{8,13}

Children with short stature without GH deficiency have also been treated with biosynthetic GH. However, there has been much controversy regarding the effects of systemic GH administration in patients with familial short stature who are not deficient in GH.^{14,15} Because of the competitive nature of Korean society, GH therapy is frequently recommended by many growth clinics, even to adolescents who are not particularly small or not deficient in GH. There have been attempts to treat malocclusion patients orthodontically while they were simultaneously receiving GH therapy.¹⁶⁻¹⁹ Case reports of patients with Turner syndrome,^{16,18} pituitary dwarfism,¹⁹ and short stature with a normal GH level¹⁷ have been published, and all have indicated that mandibular growth increased when orthodontic treatment was combined with GH treatment.

Because it has become more difficult to obtain good compliance during orthodontic treatment, compliance-free fixed functional appliances are gaining popularity.²⁰ Because GH therapy usually increases mandibular growth in GH-deficient patients, and increasing mandibular growth is the major concern of the orthodontist during the treatment of Class II patients with mandibular deficiency, functional appliance treatment combined with GH therapy would be worth assessing. See [Supplemental Materials](#) for a short video presentation about this study.

DIAGNOSIS AND ETIOLOGY

A boy, aged 13 years 7 months, came with chief complaints of proclined maxillary incisors and a retruded chin ([Fig 1](#)). He had undergone tonsillectomy when he

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All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and none were reported.

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Fig 1. Pretreatment intraoral and facial photographs.

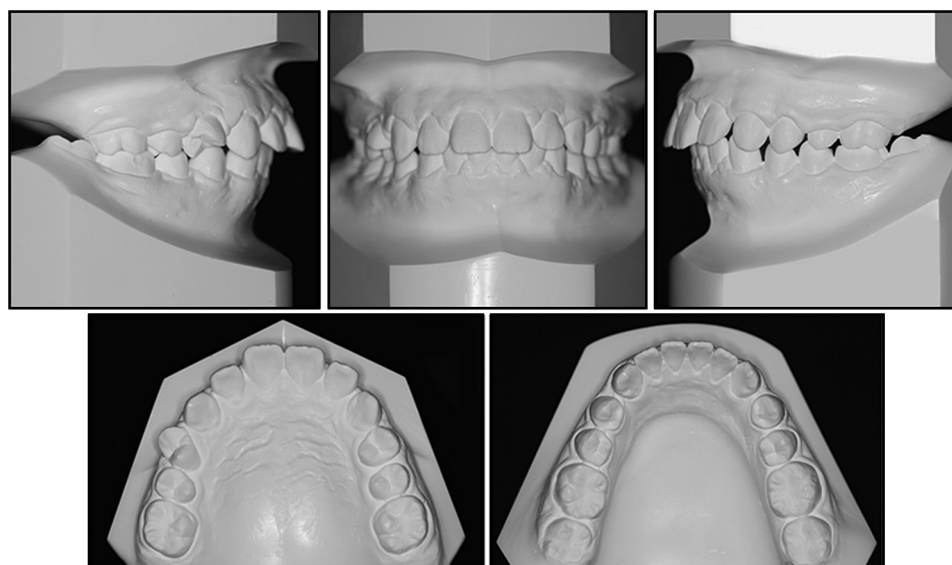


Fig 2. Pretreatment study casts.

was 7 years old but still suffered from chronic allergic rhinitis and mouth breathing.

Intraoral photographs (Fig 1), study casts (Fig 2), and panoramic radiographs (Fig 3) showed mild dental

spacing, large overbite and overjet, flared maxillary incisors, and a lingual crossbite on the right first premolar. Overbite was 4.0 mm, overjet was 5.5 mm, and there was a mild Class II molar relationship on both sides. All

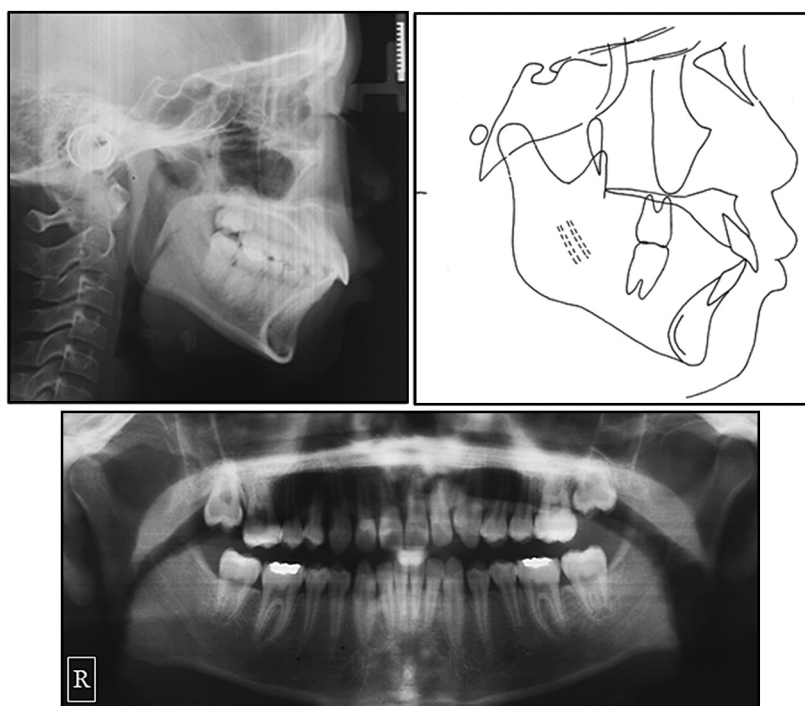


Fig 3. Pretreatment lateral cephalogram, lateral cephalometric tracing, and panoramic radiograph.

Table. Changes in cephalometric measurements

	<i>Pretreatment</i>	<i>Posttreatment</i>	<i>Retention</i>
Bjork sum (°)	393.8	389.9	386.4
Facial height ratio (%)	65.7	70.3	74.3
ANB (°)	7.6	4.4	4.1
A to N perpendicular (mm)	5.8	7.7	7.9
Pog to N perpendicular (mm)	−5.6	4.2	5.1
U1 to FH (°)	122.2	117.3	118.4
U1 to SN (°)	112.1	106.3	107.4
L1 to APog (°)	7.5	1.6	1.7
IMPA (°)	106.2	90.2	93.0
Interincisal angle (°)	108.4	133.9	134.0
Nasolabial angle (°)	100.8	108.7	112.3
UL to EL (mm)	7.0	1.0	2.5
LL to EL (mm)	6.2	−0.4	1.3

teeth other than the maxillary second molars had erupted, and there were no missing or malformed teeth. The patient also had generalized gingival inflammation and poor oral hygiene, but his alveolar bone level was intact. Both temporomandibular joints were well-formed, and there were no specific signs or symptoms.

In the facial photographs (Fig 1), the patient had a protrusive lip profile and severe lip incompetency. The pretreatment lateral cephalometric radiograph (Fig 3, Table) showed a large ANB angle (7.6°), a protrusive maxilla (A to N perpendicular, 5.8 mm),

and a retrusive mandible (Pog to N perpendicular, −5.6 mm). Protrusive, maxillary (U1 to FH, 122.2°) and mandibular incisors (IMPA, 106.2°) were also observed. The American Board of Orthodontics Discrepancy Index score was 30.

The patient and his parents were aware that his mandible was much smaller than his maxilla. His mother said that because of her son's short stature, he would start to receive GH treatment soon. His height was 154 cm, much shorter than the average for his age, near the bottom 10%.²¹

TREATMENT OBJECTIVES

The treatment objectives were to improve the profile and lip incompetency, correct the lingual crossbite of the right first premolar, establish an ideal interincisor relationship, improve incisor angulation, eliminate interdental spacing, and achieve a functional occlusion with Class I molar and canine relationships.

The prognosis for improvement of chin deficiency seemed to be poor because it was so severe.

TREATMENT ALTERNATIVES

Because of the patient's severely protrusive lip profile, retrusive chin area, and lip incompetence, a significant profile change was required. To improve these conditions, there were several options.

First, maxillary and mandibular first premolar extractions with an orthodontic mini-implant for anchorage reinforcement were considered. This option would allow great profile improvement by causing a large amount of incisor retraction. However, it would not correct the maxillary-mandibular skeletal relationship or the chin deficiency, and there was a risk that it would make the profile too retrusive.

The second option was maxillary and mandibular premolar extractions with intrusion treatment. Intrusion of the posterior teeth using an orthodontic mini-implant²² or a miniplate²³ can rotate the mandible counterclockwise and improve the chin deficiency. The patient's overbite was within normal limits, so if autorotation of the mandible was required, intrusion of not only the posterior teeth but also the anterior teeth would have been needed. Total arch intrusion using an orthodontic mini-implant is also possible, but this option was not recommended because the incisal display at rest was not large enough.²⁴

The third option was maxillary and mandibular premolar extraction with fixed functional appliance treatment. Because long-term studies on functional appliance treatment have not demonstrated significant growth of the mandible, considerable improvements in mandibular growth in the long term could not be expected.^{6,7} However, temporary enhancement of mandibular growth or a slight restriction of maxillary growth was expected.²⁵ At the least, rapid improvement of overjet and intermolar relationship could be obtained without the patient's compliance.

After receiving a detailed explanation of the treatment options, the patient and his parents chose the third option. Although the patient had interdental spacing, extraction of his maxillary and mandibular second premolars was chosen to improve the protrusive lip profile

and to compensate for the pushing effect of the fixed functional appliance on the mandibular incisors.²⁶

Additionally, we explained the possibility of genioplasty to improve his chin deficiency. A recent study demonstrated that genioplasty in the adolescent period can have good results, so genioplasty can be performed either during orthodontic treatment or after growth completion.²⁷ The patient and parents did not want a surgical procedure, so we suggested discussing it later if they felt the need after orthodontic treatment.

The patient's circulating nocturnal GH level was within normal limits, but he and his parents requested GH treatment as a possible means of increasing his height. The mother asked whether the hormone therapy would cause any problems during the orthodontic treatment. I explained that it would not have negative effects. Although I hoped that the patient's mandibular growth would significantly increase with GH treatment, there was insufficient evidence available on this topic.

TREATMENT PROGRESS

Edgewise metal brackets with 0.022-in slots (MBT setup; 3M Unitek, Monrovia, Calif) were bonded on the buccal surfaces of all erupted teeth except for the maxillary first molars. Bands were placed on the maxillary first molars for the Forsus appliance (3M Unitek). The archwire sequence progressed from 0.014-in nickel-titanium wire to 0.019 × 0.025-in stainless steel working wire, and the patient's second premolars were extracted during leveling. After alignment, leveling, and lingual crossbite correction, the extraction space was closed with working wire. When the remaining extraction space was about 2 mm, a Forsus appliance with an L-pin was placed at the gingival headgear tube of the first molar, and the hook was soldered distal to the mandibular first premolar. The estimated force vector is shown in Figure 4; a greater vertically directed force was applied than what is usually used for Forsus treatment to minimize extrusive tooth movement.²⁸ The Forsus was used for 8 months.

After correction of overbite, overjet, and molar relationship, the band was removed, and buccal tubes were placed on the maxillary first and second molars. Finally, coordinated 0.019 × 0.025-in stainless steel wires were used to detail the occlusion (Fig 5).

GH treatment commenced in the next month of bracket bonding and continued for 2 years. The patient grew 10 cm during the first year and 6 cm during the second year of GH treatment; these increases were greater than the average growth for his age group (6.7 and 4.5 cm, respectively²¹).

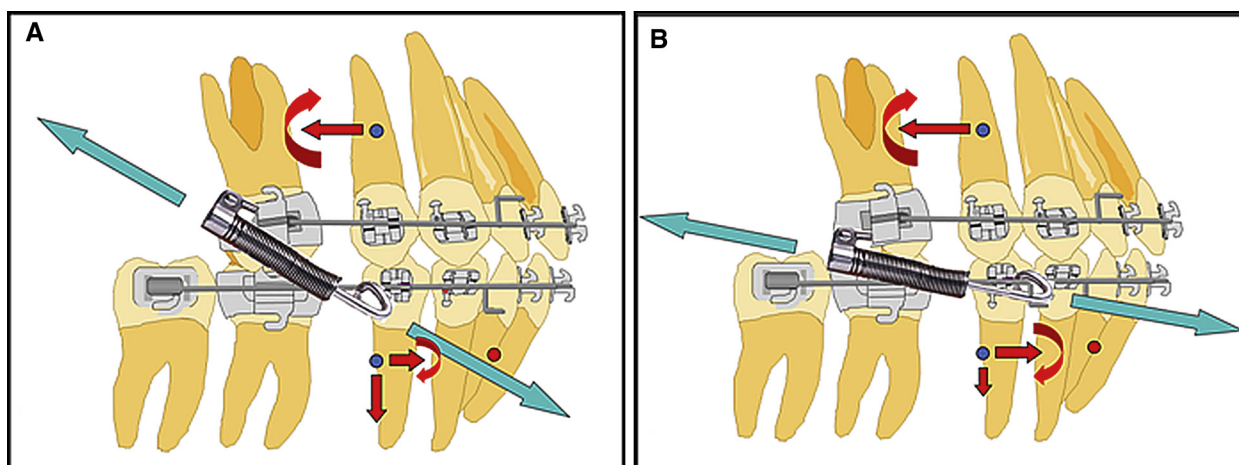


Fig 4. Schematics of force vector produced by Forsus: **A**, the Forsus device was placed on the maxillary molar gingival headgear tube and the mandibular archwire distal to the first premolar. This position can produce a more vertically directed force vector than conventional application. **B**, Conventional application of the Forsus. The module is placed on the occlusal headgear tube and the mandibular archwire distal to the canine.



Fig 5. Intraoral photographs in the finishing stage.

The patient showed poor compliance with regard to hygiene and keeping appointments. He missed 14 appointments, and the number of “poor hygiene” marks on the chart was 18. The total treatment period was 41 months, and the number of visits was 31.

Before the removal of the fixed orthodontic appliance, maxillary and mandibular lingual fixed retainers were placed. The fixed retainer at the mandibular right first premolar became detached in the next month, and the patient cut off the wire. Because he had undergone second premolar extractions, we decided against replacing the mandibular fixed retainer. After bracket removal, the

patient was given a circumferential retainer for the maxillary arch and a Hawley retainer for the mandibular arch.

RESULTS

The cephalometric analysis ([Table](#)) showed that orthodontic treatment with the Forsus device dramatically changed the mandibular growth. The pogonion point to nasion-perpendicular line moved forward by 9.8 mm, and the A-point to nasion-perpendicular line increased by 1.9 mm. The ANB decreased from 7.6° to 4.4°. Based on the large amounts of ramal growth and



Fig 6. Posttreatment intraoral and facial photographs.

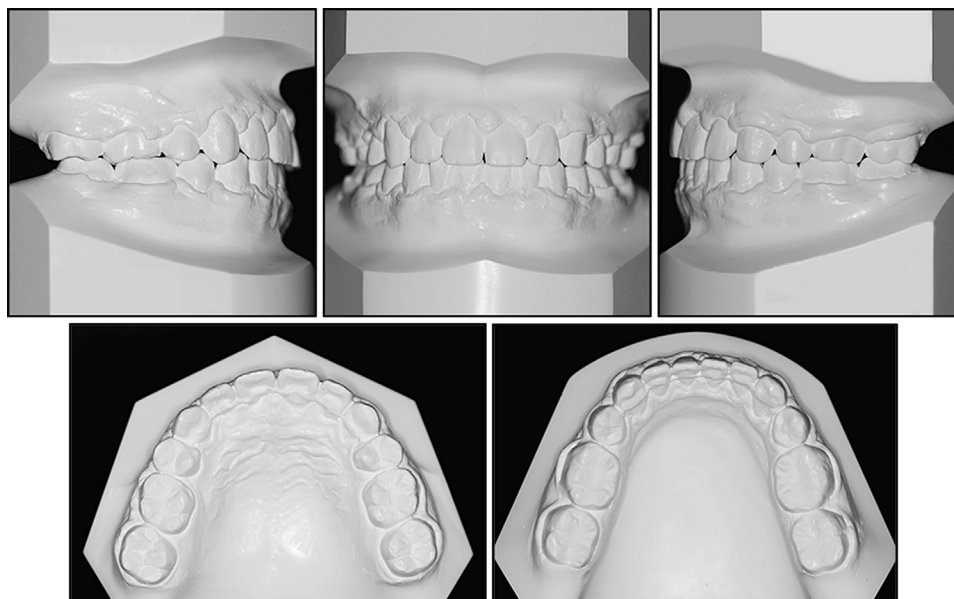


Fig 7. Posttreatment study casts.

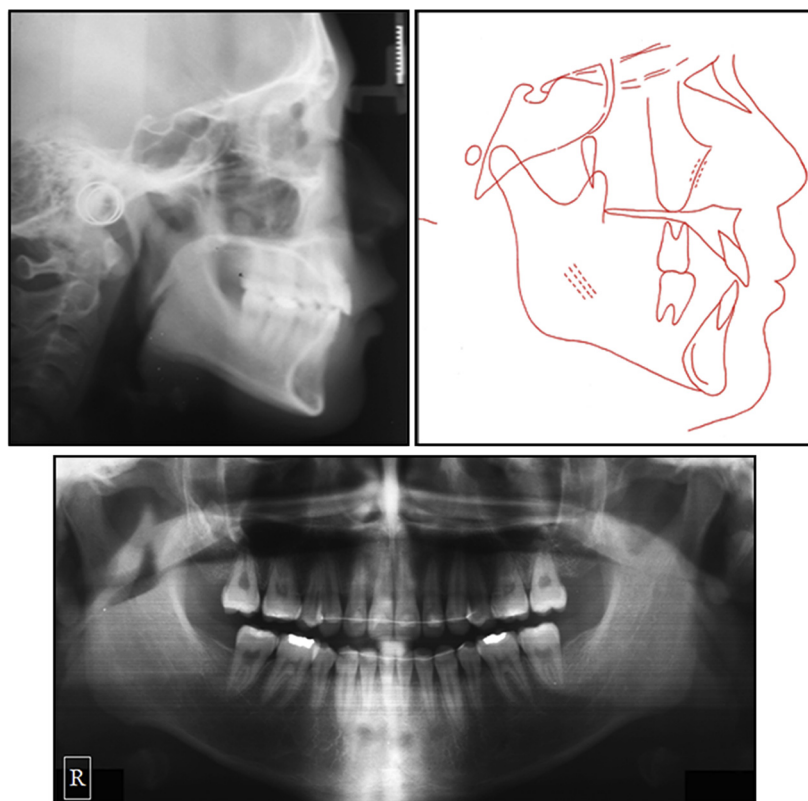


Fig 8. Posttreatment lateral cephalogram, lateral cephalometric tracing, and panoramic radiograph.

counterclockwise rotation of the mandibular plane, the profile improved significantly (Fig 6).

An acceptable occlusion with normal overbite and overjet was obtained (Figs 6 and 7). An Angle Class I molar and canine relationship was established, and the lingual crossbite was corrected. Gingival inflammation was observed because of poor oral hygiene during treatment. Fortunately, decalcification around the brackets was not severe. Posttreatment facial photographs demonstrated the achievement of a balanced facial profile and a natural form of the chin area. Lip incompetency improved, and mentalis action was eliminated. The panoramic radiograph (Fig 8) showed well-aligned roots. The American Board of Orthodontics Cast-Radiograph Evaluation score was 9.

Because his family moved to another city, the patient could not come for regular checkups. At 2 years 11 months postretention, he came to my clinic. The maxillary fixed retainer had been totally removed at a local dental clinic because of retainer detachment and deformation at about 6 months of retention. His facial profile was still acceptable, but his lip thickness had significantly increased, and as a result, his lip profile had become slightly protrusive (Figs 9 and 10). His occlusion was still stable, but his overbite had

increased slightly. White spot lesions had improved, and mild spacing was observed in the incisor region. Cephalometric superimposition showed small but significant mandibular jaw growth. The sagittal skeletal relationship was stable (ANB changed from 4.4° to 4.1°), and the mandibular plane had rotated further counterclockwise (Fig 11).

DISCUSSION

Although the effect of GH on craniofacial bone is poorly understood, it is believed that GH therapy affects the craniofacial regions, especially those where cartilage-mediated growth occurs, such as the mandibular condyle and ramus.^{11,29} In GH-deficient patients, GH replacement therapy can accelerate the growth of craniofacial components, especially the mandible.^{19,30} GH therapy combined with functional appliance treatment of a Turner syndrome patient also significantly increased mandibular length.¹⁸ There have been 2 case studies of orthodontic treatment combined with GH therapy for adolescents of short stature without GH deficiency.^{17,31} Because these patients had Class III malocclusion, the accelerated mandibular growth during GH therapy actually made treatment more difficult and worsened their profiles.



Fig 9. Intraoral and facial photographs 2 years 11 months after debonding.

Class II malocclusion is a frequently observed problem in orthodontics. Mandibular deficiency is the most common characteristic of Class II,³² and functional appliances have been used to enhance mandibular growth by positioning the mandible forward.^{5,33,34} Short-term skeletal effects of functional appliances have been reported many times, but there have not been long-term studies showing the skeletal effects of functional appliances.^{6,7,35} Even in short-term studies, functional appliances frequently yielded nonsignificant differences in mandibular growth.^{36,37} Similar results were reported after short-term^{25,38} and long-term³⁹ use of the Forsus appliance.

During the orthodontic treatment of this patient, pogonion advanced 9.8 mm, whereas A-point moved only 1.9 mm anteriorly when it was measured at the nasion perpendicular line (Table). The ANB reduction was 3.2°. The amount of skeletal change was much greater than in previous studies using the Forsus.^{25,39,40} The greater increase of ramal height than vertical growth of the anterior facial region caused counterclockwise mandibular plane rotation during treatment. The mandibular plane angle was reduced by 3.9°, and this

rotation maximized the chin point advancement. Because previous studies have demonstrated that GH therapy can significantly increase mandibular growth, especially in the ramus and condyle, the GH therapy seems to have contributed to this favorable growth change.¹⁶⁻¹⁹ A previous longitudinal study by Kjellberg and Wikland¹³ showed that GH treatment yielded a more prognathic growth pattern in both GH deficiency and idiopathic short stature without GH deficiency.

Although there is still controversy regarding the effect of GH therapy in children without GH deficiency, a recent systematic review showed that GH therapy seems to be effective in partially reducing the deficit in height as adults.⁴¹ At the beginning of orthodontic treatment, the height of this patient was near the bottom 10% for his age, but after debonding, his height was about 50% (172 cm). Because the individual response to GH therapy is highly variable, the result of this case report needs to be interpreted with caution.⁴¹

The force vector of the Forsus appliance usually causes proclination of the mandibular incisors,^{25,38,40} but in this patient, the mandibular incisor axis to the mandibular plane improved. Because the push rod of the Forsus

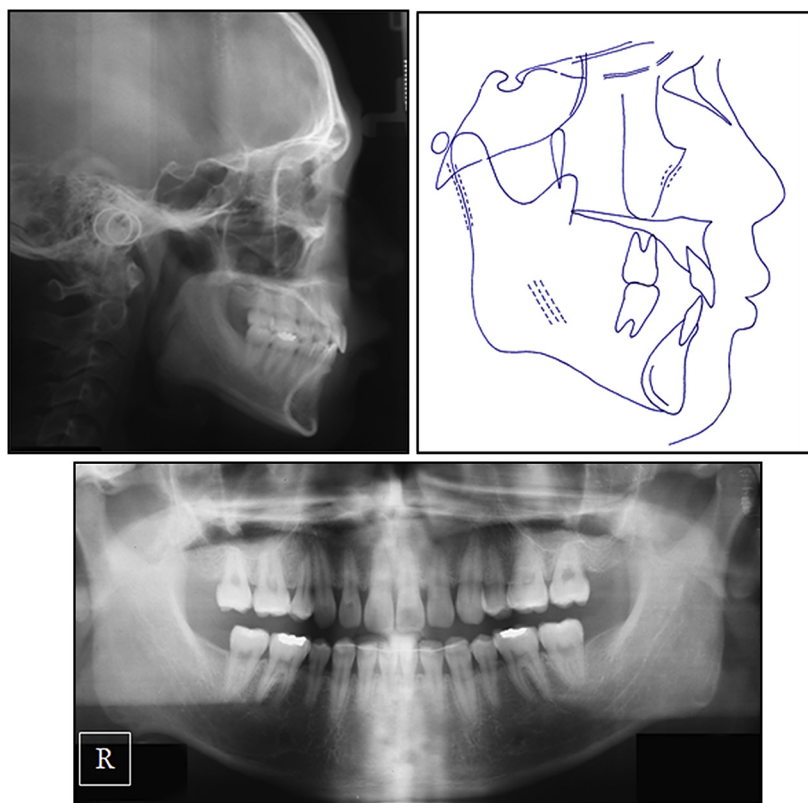


Fig 10. Lateral cephalogram, lateral cephalometric tracing, and panoramic radiograph 2 years 11 months after debonding.

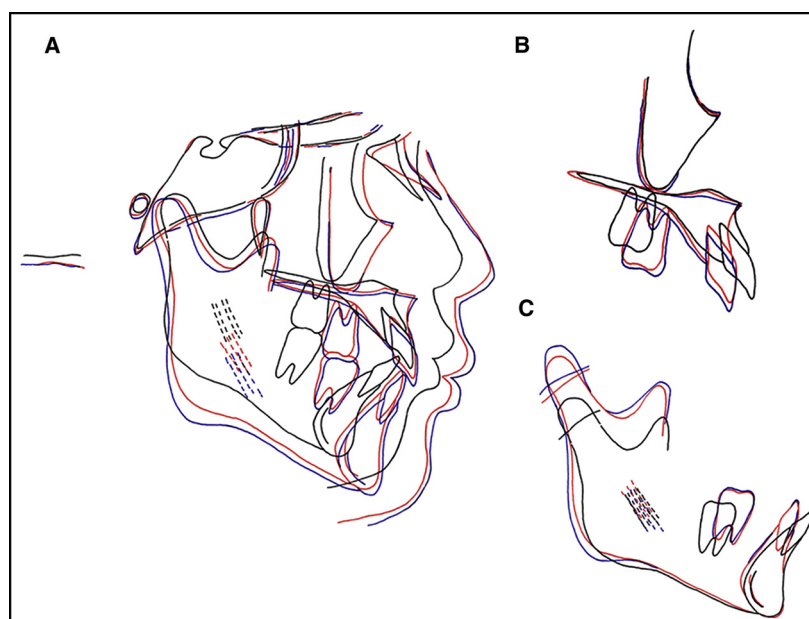


Fig 11. Superimposition of pretreatment (*black*), posttreatment (*red*), and retention (*blue*) lateral cephalometric tracings: **A**, overall; **B**, maxilla; **C**, mandible.

appliance was placed posterior to the mandibular first premolar, the force vector of the Forsus (Fig 5) seemed to pass near the center of resistance of the mandibular incisors. Extraction of the mandibular premolars also helped to improve the incisor angulation.²⁶

In this case report, it was impossible to determine whether the functional appliance treatment enhanced the effects of GH therapy, or whether GH therapy alone caused these skeletal changes. Structured prospective cohort studies are needed to evaluate whether GH therapy can induce significant mandibular growth in Class II patients and act synergistically with functional appliance treatments. However, even if GH therapy can induce clinically significant mandibular growth in Class II patients, the high cost and the possibility of adverse effects such as type 2 diabetes may be a concern of GH treatment for non-GH-deficient Class II patients.⁴²

I consulted the Division of Pediatric Endocrinology and Metabolism, Seoul National University College of Medicine, about prescribing GH for patients with Class II mandibular deficiencies. The division head noted 2 important aspects of this treatment. To use GH to enhance mandibular growth, prospective cohort studies to evaluate the adequate dose for this purpose and possible adverse effects at this level of GH administration are lacking and need to be performed. During his experience with treatment of GH in patients with idiopathic short stature, he observed a tendency for worsening facial asymmetry in some patients. Thus, facial asymmetry should be carefully evaluated during GH treatment.

CONCLUSIONS

Although long-term studies have shown that functional appliance treatment cannot increase mandibular growth in Class II retrognathic patients, various kinds of functional appliances are still used to treat these patients. This Class II boy, aged 13 years 7 months, displayed a protrusive lip profile and severe chin deficiency with skeletal Class II malocclusion. He underwent Forsus appliance treatment with premolar extraction and GH therapy. Significant profile improvement with a large amount of mandibular growth was observed during treatment, and the profile was stable for 2 years 11 months of retention. Further research is needed to evaluate the use of GH for the treatment of mandibular deficiency patients.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.ajodo.2016.08.030>.

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