

## **Revised-2**

### **Comprehensive treatment for severe periodontitis with pathologic tooth migration-related bimaxillary protrusion: a case report with 3-year follow-up**

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## **Abstract**

*Background:* Patients with severe periodontitis often experience pathologic tooth migration (PTM), which impairs esthetics and leads to occlusal disharmony (e.g., premature contacts and/or traumatic occlusion) that can further exacerbate periodontitis. Here, we describe a patient who exhibited severe periodontitis with PTM-related bimaxillary protrusion. This report includes 3-year clinical outcomes following periodontal regenerative therapy, implant-anchored orthodontic therapy, and implant prosthodontics intended to achieve both functional and esthetic improvements.

*Case Description:* A 63-year-old woman presented with the chief complaint of upper anterior tooth mobility. Clinical examination revealed excessive tooth mobility, deep periodontal pockets, and infrabony defects in all teeth. All teeth exhibited PTM; the mandibular anterior teeth exhibited marked protrusion caused by the progression of periodontitis. After initial periodontal therapy, periodontal regenerative therapy was performed in all molar regions. At 9 and 6 months postoperatively, comprehensive orthodontic treatment was initiated for the mandible and maxilla, respectively, using orthodontic anchorage devices to achieve acceptable functional occlusion. After orthodontic treatment, staged guided bone regeneration was performed and dental implants were placed in the severely resorbed maxillary anterior ridge. This comprehensive treatment yielded favorable periodontal conditions, stable occlusion, and good esthetic outcomes.

*Practical Implications:* Favorable esthetics, stable occlusion, and highly cleansable periodontal tissues were achieved with well-planned interdisciplinary and comprehensive treatment, although the patient had severe periodontitis and PTM-related bimaxillary protrusion.

**Key Words:** interdisciplinary therapy; pathologic tooth migration; periodontal regenerative therapy; implant anchored orthodontic treatment; guided bone regeneration; severe periodontitis; bimaxillary protrusion.

## Introduction

During periodontitis progression, pathologic migration may occur in one or more teeth. This pathologic tooth migration (PTM) is induced by periodontal tissue destruction, posterior bite collapse, and parafunctional habits (e.g., lip biting and tongue thrusting)<sup>1)</sup>; it can cause outward flaring of the anterior teeth, a spaced dental arch, and tooth elongation<sup>1)</sup>. For patients with no occlusal discrepancy until the onset of periodontitis, excessive occlusal force in the anterior segment caused by reduced occlusal support with progressive posterior tooth bone resorption may lead to malpositioning of anterior teeth<sup>2)</sup>. Furthermore, natural elongation and inclination of the teeth may occur with periodontal inflammation and bone resorption around the anterior teeth<sup>3)</sup>. Additionally, some patients present with PTM induced by lip and tongue pressure<sup>4)</sup>. The risk of PTM increases with periodontitis progression; moreover, the prevalence of PTM is higher in patients with more severe periodontitis<sup>5, 6)</sup>. A migrating tooth with reduced bone support may experience premature contact, occlusal interference, and secondary occlusal trauma<sup>7)</sup>. Secondary occlusal trauma may exacerbate periodontitis through attachment loss and/or the development of infrabony defects<sup>8)</sup>, which worsen the condition in a vicious cycle.

During the treatment of patients with concurrent severe periodontitis and PTM, it is crucial to provide periodontal therapy, as well as an interdisciplinary approach involving close communication and careful coordination among the periodontist, prosthodontist, and orthodontist. Here, we describe the 3-year follow-up progress and outcomes in a patient who had severe periodontitis and PTM-related bimaxillary protrusion. An appropriate occlusal relationship, stable periodontal environment, and favorable esthetic results were obtained through interdisciplinary therapy comprising periodontal regenerative therapy, implant-anchored orthodontic treatment, and prosthodontics (i.e., dental implant treatment).

## Case Report

Written informed consent was obtained from the patient for the publication of this case report.

A 63-year-old woman presented with the chief complaint of mobility in the maxillary anterior teeth. She was a non-smoker who was undergoing clinical treatment for hyperthyroidism. Her facial profile was convex with bimaxillary protrusion (Figure 1A, B). The bilateral molar relationship was Angle Class I, but the maxillary and mandibular molars were mesially inclined (Figure 1C, E). The mandibular anterior teeth exhibited outward flaring, which resulted in an anterior open bite (Figure 1D, G, J). There was no occlusal contact on the bilateral working sides during lateral movements; however, bilateral balancing side contacts were present on the second molars (Figure 1F, H). The overjet and overbite were  $-0.5$  and  $-2.5$  mm, respectively.

The patient's plaque control was poor and generalized marked gingival inflammation was evident (Figure 1). Periodontal examination showed probing depths of  $\geq 6$  mm for all teeth; 91.7% of the sites exhibited bleeding on probing. Nearly all teeth were mobile, but mobility was most noticeable in the maxillary anterior teeth and maxillary left molars (Table 1). Full-mouth periapical radiographs revealed angular bone defects in all teeth; in particular, the maxillary central incisors had minimal or no bone support. Tooth 30 had Class II furcation involvement (Figure 1L). The patient also demonstrated bruxism during sleep.

Cephalometric analysis, compared with Japanese norms<sup>9</sup>), showed a skeletal Class II jaw-base relationship (angle through A point, nasion, and B point:  $9.1^\circ$ ) with a high mandibular plane angle (mandibular plane to sella-nasion:  $44.7^\circ$ ). The mandibular central incisors were extremely labially inclined (mandibular incisor to mandibular plane:  $121.3^\circ$ ), but the inclination of the maxillary central incisors was within the

normal range (maxillary incisor to sella-nasion: 97.3°), which resulted in a reduced interincisal angle (96.7°) (Figure 1B, Table 2).

The patient's diagnosis was bimaxillary protrusion and generalized severe chronic periodontitis (stage IV, grade C, %radiographic bone loss/age > 1.0, non-smoker and no diagnosis of diabetes, according to the consensus report classification scheme<sup>10</sup>). The treatment objectives were to establish a proper interincisal relationship, as well as functional and acceptable occlusion to eliminate occlusal trauma; they also comprised the achievement of a healthy periodontal environment with high cleansability.

After initial periodontal therapy, the prognoses of teeth 7, 8, 9, and 10 were considered hopeless because of advanced tooth mobility and severe bone loss. Periodontal regenerative therapy was planned in the maxillary and mandibular molar regions to retain as many teeth as possible. More than 6 months after periodontal regenerative therapy, full-mouth orthodontic treatment was initiated. Orthodontic anchor miniscrews were placed in the rearmost molar regions and used as absolute anchorage for the uprighting and retraction of all teeth. After the completion of orthodontic treatment, staged guided bone regeneration (GBR) was performed to augment and reconstruct the alveolar ridge of the maxillary anterior region; dental implants were placed on the sites of teeth 7 and 10 (Supplemental Figure 1). Finally, metal-ceramic prostheses were inserted on all molars to establish stable and secure occlusion. A timeline of the interdisciplinary treatment plan is shown in Supplemental Figure 1.

Initial periodontal therapy mainly consisted of plaque control, scaling, and root planing. Teeth 8 and 9 exhibited severe mobility; thus, they were extracted and replaced with temporary prostheses. After reevaluation, periodontal regenerative therapy was performed in the molar regions. Combination regenerative therapy using an enamel matrix derivative (EMD) (Emdogain Gel, Straumann), freeze-dried bone

allograft (FDBA) (OraGRAFT, LifeNet Health), and expanded polytetrafluoroethylene (e-PTFE) membrane (Gore-Tex, WL Gore & Associates) was performed to manage the furcation involvement of tooth 30 (Figure 2A, B). The non-resorbable membrane was removed 5 weeks postoperatively. Regenerative therapy with EMD and FDBA was performed in other molar regions (Figure 2D, E). All molars were postoperatively fitted with provisional restorations.

At 9 months postoperatively, 0.022-in slot preadjusted edgewise appliances were placed on the mandibular arch, then leveled and aligned with nickel-titanium archwires (Figure 3A). After the extraction of bilateral mandibular wisdom teeth, miniscrews (diameter, 1.3 mm; length, 7 mm; Absoanchor, Dentos) were implanted in the wisdom teeth region. After a 1-month latency period, distal movement of the mandibular dentition was initiated with a 2-N load on nickel-titanium closed-coil springs (Sentalloy, Tomy International) (Figure 3B). A 0.016-in × 0.022-in stainless steel wire was used during distal movement. Similarly, edgewise appliances were placed on the maxillary arch at 6 months after regenerative therapy of the bilateral upper molars, then leveled and aligned. The miniscrews were implanted in the distobuccal alveolus of the maxillary first molars. They were inserted obliquely into the cortical bone surface using a self-tapping method. Distal movement of the maxillary dentition was initiated with nickel-titanium closed-coil springs (Figure 3C). Force was applied backward and upward, as parallel to the occlusal plane as possible. Prior to tooth extraction, orthodontic extrusion of teeth 7 and 10 was performed to facilitate bone ridge regeneration of the maxillary anterior region. After the removal of edgewise appliances, a wraparound-type retainer was placed on the maxillary arch; a lingual bonded retainer was applied to the mandibular dentition. The total active orthodontic treatment period was 20 months.

In the maxillary anterior region, both the interdental papillae and alveolar bone had been severely lost, resulting in poor esthetics (Figure 4A). Initially, horizontal and

vertical GBR were performed using a titanium-reinforced dense-PTFE membrane (Cytoplast, Osteogenics) and demineralized bovine bone mineral (Geistlich Bio-Oss, Geistlich Pharma) soaked in recombinant human platelet-derived growth factor-BB (GEM21S, Osteohealth) (Figure 4C, D). Six months later, appropriate alveolar morphology had not been achieved in the cervical area (Figure 4E). Therefore, additional GBR was performed using titanium screws (1.6 mm × 8 mm, Jeil Auto Screw, Jeil Medical), demineralized bovine bone mineral (Bio-Oss), and resorbable collagen membrane (OSSIX Plus, OraPharma); at that time, two implants (4/3 × 11.5 mm 3i T3 Tapered Implant, BIOMET 3i) were placed (Figure 4F–H). After the establishment of appropriate alveolar bone morphology (Figure 4I), an interpositional subepithelial connective tissue graft was performed to correct the displaced mucogingival junction and acquire optimal soft tissue thickness (Figure 4J, K). At reevaluation, the molar probing depths were reduced to approximately 4–6 mm. Periapical radiographs also showed marked improvement in radiographic translucency in the previous infrabony defects, despite a slight difference in marginal bone level. Next, osseous surgery was performed with an apically positioned flap. Improvements in bone level were noted in both the molar region and the furcation involvement in tooth 30; specifically, the previous infrabony defects were nearly filled with bone-like tissue and favorable osseous architecture was observed (Figure 2C, F). Reevaluation was performed at 3 months postoperatively; nearly all regions showed probing depths of  $\leq 3$  mm.

Individual metal-ceramic prostheses or gold restorations were placed on molars. A fixed partial denture comprising zirconia ceramics with layered porcelain was used for the implant prosthesis (Figure 4B). A nightguard was fitted and maintenance was conducted at 2-month intervals.

After comprehensive treatment, the patient exhibited a balanced facial profile with proper positioning of the upper and lower lips. Stable intercuspation of the teeth was

evident with functional Class I canine and molar relationships. Favorable anterior guidance was achieved with limited traumatic force on the molars (Figure 5). Most teeth exhibited probing depths of  $\leq 3$  mm without pathologic mobility (Table 1). The patient's plaque control was improved to exhibit full mouth plaque scores  $< 15\%$  and bleeding on probing  $< 10\%$ . Periapical radiographs demonstrated that the alveolar bone levels around all teeth were aligned and exhibited physiological morphology (Figure 5L). Post-treatment cephalometric evaluation showed a persistent Class II jaw-base relationship (A point, nasion, and B point:  $9.2^\circ$ ) and a slight enhancement of the vertical dimension of the occlusion (sella-nasion to mandibular plane:  $45.3^\circ$ ). The mandibular incisor inclinations were inclined lingually (mandibular incisor to mandibular plane:  $100.4^\circ$ ), resulting in an acceptable interincisal relationship (Table 2). By using orthodontic anchor miniscrews, successful distal traction values of 4 mm for maxillary anterior teeth and 9.5 mm for mandibular anterior teeth were achieved without premolar extraction. The bimaxillary molars were moved distally by 2.5 mm (Supplemental Figure 2). No symptoms of temporomandibular disorders were observed throughout the active orthodontic treatment period.

At 3 years after prosthodontic treatment (i.e., 6 years post-retention), the patient's occlusion and periodontal condition were stable (Figure 6). The patient's plaque control has also been stable and has kept favorable conditions. Periapical radiographs showed stability in bone levels around the teeth, as well as in the implants (Figure 6L). Cephalometric analysis and superimposition of pretreatment, post-treatment, and post-retention findings showed minimal changes (Supplemental Figure 2, Table 2).

## **Discussion**

Our patient had severe periodontitis with generalized PTM and bimaxillary protrusion. Notably, she had occlusal discrepancy-related functional instability and

serious esthetic problems. Furthermore, all of her teeth had infrabony defects and marked mobility; the maxillary anterior ridge exhibited large bony defects after tooth extraction. Treatment was challenging because it required functional and pleasing esthetics, as well as the retention of many teeth. This involved close communication and coordination among three disciplines: periodontal treatment focused on periodontal regenerative therapy, implant treatment comprising reconstruction of the alveolar ridge, and orthodontic treatment in the presence of periodontitis and teeth with minimal bone support. The findings in this report have important implications for the comprehensive and interdisciplinary treatment of patients with severe periodontitis and PTM-related occlusal collapse.

At the first visit, the patient was aware of her poor periodontal condition and had regularly visited her former dentist for treatment. She did not have congenital malocclusion; however, several years prior, her occlusion had begun to collapse and gradually deteriorated. She had no parafunctional habits (e.g., tongue thrust and lip biting), but had marked sleep bruxism. Etiological factors for PTM reportedly include occlusal abnormalities<sup>1</sup>). Although there is insufficient evidence to support bruxism as a causal factor for PTM, parafunctional habits may contribute to PTM<sup>2</sup>). These findings led us to presume that the patient's gingival inflammation had initially induced attachment loss; subsequently, additional excessive occlusal force involving bruxism may have caused aggressive periodontitis with progressive bony defects. Furthermore, the posterior bite collapse might have been induced by the shortened vertical dimension of the occlusion involving increased tooth mobility and inclination, accompanied by progressive posterior tooth bone resorption. These events led to marked outward flaring of anterior teeth, culminating in PTM throughout the mouth. Because of the severe labial inclination of the mandibular incisors, the overjet was -0.5 mm, which resulted in a bimaxillary protrusive profile with incomplete lip closure.

To achieve stable occlusion with a balanced profile, surgical treatment was considered for our patient. However, the patient was 63 years of age at the first visit and wished to avoid invasive surgical procedures involving postoperative discomfort and pain. The overall treatment goal was to regain the pre-PTM occlusal condition by means of orthodontic treatment to upright and retract all teeth with orthodontic screw anchorage after the extraction of mandibular wisdom teeth. Because the patient was originally presumed to have a high mandibular plane angle, we were concerned about the potential for an enhanced vertical dimension of the occlusion due to molar uprighting during orthodontic treatment, which would have been undesirable for this patient. Therefore, we applied minimal extrusive force to the molars. We used anchor screws and coil springs to move the maxillary dentition backward while maintaining an orientation parallel to the occlusal plane; we also applied upward force to the maxillary molars by maintaining the curve of Spee in the maxillary dentition<sup>11</sup>). Thus, we limited the change in the vertical dimension. The superimposition of cephalometric tracings before and after treatment showed distal movement of both maxillary and mandibular dental arches without further extrusion (Supplemental Figure 2). Moreover, the mandibular incisors were lingually inclined by orthodontic group distalization, which resulted in a proper interincisal relationship with an adequate interincisal angle. Although the mandibular incisors slightly relapsed in the labial direction during the 3-year follow-up period, stable and functional occlusion was maintained with Class I canine and molar relationships. After the initial periodontal therapy, multiple regenerative therapies were applied to all molars. These regenerative therapies were specifically focused on mobile teeth, which were temporarily splinted with an interim restorative device before the patient began to use the interocclusal device. Before surgical interventions, deep vertical intrabony defects were evident in all proximal surfaces of the molars; tooth 30 exhibited class II furcation involvement. Treatment of tooth 30 was expected to be

difficult because the furcation was located slightly above the adjacent alveolar bone crest. However, the combination regenerative therapy comprised of EMD, bone graft, and non-resorbable membrane<sup>12,13)</sup> yielded a favorable outcome. The timing of orthodontic treatment initiation after regenerative therapy is controversial<sup>14-17)</sup>. Several studies have advocated a relatively early initiation of orthodontic treatment (e.g., 2 to 4 weeks after regenerative therapy)<sup>15-17)</sup>. Many of these studies focused on patients who received regenerative therapy and orthodontic treatment for anterior teeth with relatively low occlusal loads. However, our patient required the application of orthodontic force to molars with heavy occlusal loading; she also demonstrated bruxism. Therefore, rather than implementing early orthodontic intervention, we waited until  $\geq 6$  months after regenerative therapy to allow maturation of the regenerated periodontal tissue<sup>18)</sup>. Following the completion of active orthodontic treatment, osteoplasty was performed to achieve appropriate osseous architecture and reduce the periodontal pockets. Furthermore, we confirmed the resolution of the intrabony defects.

The post-extraction bone defects in the maxillary anterior alveolar ridge were sufficiently large both vertically and horizontally that it was difficult to achieve an esthetic result. The ridge volume was also inadequate for implant fixture placement. For optimal reconstruction of the alveolar ridge (including the interdental papillae), it is crucial to establish three-dimensional bone and soft tissue around appropriately located implants in accordance with the design of the definitive prosthesis<sup>19)</sup>. This adequate volume of hard and soft tissue, especially on the labial side of the prosthesis, is critical for the achievement of a good soft tissue profile including interdental papillae<sup>20)</sup>. Accordingly, we planned to first perform GBR with a staged approach, then to perform additional GBR to simultaneously compensate for the shortage of bone volume during implant placement. Many investigators have indicated that it is favorable to mix similar amounts of xenograft and autogenous

bone as the graft material for GBR<sup>21-23</sup>). However, the harvesting of autogenous bone involves surgical invasion at the donor site and may lengthen the surgical time. Thus, we used a mixture of xenogeneic bone substitutes and recombinant human platelet-derived growth factor, which is reported to be effective in bone regeneration/ridge augmentation<sup>24-26</sup>). The first GBR procedure failed to fully reconstruct the labial part of the alveolar ridge to support the interdental papillae. Therefore, a second GBR procedure was performed during implant placement using a titanium screw, xenogeneic bone substitute, and resorbable membrane<sup>27</sup>). Furthermore, an interpositional subepithelial connective tissue graft with wide epithelium was applied to acquire optimal soft tissue thickness<sup>19</sup>). Using these procedures, we achieved an acceptable esthetic soft tissue profile (Figure 4B). The total treatment duration was long (68 months), but the orthodontic and surgical procedures were completed in approximately 4 years. This duration was much longer than initially anticipated to identify tooth shapes that were suitable in terms of esthetics, function, and cleansability; provisional restorations were generated, copied, and reproduced in definitive restorations. To stabilize the occlusion, an implant-supported fixed partial denture was fabricated with zirconia ceramics for the maxillary anterior restoration; the restorations for all posterior teeth comprised single crowns. At the first visit, all teeth exhibited mobility and it seemed impossible to restore each tooth with a single crown. However, tooth mobility was considerably reduced following treatment, enabling the restoration of each tooth with a single crown. The treatment goal was achieved by several therapeutic outcomes: acquisition of attachment gain by periodontal regenerative therapy; distribution of teeth with appropriate tooth axis angles by orthodontic treatment, which allowed the occlusal forces to be transmitted in a desirable direction; and regulation of the traumatic force on the molars by establishing proper anterior guidance through orthodontic treatment.

Periapical radiographs taken 3 years after the delivery of definitive restorations revealed a sharp lamina dura, which suggested periodontal tissue stability. The tooth positions have not changed since the completion of prosthetic treatment; the teeth remain stable with tight occlusal contacts. It is important to longitudinally monitor the occlusal and periodontal conditions. We instructed the patient to continue to use a nightguard and to attend regular check-ups at 2-month intervals to ensure supportive periodontal care.

### **Conclusions**

A patient who exhibited severe periodontitis with PTM-related bimaxillary protrusion underwent comprehensive treatment involving interdisciplinary therapies. Periodontal regenerative therapy enabled the preservation of more teeth, while orthodontic treatment using anchor miniscrews allowed movement of pathologically displaced teeth to appropriate positions and facilitated a functionally stable occlusal relationship. Furthermore, implant prosthetic treatment based on appropriate site development resulted in pleasing tooth and soft tissue esthetics.

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## References

- 1) Brunsvold MA. Pathologic tooth migration. *J Periodontol.* 2005;76:859-866.
- 2) Shifman A, Laufer B, Chweidan H. Posterior bite collapse-revisited. *J Oral Rehabil* 1998;25:376-385.
- 3) Martinez-Canut P, Carrasquer A, Magan R, Lorca A. A study on factors associated with pathologic tooth migration. *J Clin Periodontol* 1997;24:492-497.
- 4) Proffit W. Equilibrium theory revisited: Factors influencing position of the teeth. *Angle Orthod* 1978;48:75-186.
- 5) Towfighi PP, Brunsvold MA, Storey AT, Arnold RM, Willman DE, McMahan CA. Pathologic migration of anterior teeth in patients with moderate to severe periodontitis. *J Periodontol.* 1997;68:967–72.
- 6) Khorshidi H, Moaddeli MR, Golkari A, Heidari H, Raofi S. The prevalence of pathologic tooth migration with respect to the severity of periodontitis. *J Int Soc Prev Community Dent.* 2016 Aug;6(Suppl 2):S122-5.
- 7) Branschofsky M, Bekler T, Schafer R. Secondary trauma from occlusion and periodontitis. *Quintessence Int.* 2011;42(6):515-522.
- 8) Fan J, Caton JG. Occlusal trauma and excessive occlusal forces: narrative review, case definitions, and diagnostic considerations. *J Periodontol.* 2018 Jun;89 Suppl 1:S214-S222.
- 9) Wada K, Matsushita K, Shimazaki S, Miwa Y, Hasuike Y, Susami R. An evaluation of a new case analysis of a lateral cephalometric roentgenogram. *J Kanazawa Med Univ* 1981;6:60-70.
- 10) Papapanou PN, Sanz M, Buduneli N et al. Periodontitis: consensus report of work-group 2 of the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions. *J Clin Periodontol* 2018;45(suppl 20):s162-s170.

- 11) Yamada K, Kuroda S, Deguchi T, Takano-Yamamoto T, Yamashiro T. Distal movement of maxillary molars using miniscrew anchorage in the buccal interradicular region. *Angle Orthod.* 2009 Jan;79(1):78-84.
- 12) Hägi TT, Laugisch O, Ivanovic A, Sculean A. Regenerative periodontal therapy. *Quintessence Int.* 2014 Mar;45(3):185-92.
- 13) Reynolds MA, Kao RT, Camargo PM, Caton JG, Clem DS, Fiorellini JP, Geisinger ML, Mills MP, Nares S, Nevins ML. Periodontal regeneration - intrabony defects: a consensus report from the AAP Regeneration Workshop. *J Periodontol.* 2015 Feb;86(2 Suppl):S105-7.
- 14) Ghezzi C, Masiero S, Silvestri M, Zanotti G, Rasperini G. Orthodontic treatment of periodontally involved teeth after tissue regeneration. *Int J Periodontics Restorative Dent.* 2008;28(6):559-567.
- 15) Corrente G, Abundo R, Re S, Cardaropoli D, Cardaropoli G. Orthodontic movement into infrabony defects in patients with advanced periodontal disease: a clinical and radiological study. *J Periodontol.* 2003;74(8):1104-1109.
- 16) Cardaropoli D, Re S, Manuzzi W, Gaveglio L, Cardaropoli G. Bio-Oss collagen and orthodontic movement for the treatment of infrabony defects in the esthetic zone. *Int J Periodontics Restorative Dent.* 2006;26(6):553-559.
- 17) Ghezzi C, Vigano VM, Francinetti P, Zanotti G, Masiero S. Orthodontic treatment after induced periodontal regeneration in deep infrabony defects. *Clin. Adv Periodontics.* 2013;3:24-31.
- 18) Wikesjö UM, Nilvéus RE, Selvig KA. Significance of early healing events on periodontal repair: a review. *J Periodontol.* 1992 Mar;63(3):158-65.
- 19) Ishikawa T, Salama M, Funato A, Kitajima H, Moroi H, Salama H, Garber D. Three-dimensional bone and soft tissue requirements for optimizing esthetic results in compromised cases with multiple implants. *Int J Periodontics Restorative Dent.* 2010 Oct;30(5):503-11.

- 20) Grunder U, Gracis S, Capelli M. Influence of the 3-D bone-to-implant relationship on esthetics. *Int J Periodontics Restorative Dent.* 2005 Apr;25(2):113-9.
- 21) Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: a prospective case series in 22 patients. *Int J Oral Maxillofac Implants.* 2011 Mar-Apr;26(2):404-14.
- 22) Mordenfeld A, Johansson CB, Albrektsson T, Hallman M. A randomized and controlled clinical trial of two different compositions of deproteinized bovine bone and autogenous bone used for lateral ridge augmentation. *Clin Oral Implants Res.* 2014 Mar;25(3):310-320.
- 23) Meloni SM, Jovanovic SA, Urban I, Baldoni E, Pisano M, Tallarico M. Horizontal ridge augmentation using GBR with a native collagen membrane and 1:1 ratio of particulate xenograft and autologous bone: a 3-year after final loading prospective clinical study. *Clin Implant Dent Relat Res.* 2019 Aug;21(4):669-677.
- 24) Simion M, Rocchietta I, Dellavia C. Three-dimensional ridge augmentation with xenograft and recombinant human platelet-derived growth factor-BB in humans: report of two cases. *Int J Periodontics Restorative Dent.* 2007 Apr;27(2):109-15.
- 25) Cardaropoli D. Vertical ridge augmentation with the use of recombinant human platelet-derived growth factor-BB and bovine bone mineral: a case report. *Int J Periodontics Restorative Dent.* 2009 Jun;29(3):289-95.
- 26) Scheines C, Hokett SD, Katancik JA. Recombinant human platelet-derived growth factor-BB in human alveolar ridge augmentation: a review of the literature. *Int J Oral Maxillofac Implants.* 2018 Sep/Oct;33(5):1047-1056.
- 27) Friedmann A, Strietzel FP, Marezki B, Pitaru S, Bernimoulin JP. Histological assessment of augmented jaw bone utilizing a new collagen barrier membrane compared to a standard barrier membrane to protect a granular bone substitute material. *Clin Oral Implants Res* 2002;13:587–594.

## FIGURE LEGENDS

Figure 1. Pretreatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C–K: C–E, G, J = intercuspal position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

Figure 2. Oral photographs of periodontal surgery: A, B. Regenerative therapy for teeth 29–31 was performed using enamel matrix derivative solution (EMD), freeze-dried bone allograft (FDBA), and non-resorbable membrane. C. During re-entry surgery, newly formed bone-like tissue was observed in the furcation involvement at tooth 30. D, E: Regenerative therapy for teeth 2–5 was performed using EMD and FDBA. F: During re-entry surgery, newly formed bone-like tissue was observed in the previous osseous defects at teeth 2-5.

Figure 3. Orthodontic treatment progress. A. Orthodontic treatment of the mandible was initiated at 9 months after the completion of regenerative therapy, beginning with leveling and alignment with nickel-titanium archwires. B. Using orthodontic anchorage devices placed bilaterally in the wisdom teeth region, the lower dentition was distalized with nickel-titanium closed-coil springs. C. Orthodontic treatment of the maxilla was initiated at 6 months after the completion of regenerative therapy. The upper dentition was distalized with closed-coil springs using anchor screws placed at the bilateral distobuccal alveolus of the maxillary first molars.

Figure 4. Oral photographs of implant surgery: A. Before implant surgery. B. After delivery of the final prosthesis. C, D. Guided bone regeneration (GBR) was performed using bone filler and non-resorbable membrane. E. Six months after GBR, appropriate alveolar morphology was not evident in the cervical area. F. Two

implants were placed on the sites of teeth 7 and 10. G. Titanium screws were inserted to obtain appropriate bone morphology in the cervical area. H. Additional GBR was performed using bone filler and resorbable membrane during implant placement. I. Six months after additional GBR, appropriate alveolar morphology was achieved. J, K. An interpositional subepithelial connective tissue graft was performed to acquire optimal soft tissue thickness.

Figure 5. Post-treatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C–K: C–E, G, J = intercuspal position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

Figure 6. Three-year post-treatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C–K: C–E, G, J = intercuspal position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

## **SUPPLEMENTAL FIGURE LEGENDS**

Supplemental Figure 1. Schematic illustration and timeline of interdisciplinary treatment. White numbers indicate treatment duration (in months) after the start of treatment.

Supplemental Figure 2. Cephalometric tracings at pretreatment (black line), post-treatment (red line), and 3-year retention (green line) superimposed on A, the sella-nasion plane at sella; B, the anterior palatal contour; and C, the mandibular plane at menton.

## **TABLES**

Table 1. Periodontal examination findings at baseline, post-treatment, and 3 years post-treatment. Red-colored numbers show bleeding on probing. Blue-colored numbers show pus discharge on probing.

Table 2. Cephalometric summary.

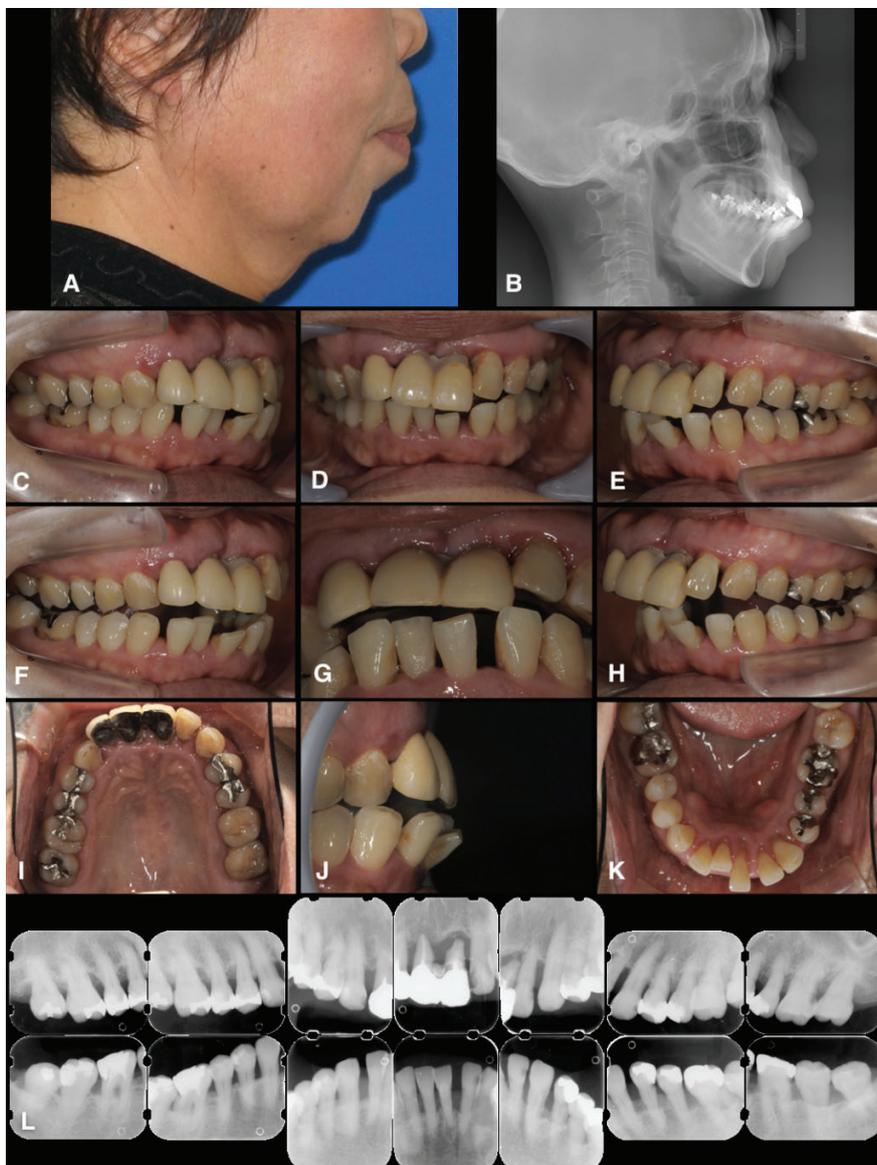


Figure 1. Pretreatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C-K: C-E, G, J = intercuspal position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

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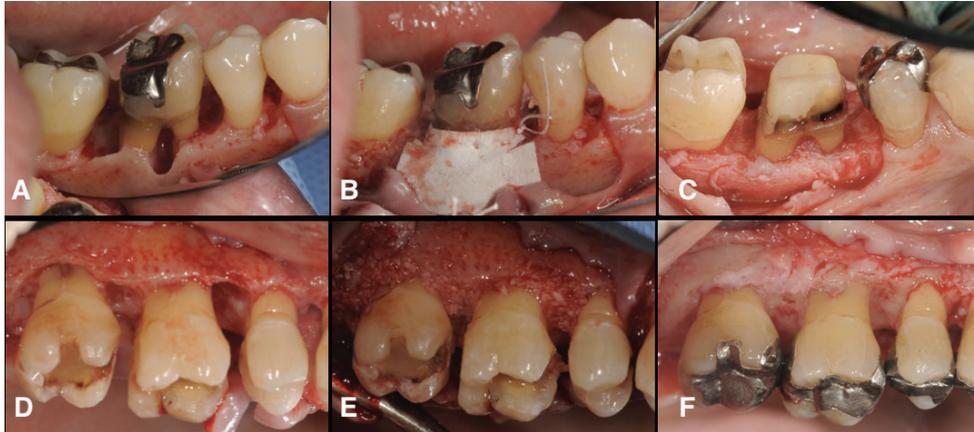


Figure 2. Oral photographs of periodontal surgery: A, B. Regenerative therapy for teeth 29–31 was performed using enamel matrix derivative solution (EMD), freeze-dried bone allograft (FDDBA), and non-resorbable membrane. C. During re-entry surgery, newly formed bone-like tissue was observed in the furcation involvement at tooth 30. D, E: Regenerative therapy for teeth 2–5 was performed using EMD and FDDBA. F: During re-entry surgery, newly formed bone-like tissue was observed in the previous osseous defects at teeth 2-5.

378x168mm (72 x 72 DPI)



Figure 3. Orthodontic treatment progress. A. Orthodontic treatment of the mandible was initiated at 9 months after the completion of regenerative therapy, beginning with leveling and alignment with nickel-titanium archwires. B. Using orthodontic anchorage devices placed bilaterally in the wisdom teeth region, the lower dentition was distalized with nickel-titanium closed-coil springs. C. Orthodontic treatment of the maxilla was initiated at 6 months after the completion of regenerative therapy. The upper dentition was distalized with closed-coil springs using anchor screws placed at the bilateral distobuccal alveolus of the maxillary first molars.

379x252mm (72 x 72 DPI)

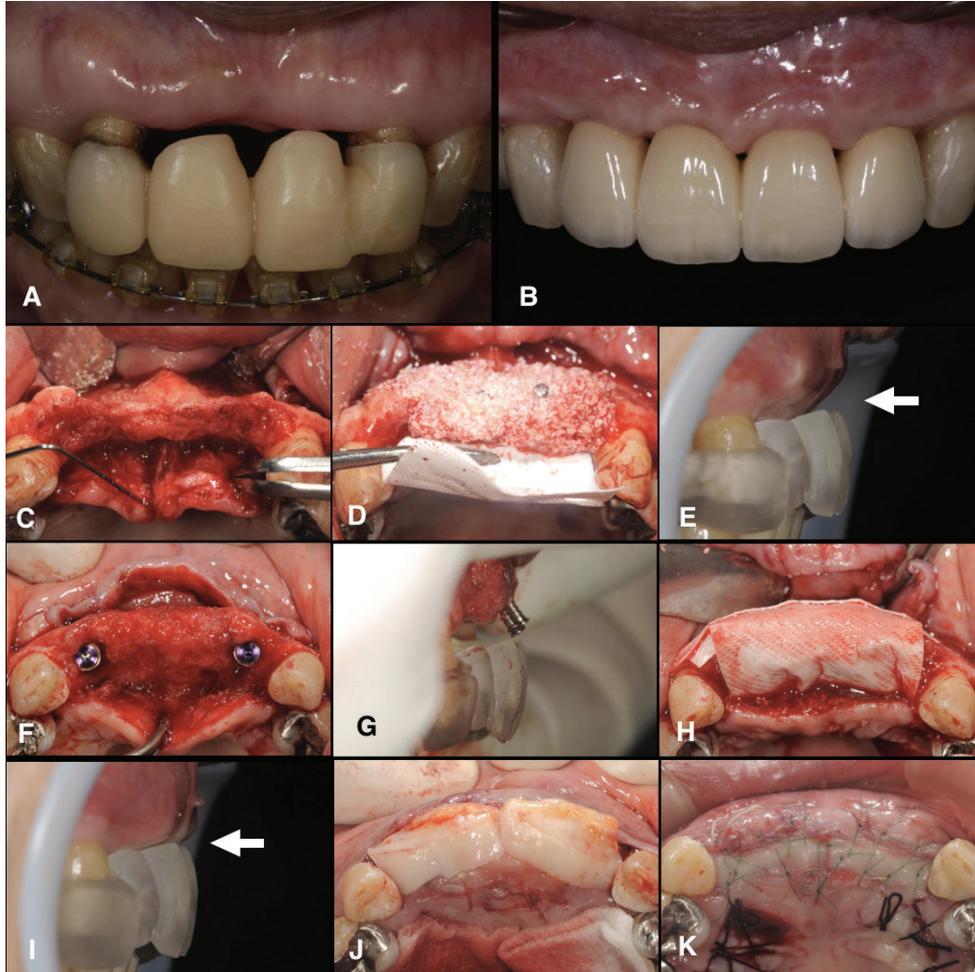


Figure 4. Oral photographs of implant surgery: A. Before implant surgery. B. After delivery of the final prosthesis. C, D. Guided bone regeneration (GBR) was performed using bone filler and non-resorbable membrane. E. Six months after GBR, appropriate alveolar morphology was not evident in the cervical area. F. Two implants were placed on the sites of teeth 7 and 10. G. Titanium screws were inserted to obtain appropriate bone morphology in the cervical area. H. Additional GBR was performed using bone filler and resorbable membrane during implant placement. I. Six months after additional GBR, appropriate alveolar morphology was achieved. J, K. An interpositional subepithelial connective tissue graft was performed to acquire optimal soft tissue thickness.

378x379mm (72 x 72 DPI)



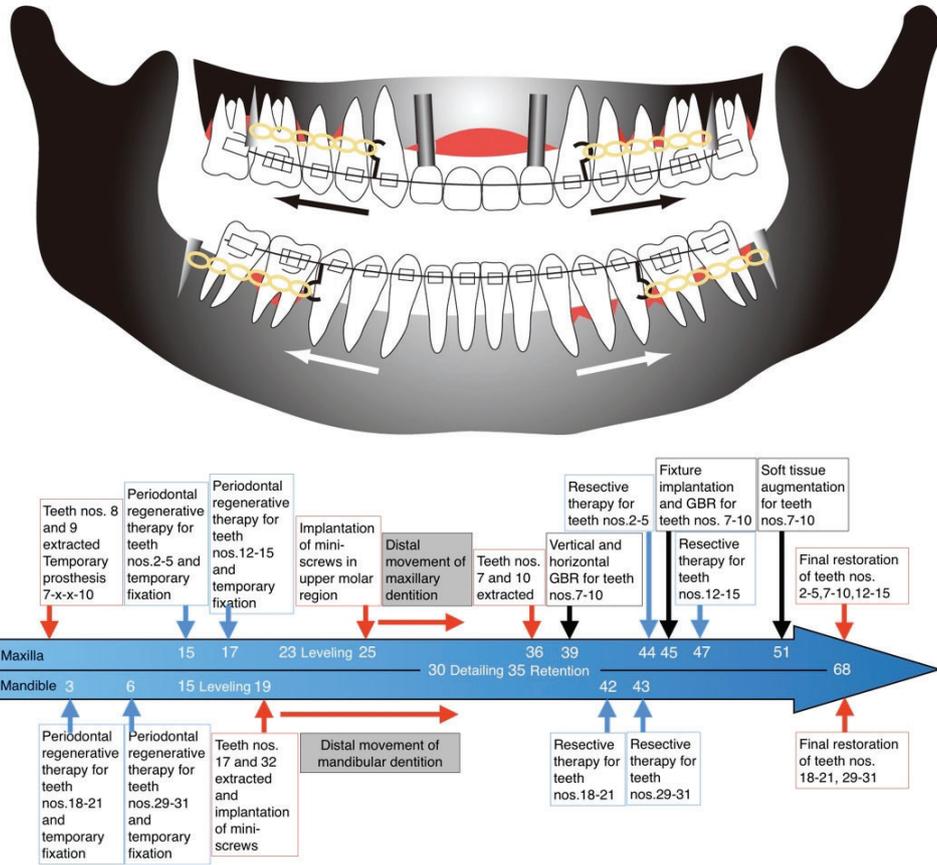
Figure 5. Post-treatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C–K: C–E, G, J = intercuspation position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

378x504mm (72 x 72 DPI)



Figure 6. Three-year post-treatment lateral facial profile (A), lateral cephalogram (B), intraoral photographs (C-K: C-E, G, J = intercuspal position; F = right lateral movement; H = left lateral movement), and periapical radiographs (L).

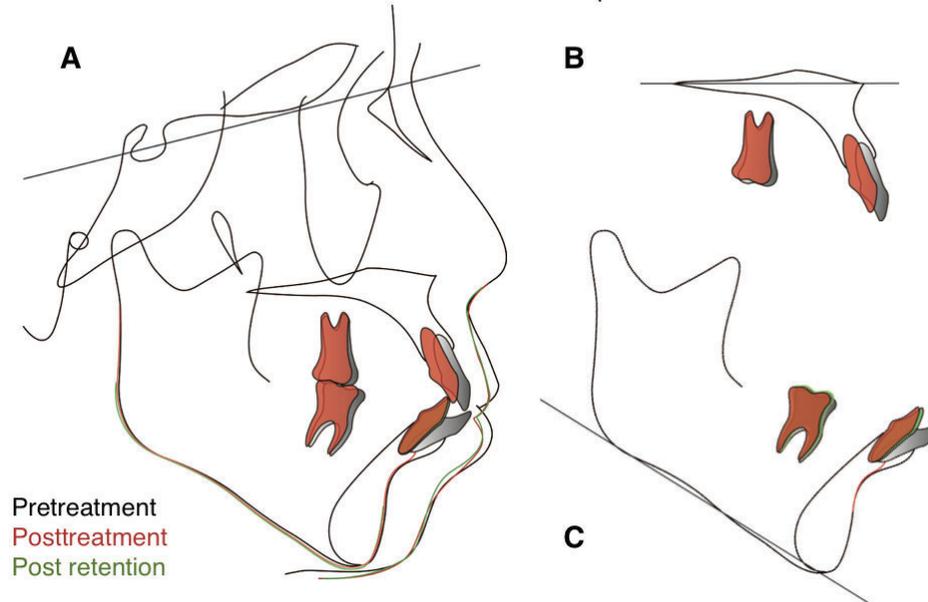
378x505mm (72 x 72 DPI)



Supplemental Figure 1. Schematic illustration and timeline of interdisciplinary treatment. White numbers indicate treatment duration (in months) after the start of treatment.

381x351mm (72 x 72 DPI)

*Superimposed on Sella-Nasion plane at Sella*



Supplemental Figure 2. Cephalometric tracings at pretreatment (black line), post-treatment (red line), and 3-year retention (green line) superimposed on A, the sella-nasion plane at sella; B, the anterior palatal contour; and C, the mandibular plane at menton.

344x236mm (72 x 72 DPI)



Table2

	Japanese Norm Adult-female±S.D.	Baseline	Posttreatment	Posttreatment after 3 years
SNA	80.8±3.61	86.0	86.0	86.0
SNB	77.9±4.54	76.9	76.8	76.6
ANB	2.8±2.44	9.1	9.2	9.3
SN-Mp	37.1±4.64	44.7	45.3	45.5
U1-SN	105.9±8.79	97.3	96.3	96.3
L1-Mp	93.4±6.77	121.3	100.4	102.9
Interincisal angle	123.6±10.54	96.7	118.0	116.9