Case Report

Marfan Syndrome—An Orthodontic Perspective

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ABSTRACT

Marfan syndrome is a heritable disorder of connective tissue that can affect the heart, blood vessels, lungs, eyes, bones, and ligaments. It is characterized by tall stature, elongated extremities, scoliosis, and a protruded or caved-in breastbone. Patients typically have a long, narrow face. A high-arched palate produced by a narrow maxilla and skeletal Class II malocclusion due to mandibular retrognathia are other common features. For a patient with no family history of the disorder, at least three body systems must be affected before a diagnosis can be made. Individuals affected by the syndrome routinely seek orthodontic treatment to correct the orofacial manifestations. In this report, the authors present the records of three patients with Marfan syndrome who were treated at a dental school. Two patients had severe periodontal disease in the absence of significant contributing local factors. The presentation of systemic symptoms and typical physical characteristics varied. The syndrome thus went unnoticed in one patient for many years. We discuss here the observed intraoral findings and the progress of orthodontic treatment to provide a brief overview of the challenges involved in treating such patients. (*Angle Orthod.* 2009;79: 394–400.)

KEY WORDS: Marfan syndrome; Orthodontics; Case report

INTRODUCTION

The National Marfan Foundation (NMF) describes Marfan syndrome as a heritable disorder of connective tissue that can affect the heart, blood vessels, lungs, eyes, bones, and ligaments. The condition was named after a French pediatrician, Antoine Bernard-Jean Marfan, who first described its occurrence in 1896 in a 5-year-old girl named Gabrielle with ''spider's legs'' or dolicostenomely (from the Greek: stenos = narrow, slender; melos = limb); the patient was noted to have disproportionately long and thin arms, legs, fingers, and toes.

Marfan syndrome is an autosomal dominant genetic disorder of the connective tissue that affects about 1 in 5000 Americans. It may be classified as type I or type II. Type I, or classic Marfan syndrome, is the most common presentation of the disorder. Males and females are equally affected. Mutations in the *FBN1* gene located on chromosome 15 cause type I Marfan syndrome.[1,2] The fibrillin-1 glycoprotein encoded by the *FBN1* gene is required for the formation of elastic fibers in connective tissue. A mutation in the gene can decrease the quantity and quality of fibrillin-1. This in turn can lead to weakened structural support, especially in areas where elastic fibers are found in abundance.[3–5] Consequently, the aorta, ligaments, and ocular muscles are among the most frequently affected parts of the body.

Type II Marfan syndrome is less common and is due to a mutation in the gene that encodes transforming growth factor-β receptor 2 *(TGFBR2).*[6] The protein synthesized by this gene transmits signals from the cell surface to the nucleus, thereby affecting cell division and growth. The clinical presentation of type II Marfan syndrome resembles that of classic Marfan syndrome, with the exception that the ocular system usually is not involved.

Marfan syndrome affects different people in different ways. Symptoms range from mild to severe, and they progress with age in most cases. Skeletal abnormalities are the most readily visible signs.[2,3,7] Affected individuals are markedly taller than their age-matched unaffected counterparts. Long slender limbs, fingers, and toes are characteristic. Arms are exceptionally

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Table 1. Summary of the Diagnostic Criteria for Type I Marfan Syndrome[9]

	Major Criteria	Minor Criteria
Skeletal system	• Pectus carinatum • Long limbs • Scoliosis	• Joint hypermobility • High-arched palate • Dolichocephaly • Retrognathia
Ocular system	• Ectopia lentis (dislocated lens)	• Flat cornea • Long globe
Cardiovascular system	• Dilatation of the ascending aorta with/without aortic regurgitation • Dissection of the ascending aorta	• Mitral valve prolapse with/without regurgitation • Dilatation/dissection of the descending thoracic or abdominal aorta
Pulmonary system	None	• Spontaneous pneumothorax • Apical blebs
Skin and integument	None	• Unexplained stretch marks • Recurrent incisional hernias
Dura	• Lumbosacral dural ectasia	None
Family/Genetic history	• Mutation in *FBN1* • Presence of an inherited haplotype around *FBN1*	None

long, and their expanse when outstretched is often greater than the height of the individual. Other typical features include abnormal curvature of the spine (scoliosis), caved-in (pectus excavatum) or protruding (pectus carinatum) sternum, and abnormal joint flexibility.

Marfan syndrome is diagnosed primarily on clinical grounds. Imaging studies such as radiography, echocardiography, and magnetic resonance imaging (MRI) facilitate detection and monitoring of cardiovascular disease.[3,8] Family history, molecular data, and involvement of organ systems must be taken into consideration before a diagnosis can be established. A panel of experts in Ghent, Belgium, put forth a set of guidelines in 1996.[9] Named for the city in which they were proposed, the Ghent criteria delineate major and minor diagnostic findings. This combination of findings in different organ systems forms the mainstay of diagnosis (Table 1). The main criteria for diagnosis consist of clinical features that are typical of the syndrome and rarely occur in the general population. These include long limbs, scoliosis, pectus carinatum, pectus excavatum, ectopia lentis, dilatation and/or dissection of ascending aorta, aortic regurgitation, and dural ectasias. Minor criteria are present in individuals with the syndrome and often are seen in the general population. These include joint hypermobility, high palate, dolichocephaly, retrognathia, flat cornea, mitral valve prolapse, dilatation or dissection of the thoracic aorta, spontaneous pneumothorax, and recurrent hernias. In the presence of a nonsignificant family history, major criteria in at least two different organ systems and involvement of a third system are required. However, if evidence of a genetic mutation in the family is found, then one major criterion in an organ system and involvement of a second system are sufficient to establish a diagnosis of Marfan syndrome.

Oral manifestations of Marfan syndrome, although not specific, are identifiable during a routine intraoral examination. Dental caries and periodontal disease have not been reported to occur more frequently in patients with Marfan, although certain orofacial defects are more prevalent.[10,11] Constriction of the maxilla and a high-arched palate are important from an orthodontic standpoint, as are concomitant crowding and posterior cross-bite.[12] A dolichofacial face type and skeletal Class II malocclusion are commonly noted. However, dental and orthodontic treatment objectives in individuals with Marfan syndrome do not differ from those in healthy counterparts. Prophylactic antibiotics might be required prior to exodontia or banding of teeth, to reduce the risks of bacteremia and subsequent endocarditis.[11] Stringent maintenance of oral hygiene also assumes special importance in minimizing the need for scaling and root planing.

Children with Marfan syndrome require orthodontic treatment to correct the malocclusion and associated orofacial anomalies.[10] Growth and development of the craniofacial complex tend to highlight the facial characteristics in a growing child. Additionally, orthognathic surgery may be indicated in patients with severe jaw and bite abnormalities. The challenge before the orthodontist is to establish the correct maxillomandibular relationship while achieving retention and stability. Patients with a high palatal vault and arachnodactyly, which are characteristic features of Marfan syndrome, commonly seek orthodontic care for crowding and excessive overjet.[13] However, the same reasons prompt the general population to seek care as well.

There is a dearth of evidence in the literature re-

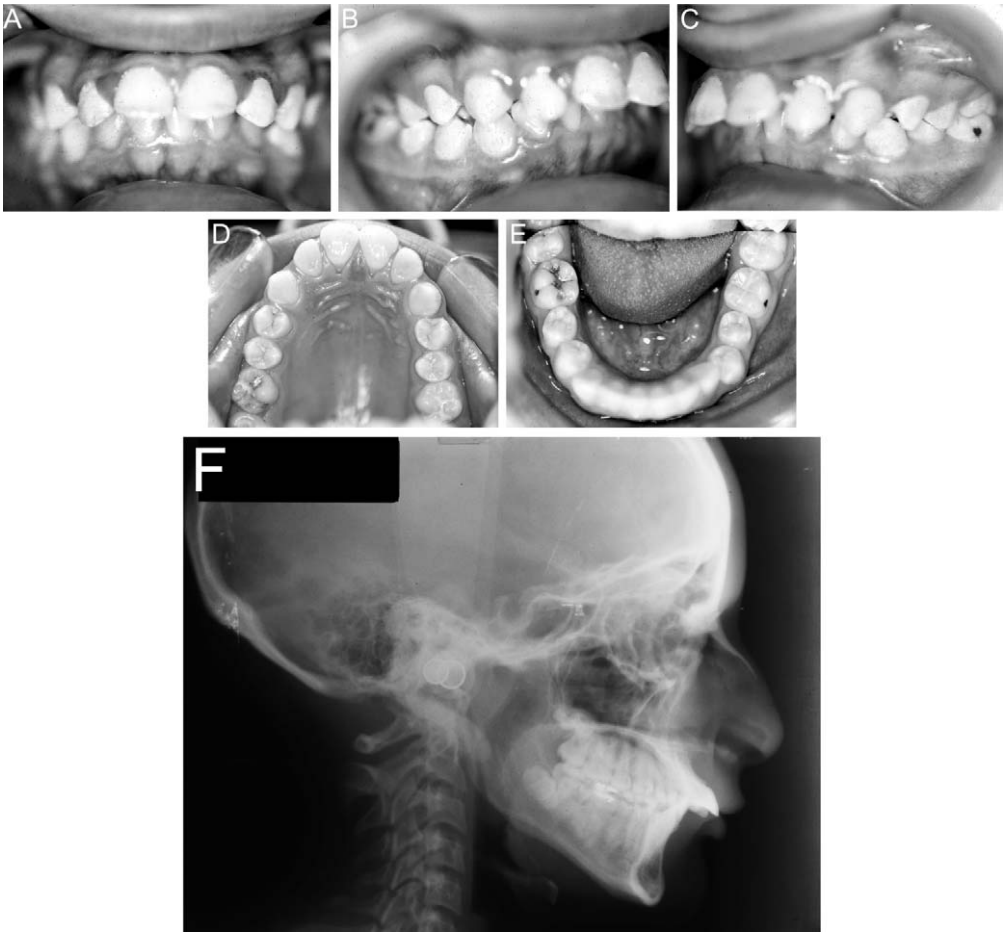

Figure 1. Pretreatment records of Case 1. (A) Frontal. (B) Right buccal. (C) Left buccal. (D) Maxillary occlusal. (E) Mandibular occlusal. (F) Lateral cephalogram.

garding the progress of orthodontic treatment in patients with Marfan syndrome. This report presents three separate cases of individuals with the syndrome who received orthodontic treatment at a dental school. Pertinent findings and the progress of treatment are presented, to facilitate evaluation of the challenges associated with such cases.

CASE REPORT 1

A 12-year-old girl presented with a chief complaint of protruding upper anterior teeth. Her past medical history included Marfan syndrome, and she was taking 25 mg atenolol bid for aortic dilation. At the time of presentation, intraoral examination revealed a permanent dentition with poor oral hygiene and absence of caries (Figure 1). Clinical examination indicated normal temporomandibular joint (TMJ) and mandibular movements. Deviation of the mandible to the right was noted on protrusion.

The patient's face had an asymmetric, dolichofacial shape. Lateral photographs revealed a convex and slightly retrognathic profile. Her nose and alar bones deviated to the right. She did not show excessive gingiva on smiling and had a normal lower facial height. Clinical examination revealed a convex and slightly retrognathic profile. The patient's lips were in poor balance and harmony in relation to the face. The mentolabial fold was abnormally accentuated, but the nasolabial angle was normal. Gingival inflammation and recession were noted on the palatal aspect of the upper central incisors.

Treatment Summary

Before the time of the first treatment appointment, we consulted the patient's cardiologist, and prophylactic antibiotics were prescribed for banding. We stressed the need for good oral hygiene and assessed it at subsequent visits. Treatment objectives included attaining Class II molar and Class I canine relationships. Maxillary first premolars were extracted. The posterior cross-bite tendency and overbite were corrected. The curve of Spee was leveled by intruding the upper and lower incisors, and crowding in the lower

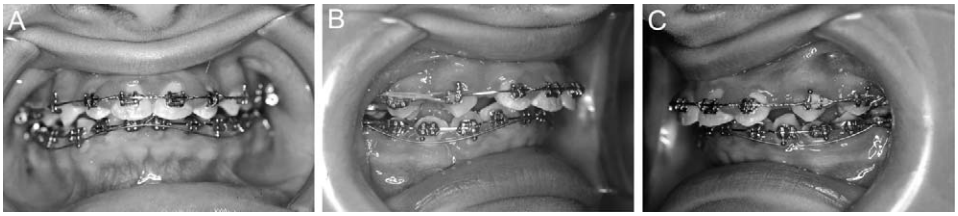

Figure 2. Generalized gingival inflammation was seen consistently at each visit during treatment. (A) Frontal. (B) Right buccal. (C) Left buccal.

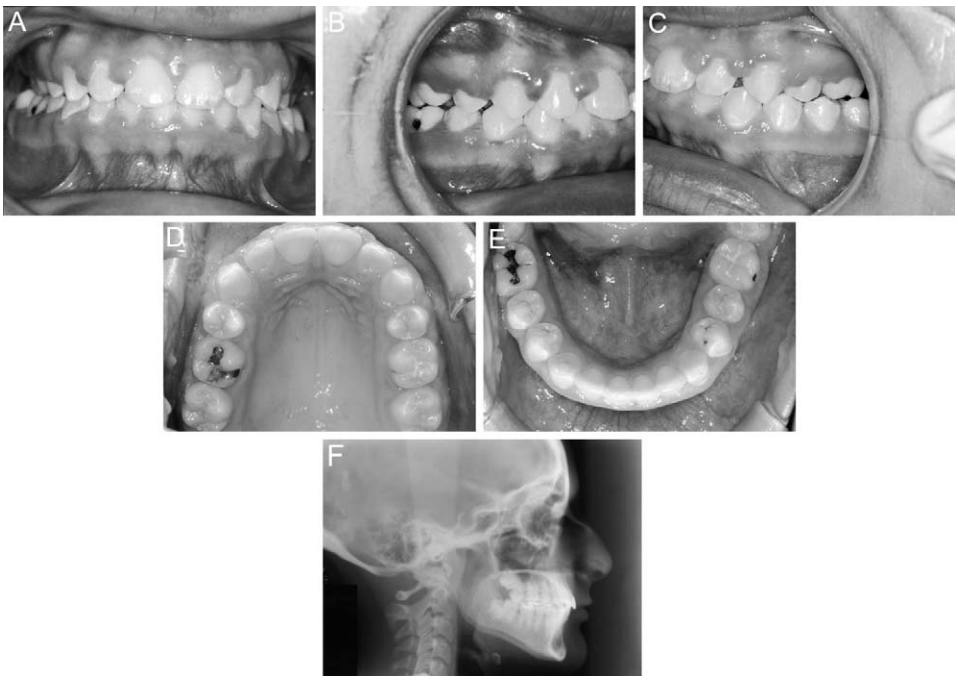

Figure 3. Poor oral hygiene can compromise the outcome of orthodontic treatment, but tooth movement occurs normally. (A) Frontal. (B) Right buccal. (C) Left buccal. (D) Maxillary occlusal. (E) Mandibular occlusal. (F) Lateral cephalogram.

arch was resolved through slight advancement of incisors.

Orthodontic treatment lasted 3 years and 9 months. Even in the absence of significant plaque deposits and other local factors, profuse gingival bleeding was noted during minor adjustment of the appliance (Figure 2). Because of the chronic inflammation that occurred in periodontal tissues, after consultation with her physician, we decided to premedicate the patient prior to each appointment to decrease the risk of bacteremia. We completed treatment with good occlusion and esthetics (Figure 3) and used an upper Hawley appliance with a biteplate and a lower Hawley during the retention phase.

CASE REPORT 2

A 13-year-old Hispanic male presented with a desire to have his teeth look like his mother's teeth. Past medical history revealed speech and learning disorders, and he had joined a program with the goal of correcting these problems. Past dental history revealed trauma to his front teeth and gingival bleeding. He had difficulty breathing through the nose and had a marked nail biting habit.

The patient's oral hygiene was fair, and generalized chronic gingivitis was aggravated in the upper anterior region by incompetent lips and mouth breathing. Pseudopockets up to 4 mm deep resulted from gingival hypertrophy.

The patient had a dolichocephalic head, a convex soft tissue profile, and a retrognathic soft tissue facial type. His lips were markedly incompetent at rest with a hyperactive mentalis muscle upon closure. He showed excessive gingiva on smiling.

The panoramic radiograph revealed the presence of a supernumerary tooth between the left lower premolars. A vertical cleft evident between the upper central incisors had been formed from intervening fibrous tissue of the upper labial frenum. All third molars were present, and the lower right and left third molars were mesially angulated.

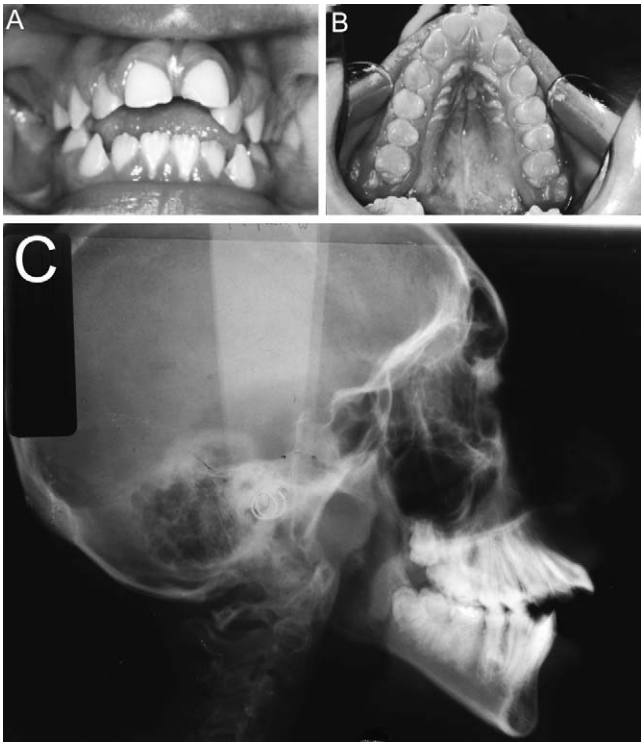

Figure 4. Anterior open bite and high-arched palate seen in Case 2. (A) Frontal. (B) Maxillary occlusal. (C) Lateral cephalogram.

An anterior open bite of 6 mm was seen anteriorly (Figure 4A). The upper and lower dental midlines coincided with the facial midline. A bilateral 50% Class II molar relationship with 13.5 mm overjet was observed. The maxillary arch was omega-shaped as the result of bilateral narrowing in the premolar and first molar areas; it was asymmetrical in the region of the lateral incisors, second premolars, and first molars (Figure 4B). Excess space measured 8 mm. The mandibular arch form was square and symmetrical, and 7 mm crowding was limited to the anterior segment.

Treatment Summary

First, we referred the patient to the periodontist to improve his gingival health, and to the surgeon for orthognathic surgery consultation. On the basis of clinical findings, the treating orthodontist recommended a thorough systemic examination to rule out the possibility of an underlying medical condition. It was only then that a pediatric cardiologist diagnosed Marfan syndrome and mitral valve prolapse.

Orthodontic treatment lasted 4 years and 8 months primarily because of the poor periodontal status of the patient and his noncompliance with appointments (Figure 5). Subgingival scaling and gingivectomy were performed routinely in all quadrants. Premedication (500 mg amoxicillin, 1 hour before appointment) was provided prior to each visit. The patient underwent orthognathic surgery, and treatment was completed with acceptable results (Figure 6). An upper Hawley appliance and a lower bonded canine-to-canine retainer were used during the retention phase.

CASE REPORT 3

A 20-year-old white female presented to the orthodontic clinic with a chief complaint of crowded teeth. A prior diagnosis of Marfan syndrome was a notable feature in her medical history. In accordance with the classical oral findings reported in patients with Marfan syndrome, the patient had a high-arched palate, a bilateral posterior cross-bite, and an anterior open bite (Figure 7A).

Treatment Summary

Surgical release of the zygomatic buttresses was performed as part of surgically assisted rapid palatal expansion (SARPE). Figures 7B and 7C show that gingival adaptation to rapid maxillary expansion and subsequent dental alignment occurred normally. Subsequently, a LeFort I osteotomy was carried out for maxillary advancement after downfracturing of the maxilla. Healing after surgery was uneventful. Treatment was not complicated or unduly prolonged by poor compliance or poor oral hygiene.

DISCUSSION

Connective tissue disorders often are associated with extensive periodontal tissue breakdown.[14] In this context, a definite correlation between Marfan syndrome and an increased susceptibility to periodontal disease is uncertain. A case described a few years back, purported to be the first report of its kind, pro-

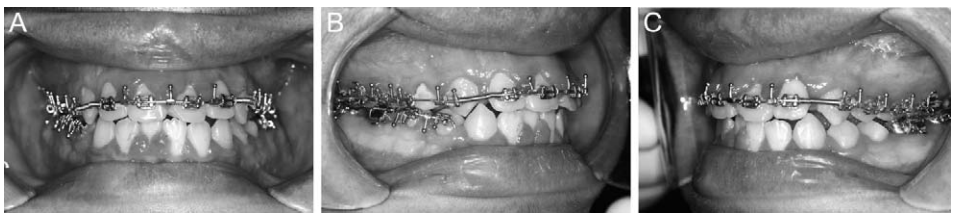

Figure 5. Orthodontic treatment was prolonged by the patient's poor periodontal condition. (A) Frontal. (B) Right buccal. (C) Left buccal.

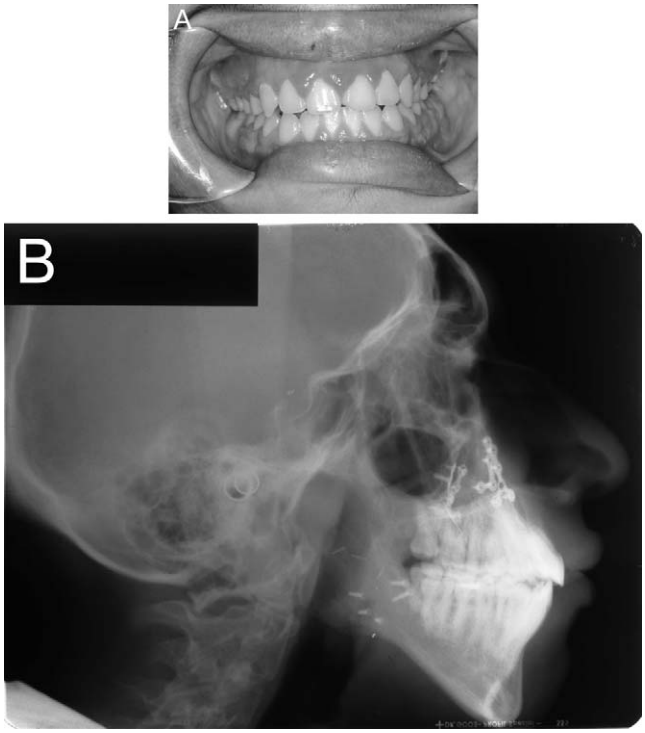

Figure 6. Orthognathic surgery to correct the open bite resulted in a stable occlusion. (A) Frontal. (B) Lateral cephalogram.

posed a link between Marfan syndrome and severe periodontitis.[15] Alveolar bone loss, high attachment level loss, furcation involvement, and tooth hypermobility were the salient features. Cases 1 and 2 as presented here involved significant plaque deposits and poor oral hygiene. Early diagnosis and treatment are important factors that play a major role in delaying or altogether avoiding the onset of severe symptoms later in life.

The high-arched palate commonly seen in Marfan syndrome has not been explained but may be accompanied by a small nasal airway and increased nasal airway resistance (NAR). High NAR may produce obstructive sleep apnea in patients with Marfan.[16,17] Compensatory oral breathing consequent to nasal obstruction may alter the natural head posture, thus influencing facial development.

The cases presented here illustrate some common oral findings typical of Marfan syndrome. Orthodontic treatment frequently is sought by individuals affected by the syndrome because of the typical presentation of symptoms.[10] Maxillary vertical excess and mandibular retrognathism combined with a high and narrow palatal vault are commonly seen. The incidence of referral for orthodontic treatment is higher in patients with Marfan than in healthy control subjects[18] because intraoral findings such as a high-arched palate, crowding, open bite, and excessive overjet are closely related to Marfan syndrome. Cases 2 and 3 presented here revealed facial features typical of the syndrome. In addition, the clinician should note skeletal abnormalities such as disproportionately long limbs, scoliosis, and abnormal joint flexibility. Often, a patient whose condition was previously undiagnosed may present for orthodontic treatment. In these situations, the orthodontist may be the first health care provider to come in close contact with the patient. This is possible because of the variable nature of the syndrome and the unpredictable extent of involvement.[12] Because the severity of symptoms may not be obvious in affected individuals, diagnosis may be missed at an early age.

For Case 1, treatment was successfully carried out in accordance with the guidelines of the cardiologist. Compliance with oral hygiene maintenance is a problem in most cases. This aspect cannot be overemphasized, especially when patients with Marfan are treated. Any long-term treatment requires utmost cooperation from the patient. Another potential complication associated with Marfan syndrome results from involvement of the cardiovascular system. Aortic dissection or rupture is the leading cause of mortality in these patients.[1] Many cardiologists recommend prophylactic antibiotics before invasive dental procedures are performed.[14] When poor oral hygiene occurs, frequent scaling and root planing might be required. This in turn increases the potential for bacteremia.

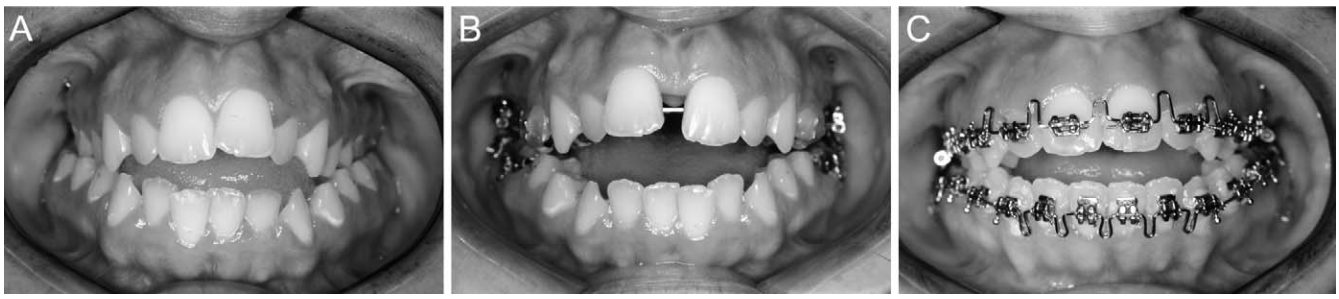

Figure 7. (A) Bilateral posterior cross-bite resulting from a narrow maxillary arch. (B) Surgically assisted rapid palatal expansion (SARPE) to expand the constricted maxilla. (C) Diastema created by rapid expansion closed well by orthodontic tooth movement.

Orthognathic surgery sometimes is required to correct severe orofacial discrepancies in patients with Marfan syndrome. The treating orthodontist may be apprehensive of including a surgical procedure in the treatment plan because of potential complications related to surgery. However, surgeons work closely with the patients' cardiologists when planning treatment. Cases 2 and 3 presented here required orthognathic surgical procedures; neither delayed bone healing following surgery nor abnormal tooth movement was observed.

Prior to the evolution of open heart surgery, patients with Marfan usually died from acute aortic dissection or rupture and thus had an average life expectancy of only 32 years.[19] Today, however, timely diagnosis and management can extend the life expectancy of patients with Marfan to over 60 years of age. Medications such as beta-adrenergic blockers reduce arterial blood pressure and the progression of aortic dilatation. Regular imaging of the aorta by echocardiography or magnetic resonance tomography allows monitoring of asymptomatic individuals. In addition, coordinated efforts of interdisciplinary teams comprising cardiologists, heart surgeons, orthopedic surgeons, ophthalmologists, pediatricians, geneticists, psychologists, and orthodontists are necessary.

CONCLUSIONS

- Patients with Marfan syndrome can undergo orthodontic treatment, just as their healthy counterparts do.
- Surgical procedures for patients with Marfan syndrome can be undertaken as long as appropriate precautions are taken.
- The fact that the patient in Case 2 was given the diagnosis during orthodontic treatment highlights the importance of awareness of the dental conditions that characterize Marfan syndrome.
- A low life expectancy in undiagnosed cases and significant improvement with currently available treatment modalities show the importance of an early diagnosis.

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