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CASE REPORT

Oral manifestations of a rare variant of Marfan syndrome

Abhishek Sinha[1], Sandeep Kaur[2], Syed Ahmed Raheel[3], Kirandeep Kaur[4], Mohammed Alshehri[5] & Omar Kujan[3,6]

[1]Department of Orthodontics, Hazaribag College of Dental Sciences and Hospital, Hazaribag, Jharkhand, India
[2]Department of Oral Medicine & Radiology, Indira Gandhi Government Dental College & Hospital, Jammu, Jammu and Kashmir, India
[3]Department of Oral Medicine & Diagnostic sciences, Al-Farabi College for Dentistry and Nursing, Al-Farabi Colleges, Riyadh, Saudi Arabia
[4]Department of Periodontology, Institute of Dental Studies & Technologies, Modi Nagar, Uttar Pradesh, India
[5]Dental Department, King Khaled University Hospital, King Saud University, Riyadh, Saudi Arabia
[6]School of Dentistry, The University of Western Australia, Nedlands, Western Australia, Australia

Correspondence
Omar Kujan, Department of Oral Pathology, School of Dentistry, The University of Western Australia, Nedlands, WA6009 Australia. Tel: +61 8 6457 7649;
Fax: +61 8 6457 7666;
E-mail: omar.kujan@uwa.edu.au

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Key Clinical Message

This article reports the oral manifestations of an unusual presentation of Marfan syndrome (MFS) and provides an evidence to the importance of recognizing the oral features in confirming the diagnosis of MFS. Dentists have a vital role in confirming the diagnosis of developmental disorders that involve the craniofacial compendium.

Keywords

Differential diagnosis, fibrillinopathies, Marfan syndrome, orofacial features.

Introduction

Marfan syndrome (MFS) is a disorder of genetic connective tissue that may involve the heart, blood vessels, lungs, eyes, bones, and ligaments [1]. The condition was firstly described by a French pediatrician, Antoine Bernard-Jean Marfan, in 1896 in a 5-year-old girl named Gabrielle with "spider's legs" or dolichostenomelia [1]. This disorder has a prevalence of at least one per 5000 [2]. Mutations in the gene for fibrillin-1 (FBN1) located on chromosome 15q-21.1 cause most cases of MFS [1–3]. However, a small number of MFS cases have linked to a mutation in the gene transforming growth factor receptor 2 (TGFBR2) [2, 4].

Marfan syndrome has previously classified into two types I and II using the Ghent diagnostic criteria. A revised version of the Ghent nosology for MFS was released in 2010 (Tables 1 and 2) [3]. Aortic involvement has been considered an essential feature [5]. Therefore, MFS has associated with high risk of mortality due to the potential hazard of dissection of dilated aortic root. Summers et al. outlined a decision tree to help in confirming the diagnosis of MFS [2]. The aim of this study was to highlight the importance of recognizing the oral manifestations of Marfan syndrome in finalizing the diagnosis and ultimately improving the patient's management.

Case Report

A 13-year-old female adolescent presented to the Department of Orthodontics, with a chief complaint of irregularly placed upper front teeth.

The child revealed partial (left side) frontal bossing since birth with abnormal visual acuity (Fig. 1A). Her mother stated that the patient is her single child. She also confirmed that her pregnancy and labor were normal.

Table 1. Diagnostic criteria for Marfan syndrome (Revised Ghent nosology 2010) [3].

Absence of family history	
1	Aortic diameter (Z ≥ 2) or aortic root dissection and Ectopia lentis or
2	Aortic diameter (Z ≥ 2) or aortic root dissection and FBN1 mutation or
3	Aortic diameter (Z ≥ 2) or aortic root dissection and a systemic score ≥7 points* or
4	Ectopia lentis and casual FBN1 mutation with known Aortic diameter (Z ≥ 2) or aortic root dissection
Prsence of family history	
5	Family history and Ectopia lentis or
6	Family history and a systemic score systemic score ≥7 points* or
7	Family history and Aortic diameter (Z ≥ 2 above 20 years old, Z ≥ 3 below 20 years)

*Without discrimentating from other syndromes and genetic conditions listed in Table 3.

Table 2. Scoring of Systemic features (Revised Ghent nosology 2010) [3].

Feature	Score (Maximum total: 20 points; score ≥7 indicates systemic involvement)
Wrist AND thumb sign	3
Wrist OR thumb sign	1
Pectus carinatum deformity	2
Pectus excavatum or chest asymmetry	1
Hindfoot deformity	2
Plain pes planus	1
Pneumothorax	2
Dural ectasia	2
Protrusio acetabuli	2
Reduced upper segment/lower segment (US/LS) AND increased arm/hight AND no severe scoliosis	1
Scoliosis or thoracolumbar kyphosis	1
Reduced elbow extension	1
Facial features (3/5) (dolichocephaly, enophthalmos, downslanting palpebral fissure, malar hypoplasia, retrognathia)	1
Skin stria	1
Myopia >3 diopters	1
Mitral valve prolapse (all types)	1

Remarkably, the mother had partial (right side) frontal bossing with decreased visual acuity, otherwise healthy and no remarkable finding was detected (Fig. 2). In compliance with the ethics code of the institution, guardian's informed consent was sought, and subsequently further clinical inspection and other investigations were carried out.

General examination revealed elongated fingers and toes (arachnodactyly) (Fig. 1B and C) with no cardiac abnormality. Also, the patient has been diagnosed with a partial displacement of the crystalline lens in her left eye. Blood and urine tests were in the normal range. The girl has relatively healthy growth with no history of seizures, lethargy, and episodic vomiting. She spoke fluently and responded to all questions confirming her natural mental health.

The clinical examination showed that the patient has an asymmetric face with frontal bossing on the left side with dolichofacial pattern and retrognathic profile (Fig. 1A). The intra-oral inspection revealed a permanent dentition characterized by microdontia and enamel hypoplasia, and with an absence of caries and a deep palatal vault (Fig. 1D). The maxillary arch was high and has spaced dentition with the mesiolabial rotation of upper right central incisor. She had excessive gingiva on smiling and increased lower facial height. The patient had an increased overjet of 12 mm, and her overbite was 70%. The patient's lips competency was in a bad balance and was not in harmony about the face. The mentolabial fold and nasolabial angle were abnormally accentuated. The orthopantograph revealed no significant finding except lower premolar roots incompletion (Fig. 1E).

On overall assessment, the patient was diagnosed as a variant of Marfan syndrome using the 2010 revised Ghent nosology [3]. As the skeletal malformation was severe, the symptomatic treatment modality was selected to correct the proclination and rotation of the upper and lower anterior teeth with the pre-adjusted fixed orthodontic appliances. The bonding procedure was complicated as the dental structure was affected with microdontia and enamel hypoplasia; hence, some teeth were banded to achieve the treatment goal (Fig. 3). As the proclination and rotation were the primary concern of the patient, the surgical intervention was not advised at this stage.

Discussion

The diagnosis of Marfan syndrome is mainly formulated by clinical examination [6]. The personal and family history, molecular data, and contribution of organ systems radiography, echocardiography, and magnetic resonance imaging (MRI) investigations are the supplemental aids to facilitate the diagnosis of the defects that may present in the spectrum of MFS signs [7].

The diagnostic guidelines of Marfan syndrome have been revised and updated several times [2, 3, 8–10]. During 1996, the experts' panel in Ghent, Belgium, put forth the first set of diagnostic guidelines [8]. The revised Ghent nosology guidelines produced a framework that would help clinician recognize MFS cases with higher

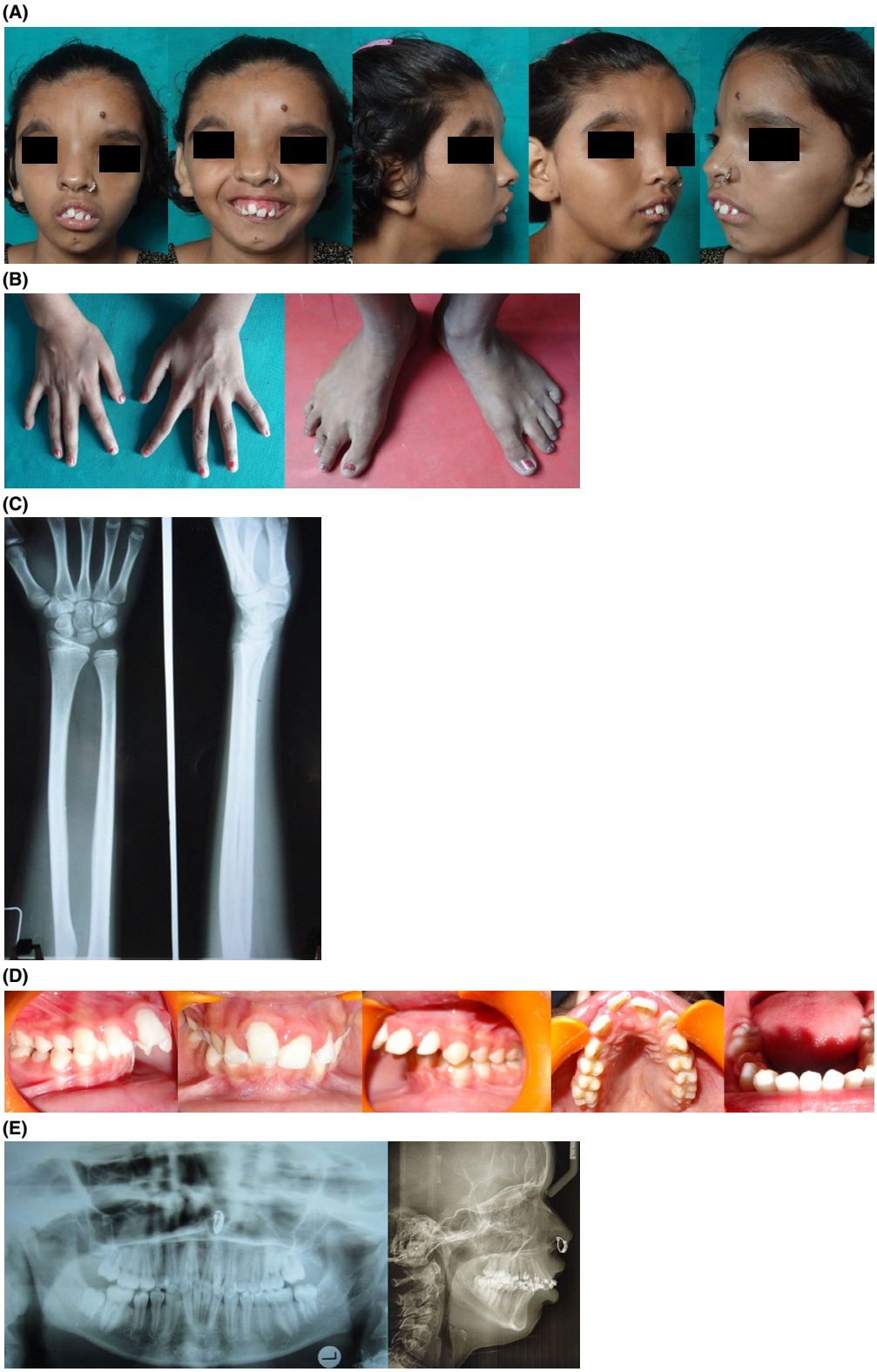

Figure 1. (A) Patient's extra-oral clinical photographs. (B) Patient's spidery long fingers and long toes photograph. (C) Hand wrist radiograph showing arachnodactyly. (D) Patient's intra-oral clinical photographs. (E) Panoramic X-ray and midtreatment lateral cephalogram depicting severity of mandibular retrognathia.

Figure 2. Patient's mother extra-oral clinical photogrphs.

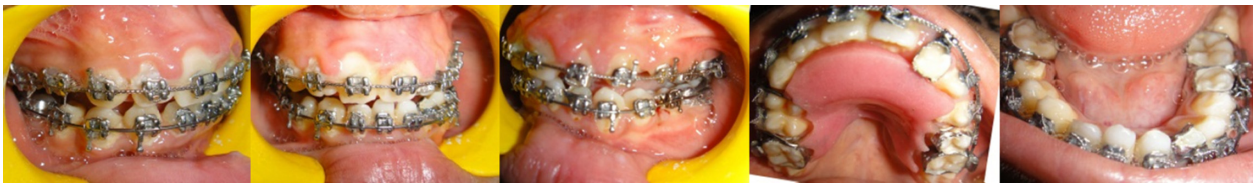

Figure 3. Pre-adjusted orthodontic appliance with anterior bite plane in the patient.

accuracy (Tables 1 and 2) [3]. The tabulated criteria are distinctive features of the syndrome and rarely occur in the general population. However, the diagnostic challenge of such similar cases is to exclude other conditions or syndromes that are caused by the fibrillin gene disruption that is responsible for the genesis of MFS [1]. A mutation in the gene for fibrillin diminishes the quantity and quality of fibrillin [11]. The fibrillin is described as three types: fibrillin 1, 2, and 3. The fibrillin-2 and fibrillin-3 have a domain organization identical to that of fibrillin-1. All three fibrillin are structural components of microfibrils in a cellular structure. The fibrillin-1 glycoprotein is necessary for the formation of elastic fibers in connective tissue. As a result weakened structural support would materialize, especially in areas where elastic fibers are found in large quantity [11]. Consequently, the most frequently affected parts of the body are the aorta, ligaments, and ocular muscles. FBN1 mutations have been identified in an array of phenotypes, the type 1 fibrillinopathies, with greater or lesser degrees of clinical overlap with MFS (Table 3).

Table 3. Clinical differential features of Fibrillinopathies types.

Syndrome	Discriminating features
Ectopia lentis syndrome [15, 16]	Mainly ocular findings with lack of aortic root dilatation
Kyphoscoliosis [17]	Mainly ocular findings
Familial arachnodactyly [18]	Dolichostenomelia and arachnodactyly
Shprintzen–Goldberg syndrome [19, 20]	Craniosynostosis, mental retardation
Isolated skeletal features [21]	Tall stature, scoliosis, pectus excavatum, arachnodactyly
MASS phenotype	Mitral valve prolapse, aortic dilatation without dissection, skeletal and skin abnormalities
Weill–Marchesani syndrome [22]	Short stature, brachydactyly, joint stiffness, and characteristic eye abnormalities
Loeys–Dietz syndrome [23]	Bifid uvula/cleft palate, arterial tortuosity, hypertelorism, diffuse aortic and arterial aneurysms, craniosynostosis, clubfoot, velvety skin, easy bruising

The challenging nature of the diagnosing of this present case is the absence of both the family history of MFS and the aortic involvement despite the fact that her mother has suggestive features of Marfan-like condition or syndrome. The ophthalmology examination has revealed that patient has a partial displacement of the crystalline lens in the left eye, which was compatible with ectopia lentis diagnosis and suggestive of a link to Marfan or Marfan-like syndrome. After careful consideration of

the differential features of fibrillinopathies and the exclusion of both Ehler–Danlos syndrome and homocystinuria on the basis that the patient has no feature of skin hyperextensibility, malar flush, osteoporosis, or a positive urinary nitroprusside test. The case's final diagnosis was then clinically confirmed as a rare variant of MFS given her the orofacial features, the high score of the systemic features, the diagnosis of ectopia lentis, and the absence of mental retardation.

The orofacial features of the presented case included dolichocephaly, malar hypoplasia, retrognathia, skeletal class II malocclusion, severe maxillary crowding, and large overbite. However, the movement of the temporomandibular joint was in the normal range. Her reported orofacial features were consistent to those reported in the literature [6, 12, 13]. The orofacial features in our case have played a confirmatory role in making the MFS diagnosis. It is well accepted that these features are more specific than sensitive and are postulated to be used in prioritizing patients for appropriate referrals and detailed examination [12, 14].

It is generally the MFS patients warrants special care protocols given the potential risk of cardiac defects [6, 12, 13]. However, in our case, the patient has no cardiac anomalies or pathologies, and therefore, no special management protocol was devised. Thus a standard orthodontic treatment has been applied.

Conclusion

Dentists should be vigilant to recognize the oral manifestations of Marfan syndrome and other similar craniofacial developmental disorders as rare presentations of fibrillinopathies. Knowledge about this rare syndrome's diagnosis, general health, and treatment modes help dentists to offer more appropriate treatment for their patients.

Conflict of Interest

None declared.

Authorship

AS, SK, and KK: have developed the conception and the acquisition of the case report and drafted the manuscript. SAR, MA, and OK: analyzed the case details and finalized the manuscript.

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