

## Case Report

## The Early Diagnosis of the Marfan Syndrome: What is the Role of the Pediatric Dentist?

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**Abstract:** Marfan syndrome (MIM 154700) is a variable, autosomal dominant disorder of connective tissue whose cardinal features affect the cardiovascular system, eyes and skeleton. The diagnosis of Marfan syndrome (MFS) relies on defined clinical criteria (Ghent nosology), outlined by international expert opinion to facilitate accurate recognition of this genetic aneurysm syndrome. The patient with MFS has multiple oral decrease that may be diagnosed and treated on time to increase the life quality of the patient. Treatment planning is related to the age of the patient, the type and severity of the disorder, and the oral health of the patient. **AIM:** The aim of this article was to describe through two cases the orofacial manifestations of Marfan syndrome and to demonstrate the role of the pediatric dentist in the early diagnosis of this genetic defect from the oral pathognomonic signs of this syndrome and and the therapeutic management of those children.

**Keywords:** Marfan Syndrome, dental management, clinical manifestations, orofacial features, fibrillinopathies, treatment.

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### INTRODUCTION

Marfan's syndrome is a variable, autosomal dominant rare disorder of connective tissue typically involving the cardiovascular, skeletal, and ocular systems. (Sinha A, *et al.*, 2017) (Dean JCS *et al.*, 2007) (Prashanth S *et al.*, 2012) (Meester JAN *et al.*, 2017) (Jondeau G, 2019). This condition represents an incidence of 1 per each 9800 individuals without any gender or ethnic distinction (Dean JCS *et al.*, 2007).

A consent regarding diagnostic criteria was defined at the International Nosology of Heritable Disorders of Connective Tissue Meeting in Berlin in 1986 (Dean JCS *et al.*, 2007). In 1991, fibrillin-1 gene mutation on chromosome 15 was identified as a cause of Marfan syndrome but molecular testing is not as diagnostically useful as was originally hoped. In fact, the recognition that many individuals diagnosed with the disorder do not carry the *FBN1* mutation identified in more severely affected family members conducted to revise the Berlin diagnostic criteria of 1988 and the clinical features codified as the Ghent nosology in 1996 several years later in order to make the diagnosis of Marfan syndrome more consistent and of more prognostic value (De Paepe A *et al.*, 1996) (Sakai LY *et al.*, 2016). The last revised version of the Ghent nosology for MFS was released in 2010 (table 1, table

2) (Loeys BL *et al.*, 2010). It helps to identify which patients with a Marfan-like build are at risk of cardiovascular complications, needing regular follow-up with prophylactic medical and surgical treatment.

Several orofacial manifestations are frequently present, but are not specific enough to the disorder for inclusion in the major criteria. These comprehend a long narrow skull (dolichocephaly), a high-arched palate, tooth crowding, retrognathia (recessed lower mandible) or micrognathia (small chin), malar flattening, and downward-slanting palpebral fissures. (Morales-Chavez Mc *et al.*, 2010)

The aim of this study was to spotlight the orofacial manifestations of Marfan syndrome and to demonstrate the role of the pediatric dentist in the early diagnosis of this genetic defect from the oral pathognomonic signs of this syndrome and eventually offering more appropriate treatment for the patient.

### CASES REPORT

**Case 1:**

A 12-year-old female adolescent was addressed to the department of Pediatric Dentistry, La Rabta Hospital, Tunisia. With regard to the patient's

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medical background, her mother affirmed that the young girl was diagnosed with Marfan Syndrome:

- The cardiovascular manifestations were dilatation of the ascending aorta with aortic regurgitation and risk of root dissection. These manifestations were managed with beta blocker medication.
- Dislocated lenses and myopia were the ocular manifestations
- Spontaneous pneumothorax had been surgically intervened at an early age

For the physical examination, a seize of 1.72 cm range was determined from upper to average with elongated extremities (dolichostenomelia) (Fig1). Anterior chest deformity caused by overgrowth of the ribs pushing the sternum anteriorly (pectus carinatum) was observed (Fig2, A, B). Arachnodactyly, wrist signs (full overlap of the distal phalanges of the thumb and fifth finger when wrapped around the contralateral wrist) and thumb sign (the distal phalanx of the thumb fully extends beyond the ulnar border of the hand when folded across the palm) were present (Fig2, E).

The extra-oral examination revealed an elongated and narrowed cranium: dolichocephalism, malar hypoplasia and micrognathia. (Fig2, C, D).

Intra-orally, highly arched palate with tooth crowding, enamel hypoplasia and several caries were observed (Fig3, A, B, C).

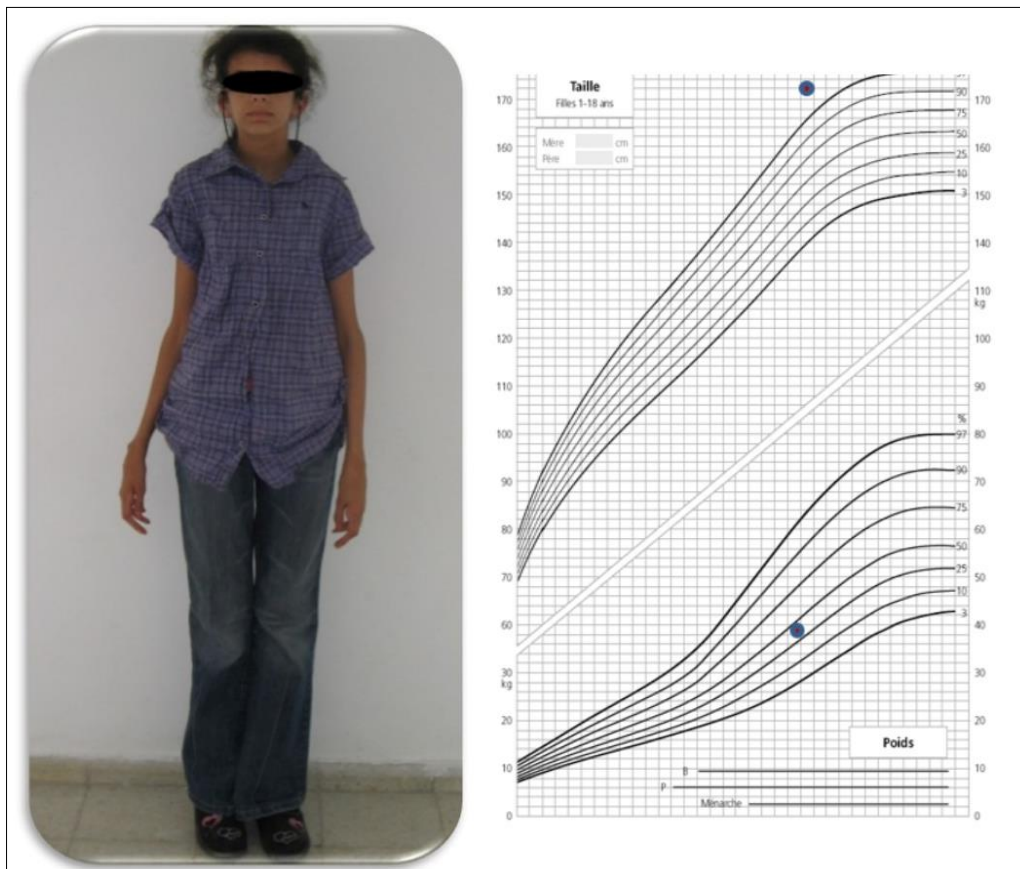
Radiology, abnormal form of pulp chamber and radicular deformities were present especially in permanent molars (Fig3, D).

Treatment objectives taken into account were:

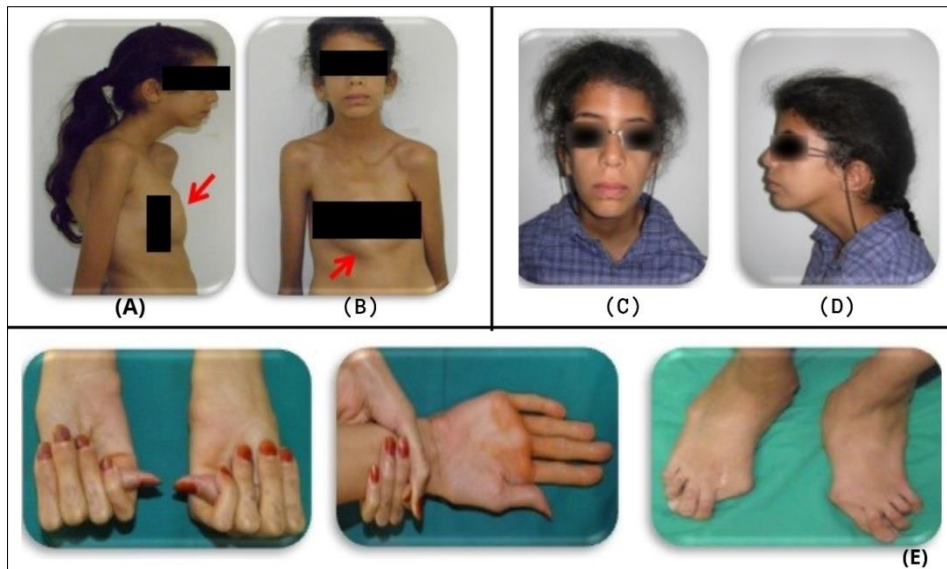
- Preservation of tooth integrity and vitality of permanent teeth
- Reducing sensitivity and improve esthetics
- Normalization of oral functions

Treatment included oral prophylaxis, caries curettage and placement of a resin on 11 and 21 and glass ionomer cement on 24 and extraction of 26 and the radicular rests of 63, 65, 54, 55, 83, 85. All of these procedures were carried out following a 2 g amoxicillin antibiotic prophylaxis intake, which was taken one hour prior to the medical visit, due to the patient's cardiac pathology (Fig3, E).

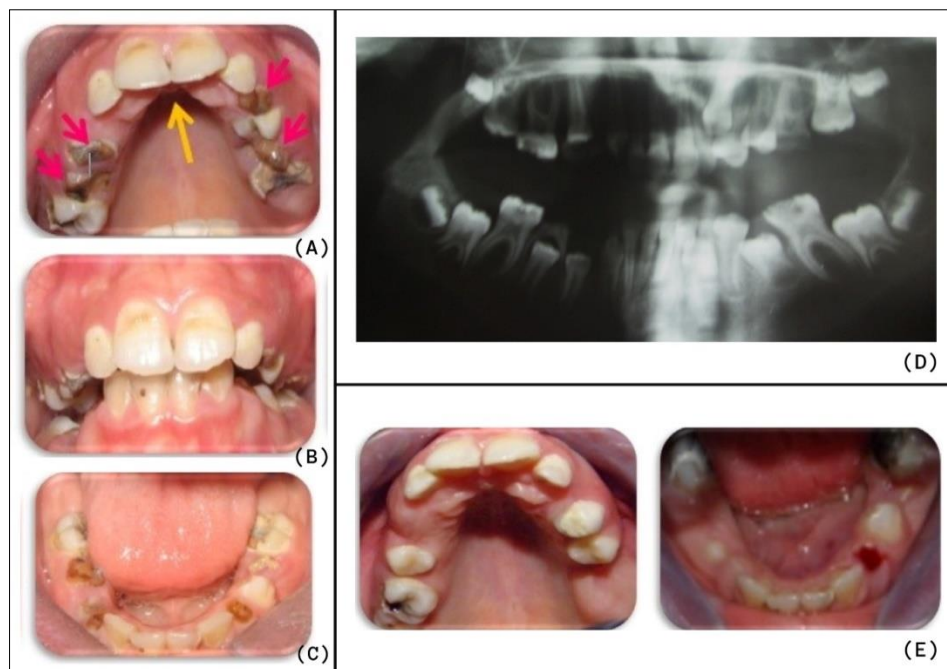
Removable partial dentures for the absent teeth were made and the patient was sent to the Orthodontic's Department for the proper evaluation and occlusion's treatment.



**Fig-1: Case 1: Physical characteristics of Marfan syndrome a seize of 1.72 cm with elongated extremities (Dolichostenomelia)**



**Fig-2: Case 1 (A, B) Anterior chest deformity (C) Elongated and narrowed cranium (D) Micrognathia (E) Arachnodactyly, wrist sign and thumb sign**



**Fig-3: Case 1 (A) intraoral occlusal frontal view before treatment (B) intraoral occlusal maxillary view before treatment (C) intraoral occlusal mandibular view before treatment (D) panoramic radiography (E) intraoral frontal and intraoral occlusal mandibular after treatment**

**Case 2**

A 13-year-old girl was referred to the department of Pediatric Dentistry, La Rabta Hospital, Tunisia with an aesthetic chief complaint. The interrogatory of her parent revealed that she came from a consanguineous marriage (second degree) and other members of her family had the same physical and dental anomalies.

The interrogation revealed that the patient had myopia and no cardiac abnormality. The physical

examination showed a tall stature, elongated extremities known as dolichostenomelia in absence of spine deformation with a reduced upper /lower segment and increased Arm/Height. She represented also arachnodactyly of the hands and feet and joint hypermobility (Thumb and wrist signs were positive) (Fig4, B). Her facial features showed a broad curved forehead and long, narrow face (dolichocephaly) (Fig4, A).

Intraoral examination revealed that the patient had been an incomplete permanent dentition with delayed eruption and several impacted and conical teeth crown. No abnormalities were found on the tongue or floor of the mouth. (Fig4, C)

Panoramic radiography (Fig4, D) showed multiple dental agenesis:

- All the permanent mandibular teeth expect the two first molars (36/46) with persistence of the anterior primary teeth
- Three maxillary premolars (14/15/25) and one maxillary lateral incisor 12
- Root malformation of the maxillary premolar and molars (26/24/16)
- Infraclusion of the two primary maxillary molars (55/65)

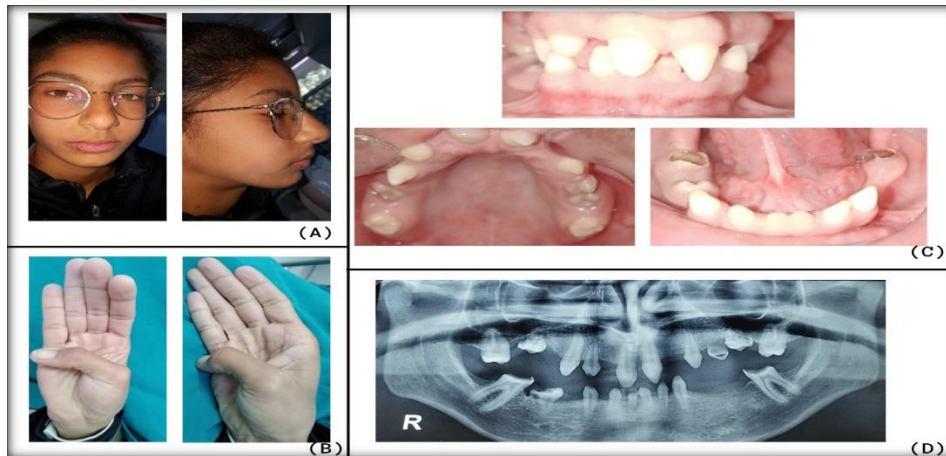
A treatment plan was developed which the main objective was to:

- Improve esthetics
- Restore masticatory function.

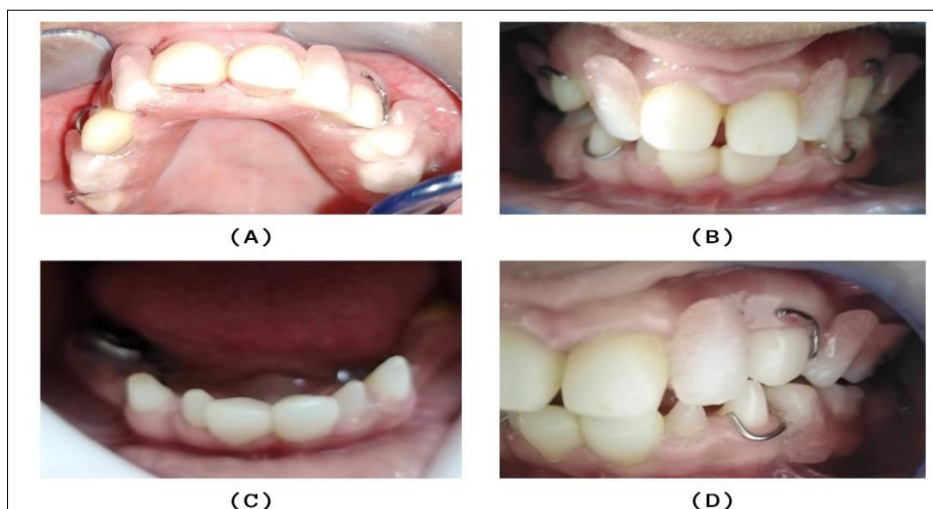
First, the patient was advised to brush her teeth with normal fluoride toothpaste. Second, Restorative treatment was performed:

- 11 and 21: Reconstitution with composite resin
- 36: Pulpectomy, root canal filling and reconstitution with composite resin.
- 46: Caries curettage, cupping with calcium hydroxide, reconstitution with composite resin and stainless-steel crown

Then, extraction of primary molars 55, 64 and 65 was carried out. Finally, removable partial dentures for the absent teeth were made to obtain normal occlusion. A genetic test was performed to confirm the diagnosis. (Fig5, A B C D).



**Fig-4: Case 1 (A) Front view : Elongated face / Profile view : micrognathia (B) (C) intraoral views before treatment (D) panoramic radiography (intraoral frontal view after treatment (g) intraoral occlusal maxillary view after treatment (h) intraoral occlusal mandibular view after treatment**



**Fig-5: Case 2 (A) intraoral occlusal maxillary view after treatment (B) intraoral occlusal view after treatment (C) intraoral occlusal mandibular view after treatment (D) intraoral occlusal left view after treatment**

## DISCUSSION

Marfan syndrome MFS is an autosomal dominant inherited rare connective tissue disorder mostly caused by mutations in *FBNI*, the gene encoding fibrillin 1, a structural component of the extracellular matrix also involved in the regulation of transforming growth factor bioavailability (Sinha A *et al.*, 2017) (Bitterman AD *et al.*, 2017) (Pepe G *et al.*,

2016). This disease is characterized by three clinical criteria (thoracic aortic aneurysm and/or dissection, ectopia lentis, and multisystemic manifestations) and two genetic criteria (the presence of a first-grade relative with MFS diagnosed according to revised Ghent-2 criteria (table 1, table 2) and presence of a pathogenic mutation in *FBNI* (Pepe G *et al.*, 2016).

**Table-1: Diagnostic criteria for Marfan syndrome (Revised Ghent nosology 2010) (Loeys BL *et al.*, 2010).**

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

\*Without discriminating from other syndromes and genetic conditions.

**Table-2: Scoring of Systemic features (Revised Ghent nosology 2010) (Loeys BL *et al.*, 2010).**

Feature systemic involvement)	Score (Maximum total:20 points; score $\geq 7$ indicates
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

In the described cases, we noticed that the two patients presented many common manifestations touching the skeletal system such as disproportionate overgrowth of the long bones which is often the most striking and immediately evident sign of this genetic defect.

Several craniofacial manifestations were also present such as a long narrow skull (dolichocephaly), a high-arched palate, teeth abnormalities, retrognathia (recessed lower mandible). A minor criterion was noticed about the two girls: severe myopia. In fact, this condition that affects the eyes has been shown to occur in most of the patients with the disorder. When

identified, it should prompt further assessment for Marfan’s syndrome. (Khonsari RH *et al.*, 2010).

The diagnosis of Marfan syndrome in the first case is confirmed by clinical examination, her personal and family history, the contribution of organ systems radiography and the genetic test.

The challenging nature of the diagnosing of the second case is the absence of both ectopia lentis and the aortic involvement despite the fact that her mother has reported that other members of her family have the same features of Marfan-like condition or syndrome. Many different heritable connective tissue disorders (HCTD) have been described over the past decades.

These diseases often affect the connective tissue of various organ systems. Three typical examples of HCTD are Marfan syndrome, Ehlers-Danlos syndrome (EDS), and Loeys-Dietz syndrome (LDS). These syndromes show some degree of phenotypical overlap of cardiovascular, skeletal, and cutaneous features (Prashanth S *et al*, 2012) (Meester JAN *et al.*, 2017).

After careful consideration of the differential features of fibrillinopathies and the exclusion LDS on the basis that the patient has no feature of the unique presence of hypertelorism, bifid uvula or cleft palate, and widespread aortic and arterial and EDS with the absence of tortuosity skin hyperextensibility, malar flush and osteoporosis. (Prashanth S *et al.*, 2012) (Meester JAN *et al.*, 2017).

The orofacial manifestations of the second case were dolichocephaly, micrognathia, several impacted and conical teeth crown, multiple agenesia, and large overbite. The dental malformations in this case were more similar to anhidrotic ectodermal dysplasia (AED) than MFS. The diagnosis of AED was highly unlikely because this syndrome is always associated with lack of or diminished sweating (anhidrosis or hyperhidrosis), heat intolerance, and fever; abnormally sparse hair (hypotrichosis). (De Paepe A *et al.*, 1996).

On overall assessment of the personal and family history, the orofacial manifestations and the high score of the systemic features, the second case's final diagnosis was then mainly confirmed as a rare variant of Marfan syndrome using the 2010 revised Ghent nosology.

Patients with MFS often exhibit three types of dental anomalies involving dentin formation: root deformities; calcified pulp inclusions; and abnormal pulp shape. These deformations were found in the two presented cases. They may be explained by multiple endothelial ruptures in pulpar vessels or by abnormal mechanical constraints around the tooth germ due to periosteal and stromal microfibrillar dysfunction (Meester JAN *et al.*, 2017).

The treatment of dental anomalies is a key issue in the follow-up of MFS patients. MFS patients have a high frequency of cardiovascular disorders and may theoretically have an abnormal bone response to mechanical stress. Three points have to be taken into account by the dentists the use of local anesthesia containing epinephrine needs careful management; high-risk protocols to prevent bacteremia during and after oral surgery are mandatory; and alveolar bone may not react as expected to orthodontic treatments. (Morales-Chavez Mc *et al.*, 2010). However, in the first case, the patient has no cardiac anomalies or pathologies, and therefore, no special management protocol was devised.

Early diagnoses of both dental and craniofacial anomalies allow more appropriate clinical follow-ups and an adequate treatment which could definitely develop a satisfactory prognosis of these type of patients with great advantage to the quality of life of patients (Judge DP *et al.*, 2005).

## CONCLUSION

Pediatric dentists should be aware to recognize since an early age the orofacial manifestations of Marfan syndrome and other similar craniofacial disorders in order to establish a proper diagnosis and offer an appropriate treatment for these patients.

## REFERENCES

1. Bitterman, A. D., & Sponseller, P. D. (2017). Marfan Syndrome: A Clinical Update. *Journal of the American Academy of Orthopaedic Surgeons*, 25(9), 603-609.
2. De Paepe, A., Devereux, R. B., Dietz, H. C., Hennekam, R. C. M., & Pyeritz, R. E. (1996). Revised diagnostic criteria for the Marfan syndrome. *American Journal of Medical Genetics*, 62(4), 417-426.
3. Dean, J. C. S. (2007). Marfan syndrome: Clinical diagnosis and management. *European Journal of Human Genetics*, 15(7), 724-733.
4. Jondeau, G., Boileau, C., & Milleron, O. (2017). Marfan Syndrome: Always Evolving. *Circulation: Cardiovascular Genetics*, 10(3).
5. Judge, D. P., & Dietz, H. C. (2005). Marfan's syndrome. *The Lancet*, 366(9501),
6. Khonsari, R. H., Corre, P., Boukerma-Vernex, Z., Schmidt, J., Renaudin, K., Frayssé, C., Gayet-Delacroix, M., Khau Van Kien, P., & David, A. (2010). Extreme oral manifestations in a Marfan-type syndrome. *International Journal of Oral and Maxillofacial Surgery*, 39(6), 622-625.
7. Loeys, B. L., Dietz, H. C., Braverman, A. C., Callewaert, B. L., De Backer, J., Devereux, R. B., Hilhorst-Hofstee, Y., Jondeau, G., Faivre, L., Milewicz, D. M., Pyeritz, R. E., Sponseller, P. D., Wordworth, P., & De Paepe, A. M. (2010). The revised Ghent nosology for the Marfan syndrome. *Journal of Medical Genetics*, 47(7), 476-485.
8. Meester, J. A. N., Verstraeten, A., Schepers, D., Alaerts, M., Van Laer, L., & Loeys, B. L. (2017). Differences in manifestations of Marfan syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome. *Annals of Cardiothoracic Surgery*, 6(6), 582-594.
9. Morales-Chavez, Mc., & Rodriguez-Lopez, Mv. (2010). Dental Treatment of Marfan Syndrome. With regard to a case. *Medicina Oral Patologia Oral y Cirugia Bucal*, e859-e862.
10. Pepe, G., Giusti, B., Sticchi, E., Abbate, R., Gensini, G., & Nistri, S. (2016). Marfan syndrome: Current perspectives. *The Application of Clinical Genetics*, 55.

11. Prashanth, S., & Deshmukh, S. (2012). Ectodermal Dysplasia: A Genetic Review. *International Journal of Clinical Pediatric Dentistry*, 5(3), 197-202.
12. Sakai, L. Y., Keene, D. R., Renard, M., & De Backer, J. (2016). FBN1: The disease-causing gene for Marfan syndrome and other genetic disorders. *Gene*, 591(1), 279-291.
13. Sinha, A., Kaur, S., Raheel, S. A., Kaur, K., Alshehri, M., & Kujan, O. (2017). Oral manifestations of a rare variant of Marfan syndrome. *Clinical Case Reports*, 5(9), 1429-1434.

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