Genetic and epigenetic aspects related to malocclusion—report of cases of monozygotic twins

Aspectos genéticos e epigenéticos relacionados com relatório de maloclusão-caso de gêmeos monozigigóticos

DOI:10.34119/bjhrv2n5-071

Recebimento dos originais: 27/09/2019
Aceitação para publicação: 25/10/2019

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ABSTRACT

Introduction: The multifactorial etiology of malocclusion involves several factors such as genetic, epigenetic and environmental factors. Among various dental anomalies, the development of supernumerary teeth is also directly related to genetic factors and mesiodens is the most frequent type of anomaly. Case Report: Two monozygotic twin sisters, both of which presented mesiodens, but only one with associated anterior open bite. Supernumerary removal was performed in the two sisters, and the anterior open bite was treated with the use of a fixed palatine grid. Results: The case was finished with proper occlusion and intercuspidation, contemplating facial and dental esthetics. Conclusion: Observing the possible differences that occur in pairs of monozygotic twins, it can be concluded that the development of malocclusions is associated with an interaction between genetic, epigenetic and environmental factors. Thus, the diagnosis and treatment of malocclusion should be individualized for each patient.

Keywords: Twins, Monozigotic. Tooth, supranumerary. Epigenetic Repression.

RESUMO

Introdução: A etiologia multifatorial da má oclusão envolve vários fatores, como fatores genéticos, epigenéticos e ambientais. Entre as várias anomalias dentárias, o desenvolvimento de dentes supranumerários também está diretamente relacionado a fatores genéticos e o mesiodens é o tipo de anomalia mais frequente. Relato de Caso: Duas irmãs gêmeas monozigóticas, as quais apresentaram mesiodens, mas apenas uma com mordida aberta anterior associada. A remoção supranumerária foi realizada nas duas irmãs e a mordida aberta anterior foi tratada com o uso de uma grade palatina fixa. Resultados: O caso foi finalizado com oclusão e intercuspidação adequadas, contemplando estética facial e dentária. Conclusão: Observando as possíveis diferenças que ocorrem em pares de gêmeos monozigóticos, pode-se concluir que o desenvolvimento de más oclusões está associado a uma interação entre fatores genéticos, epigenéticos e ambientais. Assim, o diagnóstico e o tratamento da má oclusão devem ser individualizados para cada paciente.

Palavras-chave: Gêmeos Monozigóticos. Dente supranumerário. Repressão Epigenética.

1. INTRODUCTION

Malocclusion is an anomaly of dental development and/or dental arches, causing esthetic and functional problems.¹ It has a multifactorial etiology, in which an interaction of factors can influence the growth and development of the jaws,² including the genetic, epigenetic
and environmental factors. The pattern of growth and development is strongly influenced by hereditary factors as well as dental morphology.

Among the number dental anomalies, the development of supernumerary teeth is directly related to genetic factors, since these teeth have already been diagnosed in twins, siblings and several generations of the same family. In the recent study by Kim et al. (2017), the authors identified a set of genes associated with the development of supernumerary teeth, involving BMP (bone morphogenetic proteins), SHH (sonic hedgehog) and WTN (wingless integrated).

Clinically, this pathology can cause several local disorders that require surgical or orthodontic intervention. These include retention, delayed or ectopic eruption of the central incisors, dental dislocations, development of dentigerous cysts, root resorption and the appearance of midline diastema. In monozygotic twins, there is generally the same number of supernumerary teeth located in similar regions of the mouth and cases of unilateral mesiodens; they may present as mirror images in each twin. Besides, reports of mesiodens in monozygotic twins have been more frequent than in dizygotic twins.

The role of genetic factors in the studies of identical twin malocclusions represents vital importance in the determination of morphological and dentofacial characteristics. The main factor of facial growth is genetic but extrinsic to the bone, then associated with epigenetic factors, defined as functional matrices, according to Cabrera and Enlow (1997), based on the growth theory introduced by Moss. Monozygotic twins usually present the same malocclusion, which does not necessarily occur in dizygotic twins. This is because monozygotic twins develop from the same egg cell and therefore share the same genetic load, thus demonstrating that the differences between them depend on epigenetic and environmental factors. Among these, we can mention the non-nutritive sucking habits, which are associated with the development of several types of malocclusions, such as the anterior open bite, characterized by the lack of vertical anterior teeth.

The aim of this study is to report two clinical cases of monozygotic twin sisters, both of which presented a supernumerary tooth, but with different occlusion patterns, explaining the appropriate diagnosis and treatment.

2. CASE REPORT

14-year-old monozygotic twin female patients attended the Unichristus Dental Clinic, in Fortaleza, Brazil, for a dental evaluation. Both family medical history did not show any systemic impairment.
Intraoral examination showed good oral hygiene, the presence of permanent dentition, the absence of carious lesions and periodontal problems, and the existence of cusp of a possible supernumerary erupted on the palate in both patients, compatible with the diagnosis of mesiodens. During the anamnesis, one of them reported having a finger sucking habit, and after the clinical examination, the presence of anterior open bite was observed only in this patient (Figure 1).

Figure 1: Initial photos. A and B) Extraoral; C and E) Frontal and occlusal view of the twin dentition without anterior open bite; D and F) Frontal and occlusal view of the twin dentition with anterior open bite.

As part of the clinical protocol adopted by our service, intraoral and panoramic radiographs were carefully requested to complement the diagnosis and care plan for this case. In each twin, the presence of a supernumerary tooth in the region of the upper central incisors on the left side was observed radiographically, with apparent gyroversion (Figure 2). A tomographic examination was not performed, as it was possible to confirm the location of the palatine in the clinical examination.

Figure 2: Panoramic radiographs of both twins demonstrating the presence of supernumerary teeth in the region of upper central incisors on the left side, with apparent gyroversion.

Surgical removal of the supernumerary was indicated in both patients in order to avoid the possible disturbances that may be caused by the presence of these teeth. The patients had biweekly dental care, including a prevention program with oral hygiene instruction and nutritional recommendations. The proposed plan of care consisted of topical application of fluoride, surgical removal of supernumerary teeth in both patients, and treatment of anterior open bite with fixed palatine grid only in the twin that developed malocclusion due to parafunctional habit (Figure 3). After removal of the supernumerary teeth, the anatomical similarity between them was observed, both of which presented root dilaceration (Figure 4).

Figure 3: Fixed palatine grid installation in a patient with anterior open bite. A) front view; B) right lateral; C) left lateral; D) occlusal view.

Figure 4: Mesiodens of both twins after surgical removal.

The patient in whom the palatine grid was installed remained with the appliance for five months and, after this period, the open bite was corrected (Figure 5). Follow-up visits were initially established monthly and then started quarterly for a total of one year. Subsequently, the orthopedically treated patient was referred to the Orthodontics service for completion of the treatment.
3. DISCUSSION

It is a consensus among the authors that all malocclusion has a multifactorial etiology, including genetic and environmental factors, with high prevalence in the general population. Epigenetics stands out as one of the most studied current branches, demonstrating that gene expression can be influenced by environmental factors. Several studies have also been carried out on pairs of monozygotic and dizygotic twins in order to demonstrate the contribution of genetics to the development of dentition and occlusion. In relation to the development of supernumerary teeth, some studies claim that their etiology is not yet fully elucidated, but they believe that they can be transmitted as an autosomal dominant trait lacking penetrance in some generations. Corroborating with this thinking, results from recent studies attempt to elucidate some genes that may be directly related to the development of this anomaly.

In the present study, both monozygotic twins presented a number anomaly with the presence of unilateral mesiodens on the palate, emphasizing the great anatomical similarity between the supernumerary ones, both with root dilaceration. These findings corroborate with studies that demonstrate the genetic influence on the dental development pattern. Thus, on the affected side, in the cases reported in this article, the sisters presented the supernumerary on the left side, differing from other studies that reported the presence of unilateral mesiodens on opposite sides of each monozygotic twin, such as mirror images.

It is known that the presence of environmental factors leads to a break in the equilibrium relationship between the bony bases, the teeth, and the musculature, favoring the development of malocclusions. Among the functional conditions acquired, the sucking habit appears as one of the leading causes of various types of malocclusions. In the present report, only one of the twins developed an anterior open bite type malocclusion, with only the parafunctional finger suction habit, thus demonstrating that even in cases in which patients have the same genetic load, there is a strong influence of epigenetic and environmental factors on the development of malocclusion. It is also important to note that although one of the twins had a sucking habit for a total of 14 years, the open bite developed by the twin was mild. We can, therefore, suggest that the patient has a favorable growth pattern - which is determined genetically - because, despite the duration, frequency, and intensity of the habit, it did not develop a severe malocclusion. This finding corroborates some previous studies in which the
authors state that the differences between monozygotic twins depend on the influence of epigenetic and environmental factors.2,14,15

In both patients, the mesiodens was partially erupted by palatine, without damaging the occlusion of the mesiodens, with the central incisors erupted and aligned. This result disagrees with the studies of Gunduz et al.11 (2008) and Colak et al.26 (2013) in which there was a higher prevalence of mesiodens impacted when compared to those erupted. Also, other studies have demonstrated that in the majority of cases the presence of mesiodens impairs the correct eruption of the upper incisors and also their alignment in the arch.6,8,11,12 Regarding the proposed treatments, the literature demonstrates that the extraction of mesiodens should be performed at an appropriate time, usually at the beginning of the mixed dentition, to avoid the possible complications related to its presence, thus minimizing the need for orthodontic treatment and complexity of surgical management.6,8,11 In the cases reported in the present study, the diagnosis and removal of the mesiodens were performed in permanent dentition, without any complications during the supernumerary surgical removal.

The anterior open bite has a multifactorial etiology, which may be of skeletal or dental origin, and is often associated with the presence of parafunctional habits.20 Some alternatives for the treatment of this malocclusion are described in the literature, among them: habit-preventing devices, fixed apparatus, mini-implants, mini-plates and surgical correction.27,28 However, an adequate diagnosis and treatment plan are needed before deciding on the best approach. Regarding the use of the fixed palatine grille for the treatment of anterior open bite, the present report is in agreement with previous studies, which opted for the same treatment, being successful at the end of the therapy.29,30

4. CONCLUSION

Although the genetic studies are still few regarding the genes related to the appearance of the mesiodens, the reports with homozygous twins verify the genetic imprint involved in the development of those.

Our findings show that any differences observed in pairs of monozygotic twins in the development of malocclusions are associated with an interaction between genetic, epigenetic and environmental factors. Thus, the diagnosis and treatment of malocclusion should be individualized for each patient.
REFERENCES

1 Thomaz EBAF, Valença AMG. Prevalência de má-oclusão e fatores relacionados à sua ocorrência em pré-escolares da cidade de São Luís – MA – Brasil. RPG Rev Pós Grad. 2005;12(2):212-21.

2 Almeida RR, Almeida-Pedrin RR, Almeida MR, Garib DG, Almeida PCMR, Pinzan A. Prevalência das más oclusões: características hereditárias e congênitas, adquiridas, gerais, locais e proximais (hábitos bucais). Rev Dental Press Ortod Ortop Facial. 2000;5(6):107-29.

3 Almeida MR, Pereira ALP, Almeida RR, Almeida--Pedrin RR, Silva Filho OG. Prevalência de má oclusão em crianças de 7 a 12 anos de idade. Dental Press J Orthod. 2011 July-Aug;16(4):123-31.

4 Huh A, Horton MJ, Cuenco KT, Raoul G, Rowlerson AM, Ferri J, et al. Epigenetic influence of KAT6B and HDAC4 in the development of skeletal malocclusion. Am J Orthod Dentofacial Orthop. 2013 Oct;144(4):568-76.

5 Mas C, Frapier L. A genetic heritage; the same yet different: A comparative study in twins. International Orthodontics. 2017;15(3):483-497.

6 Rocha SCC, Vidigal BL, Pereira AC, Fonseca MS, Manzi FR. Etiologia, Diagnóstico e Tratamento do Mesiodens – Relato de Caso Clínico Atípico. Arq Bras Odontol. 2012;8(2):49-54.

7 Nunes KM, Medeiros MV, Ceretta LB, Simões PW, Azambuja FG, Sônego FGF, Pires, PDS. Dente supranumerário: revisão bibliográfica e relato de caso Clínico. Rev Odontol Univ Cid São Paulo. 2015 Jan-Apr;27(1):72-81.

8 Russell KA, Folwarczna MA. Mesiodens—diagnosis and management of a common supernumerary tooth. J Can Dent Assoc. 2003;69(6):362–366.

9 Gurgel CV, Cota ALS, Kobayashi TY, Silva SMB, Machado MAAM, Rios D, et al. Bilateral Mesiodens in Monozygotic Twins: 3D Diagnostic and Management. Case Rep Dent. 2013;2013.
10 Kim YY, Hwang J, Kim HS, Kwon HJ, Kim S, Lee JH, Lee JH. Genetic alterations in mesiodens as revealed by targeted NGS and gene co-occurrence network analysis. Oral Dis. 2017 Oct;23(7):966-972.

11 Gunduz, K., Celenk, P., Zengin, Z. & Sumer, P. 2008. Mesiodens: a radiographic study in children. J Oral Sci. 2008;50(3):287-91.

12 Seddon RP, Johnstone SC, Smith PB. Mesiodentes in twins: a case report and a review of the literature. Int J Paediatr Dent. 1997;7(3):177–184.

13 Cassetta M, Altieri F, Giordano A. Mirror imaging of impacted and supernumerary teeth in dizygotic twins: A case report. J Clin Exp Dent. 2015 Feb;7(1):e167–e169.

14 Townsend G, Hughes T, Luciano M, Brook A. Genetic and environmental influences on human dental variation: limitations and advantages of studies involving twins. Arch Oral Biol. 2009;54:S45–51.

15 Townsend G, Bockmann M, Hughes T, Brook A. Genetic, environmental and epigenetic influences on variation in human tooth number, size and shape. Odontology. 2012;100:1–9.

16 Hughes T, Bockmann M, Mihailidis S, Bennett C, Harris A, Seow WK, et al. Genetic, epigenetic, and environmental influences on dentofacial structures and oral health: ongoing studies of Australian twins and their families. Twin Res Hum Genet. 2013 Feb;16(1):43-51.

17 Cabrera CAG, Enlow DH. Crescimento e desenvolvimento craniofacial. In: Cabrera CAG, Cabrera MC. Ortodontia clínica. Curitiba: produções interativas, 1997; cap. 1, p 1-41.

18 Weber DM, Vares MA, Mota HB, Keske-Soares M. Desenvolvimento do sistema fonológico de gêmeos monozigóticos com desvio fonológico: correlação a fatores genéticos e ambientais. Rev CEFAC. 2007 Jan-Mar;9(1):32-39.

19 Lopes-Freire GM, Cárdenas ABC, Deza JEES, Ustrell-Torrent JM, Oliveira LB, Quesada Jr JRR. Exploring the association between feeding habits, non-nutritive sucking habits, and malocclusions in the deciduous dentition. Prog Orthod. 2015 Dec;16(43):1-7.

20 Reichert I, Figel P, Winchester L. Orthodontic treatment of anterior open bite: a review article—is surgery always necessary? Oral Maxillofac Surg. 2014 Sep;18(3):271-277.
21 Souza BS, Bichara LM, Guerreiro JF, Quintão CC, Normando D. Occlusal and facial features in Amazon indigenous: An insight into the role of genetics and environment in the etiology dental malocclusion. Arch Oral Biol. 2015 Sep;60(9):1177-86.

22 Consolaro A, Cardoso MA, Consolaro RB. "Maxillary lateral incisor partial anodontia sequence": a clinical entity with epigenetic origin. Dental Press J Orthod. 2017 Nov-Dec;22(6):28-34.

23 Odeh R, Townsend G, Mihailidis S, Lahdemaski R, Hughes T, Brook A. Infraocclusion: Dental development and associated dental variations in singletons and twins. Archives of oral biology. 2015;60:1394-1402.

24 Lei HH, Liu H, GE LH. PAX6 polymorphisms in 20 Chinese children with supernumerary teeth in the maxillary incisor area. Int J Paediatr Dent. 2011;21:271-7.

25 Carton A, Rees RT. Mirror image dental anomalies in identical twins. Br Dent J. 1987;162:193-94.

26 Colak H, Uzgur R, Tan E, Hamidi MM, Turkal M, Colak T. Investigation of prevalence and characteristics of mesiodens in a non-syndromic 11256 dental outpatients. Eur Rev Med Pharmacol Sci. 2013 Oct;17(19):2684-9.

27 Matsumoto MA, Romano FL, Ferreira JT, Valério RA. Open bite: diagnosis, treatment and stability. Braz Dent J. 2012;23(6):768-78.

28 Al Hamadi W, Saleh F, Kaddouha M. Orthodontic Treatment Timing and Modalities in Anterior Open Bite: Case Series Study. Open Dent J. 2017 Nov;11:581-594.

29 Slaviero T, Fernandes TM, Oltramari-Navarro PV, de Castro AC, Conti F, Poleti ML, Almeida MR. Dimensional changes of dental arches produced by fixed and removable palatal cribs: A prospective, randomized, controlled study. Angle Orthod. 2017 Mar;87(2):215-222.

30 Rossato PH, Fernandes TMF, Urnau FDA, de Castro AC, Conti F, de Almeida RR, Oltramari-Navarro PVP. Dentoalveolar effects produced by different appliances on early treatment of anterior open bite: A randomized clinical trial. Angle Orthod. 2018 Nov;88(6):684-691.
ATTACHMENTS

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Figure 3: Fixed palatine grid installation in a patient with anterior open bite. A) front view; B) right lateral; C) left lateral; D) occlusal view.

Figure 4: Mesiodens of both twins after surgical removal.
Figure 5: 5-month follow-up after the palatine grid installation. A) front view; B) right lateral; C) left lateral.