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Genetic Implications in Class II Subdivision 2 Malocclusion in Two Siblings. Case Report

Medical Science

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ABSTRACT

The aim of this study was to find genetic implication in the etiology of Class II subdivision 2 malocclusion using single nucleotide polymorphism as genetic marker in two siblings with Class II subdivision 2 malocclusion, starting from the literature's opinions regarding the inherited patterns of this anomaly. Clinical aspects knowing as being hereditary were found out after the extra oral, intraoral and radiological examination. Genomic DNA was also extracted from the buccal mucosa of the two siblings in order to determine their genotype. Four markers were selected from each patient, MyoH1, VDR, PAX9 and RUNX2. Genetic association was found between single nucleotide polymorphism and this malocclusion for PAX9 gene. Even though genetic analyze demonstrated the hereditary etiology of the Class II subdivision 2 malocclusion, some clinical features were different in the two siblings.

INTRODUCTION

Craniofacial structures are developed from complex processes of tissue interactions, cell migrations, and coordinated growth (Kouskoura et al., 2011; Nieminen et al., 2011). Among the 5500 inherited diseases known in humans, more than 700 are craniofacial anomalies, but only in 20% of them the genetic determinism was proofed. (National Institute of Dental and Craniofacial Research Genetics Workgroup, 1999).

Class II subdivision 2 anomaly is relatively rare and comprises 1.5% to 7% of all malocclusions found in white western population. (Steigman, Kawar & Zilberman, 1983), affecting especially the womens. (Hartsfield Jr., Morford & Otero, 2012)

It consists of a unique combination of deep overbite, retroclined incisors, Class II skeletal discrepancy, high lip line with strap-like activity of the lower lip, and active mentalis muscle. This is often accompanied by particular morphometric dental features also, such as a poorly developed cingulum on the upper incisors and a characteristic crown root angulation. There is strong evidence for genetics as the main etiological factor in the development of Class II division 2 malocclusions, in some authors opinions. (Mossey, 1999) Other, like Ruf and Pancherz (1999) considered the etiology of this malocclusion being unclear, or a combination between genetic and environmental factors. Orthodontic treatment of this anomaly, but especially the long term stability of the results, can be difficult because of its genetic determinism.

AIM

The aim of this study was to demonstrate the genes implication in the etiology of Class II subdivision 2 malocclusion in two siblings.

MATERIAL AND METHOD

Two siblings with Class II subdivision 2 malocclusion, one brother, 11 years old and his sister, 17 years old were selected. Clinical and radiological examination was performed and inherited patterns were registered. Also genomic DNA was extracted from the buccal mucosa using Animal and Fungi DNA Preparation Kit (Jena BioScience). Gene fragments (Myo1H, VDR, PAX9 and RUNX2) were amplified with Polymerase Chain Reaction.

RESULTS

Case 1 – 11 years old –Class II/2. His genotype distribution was: GG for Myo1H, AA for PAX9, CT for RUNX2 and TT for VDR. (A and T are the mutant allele genes).

Figure1: Facial profile



The patient shows a class II profile with slightly retruded mandible and increased nasal-labial angle. (fig.1)

Figure 2: Dental arches





The upper arch is narrow with palatally displaced small lateral incisors and ectopic erupting canines. The frontal teeth are retruded and crowded. Lower arch shows only slight malposition of the incisors and persistence of temporary second molars. (fig.2)

Figure 3: Occlusal relationships



The patient has half cusp, class II occlusal relationships im molar and canines, deep - bite and reversed bite in 2.2. (fig.3)

Figure 4: Cephalometry



The cephalometric examination shows skeletal class II of 6 mm, retrusion in upper and lower incisors, tendency toward posterior rotation of the mandible. The upper and especially the lower lip are thick. (fig.4)

The patient underwent orthodontic treatment with fixed appliance. (fig.5)

Figure 5: Post - treatment profile and occlusion



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Case 2 CA – 14 years old – the sister of the first patient, with the same malocclusion. Her genotype distribution was: GG for MyoH1, AG for PAX9, CT for RUNX2 and TT for VDR.

Figure 6: Facial profile



She shows almost the same profile like her brother, but more typical for Class II/2 compared with him (decreased lower face height, prominent chin and nose, tendency to concave profile). (fig.6)

Figure 7: Dental arches



The maxilla is narrow with retruded and crowded upper incisors. Lower incisors are over erupted that increseases the curve of Spee. (fig.7)

Figure 8: Occlusal relationships



There is half cusp class II in one side and false class I on the other side, deep-bite and midline shifted to the left with 2 mm. (fig.8)

Figure 9 : Cephalometry



In cephalometry she was skeletal class II of 5 mm with slightly retruded upper incisors and protruded lower incisors, mandibular anterior rotation, thick lips and thick soft chin . (fig.9)

Orthodontic treatment was carried out using fixed appliance. (fig.10)

Figure 10: Post-treatment profile and occlusion



DISCUSSION

The controversy regarding the etiology of the Class II division 2 malocclusion arises from a failure to appreciate the synergistic effects of genetics and environment on facial morphology. Familial occurrence of Class II division 2 has been documented for a long time in several published reports including twin and triplet studies (Kloeppel, 1953; Markovic, 1992) and in family pedigrees from Korkhaus and Rubbrecht (1930) and Peck *et al.* (1998). Many studies point to incontestable genetic influence in Class II subdivision 2 (Graber, 1972; Markovic, 1992) probably autosomal dominant with incomplete penetrance and variable expressivity. This anomaly could also be explained by a polygenic model with a simultaneous expression of a number of genetically determined morphological traits, rather than being the effect of a single controlling gene. (Mossey, 1999)

Further evidence for a polygenic complex etiology for Class II/2 was found in the studies of Basdra et al. (2000) which showed that 13.9% of Class II/2 subjects had agenesis of maxillary lateral incisors and 7.5% had peg-shaped or small maxillary lateral incisors. In contrast, Morrison (2008) found none of the probands had agenesis of/or small maxillary lateral incisors, although first-degree relatives of the Class II/2 probands showed similar frequencies of hypodontia and microdontia .

A step forward in the genetic polymorphism assessment was made when DNA markers (single nucleotide polymorphisms) in genes associated with dental development. MSX1, PAX9, AXIN2, RUNX2 and RUNX3 were investigated in Class II/2 Caucasian subjects by Morford et al. (2010) Borderline-association of all Class II/2 subjects with the PAX9 was identified (p=0.06). There was a significant association (p=0.0286) for Class II/2 subjects and the RUNX2. Genetic analyze in our cases found identical genotypes for all these genes except the PAX9 where the genotype is AA in brother and AG in sister. Both had the mutant allele gene, A.

Clinical examination of the two siblings revealed class II profile, with retruded chin in male and concave, typical class II/2 profile with prominent chin and thick lower lip, in female. Thicker upper and lower lips were found in Class II division 2 patients compared to Class I controls in the study of McIntyre and Millett (2006). In addition, the Class II division 2 subjects had greater lower lip contact and thus increased resting pressure on the maxillary incisors than the controls. This could be a causal effect in producing maxillary incisor retrusion and can be a concern with post-treatment stability (Lapatki et al., 2007 ; McIntyre & Millett, 2006). In opinion of Howe (2012), the position, morphology and behavior of the lower lip are genetically determined or influenced.

Intraoral examination of our cases showed inherited characters present in both siblings like narrow maxilla, poorly developed cingulum of the upper incisors and small upper lateral incisors, especially in the male patient. The reduced mesio-distal mean dimension of the maxillary lateral incisor in the group in which retroclination involved all maxillary incisors can be justified by the high prevalence of congenital microdontic lateral incisors found in Class II subdivision 2 anomaly. (Pereira et al., 2013)

Another inherited feature of the Class II division 2 syndrome is the tendency to a forwardly rotating mandibular development, which contributes to the deep bite, chin prominence, and reduced lower face height. This last feature, in turn, has an influence in the position of the lower lip relative to the upper incisors, and an increase in masticatory muscle force. (Quinn & Yoshikawa, 1985). Cephalometric examination in our cases found this characteristic Class II/2 pattern only in female.

The inherited Class II/2 soft tissue patterns were strongly in sister than in brother while the genetic dental features were more accentuated in male. Also the rotation of the mandible was different.

After the treatment it can be seen that the dental arches were completely aligned and the occlusion was completely corrected in both siblings. In male posterior rotation of the mandible was changed by the orthodontic treatment so the facial profile was improved through mandibular advancement. In female, some concavity of the profile still persisted at the end of treatment, probably because the genetic involvement was stronger in soft tissue characteristics than in teeth position in her case. Attention must be paid for the future stability of this case as long as soft tissues did not follow in the same manner the changes in teeth position. The identification of genetic influences in Class II malocclusion can aid in the prevention and improve treatment modalities. (Ionescu et al., 2008)

CONCLUSIONS

Even though genetic analyze demonstrated the hereditary etiology of the Class II subdivision 2 malocclusion, some clinical features were different in the two siblings. The inherited soft tissue patterns were stronger in female compared with his brother; in consequence, post-treatment changes in facial aspect were different. Future studies, on larger groups of Class II subdivision 2 patients are necessary to investigate the association between genetic polymorphism and this anomaly.

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REFERENCE

[1]Basdra, E.K., Kiokpasoglou, M. & Stellzig, A. (2000). The Class II Division 2 craniofacial type is associated with numerous congenital tooth anomalies. European journal of orthodontics, 22(5), 529-535. | [2]Graber, T. M. (1972). Orthodontics—Principles and Practice (ed. T. M. Graber) p. 46, Philadelphia, PA: W B Saunders Co. | [3]Ionescu, E., Teodorescu, E., Badarau, A., Grigore, R., & Popa, M. (2008). Prevention perspective in orthodontics and dento-facial orthopedics. Journal of Medicine and Life, 1(4), 397- 402. | [4]Kloeppel, W. (1953). Deckbiss bei Zwillingen. Fortschr Kieferorthop, 14(2), 130–135. | [5]Korkhaus, G. (1930). Investigations into the inheritance of orthodontic malformations. Dental Record, 50, p. 271–280. | [6]Kouskoura, T., Fragou, N., Alexiou, M., John, N., Sommer, L., Graf, D., et al. (2011).The genetic basis of craniofacial and dental abnormalities. Schweizer Monatsschrift Fur Zahnmedizin / SSO, 121(7-8), 636-646. | [7]Hartsfield, J.K.Jr., Morford, L.A. & Otero, L.M. (2012). Genetic Factors Affecting Facial Growth. In Bourzguil, F. (Eds.) Orthodontics - Basic Aspects and Clinical Considerations (pp 125-154). Janeza Trdine, Croatia: InTech. | [8]Howe, S.C. (2012) Phenotypic characterization of Class II malocclusion. (Master of Science thesis), University of Iowa. | [9]Lander, ES. (2001). International Human Genome Sequencing Consortium et al., Nature, p. 409, 860, 921. | [10]Lapatki, B. G., Klatt, A., Schulte-Monting, J. & Jonas, I. E. (2007). Dentofacial parameters explaining variability in retroclination of the maxillary central incisors. Journal of Orofacial Orthopedics, 68(2), 109-123. | [11]Markovic, M. D. (1992). At the cross-roads of orofacial genetics. European Journal of Orthodontics, 14, 469–481. | [12]McIntyre, G. T., & Millett, D. T. (2006). Lip shape and position in class II division 2malocclusion. The Angle Orthodontist, 76(5), 739-744. | [13]Morrison, M.W. (2008). Relative Risk of Class II division 2 Malocclusion in First-Degree Relatives of Probands with Class II division 2 Malocclusion. Master of Science in Dentistry degree Department of Orthodontics and Oral Facial Genetics. Indiana University School of Dentistry. | [14]Mossey, P. A. (1999). The heritability of malocclusion: Part 1- Genetics, principles and terminology. British Journal of Orthodontics, 26(2), 103-113. | [15]Mossey, P. A. (1999). The heritability of malocclusion: Part 2 - The influence of genetics in malocclusion. British Journal of Orthodontics, 26(3), 195-203. | [16]National Institute of Dental and Craniofacial Research. (1999). Genetics and craniofacial and dental anomalies: report of the National Institute of Dental and Craniofacial Research Genetics Workgroup. www.nidcr.nih.gov/NewsAndReports/Reports Presentation/default.htm. 2008. | [17]Nieminen, P., Morgan, N. V., Fenwick, A. L., Parmanen, S., Veistinen, L., Mikkola, M.L., et al. (2011). Inactivation of IL11 signaling causes craniosynostosis, delayed tooth eruption, and supernumerary teeth. American Journal of Human Genetics, 89(1), 67-81. | [18]Peck, S., Peck, L. & Kataja, M. (1998). Class II Division 2 malocclusion: a heritable pattern. The Angle Orthodontist, 68, 9–17. | [19]Pedro, M.P., Perreira, A.P., Tavares, P. & Braga, A.C. (2013). 3 Different manifestations of Class II Division 2 incisor retroclination: A morphologic study. Am J Orthod Dentofac Orthop 143, 310-315. | [20]Quinn, R.S.& Yoshikawa, D.K. (1985). A reassessment of force magnitude in orthodontics. Am J Orthod, 88, 252-260. | [21]Rubbrecht, O. (1930). Les variations maxillo-faciale sagittales et l'hérédité mendélienne. Revue Belge Stomat, 27, 1–24, 61–91, 119–153. | [22]Ruf, S. & Pancherz, H. (1999). Class II division 2 malocclusion: Genetics or environment? A case report of monozygotic twins. The Angle Orthodontist, 69(4), 321-324. | [23]Steigman, S., Kawar, M. & Zilberman, Y. (1983). Prevalence and severity of malocclusion in Israeli Arab urban children 13 to 15 years of age. Am J Orthod. 84, 337–343. | [24]Zilberman, Y., Cohen, B. and Becker, A. (1990). Familial trends in palatal canines, anomalous lateral incisors, and related phenomena. European Journal of Orthodontics, 12, 135–139. |