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Case Report

Discordant tooth agenesis and peg-shaped in a pair of monozygotic twins: Clinical and molecular study

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ABSTRACT

The present report aimed to study an uncommon case of a pair of twins that presented a discordant dental phenotype. Family investigation, clinical, radiographic examination and molecular analysis were performed in both girls. Molecular analysis confirmed the monozygosity by deoxyribonucleic acid chip technology. One twin presented tooth agenesis in left upper lateral incisor and peg-shaped on the contra lateral side while the other twin had no dental alterations. The dental casts study employed digital caliper to compare morphological dimensions and showed alteration only in peg-shaped tooth. In conclusion, this study provide support that one or more mutated gene could cause discordances in dental phenotype in these monozygotic twins.

Key Words: Dental anomalies, dental development, monozygotic twins, tooth agenesis

INTRODUCTION

Tooth agenesis and small peg-shaped constitutes common developmental abnormalities in human. Tooth agenesis is defined as congenital absence of one or a few permanent teeth without any systemic disorders and the prevalence varies from 2.6% to 11.3% (excluding third molars). Peg-shaped is defined as a developmental alteration in dental shape, which incisal mesio-distal width of the tooth crown is narrower than the cervical.[1] Its prevalence varied from 0.8% to 2.3%.[1,2] Upper lateral incisor agenesis is commonly associated to a peg-shaped in the contralateral.[3-6] A previous study suggested that tooth agenesis and peg-shaped or strongly mesio-distally reduced upper lateral incisors could share the same genetic background.[7]

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The etiology of tooth alterations in human is still unclear and has been the subject of numerous investigations to determine the patterns of development of different teeth, associations within and between the dental alterations and the relative degrees of influence of genetic and environmental factors.[8-10]

Tooth development may fail due to both environmental and genetic factors. Irradiation and chemotherapeutic agents[11] can arrest tooth development. However, most developmental dental failure are caused by genetic factors.[12] Severe forms of tooth agenesis (oligodontia) have been linked to mutations or deletions in msh homeobox 1, paired box 9, axin2, bone morphogenetic protein 4 and transforming growth factor beta 3.[9,13-15] Familial clustering and higher concordance in monozygotic (MZ) than in dizygotic twins also show the importance of genetic factors.[16]

The present case report aimed to study an uncommon case of MZ twins, confirmed by deoxyribonucleic acid (DNA) chip technology, which showed a discordant dental phenotype in primary and permanent dentition.

CASE REPORT

MZ twins Caucasian girls were examined in a Pediatric Dental Clinic at age 11 months. During intra-oral clinical and periapical radiograph examination, the twin A (TA) revealed a congenital absence of left primary upper lateral incisor [Figure 1a] and the twin B (TB) had all the primary incisors. Clinical examination of others tissues of ectodermal origin was also carried out and showed no abnormalities.

During the anamnesis, the mother reported no previous history of dental anomalies and/or others congenital alterations on neither side of the family. According to maternal reports, the twins share the same placenta, being MZ (identical), monochorionic. The mother reported no history of tabagism, smoking and alcohol exposure during pregnancy. The twins were born prematurely (28 weeks). They did not need any special care. The TA was born first, weighing 1.630 kg. The TB, weighing 1.450 kg was born 3 min later.

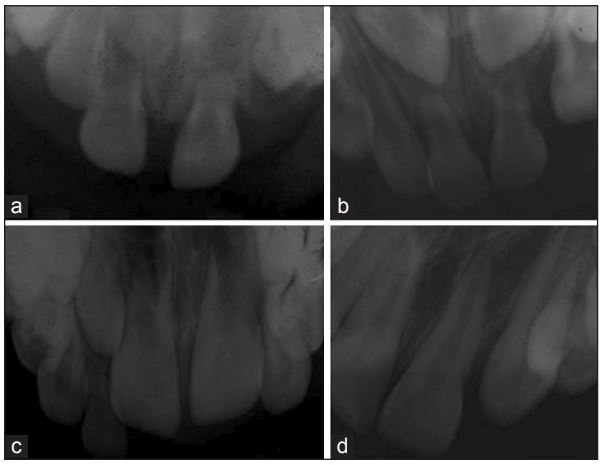

Figure 1: Dental development in twin A (a = 11 months of age; b = 3 years of age; c = 7 years of age; d = 9 years of age)

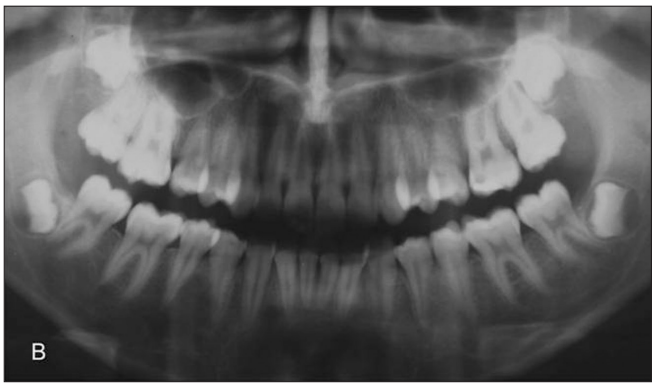

Figure 3: The panoramic radiograph of twin B at 12 years of age

Patients had follow-up twice a year and the dental development was clinically and radiographically observed [Figure 1b-d].

By the age 12 years, an orthopantomography confirmed that the left upper permanent lateral incisor was also absent and the right permanent upper lateral incisor was peg-shaped in the TA while TB had normal shaped permanent dentition [Figures 2 and 3].

The treatment of TA demands a multidisciplinary approach since it causes poor esthetics and functional problems. The peg-shaped tooth was restored with composite resin. A prosthetic treatment using the esthetic space maintenance was carried out to the absent lateral. An implant procedure will be carried out in the future [Figures 4 and 5]. Patients are still being attended in regular visits.

Molecular analysis for monozigotic confirmation

Genomic DNA of TA and TB were isolated from buccal epithelial cells following established protocol.[17] The DNA extraction was achieved by

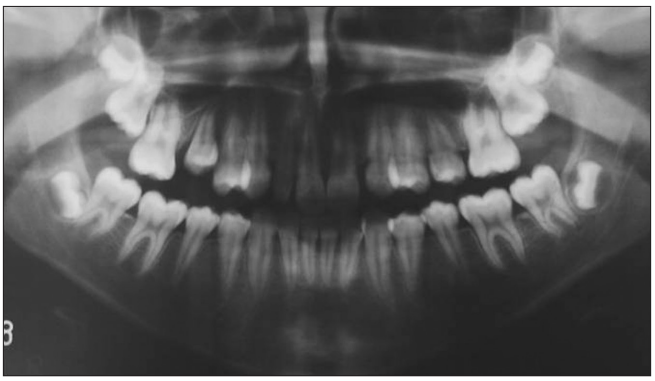

Figure 2: The panoramic radiograph of twin A at 12 years of age

Figure 4: Intra-oral pictures after peg-shaped upper lateral incisor restoration and prosthetic treatment of the twin A

Figure 5: Intra-oral pictures of twin B

salting out the cellular proteins by dehydration and precipitation with a saturated ammonium acetate solution. Polymerase chain reaction amplified the purified DNA sample from both twins that presented a 260/280 ratio higher than 1.8.

Monozigotic was evaluated by comparisons of markers in the blood (ABO, Rh), together with several DNA variations. We used the Affymetrix GeneChip® Human Mapping 500K Array Set provides consistently high coverage across different populations. It is comprised of two arrays, each capable of genotyping on average 250,000 SNPs (approximately 262,000 for Nsp arrays and 238,000 for Sty arrays). After that, we were able to verify that both girls presented strong similarities that confirmed the monozigosity.

Study dental casts analysis

At 12 years old, dental casts were obtained from irreversible hydrocolloid impressions. This investigation (Dental Casts Analysis) was undertaken to compare morphological aspects and mesio-distal and vestibulo-lingual crown dimensions of the permanent dentition in TA and TB. An electronic digital caliper was used to record the maximum dimension. Based on dental features, except for the upper lateral incisors, there were no differences in the crown diameters of the two twins.

DISCUSSION

MZ share similar DNA sequences; however, they are often discordant for some phenotypes.[18-20] These discordances in MZ twins are of great interest to the human genetics research, which wishes to gain further insight into the complexities of genetic-environmental interaction in development.

In fact, tooth agenesis and peg-shaped seem to have a genetic determination. Dental anomalies may represent a complex multifactorial trait, influenced by a combination of gene function, environmental factors and developmental timing.[9]

Environmental factors involved with tooth agenesis have been revised by Pemberton *et al*.,[21] that highlight some factors such as jaw fractures, surgical procedures, extraction of the preceding primary tooth, chemotherapy, irradiation, thalidomide during mother's pregnancy, nutrient deprivation and serious illness. In our case report, the etiology of tooth agenesis could not be clearly associated with any of these environmental factors. Townsend *et al*.[22] displayed discordance for agenesis of permanent maxillary lateral incisor in five pair of MZ twins and suggested a possible link with disparate birth weights of the twins. However, we do not suggest this relationship since the twin with the lower birth weight (TB) had all the teeth formed. It was expected that the twin who was born with lower weight had the absence of the missing tooth to prove the relationship between birth weight and agenesis.

Assuming that genetic information is identical for each MZ twin, differences between them can be interpreted as a consequence of environmental factors. It is possible that epigenetic events may be responsible for discordant expression in genetically identical individuals. However, during pregnancy, the mother is the environment of the children,[23] so this pair of twins were exposed to the same environmental factors.

We can propose that differences between MZ twins could be a consequence of gene mutation. In addition, the fact that the same individual (TA), with no known family history for dental anomaly, was affected by both tooth agenesis and peg-shaped suggested that the same mutated gene could cause both anomalies. The inheritance pattern of tooth agenesis and peg-shaped upper lateral incisors demonstrated that they are different expressions of one gene with reduced penetrance.[7]

Tooth agenesis is a complex condition affecting several parameters of oral development that may include the association of reducing in dental crown size dimension.[24] In addition, in the dental casts analysis, we were able to note that only upper lateral incisor group were affected in TA and there was not

differences between the others teeth dimensions. This finding reflected the possibility that different types of teeth may have independent developmental mechanisms and different genetic factors may be involved. In this case, a mutated gene probably affected only upper lateral incisor.

Contrary to previous beliefs, nowadays, it is assumed that MZ twins are not genetically identical. Previous studies have induced a paradigm shift to twin research, focusing on the genetic or epigenetic difference between MZ discordant twins.[25-27] Townsend *et al*. (2005)[27] studied dental alterations in MZ twins and reinforce the point that using the term "identical" when referring to "MZ" twin pairs can be misleading. We believe that a widely molecular investigation in MZ twins with dental phenotype discordances are needed to allow the determination of genes involved with dental alterations.

CONCLUSION

The clinicians need to recognize that MZ twins may have different clinical characteristics, becoming of great importance the early diagnosis and implementation of appropriate treatment and monitoring, as performed in this case, minimizing the problems that can cause such a difference to the esthetic, functional and psychological aspects.

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