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Dokuzuncu Kromozomun Perisentrik İnversiyonuna Bağlı Ailesel Non-Sendromik Oligodonti*

Familial Non-Syndromic Oligodontia Attributable to Pericentric Inversion of Ninth Chromosome

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Öz

Non-sendromik oligodonti, herhangi bir sendromun eşlik etmediği, üçüncü azı dişleri hariç, altı veya daha fazla dişin konjenital eksikliği olarak tanımlanır. Etiyolojisinin, kalıtsal ve çevresel faktörlere bağlı olduğuna inanılmakla birlikte bu konu henüz aydınlatılamamıştır.

Ailesel sendromik olmayan oligodontinin ayırıcı tanısı için dental muayene ile birlikte klinik testler ve aile görüşmesi ve genetik danışmanlık ile G-bant karyotip analizi yapıldı. Klinik ve genetik bulgular, 18 yaşındaki erkek hastanın, dokuzuncu kromozomunun perisentrik inversiyonu anlamına gelen 46, XY, inv (9)(p21,q31) karyotipi ile ailesel non-sendromik oligodontiden etkilendiğini gösterdi.

Bu çalışmada, daha önce ailesel non-sendromik oligodonti ile korelasyon göstermeyen ve özel bir karyotipe sahip inv(9)(p21,q31) nadir bir heteromorfizm olan özel ailesel sendromik olmayan oligodontili bir bireyi bildiriyoruz.

Anahtar sözcükler: otozomal dominant kalıtım, kromozom 9, inversiyon, oligodonti, oligodonti fenotip pedigrisi

Abstract

Non-syndromic oligodontia is defined as the congenital lack of six or more teeth, excluding the third molars without any accompanying syndrome. Its etiology is believed to be rooted in hereditary and environmental factors however, not resolved yet.

Dental examinations with clinical tests for differential diagnosis of familial non-syndromic oligodontia and G-banding karyotype analysis with family interview and genetic counseling were done. Clinical and genetic findings revealed that a 18-year-old male patient was suffering from familial non-syndromic oligodontia with 46,XY,inv(9)(p21,q31) karyotype which means pericentric inversion of ninth chromosome.

Here we report an individual who has familial non-syndromic oligodontia with a special karyotype of inv(9)(p21,q31) of which is a rare heteromorphism with no previously correlation to familial non-syndromic oligodontia.

Keywords: *autosomal dominant inheritance, chromosome 9, inversion, oligodontia, pedigree of oligodontia phenotype*

Introduction

Agenesis of one or more teeth is one of the most common anomalies in permanent dentition. Hypodontia describes the agenesis of one or a few teeth; oligodontia is a severe and rare form of tooth agenesis involving six or more congenitally missing teeth, excluding the third molars.[1] A prevalence of 0.16% has been reported for oligodontia.[2] The mandibular second premolar is the most frequently missing tooth after the third molar, followed by the maxillary lateral incisor and the maxillary second premolar. Agenesis of maxillary central incisors, canines or first permanent molars seems to be rather exceptional.[3]

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Hypodontia and oligodontia are classified into two subgroups: non-syndromic (isolated) and syndromic. Non-syndromic hypodontia/oligodontia are generally not accompanied by another syndrome and are observed to be more common than syndromic hypodontia/oligodontia.[4] The most characteristic dental symptoms for non-syndromic hypodontia/oligodontia are a reduced number of teeth, a reduction in tooth size, anomalies of tooth form and delayed eruption.[5] On the other hand, syndromic hypodontia/oligodontia are usually accompanied by additional abnormalities like cleft lip/palate or syndromes like ectodermal dysplasia, Down syndrome, Rieger syndrome and Van der Woude syndrome.[4]

Etiopathogenesis of hypodontia/oligodontia is yet unknown. Previous studies show that congenital tooth absence may be related to multifactorial contributors like environmental, nutritional, traumatic, infectious, and hereditary influences.[6] However, familial tooth agenesis is reported to be inherited in various patterns like autosomal dominant, autosomal recessive and X-linked conditions.[7]

In familial non-syndromic oligodontia, although several mutations in two transcription factor coding genes, MSX1 and PAX9, and Wnt signal receptor AXIN 2 were blamed for the phenotype.[8] A study with a cohort of 79-Belgium hypodontia/oligodontia families reported that not only a simple monogenic condition but also additional genetic or environmental factors may modify the expression of the phenotype; despite familial aggregation and expected Mendelian segregation, the number of missing teeth in the familial hypodontia/oligodontia phenotypes and the tooth agenesis patterns were highly variable even between the affected same family members.[8]

In this report, we present a patient with non-syndromic oligodontia and provide his family tree. The patient's karyotype had never been associated with oligodontia in the literature.

Case Report

The diagnosis of oligodontia was first made when an orthopantograph revealed 12 congenitally missing teeth in the 18-year-old patient (Figure 1A). The patient was referred to our clinic for gingival bleeding. He was born to non-consanguineous parents through a term, vaginal birth without any birth complications. The patient had no history of trauma or extractions. An extra-oral examination revealed a normal facial profile and skeletal dental base relations. In clinical and radiographical examinations, it was clear that all the permanent first and second premolars, mandibular left lateral incisors and all first molars except the mandibular right molar were missing (Figures 1B-D).

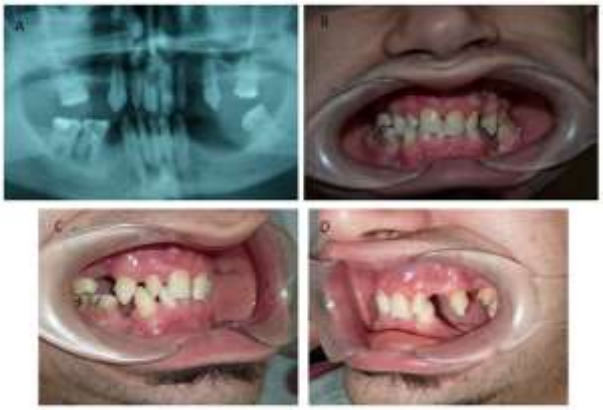

Figure 1 A, Panoramic radiograph of proband shows congenital teeth absence. **B, C and D**, Clinical aspects of oral and dental status.

Figure 2 Karyotype of the patient.

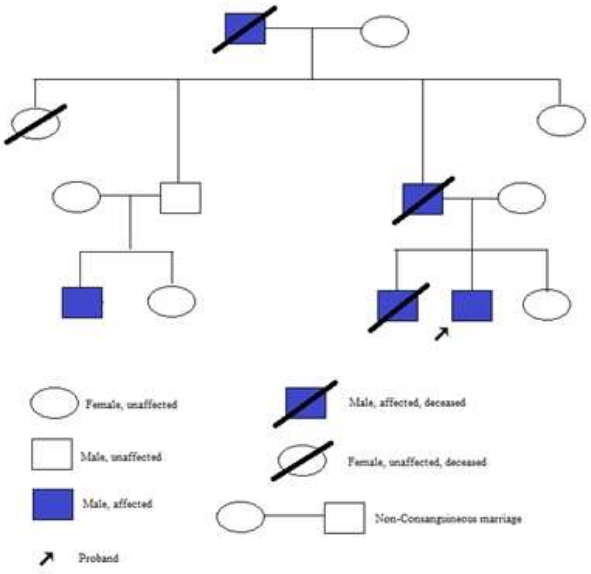

Figure 3 Pedigree of the three-generation family and oligodontia phenotypes. Pedigree showing autosomal dominant inheritance of oligodontia.

A complete set of investigations was done, which included a routine examination of blood comprising serum calcium, alkaline phosphatase, TSH, T3 and T4. The findings of these investigations were normal. His hair was normal and his nails were not brittle; also, no difficulty in perspiration was observed. These all ruled out ectodermal dysplasia. Upon ocular examination, no signs of glaucoma were seen, which eliminated Rieger syndrome. Lastly, Van der Woude syndrome was excluded, as there was no cleft palate and there were no mucosal cysts in the lower lip. The hand-wrist radiographic examination was normal. Based on the above findings, non-syndromic oligodontia was justified as the final diagnosis.

A blood sample was taken for determining the karyotype. The patient had a 46,XY,inv(9)(p21,q31) karyotype (Figure 2), which indicated that he had a pericentric inversion at the ninth chromosome. According to reports from the patient and his mother, we drew a pedigree and saw that other members of the family also exhibited tooth agenesis, such as the patient's father, cousin, grandfather and late brother (Figure 3).

The treatment plan considered for the patient primarily included scaling, root planning and polishing. The patient was referred for orthodontic treatment once the gingiva healed. After the bone and tooth discrepancies are corrected, implant placement will be considered for aesthetic and functional rehabilitation of the patient. In addition, follow-up consultations will be scheduled regularly for oral hygiene instructions.

Discussion

Familial tooth agenesis is reported to be inherited in various patterns like autosomal dominant, autosomal recessive and X-linked conditions, although variability does exist even between the affected same family members.[7,8] The patient's pedigree shows that his oligodontia may be autosomal dominantly or X-linked recessively inherited. Since we do not have karyotypes of other family members, the effect of this inversion on the oligodontia phenotype is questionable.

Pericentric inversion of the heterochromatic region of chromosome 9 (karyotype: inv(9)(p21q31)) is a rare heteromorphism. There is no known clinical significance of this specific karyotype. Recently, Wan et al.[9] reported a patient with thrombocythemia and an acquired inv(9), described as the common inv(9) heteromorphism: inv(9)(p11q13). This represented the first documented case of an acquired pericentric inversion of chromosome 9 heterochromatin. Betz et al.[10] reported two cases of acquired inv(9) chromosomes: one patient with acute myeloid leukemia, 46,XY,inv(9)(p11q13)[11]/46,XY, and a second with severe anemia, 46,XX,inv(9)(p11q13)[14]/46,XX.

Conclusion

In the present study, the chromosomal abnormality was found as 46,XY,inv(9)(p21,q31). This chromosomal anomaly may be a condition that has not been identified before in congenital tooth agenesis investigation.

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