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Patterns of non-syndromic permanent tooth agenesis in a large orthodontic population

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ABSTRACT

Objective: The aim of this study is to explore patterns of non-syndromic permanent tooth agenesis in a large orthodontic patient group.
Design: A record review was performed in various orthodontic clinics to identify white patients with non-syndromic permanent tooth agenesis, excluding 3rd molars. Four hundred and fourteen subjects fulfilled the inclusion criteria.
Results: In the 414 subjects with tooth agenesis, approximately 70% presented 1–2 missing teeth. Symmetric agenesis patterns were often observed in the sample (by jaw, by side, or crossed quadrants), with prevalence approaching 30% for cases with contralateral tooth agenesis within a jaw. In cases with 1 or 2 missing teeth, from the total number of potential tooth agenesis patterns in the sample, a certain part was evident, limiting the variation to 27.8% (44/158). In the entire sample, both in the maxilla and the mandible a certain incisor/premolar agenesis phenotype was observed in 59.0% of cases in isolated form.
Conclusions: Although there was variation in the tooth agenesis patterns, our findings suggest the involvement of particular genetic, epigenetic, and/or environmental factors in the formation of the entire dentition, which often lead to specific tooth agenesis phenotypes in cases where this process is disrupted. The present study provides a comprehensive categorization of orthodontic cases with tooth agenesis and can assist in planning future epidemiological and genetic studies.

1. Introduction

Tooth agenesis is among the most common dental anomalies in humans. The overall prevalence of tooth agenesis is 6.4% (95% CI: 5.7, 7.2) and exhibits racial, ethnic and gender differences (Khalaf, Miskelly, Voge, & Macfarlane, 2014; Polder, Van't Hof, Van der Linden, & Kuijpers-Jagtman, 2004). Females have 1.22 times higher risk of having tooth agenesis compared to males. The most commonly affected teeth in the permanent dentition seem to be the mandibular second premolars, followed by the maxillary lateral incisors and the maxillary second premolars with a varying prevalence of 1.5–3.1%. Agenesis of other teeth occurs in less than 0.1% in the general population (Khalaf et al., 2014; Polder et al., 2004).

So far, many studies have assessed the prevalence of tooth agenesis in the population and the possibility of non-formation for any tooth type (Khalaf et al., 2014; Polder et al., 2004). The severity of this condition is usually defined based on the number of missing teeth (Acharya, Jones, Moles, Gill, & Hunt, 2010; Ben-Bassat & Brin, 2009; Chan, Samman, & McMillan, 2009; Gungor & Turkkahraman, 2013). Hence, individuals with six or more missing teeth are considered to have a distinct pattern called oligodontia, individuals with less than six missing teeth are considered to have hypodontia, and in cases where all permanent teeth are missing, the condition is described as anodontia. Patients with oligodontia comprise 3.1% of patients with tooth agenesis (Khalaf et al., 2014). However, such classifications are arbitrary, since they are not based on solid scientific data. When considering the percentage of people with a certain number of missing teeth, people with one or two missing teeth comprise 83% of all individuals with missing teeth. 7% of the same population has 3 missing teeth, 6% has 4 missing teeth, while less than 1.4% of people have 5 missing teeth. The percentage decreases gradually thereafter by increasing number of missing

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teeth (Polder et al., 2004). In any case, a report of the total number of missing teeth is not an adequate description of an individual's phenotype. Similarly, the possibility for failure of formation of a single tooth, without considering the rest of the dentition, does not adequately define a certain phenotype within a population.

Tooth agenesis is also classified as syndromic or non-syndromic, based on the presence of other accompanying medical signs and symptoms (Cobourne, 2007; Vastardis, 2000). Whereas commonly missing teeth such as mandibular second premolars, maxillary lateral incisors and maxillary premolars occur often in cases with non-syndromic tooth agenesis, the absence of permanent canines, first or second molars is usually related to a generalized genetic condition (Cobourne, 2007). However, a significant contribution of various genetic factors has also been reported in non-syndromic tooth agenesis (Arzoo, Klar, Bergendal, Norderyd, & Dahl, 2014; Lammi et al., 2004; Vastardis, Karimbux, Guthua, Seidman, & Seidman, 1996). Although it is quite difficult to link certain mutations/genotypes to specific phenotypes, the identification of the various phenotypes of non-syndromic tooth agenesis on the population could facilitate patient selection for future genetic studies.

Depending on the pattern and the severity of tooth agenesis, it can have a significant impact on oral health related quality of life (Laing, Cunningham, Jones, Moles, & Gill, 2010). The successful management of the problem requires proper oral rehabilitation procedures. Patients with tooth agenesis usually require multidisciplinary treatment approaches and long-term follow-up (Kokich et al., 2011). These may include tooth size, shape and color alterations, tooth replacement and changes in tooth position through orthodontic treatment. Thus, the knowledge of tooth agenesis patterns that may be present in a population is of high clinical interest.

A recently developed numeric system for identifying patterns of missing teeth (TAC, Tooth Agenesis Code) can provide a viable solution for classification problems (van Wijk & Tan, 2006). The system assigns a binary value to each tooth providing a unique numeric value for each tooth agenesis pattern.

The comprehensive investigation of patterns of non-syndromic tooth agenesis in human populations has yet not been published in the literature. Although several studies have tested tooth agenesis patterns in patients with certain pathologies (Antonarakis & Suri, 2014), there is only one study that explored patterns of human tooth agenesis in otherwise normal patients and this focused only on severe hypodontia (>6 teeth) (Tan, van Wijk, & Prahl-Andersen, 2011). This information could be useful for treatment planning, as well as epidemiological and genetic research.

Therefore, the aim of this study was to explore all patterns of non-syndromic tooth agenesis in an otherwise normal orthodontic population.

2. Materials and methods

2.1. Study sample

To obtain the study population, orthodontic patient records from the following orthodontic clinics were accessed: a) University of Bern, Switzerland, b) University of Athens, Greece, c) two private practices in Athens and two in Thessaloniki, Greece, and d) one private practice in Biel, Switzerland. Consecutive patient files of various time periods within the last 10 years (depending on the place of sample collection) were searched for the identification of eligible subjects. Every patient included in the study was assigned a randomly generated code, and all identification information was immediately removed at the place of sample collection.

2.1.1. Inclusion criteria

- Individuals older than 9 years of age and younger than 40 years of age when the pre-treatment radiograph was obtained
- Individuals with tooth agenesis (congenitally missing teeth), except from 3rd molars
- No syndromes, systemic diseases or any other defects that affect craniofacial morphology as reported in the subjects' medical record
- White racial background
- High diagnostic quality panoramic radiographs for identification of missing teeth
- No patient where the reason of absence of any tooth apart third molars was not definite

In cases younger than 12 years old at the time of the pre-treatment radiographs, radiographs obtained at older ages were also examined to confirm potential agenesis of late forming teeth, such as the 2nd premolars and the 2nd molars. Subjects where diagnosis could not be confirmed at least at the age of 12 were excluded from the study. Finally, 414 subjects (170 males; 244 females) who fulfilled the inclusion criteria were selected from more than 8.000 orthodontic patient records, and comprised the study population.

2.2. Data collection

Four researchers (H.K., E.O., G.K., M.K.) evaluated patient files (medical and dental history, intraoral and extraoral photos, radiographs) and recorded all data in an Excel sheet (Microsoft Excel®, Microsoft Corporation, Redmond WA, USA). The following variables were recorded: gender, race, date of birth, date of panoramic image acquisition, congenitally missing teeth. The third molars were not considered. All panoramic radiographs were viewed on screen to identify tooth agenesis. For this purpose, hard copy radiographs were scanned using an Epson Perfection V700 scanner with a resolution of 600 dpi at a scale of 1:1 and saved in .tiff (tagged image file format) format. A single researcher (H.K.) re-assessed the data extraction procedure of the entire sample and any disagreements were resolved by consensus between all researchers. To evaluate the error in tooth agenesis pattern identification, the same researcher repeated the data extraction process for 40 randomly selected subjects (https://www.random.org/) following a 1-month washout period.

To explore patterns of non-syndromic tooth agenesis in an otherwise normal human population the TAC system was used (van Wijk & Tan, 2006). As mentioned previously, this system assigns a binary value to each tooth providing a unique numeric value for each tooth agenesis pattern. Each dental quadrant is analyzed separately, and thus, the combined values assigned to each of the quadrants (q1, q2, q3, and q4) in the dentition represent a unique tooth agenesis pattern (van Wijk & Tan, 2006).

2.3. Statistical analysis

All statistical analyses were conducted with SPSS software (The Statistical Package for the Social Sciences, v.17.0, SPSS Inc., Chicago, Illinois, U.S.A). Descriptive statistics were also calculated through the Tooth Agenesis Code Data Analysis Tool (http://www.tooth-agenesiscode.com/, last accessed 10 October 2016). Intra-rater agreement was evaluated through the percentage of different patterns identified in the two repeated assessments. The two-tailed Fisher's exact test was used to assess differences in the total number of missing teeth within jaws between genders and in patients with symmetric and asymmetric tooth agenesis patterns.