Tooth agenesis and craniofacial morphology in pre-orthodontic children with and without morphological deviations in the upper cervical spine

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Tooth agenesis and craniofacial morphology in pre-orthodontic children with and without morphological deviations in the upper cervical spine

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Abstract

AIM: To analyze differences in prevalence and pattern of tooth agenesis and craniofacial morphology between non syndromic children with tooth agenesis with and without upper cervical spine morphological deviations and to analyze associations between craniofacial morphology and tooth agenesis in the two groups together.

METHODS: One hundred and twenty-six pre-orthodontic children with tooth agenesis were divided into two groups with (19 children, mean age 11.9) and without (107 children, mean age 11.4) upper spine morphological deviations. Visual assessment of upper spine morphology and measurements of craniofacial morphology were performed on lateral cephalograms. Tooth agenesis was evaluated from orthopantomograms.

RESULTS: No significant differences in tooth agenesis and craniofacial morphology were found between children with and without upper spine morphological deviations (2.2 ± 1.6 vs 1.94 ± 1.2, P > 0.05) but a tendency to a different tooth agenesis pattern were seen in children with morphological deviations in the upper spine. In the total group tooth agenesis was associated with the cranial base angle (n-s-ba, r = 0.23,
INTRODUCTION

Tooth agenesis is a common congenital malformation that can occur either as an isolated finding or as part of a syndrome[1]. The complex and multifactorial etiology behind tooth agenesis is yet to be fully understood[2,3]. Tooth agenesis can occur as a result of mutations in genes involved in normal tooth development. Defects in the MSX-1 and Sonic Hedgehog genes have been identified as causing tooth agenesis[2]. Furthermore, normal tooth development is dependent on the maturation of the bone surrounding the tooth germ and the nerve innervation of the teeth[14].

The prevalence of tooth agenesis among a healthy Danish population is between 7.8% and 8.2%[5,6]. Agenesis of the mandibular second premolar is most often observed (4.1%), followed by the maxillary second premolar (2.2%), the maxillary lateral incisors (1.7%) and the mandibular central incisors (0.2%)[6].

Previous studies have found an association between tooth agenesis and craniofacial morphology in non syndromic individuals[5,7-12]. It is generally agreed that tooth agenesis affects the craniofacial morphology in the sagittal and vertical dimension and that the deviation in the craniofacial morphology is associated with the prevalence and pattern of tooth agenesis[5,7-14]. In patients missing more than 12 teeth the prognathia of the mandible was more pronounced and the face was more squared compared to patients with less tooth agenesis[10].

The craniofacial morphology is also associated with upper cervical spine morphology in non syndromic individuals. In patients with severe skeletal malocclusion traits such as skeletal deep bite, skeletal open bite, skeletal maxillary and mandibular overjet, the prevalence of morphological deviations in the upper cervical spine was significantly higher compared to subjects with neutral occlusion and normal craniofacial morphology[13-16]. The pattern of morphological deviations in the upper cervical spine in these patients with severe skeletal malocclusions indicated fusion between the second and third cervical vertebra, block fusion between the second, third and fourth cervical vertebrae, occipitalization as assimilation of the first cervical vertebra with the occipital bone and partial cleft of the first cervical vertebra[13-16]. Furthermore, deviations of the upper cervical spine morphology were significantly associated with a large cranial base angle, retrognathia of the jaws and a large inclination of the jaws[13-16].

As associations between tooth agenesis and craniofacial morphology and associations between craniofacial morphology and upper cervical spine morphology have been described there may be an association between upper cervical spine morphology and tooth agenesis. To our knowledge the relation between upper cervical spine morphology and tooth agenesis has not yet been investigated.

Therefore, the aims of the present study are: (1) to analyze the differences in prevalence and pattern of tooth agenesis and craniofacial morphology between non syndromic children with tooth agenesis with and without upper cervical spine morphological deviations; and (2) to analyze the associations between craniofacial morphology and tooth agenesis in the two groups together.

MATERIALS AND METHODS

The materials included cephalograms and orthopantomograms from non syndromic pre-orthodontic children registered between 1966 and 1997 at the orthodontic clinic, Municipal Dental Service of Farum, Denmark. All the children with tooth agenesis that met the below inclusion criteria were included in the study: Children between 8 and 18 years old referred for orthodontic treatment before the orthodontic treatment began;
one orthopantomogram and one lateral cephalogram before orthodontic treatment; agenesis of at least one permanent tooth, excluding the third molars; the first five cervical vertebrae visible on the lateral cephalogram. The exclusion criteria were: Children with known craniofacial or other syndromes; children with no tooth agenesis, excluding the thirds molars; children with insufficient medical records and X-rays.

A total of 126 children met these criteria and were included in the present study: 62 girls (aged 8-16 years, mean age 11.32 years) and 64 boys (aged 8-16 years, mean age 11.7 years) with an overjet ranging between -2.5 and 11 mm (mean 4.5 mm) and with an overbite ranging between -5 and 8 mm (mean 3.3 mm). According to the upper cervical spine morphology the children were divided into two groups: One group with upper cervical spine morphological deviations consisted of 19 children, 12 boys and 7 girls aged 9-14 years (mean age 11.9) and one group without upper cervical spine morphological deviations consisted of 107 children, 52 boys and 55 girls 8-16 years (mean age 11.4).

The study was approved by the Danish Data Protection Agency (No. 2013-54-0509).

Tooth agenesis was registered on orthopantomograms and the craniofacial and upper cervical spine morphology was registered on lateral cephalograms.

**Registration of tooth agenesis**

The registration of tooth agenesis was performed by visual assessment of the orthopantomograms. Only the permanent dentition was analyzed and the third molars were excluded from the study. Each registration on the orthopantomogram was compared with the individual child’s medical record and available information of the dentition. Only tooth agenesis where a tooth and its tooth bud was missing from the orthopantomogram and no history of extraction could be found in the corresponding medical record was registered. The registration included: Number of missing teeth; registration of multiple tooth agenesis (more than 4 missing teeth); location of the tooth agenesis with regards to which jaw; agenesis pattern with regards to which tooth group (Tables 1 and 2).

**Registration of upper cervical spine morphology**

The cephalograms were studied for deviations in the morphology of the first five cervical vertebrae by visual assessment according to Sandham[17] and divided into two groups: Posterior arch deficiencies (PAD) and fusion anomalies. PAD consists of partial cleft and dehiscence. Partial cleft is defined as lack of fusion of the posterior arch (Figure 1). Dehiscence is defined as inadequate development of a portion of the vertebra[18]. Fusion anomalies consist of fusion, block fusion and occipitalisation. Fusion is defined as fusion of two vertebrae at the articular facets, the posterior arch or the transverse process (Figure 2). Block Fusion is defined as fusion of more than two vertebrae at the vertebral bodies, the articular facets, the posterior arch or the transverse processes. Occipitalisation is defined as partial or complete fusion of the atlas (C1) with the occipital bone[17,18]. Morphological deviations were only registered if they were visible on all the cephalograms available in the medical record of the child. If, in the visual assessment of a cephalogram, any doubts occurred about the presence of morphological deviations, the subject was registered as having no morphological deviations in the upper spine. All cephalograms were reviewed together with supervisor LS.

**Registration of the craniofacial morphology**

The craniofacial morphology was registered on lateral cephalograms of the children standing in the standardized head posture with their teeth in occlusion according to Siersbæk-Nielsen et al[19]. Twelve reference

### Table 1 Mean (X-bar) and SD of number of tooth agenesis and craniofacial morphology in children with and without upper spine morphological deviations

<table>
<thead>
<tr>
<th>Variable</th>
<th>With upper spine deviations (n = 19)</th>
<th>Without upper spine deviations (n = 107)</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>X-bar</td>
<td>SD</td>
<td>X-bar</td>
</tr>
<tr>
<td>No. ageneses</td>
<td>11.9</td>
<td>1.2</td>
<td>11.5</td>
</tr>
<tr>
<td>n-s-ar</td>
<td>123.4</td>
<td>4</td>
<td>123.5</td>
</tr>
<tr>
<td>n-s-ba</td>
<td>130</td>
<td>4.3</td>
<td>130.2</td>
</tr>
<tr>
<td>ML/RLar</td>
<td>121</td>
<td>4.9</td>
<td>123.1</td>
</tr>
<tr>
<td>s-n-ss</td>
<td>81.5</td>
<td>3.4</td>
<td>80.5</td>
</tr>
<tr>
<td>s-n-pg</td>
<td>79.5</td>
<td>3.2</td>
<td>78.7</td>
</tr>
<tr>
<td>ss-n-pg</td>
<td>2</td>
<td>1.7</td>
<td>1.8</td>
</tr>
<tr>
<td>NSL/ML</td>
<td>8</td>
<td>2.7</td>
<td>7.1</td>
</tr>
<tr>
<td>NSL/ML</td>
<td>30.4</td>
<td>4.5</td>
<td>31.6</td>
</tr>
<tr>
<td>NL/ML</td>
<td>22.4</td>
<td>4.3</td>
<td>24.5</td>
</tr>
<tr>
<td>Overjet</td>
<td>5</td>
<td>2.4</td>
<td>4.4</td>
</tr>
<tr>
<td>Overbite</td>
<td>3.8</td>
<td>3.2</td>
<td>3.7</td>
</tr>
</tbody>
</table>

NSL: Nasion-Sella line; NL: Nasal line; ML: Mandibular line; NS: Not significant, Fisher’s exact test.

### Table 2 Pattern of tooth agenesis in children with and without upper spine morphological deviations

<table>
<thead>
<tr>
<th>Variable</th>
<th>With upper spine deviations (n = 19)</th>
<th>Without upper spine deviations (n = 107)</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>63.2</td>
<td>52</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>36.8</td>
<td>55</td>
</tr>
<tr>
<td>Multiple ageneses</td>
<td>1</td>
<td>5.3</td>
<td>5</td>
</tr>
<tr>
<td>Agenesis localization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>16</td>
<td>84.2</td>
<td>81</td>
</tr>
<tr>
<td>Maxilla</td>
<td>8</td>
<td>42.1</td>
<td>52</td>
</tr>
<tr>
<td>Both jaws</td>
<td>5</td>
<td>26.3</td>
<td>26</td>
</tr>
<tr>
<td>Agenesis tooth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incisor</td>
<td>3</td>
<td>15.8</td>
<td>25</td>
</tr>
<tr>
<td>Canine</td>
<td>0</td>
<td>0.00</td>
<td>2</td>
</tr>
<tr>
<td>Premolar</td>
<td>17</td>
<td>89.5</td>
<td>85</td>
</tr>
<tr>
<td>Molar</td>
<td>2</td>
<td>10.5</td>
<td>3</td>
</tr>
<tr>
<td>Several tooth groups</td>
<td>3</td>
<td>15.8</td>
<td>7</td>
</tr>
</tbody>
</table>

NS: Not significant, unpaired t-test.
points were digitalized on cephalograms using the TIOPS™ software (Tiops 2005, Version 2.12.4) and nine angular measurements were measured according to Siersbæk-Nielsen et al. Because the cephalograms were not scanned in a 1:1 scale, the overbite and overjet was measured by hand on analog cephalograms and taking into account the magnification of 5.6%. The points and lines are illustrated in Figure 3 and the mean values are shown in Table 1.

Reliability of the method
The reliability of the variables describing the cranial base and the vertical and sagittal craniofacial dimensions was assessed by re-measuring 25 lateral cephalograms selected at random from the previously evaluated cephalograms. The lateral cephalograms were marked and measured again, and paired t test found significant differences between the two sets of recordings related to the measurement of NSL/NL, NL/ML and ML/RLa. The method errors calculated by Dahlberg’s formula ranged from 0.01 to 1.32 degrees[20] and the Houston reliability coefficient from 0.89 to 1.00[21]. The reliability was within the average range as traditional film-based radiographs[22]. The reliability of the visual assessment of the morphological characteristics of the cervical vertebral units has previously been reported (k = 0.82)[23].

Statistical analysis
Regarding the craniofacial dimensions, the effect of age was assessed by linear regression analysis and for the occurrence of morphological deviations of the cervical column by logistic regression analysis. Differences in means of the craniofacial dimensions and number of tooth agenesis between genders and between the groups were assessed by unpaired t test. Differences in tooth agenesis pattern between genders and between the groups were assessed by Fisher’s exact test. Associations between tooth agenesis and craniofacial morphology and the possible effect of age and gender were tested by linear regression analyses. The results were considered significant at P values below 0.05. The statistical analyses were performed using SPSS 20.00 (Inc., Chicago, Illinois, United States).

RESULTS
No significant age and gender differences were found between children with and without morphological deviations in the upper cervical spine (Tables 1 and 2). In the group of children with morphological deviations in the upper spine (15.1% of the total group) the deviations occurred only as fusion between the second and third vertebra (42.3%) and partial cleft of the atlas (63.2%). Both morphological deviations occurred in 5.3% of the children with morphological deviations in the upper spine.

No statistically significant differences in tooth agenesis and craniofacial morphology were observed between children with and without morphological deviations in the upper spine. However, in children with morphological deviations in the upper spine a tendency to a different tooth agenesis pattern was seen as a larger occurrence of molar agenesis and agenesis of several tooth groups compared to the children without morphological deviations in the upper spine (Table 2).

In the total group, statistically significant associations were found between tooth agenesis and craniofacial morphology (Table 3). Multiple agenesis was positively associated with the gonial angle (ML/RLa; P <0.05) and significantly negatively associated with horizontal overjet (P < 0.05) and vertical overbite (P < 0.01; Table 3). Agenesis of incisors was negatively associated with the sagittal jaw relationship (ss-n-pg; P < 0.01). Agenesis of premolars was significantly positively associated with the cranial base angle (n-s-ba, P < 0.01) and the sagittal jaw relationship (ss-n-pg, P < 0.05; Table 3). Agenesis of the molars was significantly positively associated with the mandibular prognathia (s-n-pg, P < 0.01) and significantly negatively associated with the sagittal jaw relationship (ss-n-pg, P < 0.05) and the mandibular inclination (NSL/ML, P < 0.05; Table 3).
Healthy non syndromic population agenesis of the third
molars are often seen, but agenesis of first and second
molars as reported in children with morphological
deviations in the upper spine in the present study almost
never occurs\cite{2,5} because normal tooth development
is dependent on the maturation of the bone surrounding
the tooth germ and the nerve innervation of the teeth\cite{3,4}. Therefore it may be hypothesized that the
etiology of tooth agenesis could be different in non
syndromic children with morphological deviations in
the upper spine as the tooth agenesis does not follow
the normal pattern of tooth agenesis according to the
nerve innervation. Previously, an association between
the craniofacial skeleton and the upper cervical spine
has been established\cite{24-26}. An explanation for the
association between the craniofacial skeleton including
the jaws and teeth and the cervical spine could be found
in the early embryogenesis. The notochord determines
the development of the cervical spine, especially the
vertebral bodies, and also the basilar part of the occipital
bone in the cranial base which is the posterior part of
the cranial base angle\cite{27-33}. The para-axial mesoderm
forming the vertebral arches and remaining parts of
the occipital bone is also formed from the notochordal
inductions. Therefore, a deviation in the development
of the notochord may influence the surrounding bone
tissue in the upper spine as well as the posterior part of
the cranial base to which the jaws including the teeth
are attached\cite{24-26}. Only a non-significant tendency of
differences in tooth pattern between children with and
without morphological deviations in the upper cervical
spine was found in the present study. This may be
because the malocclusion and tooth agenesis were not
extreme in the present sample and therefore a clear
pattern could not be found.

Surprisingly, no statistically significant differences
in the craniofacial morphology between the children
with and without upper cervical spine morphological
deviations were found. Previously, it has been shown
that deviations of the upper cervical spine morphology
were significantly associated with a large cranial base
angle, retrognathia of the jaws and a large inclination of
the jaws in non syndromic patients with severe skeletal
malocclusion\cite{13-16,18}. Therefore it was expected to find a

### DISCUSSION

The present study has analyzed the differences in tooth
agenesis and craniofacial morphology in pre-orthodontic
children with tooth agenesis with and without upper
cervical spine morphological deviations. To our know­
ledge this has not previously been reported in the
literature. Additionally, the associations between tooth
agenesis and craniofacial morphology in the two groups
together were investigated.

In the total group of 126 non syndromic children with
tooth agenesis, 15.1% had morphological deviations
in the upper cervical spine which is in agreement with
previous reported occurrence of morphological spine
deviations in healthy adults with neutral occlusion, no
tooth agenesis and normal craniofacial morphology
(14.3%)\cite{18}. Previous studies have shown that patients
with severe skeletal malocclusions such as large overjet
and overbite had a significantly higher occurrence of
upper spine morphological deviations compared to
controls\cite{13-16}. Therefore a higher occurrence of morp­
holological deviations in the upper spine was expected
in the present study of children with tooth agenesis.
One explanation for the relatively low occurrence of
morphological deviations in the upper spine could be
that the mean values for the overjet and overbite in the
present study was within normal range and therefore
children with severe malocclusion was few.

In the present study, no statistically significant
differences in prevalence or pattern of tooth agenesis
were found between non syndromic children with and
without upper cervical spine morphological deviations.
However, the non syndromic children with morphological
deviations in the upper spine did show a tendency to
have a greater percentage of molars agenesis and
agenesis of several tooth groups compared to children
without upper spine morphological deviations. In a
healthy non syndromic population agenesis of the third

### Table 3 Significant associations tested for age and gender
effect between tooth agenesis and craniofacial morphology in
the total group

<table>
<thead>
<tr>
<th>n-s-ba</th>
<th>ML/RLar</th>
<th>s-n-pg</th>
<th>ss-n-pg</th>
<th>NSL/ML</th>
<th>Overjet</th>
<th>Overbite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple agenesis</td>
<td>0.19&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-0.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-0.25&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agenesis of incisor</td>
<td>-0.24&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agenesis of premolar</td>
<td>0.23&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.22&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agenesis of molar</td>
<td>0.25&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.23&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-0.21&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>P < 0.05, linear regression; <sup>b</sup>P < 0.01, linear regression; <sup>c</sup>P < 0.05 gender
effect. NSL: Nasion-Sella line; ML: Mandibular line.
difference in the craniofacial morphology between the two groups in the present study.

In agreement with previous studies\(^{(15,7-12)}\), an association between tooth agenesis and the craniofacial morphology was found in the present study. In general, it was found that tooth agenesis was positively associated with the cranial base angle, gonial angle and the mandibular prognathia and negatively associated with the sagittal jaw relationship (except from agenesis of the premolars), mandibular inclination, overjet and overbite in the present study. The pattern of the association between the craniofacial morphology and tooth agenesis was in agreement with previous studies of non-syndromic individuals\(^{(15,7-12)}\).

In conclusion no significant differences in tooth age­
genesis and craniofacial morphology were found between the groups of children with and without morphological deviations in the upper spine, but a non-significant tendency to a different tooth agenesis pattern between the groups was seen. In the total group significant associations between tooth agenesis and craniofacial morphology were found. A different etiology for tooth agenesis in children with morphological deviations in the upper spine was suggested as these children may have a tendency for developing a different tooth agenesis pattern compared to children without upper spine morphological deviations. The results may be valuable in the early diagnosis and treatment planning of non-syndromic children with tooth agenesis.

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