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Signs and symptoms from ectodermal organs in young Swedish individuals with oligodontia

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Summary. *Objectives*. The aim was to assess signs and symptoms from other ectodermal organs in addition to teeth in young individuals with oligodontia and to establish the prevalence of oligodontia.

Sample and methods. Children born 1981–94 reported by dental teams in the Public Dental Service to have oligodontia were asked to participate in a clinical study. The examinations comprised a structured interview on symptoms from ectodermal organs, and testing of salivary secretion.

Results. One hundred and sixty-two individuals met the inclusion criteria, and 123 individuals (75·9%) participated in the clinical study. Half of the individuals had one to four signs or symptoms from ectodermal organs beside oligodontia. The most common sign was low salivary secretion. Twelve individuals (9·6%) with isolated oligodontia reported impaired function of the sweat glands, hair, or nails. The prevalence of oligodontia was 0·090%.

Conclusions. An early identification of individuals with oligodontia can be made in a majority of cases by checking that all permanent incisors have erupted at the age of 8 years. The validity in asking individuals about normal and abnormal function of ectodermal organs was found to be low. This indicates that there is a strong need to establish routine clinical criteria for dysplasia of ectodermal organs.

Introduction

Recent reports have shown that many individuals with oligodontia also have signs and symptoms from other ectodermal organs. In a Norwegian patient material of 68 individuals with oligodontia, 57% had disturbances in the hair, nails, and/or sweat production, and whole salivary secretion rates were lower than in a control group [1]. Aplasia and hypoplasia of several major salivary glands were reported in a case presentation of a male individual with the typical clinical expression of hypohidrotic ectodermal dysplasia [2]. Nordgarden *et al*. [3] established that individuals with ectodermal dysplasia (ED) syndromes often have reduced salivary secretion. These reports indicated that some individuals with oligodontia have an ED syndrome, albeit in many cases with a rather mild clinical expression. In general, clinical signs and symptoms in rare disorders vary from very mild to very evident [4]. Although many of the ED syndromes are among the most well-known heritable syndromes, defined clinical criteria and cut-off points for the respective signs and symptoms are lacking. As missing teeth are often the only reason that patients seek care, dentists are ideally placed to evaluate ectodermal signs and symptoms in individuals with oligodontia.

The definition of an ED syndrome is the presence of two or more of the following symptoms: trichodysplasia, dental anomalies, onychodysplasia, and dyshidrosis [5]. In the thesis by Nordgarden [6], the diagnosis ‘oral ectodermal dysplasia’ was suggested when only the teeth and the salivary glands are affected. Schalk van der Weide [7] suggested that the diagnosis of oligodontia be divided into oligodontia/I for isolated oligodontia and oligodontia/S for oligodontia that is part of a syndrome. A search on features in the London Dysmorphology Database (LDDB, Oxford Medical Databases, Oxford University Press, version 2·2, 2000) resulted in 142 syndromes that matched the search term ‘oligodontia’.

The prevalence of oligodontia–or severe hypodontia–defined as the congenital absence of six or

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more permanent teeth, third molars excluded, was reported by Hobkirk and Brook [8] to occur in about one in 15 individuals with hypodontia–a prevalence of 0·3%. Rolling and Poulsen [9] reported the prevalence in a large Danish sample to be 0·16%, and Nordgarden *et al*. [10], in a study of agenesis of teeth in 18-year-old in two counties in Oslo, Norway, found eight individuals with oligodontia–a prevalence of 0·084%. In a study of 196 patients with oligodontia referred from specialist clinics in the Netherlands, the prevalence was calculated to be 0·08% [7]. The aim of this study was to assess signs and symptoms from other ectodermal organs in individuals with oligodontia and to establish the prevalence of oligodontia in three counties in Sweden.

Materials and methods

Inclusion criteria for the study were oligodontia, defined as agenesis of six or more permanent teeth, third molars excluded, verified by a panoramic radiograph; birth year 1981–94; and place of residence, one of the three Swedish counties: Jönköping, Östergötland, or Kalmar. The exclusion criterion was radiation therapy to the jaws during the first years in life. The study protocol was approved by the ethics committee at the University of Linköping, Linköping, Sweden.

Sample

An inquiry was sent to all public dental service (PDS) clinics for general dentistry and in the specialities of paediatric dentistry, orthodontics, and prosthetic dentistry, in the three Swedish counties participating in the study. The combined population of the three counties was 900 000, which constitutes about one-tenth of the entire Swedish population. More than 95% of the children in these counties receive their regular dental care in the PDS. No digital data on children with oligodontia could be obtained by a search of the patient records. In a mailed inquiry, the dental teams were asked to report all children who fulfilled the inclusion criteria.

The reported children were then asked to participate in a clinical study comprising a structured interview focusing on symptoms from ectodermal organs, and testing of salivary secretion rates. The parents, or the children if they were 18 years or older, gave their written consent to participate in the study.

Saliva testing

Salivary secretion rates were tested using standard clinical routines: unstimulated whole saliva was collected for 15 min and chewing-stimulated whole saliva for 5 min in a graduated measuring glass. The testing procedures were in most cases performed in the morning, but afternoon appointments were accepted if they were more convenient for the patient. A salivary flow rate of 0·1 mL/min or less for unstimulated whole saliva or 0·7 mL/min or less for chewing-stimulated whole saliva was considered low [11].

Structured interview on ectodermal signs and symptoms

The structured interview focusing on questions about symptoms from ectodermal organs was worked out and tested for calibration of all four examiners (the authors) in a small number of children with tooth agenesis. The interview contained four questions about skin problems, four questions about sweating problems, and one question each about whether or not the hair and nails were normal. After completion of the structured interview, the examiners were asked to judge whether they considered the facial features of the patient–especially the lips–to be similar to those of persons with hypohidrotic ED and whether they anticipated the individual to have an ED syndrome.

Results

Examined individuals and prevalence of oligodontia

From the inquiry, 164 individuals with oligodontia were identified. Two individuals who had undergone radiation therapy in their jaws during their first years in life were excluded from the study. Thus, 162 individuals were diagnosed with oligodontia–91 girls (56·2%) and 71 boys (43·8%). The total number of children born 1981–94 in the three counties was obtained from Statistics Sweden and was 179 716, a prevalence of oligodontia of 0·090%.

When contacted for participation in the clinical study, 33 declined to participate, 2 could not cooperate with examinations, and 4 had moved. Thus, 123 (75·9%) of the children with oligodontia–71 girls (57·7%) and 52 boys (42·3%)–were examined. At the time of the examination, the children ranged

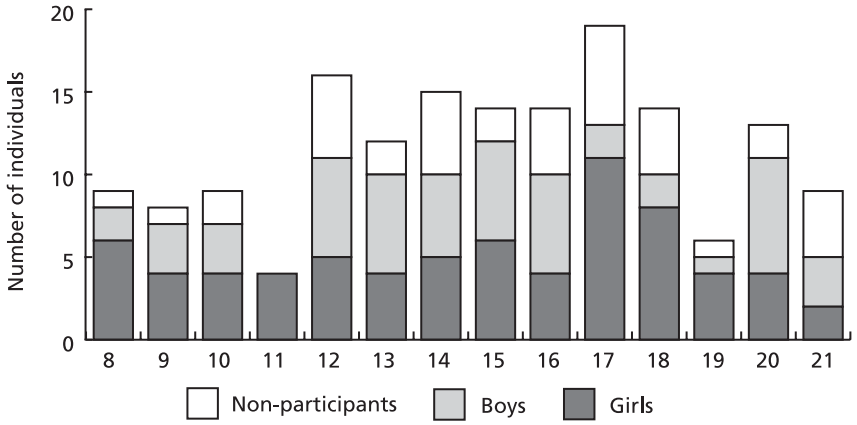

Fig. 1. Age and gender in 162 individuals with oligodontia.

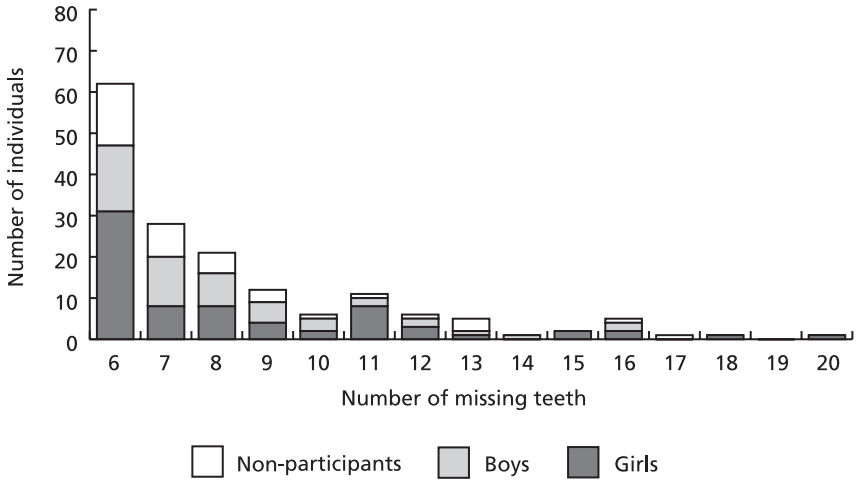

Fig. 2. Number of missing teeth in 162 individuals with oligodontia.

in age from 8 to 21 years. The age and gender distribution of the individuals with oligodontia who were examined is shown in Fig. 1.

In the 12- to 18-year-olds, the numbers of reported individuals were higher than in the younger and the older age-groups. If calculated from the total number of 12- to 18-year-olds, 90 863, the prevalence of oligodontia in this age range was 0·115%. When divided into county level, the prevalence figures were 0·144%, 0·072%, and 0·060%, respectively.

Tooth agenesis

The number of missing teeth for all 162 individuals with oligodontia was assessed from panoramic radiographs, and varied from six to 20, with a median of 7 and a mean of 8·3. The number of missing permanent teeth is shown in Fig. 2. Ninety individuals (55·6%) were missing six or seven permanent teeth and 16 individuals (9·9%) were missing more than 12 teeth. Agenesis of individual teeth is shown in Fig. 3. The teeth most commonly missing were the second premolars of the upper and lower jaw, followed by the upper lateral incisors; these teeth constituted 51·3% of the missing teeth. The upper central incisors were not missing in any individual. Ten individuals (8·1%) had a known syndrome: six had Down syndrome, one ichtyosis, one incontinentia pigmenti, one Kawasaki syndrome, and one Prader–Willi syndrome. The number of missing teeth in individuals with a syndrome varied from six to 16 with a mean of 8·5. No typical case of hypohidrotic ED was found among the examined individuals.

One or more of the permanent incisors were missing in 65·0% of all individuals with oligodontia. Of the 72 individuals who were missing eight teeth or more, 77·8% were missing one or more incisors, and of the 51 individuals missing nine teeth or more, 84·3% were missing one or more incisors. Seventeen percent were missing only premolars and 10% had no premolars.

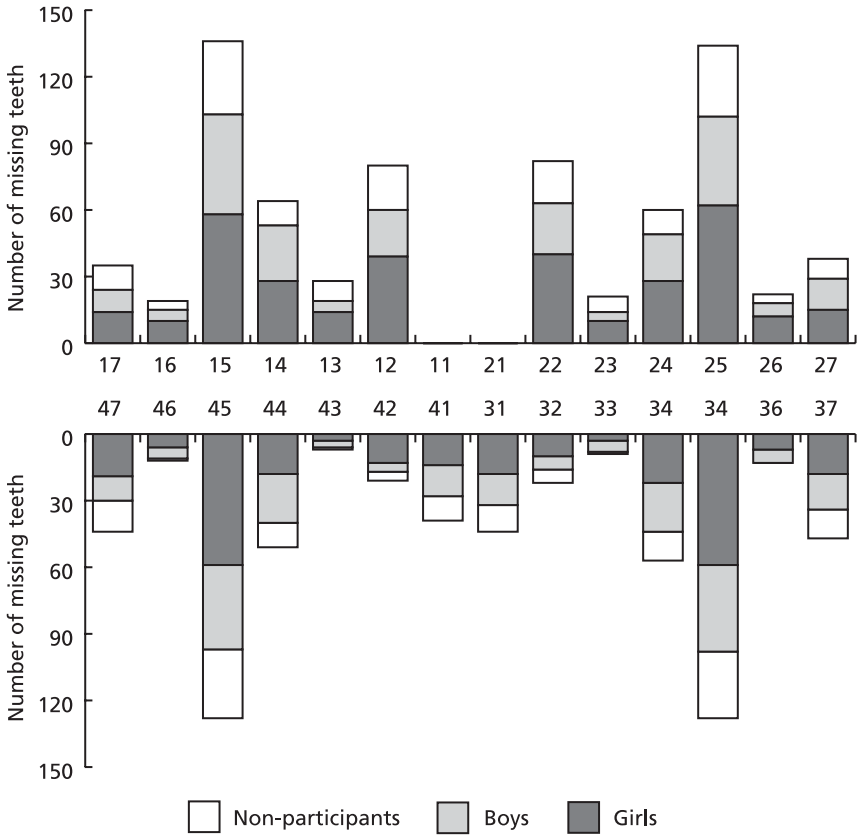

Fig. 3. Agenesis of individual teeth in 162 individuals with oligodontia.

Ectodermal signs and symptoms

Salivary function was recorded through clinical testing of salivary flow rates, and data on symptoms from sweat glands, skin, hair, and nails were collected through answers to the questions in the structured interview. Criteria for impaired function were established after completion of the study, when the question with the best discriminative potential was chosen (Table 1).

Four individuals were not able to co-operate in the two salivary tests and three were not able to co-operate in one of the tests. Therefore, data on ectodermal signs and symptoms were calculated from the results of 116 individuals. Of these, 58 individuals (50%) had one or more signs or symptoms from ectodermal organs in addition to oligodontia.

The structured interview comprised four questions about skin problems. A positive answer to the question 'Do you have eczema now?' was chosen as a criterion for symptoms from the skin. The other questions on symptoms from the skin were not found to be discriminative; the examinations were performed during the winter season and most of the children considered their skin to be dry. Of the four questions on sweating, a negative answer to the question 'Do you sweat normally?' was chosen as a criterion for the symptom of reduced sweating capacity. The answer to this question was usually given after the other questions about sweating had been answered ('Did you have episodes of fever cramps as a child?', 'Can you participate in PE

Table 1. Frequency of ectodermal signs and symptoms in 116 individuals with oligodontia (seven individuals could not co-operate with one or both salivary tests).

	Individuals who fulfil criteria	
Ectodermal organ	Number	%
Salivary glands*	35	30·2
Skin†	22	19·0
Sweat glands‡	12	10·3
Hair§	5	4·3
Nails¶	4	3·4

*unstimulated whole saliva ≤ 0·1 mL/min and/or stimulated whole saliva ≤ 0·7 mL/min.
†answered yes to the question 'Do you have eczema now?'
‡answered no to the question 'Do you sweat normally?'
§answered no to the question 'Is your hair normal?'
¶answered no to the question 'Are your nails normal?'

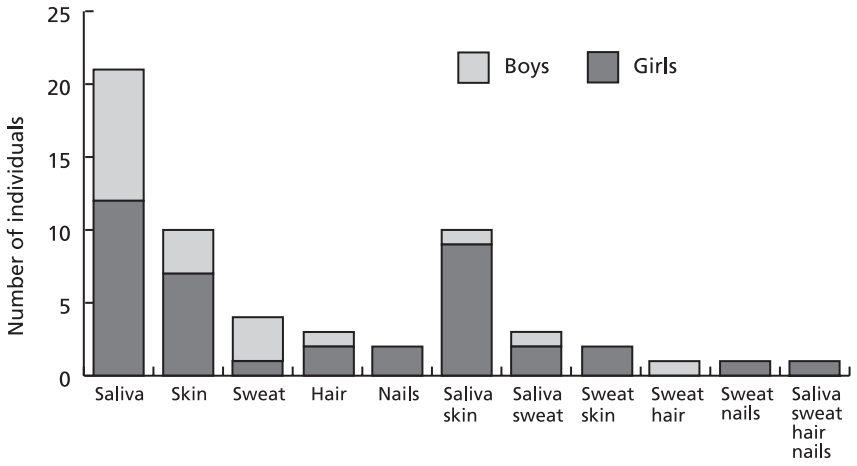

Fig. 4. Self-reported symptoms from ectodermal organs and clinically tested salivary flow rates in 116 individuals with oligodontia.

Table 2. Number of ectodermal signs and symptoms in 116 individuals with oligodontia (seven individuals could not co-operate with one or both salivary tests).

Number of symptoms from ectodermal organs	Number of individuals
0	58 (50·0%)
1	40 (34·5%)
2	17 (14·7%)
4	1 (0·9%)

lessons in school?', 'Can you sit in the sun as long as your friends?') and often after a discussion of what symptoms are related to reduced sweating. Negative answers to the question 'Is your hair normal?' and 'Are your nails normal?' were chosen as criteria for symptoms from the hair and nails, respectively. The combinations of ectodermal signs and symptoms in 116 individuals are shown in Fig. 4. The frequency of ectodermal signs and symptoms in 116 individuals is shown in Table 1, and the number of signs and symptoms per individual is shown in Table 2. Of the five ectodermal organs studied, low salivary secretion was the most frequent dysfunction, which was found in 35 individuals–in 21 as a single trait and in 14 in combination with one or more other symptoms. In all, 17 individuals (14·7%), 11 girls and 6 boys, reported symptoms from hair, nails, or sweat glands; five of them had a known heritable syndrome. Thus, 12 individuals (10·3%) with oligodontia/I reported symptoms from sweat glands, hair, or nails.

After completion of the structured interview, the examiners answered the question 'Do you think the patient has an ectodermal dysplasia syndrome?' The examiners thought that 19 of the children had an ED syndrome. Only six individuals, four girls and two boys, were among those who had symptoms from hair, nails, or sweat glands, and all six had reduced sweating. The appearance of the lips of 12 of the 19 patients who were suspected to have an ED was judged to be similar to what is often seen in persons with ED. No individual who reported symptoms from the nails or hair was by the examiners judged to have an ED syndrome.

Discussion

In this study of individuals born 1981–94, 162 of 179 716 children in a population of 900 000 inhabitants were identified with oligodontia–a prevalence of 0·090%. The identification of individuals with oligodontia depended on the memory of the PDS teams in the three participating counties, and all individuals with oligodontia were most likely not reported. The diagnosis of oligodontia is usually not established until the age of 8–10 years, which is why some individuals in the younger age-groups may not yet be diagnosed. The older age-groups, 19 years and older, no longer attend the children's dental service and often move from the area where they grew up. These factors may explain why there were fewer individuals reported in the youngest and oldest age-groups (Fig. 1). The reported prevalence of oligodontia was much lower in two of the three counties, and from these two counties, only one individual with a heritable syndrome was reported, in contrast to eight from the third county. This strengthens the notion that the identified individuals do not represent all individuals with oligodontia, and the reported prevalence of 0·090% is likely to be lower than the true population prevalence. Schalk van der Weide [7] found a prevalence of 0·08% in a patient material, and Nordgarden [10] reported a prevalence of 0·084% in one age-group in a smaller

population study. Rolling and Poulsen [9] reported the prevalence of oligodontia to be 0·16% in a study where data on Danish schoolchildren in several earlier studies were combined, and this large material represents the most complete Scandinavian sample to date. A British study reported oligodontia to occur in 0·3% [8], and a recent metaanalysis reported different prevalences of agenesis of teeth in different parts of the world [12], which indicates that there may be ethnic and geographical variations. The mean number of missing teeth in all 162 identified individuals was 8·3, and in the 10 individuals with a known syndrome, the mean number of missing teeth was 8·5. In a large Dutch material of 196 individuals with oligodontia, 62 patients with oligodontia/S were missing significantly more teeth than patients with oligodontia/I [7]; however, the patients in this material were referred from specialist clinics. In this study, more girls than boys had oligodontia, which is in accordance with a metaanalysis on tooth agenesis [12]. The pattern of missing teeth found in this study was similar to what has been presented in previous Swedish studies [13–15]. The teeth most frequently missing were second premolars followed by maxillary lateral incisors. These teeth constituted a little more than half of the missing teeth, as opposed to the findings by Rolling and Poulsen [9], who reported these teeth to represent two of three missing teeth in individuals with oligodontia.

One or more of the incisors in the upper and lower jaw were missing in 65·0% of individuals with agenesis of six or more teeth, in 77·8% missing eight or more teeth, and in 84·3% missing nine or more teeth. Thus, a recommendation to the PDS that all children who at the age of 8 have not yet got all their permanent incisors should have a panoramic radiograph taken to identify a majority of the children with oligodontia. An early identification is valuable as it increases the possibilities to use growth adapted measures in the multidisciplinary treatment planning of this patient group. The examiners judged 19 individuals to have an ED syndrome, only six of which had subjectively perceived symptoms from the sweat glands, hair, or nails. Their judgement seemed to be based more on facial features, especially on the appearance of the lips, than on subjectively perceived ectodermal symptoms. They also seemed to place more importance on symptoms of impaired sweating capacity than on symptoms from the hair and nails, which were probably considered vague and difficult to distinguish from what is normal.

From 10 years of age, the normal mean values for stimulated whole saliva exceeds 1·0 mL/min [16]. The youngest children in this study were 8 years at the time of the clinical examinations and the same criteria for low salivary secretion rates were used in all age-groups. Seven of the individuals could not co-operate with saliva testing: four of them had Down syndrome, and one had Prader–Willi syndrome. The most common ectodermal sign was low salivary secretion, found in 30·2%. Thus, the diagnosis 'oral ED', suggested by Nordgarden [6] for patients who only have signs from the teeth and salivary glands, was found in one of three individuals with oligodontia in this study. Low salivary secretion and dry skin/eczema have been described to coexist in persons with oligodontia [1], a finding that was validated in this study. Testing of salivary flow is strongly recommended in individuals with oligodontia as most of individuals with an inborn low salivary secretion will not subjectively perceive dryness of the mouth.

According to the definition of an ED syndrome, two or more of the four tissues hair, teeth, nails, and sweat glands should be affected [5]. In this study, half had one or more signs or symptoms from the five tested ectodermal organs, and only one in 10 individuals with oligodontia/I had symptoms from the hair, nails, and sweat glands. The gene for x-linked hypohidrotic ED was identified in 1996 by Kere *et al.* [17], but mutation analysis of the *EDA1* gene is still only available at a few genetic laboratories at a high cost. The understanding that many different genes are involved in the development of teeth [18,19] as well as in the different forms of EDs [20] makes it likely that we will continue to rely on clinical diagnostics in the near future.

The questions in the structured interview of this study contain the concept of 'normality', which covers a broad range of values when applied to sweating capacity, dry skin, thin hair, and brittle nails. The validity of self-reported symptoms can therefore be suspected to be low. Oligodontia was the inclusion criterion, and of the five organs studied, only three are among the criteria for an ED syndrome. Seventeen individuals (14·7%), more girls than boys and five of them with a diagnosis of a syndrome, reported impaired function from the hair, nails, and/or sweat glands in the present population-based study, in contrast to 57% in a patient material where clinical signs and symptoms were recorded [1]. This indicates that there is a strong need to establish routine clinical criteria for dysplasia of ectodermal organs

as well as to revise the criteria for ED syndromes, even if the overall picture will not be known in full until understanding of the molecular genetics in ED syndromes improves. Until then, low salivary secretion and dry skin/eczema should be recognized as concomitant symptoms in oligodontia.

What this paper adds

- In young individuals with oligodontia one out of three had low salivary secretion but only one out of ten had subjective symptoms from other ectodermal organs than teeth.

Why this paper is important to paediatric dentists

- Early identification of children with oligodontia could be made in a majority of cases by following a recommendation to take an OPG in children with one or more permanent incisor missing.
- Salivary secretion rates should be assessed in children with oligodontia.

Conclusions

- Half of young individuals with oligodontia had one or more signs and symptoms from ectodermal organs.
- One in three individuals with oligodontia had low salivary secretion.
- One in 10 individuals with oligodontia/I had symptoms from hair, nails, or sweat glands.
- The prevalence of oligodontia was 0·090%.
- An early identification of individuals with oligodontia can be made in 65% by checking that all permanent incisors have erupted at the age of 8. This recommendation will identify 85% of individuals missing nine teeth or more.
- Dentists are recommended to assess salivary secretion in children and adolescents with oligodontia.

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