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BRIEF REPORT

Ectodermal Dysplasia: Retrospective Study of Fifteen Cases

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The aim of this article is to review possible cranio-maxillofacial deformative consequences associated with hypohidrotic ectodermal dysplasia and embryonic malformations, which include dental ageneses, and describe the oral habilitation. Hypohidrotic ectodermal dysplasia patients had a clinical examination and underwent radiographic and Steiner's analyses and a respiratory capability test before assessment and treatment. Fifteen patients (eight males and seven females, aged 5–45 years) had tooth ageneses (from hypodontia to anodontia) associated with cutaneous dyshydrosis and hair and nail dystrophy. Most patients had sparse or absent hair, a short face with an unusual facial concavity, a maxillary retrusion and a relative mandibular protrusion. Dentists must conduct a comprehensive and multidisciplinary approach to these patients in order to improve their dental, masticatory, growth and orthognathic conditions. © 2006 IMSS. Published by Elsevier Inc.

Key Words: Hypohidrotic ectodermal dysplasias, Denture, Tooth ageneses.

Introduction

Ectodermal dysplasia (ED) is a large and complex group of disorders defined by the abnormal development of two or more structures derived from the ectodermal layer. The most frequently reported manifestation of ED is hypohidrotic dysplasia (HED), also termed Christ-Siemens-Touraine syndrome, and anhydrotic dysplasia, as in our cases. The ectoderm, one of three germ layers present in the developing embryo, gives rise to the central nervous system, peripheral nervous system, sweat glands, hair, nails, and tooth enamel (1,2).

As a result, HED patients exhibit the following clinical signs: hypotrichosis, hypohidrosis, and cranial abnormalities. Patients often exhibit a smaller than normal face because of frontal bossing, a depressed nasal bridge, the absence of sweat glands resulting in very smooth, dry skin and/or hyperkeratosis of hands and feet. Oral traits may express themselves as anodontia, hypodontia, and conical teeth. Anodontia also manifests itself by a lack of alveolar ridge development (1,3,4).

The earliest recorded cases of ED were described in 1792 (1). Since then, more than 200 different pathologic clinical conditions have been recognized and defined as ED. These disorders are considered relatively rare, 1 in 10,000–1 in 100,000 births (1–3,5,6).

Clinical manifestations of HED also cause considerable social problems in affected patients. Dental treatments of the clinical traits of HED can have a profound impact on these patients. The ability to look and feel like their peers is imperative for the psychological development of these patients. The literature has demonstrated the benefits that corrective dentistry has for the self-esteem and social well being of these patients (1,7,8).

Our major goals of providing dental and medical management were to provide comfort to patients to be as other healthy individuals. Depending on their ages and their abnormalities, patients underwent periodontal therapy, caries

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management or prosthodontic or orthodontic treatment. Implanting and orthognatic surgery was reserved for full-grown patients.

Patients and Methods

This retrospective study was carried out using patients applying to our university dental clinic from 1997–2005. In our dental faculty, 15 cases (eight males and seven females, aged 5–45 years) with a diagnosis of HED were included.

All major signs of HED were studied, such as sparse hair (trichodysplasia), smooth skin (hypohidrosis), abnormal fingernails and toenails, and cranial and facial abnormalities. The pedigree of the patients was researched (Table 1, Figures 1–9).

Each patient had the benefit of a rigorous clinical examination for diagnosis and therapy: minor or major abnormalities had to be detected in both patients and family. Examination included the skull, face, hair, teeth, nails, skin, lungs, sweat glands, etc. (Table 2).

Results of the maxillofacial cephalometric analyses are summarized in Table 3, and Steiner analysis was used to determine abnormalities.

Results

Fifteen cases (eight males and seven females, aged 5–45 years) had tooth ageneses (all cases: from hypodontia to anodontia), associated with cutaneous dyshidrosis, sparse or absent hair (cases 1–8, 12–15), nail dystrophy (cases 1, 3, 4, 6, 11–15), and hypohidrosis (all except patient 11).

The skin on most of the body was abnormally thin, dry, and soft with an abnormal lack of pigmentation (hypopigmentation: patients 4, 6, 7, and 12); however, the skin around the eyes (periorbital) was darkly pigmented (hyperpigmentation: cases 1, 6, 7, 11, 12, 15) and finely wrinkled, appearing prematurely aged (Tables 1 and 2).

Fifteen cases had hypodontia, six cases with fewer than ten teeth (cases 1, 2, 6, 11–13), and nine cases with more than ten teeth (cases 1, 3–5, 7–10, and 15).

Table 1. Report of clinical characteristics for each of the 15 cases

Abnormality	15 cases (100%)
Trichodysplasia (sparse or lack of hair)	12 cases (80%)
Hypohidrosis (from moderate to severe)	13 cases (86%)
Abnormal finger and toenails	12 cases (80%)
Protuberant lips	14 cases (93%)
Saddle nose	11 cases (73%)
Fever history	12 cases (80%)
Asthma and difficulty in breathing	7 cases (46%)
Peeling skin	14 cases (93%)
Deafness (hearing loss from moderate to severe)	8 cases (53%)
Relationship of parents to each other	8 cases (53%)

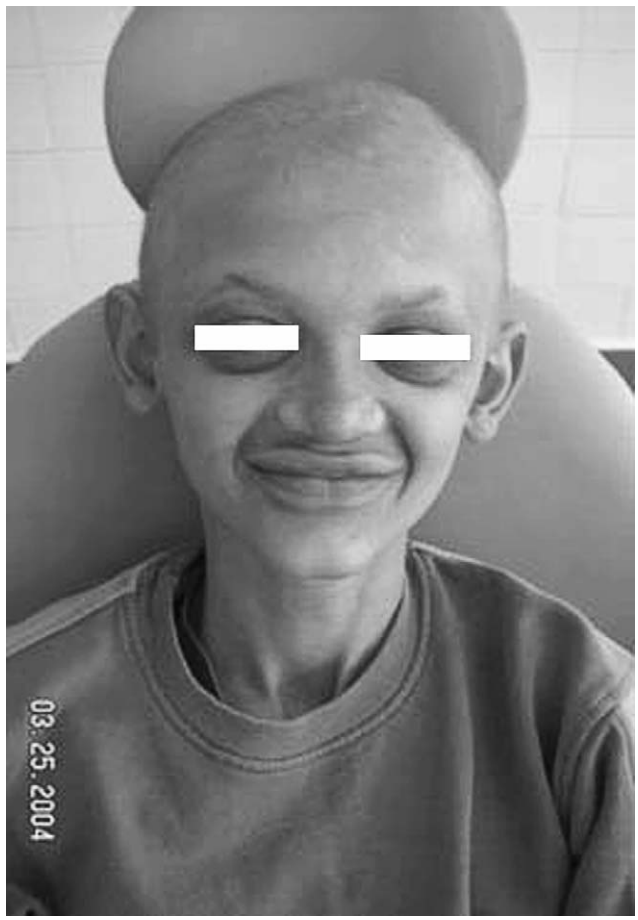

Figure 1. Maxillofacial examinations point out a significantly reduced anterior facial height caused by the collapse of the distance from anterior nasal spine to chin. The presence of a prognatic mandible also contributes to the mild or severe facial profile concavity. Also, HED is presented with an abnormal bulging forehead with high-implanted brittle hair (patient 6).

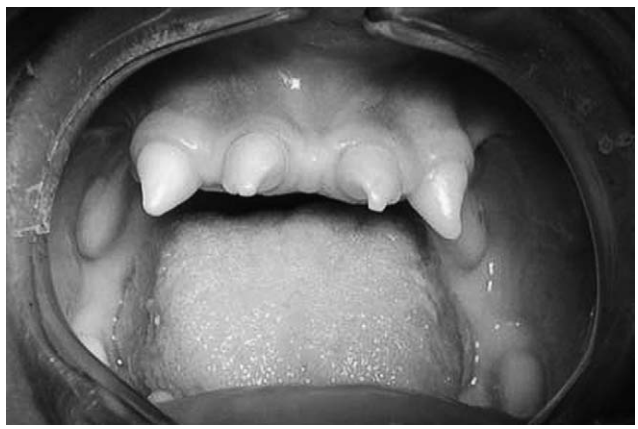

Figure 2. Mouth examination is of primary necessity. It allows mucosal assessment (dryness, thickness, and brittleness), dental inspection (number, form, and dysenamelogeneses) and an alveolar crest height estimation (patient 6).

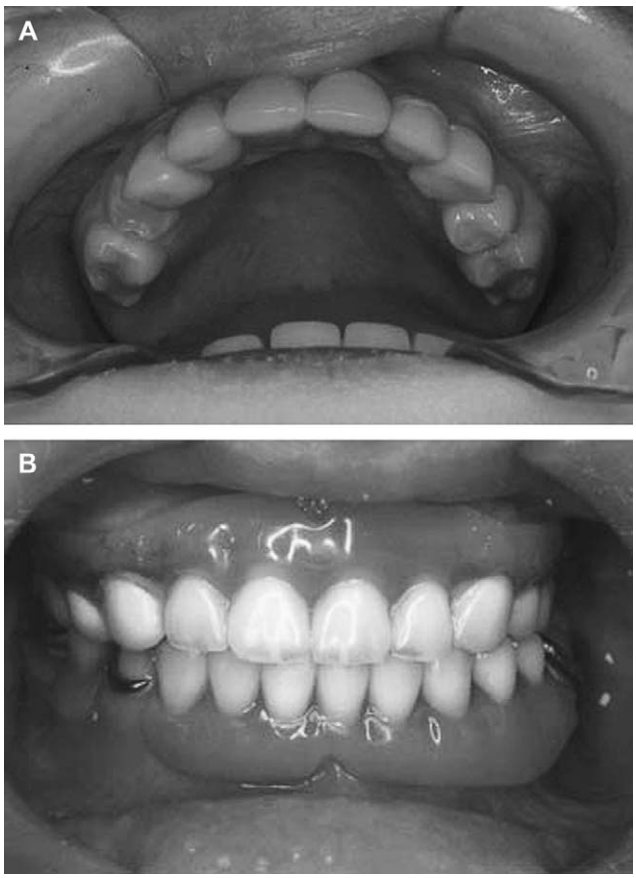

Figure 3. Fixed or non-fixed overdenture could be considered as solution. (A) Patient 4. (B) Patient 15.

Steiner analyses revealed a facial height reduction and concavity in eight of the cases (cases 4–7, 9–11, and 13), compared with normal values of Turkish persons. It was also found that maxillary hypotrophy and retrusion, forward-upward-displaced-protused mandible, skeletal class III were present, and labial retrusion, chin prominence and nasolabial and chin reinforcement was observed due to low angles.

Figure 4. Most of the patients present dry or scaly palmar skin (patient 4).

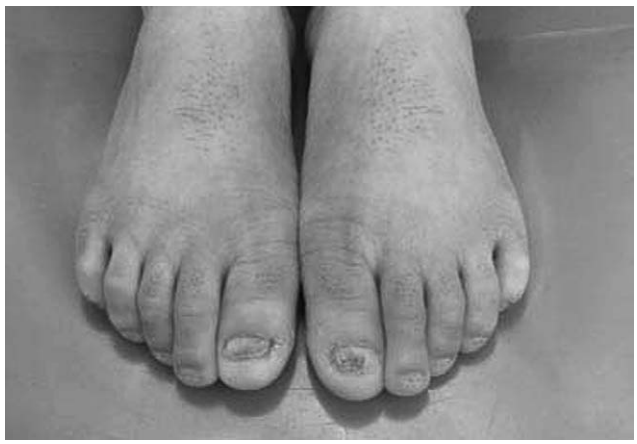

Figure 5. Nails affected with slow growth, poor development and brittleness. In addition, the toenails of some patients were discolored and had a bad odor because of fungal infection (patient 14).

Many affected cases had experienced recurrent attacks of wheezing and breathlessness (asthma) and respiratory infections (cases: 1, 4, 6, 12, and 15).

With respect to sex differentiation, there was no differentiation between genders.

Some of the cases were related to each other (cases 5, 7, and 9/cases 11, 13, and 14/cases 4 and 15) and their parents had similar features of HED. These may include absence and/or malformation of certain teeth, sparse hair, and/or reduced sweating (such as mother of cases 5, 7, and 9 and father of case 4).

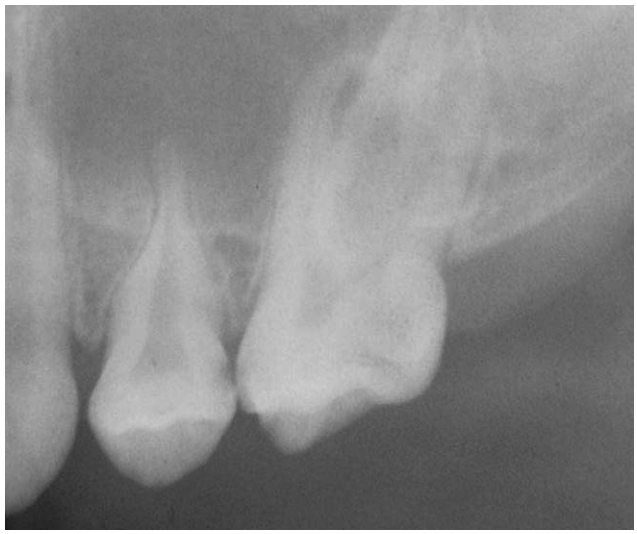

Figure 6. Tooth that is present has malformed external root resorption (patient 4).

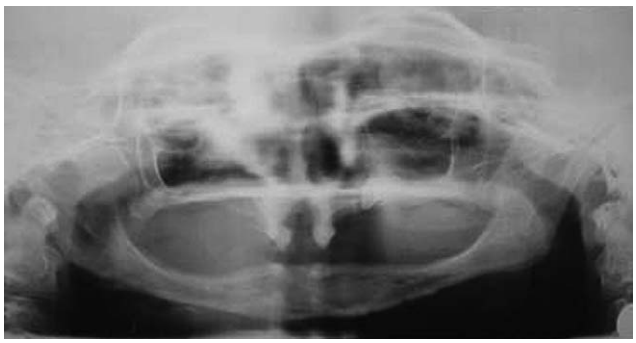

Figure 7. An orthopantomogram is useful for the rigorous assessment of the patient's real dental capital with respect to age; both deciduous and permanent dentitions are visualized (patient 2).

Discussion

HED is a rare, inherited, multisystem disorder. In our patients, after a discussion of the family and medical history, it was found that the parents of some of the patients were related to each other (patients 5, 7, and 9/patients 11, 13, and 14/patients 4 and 15) and they had similar features of HED in their parents confirming the hereditary nature of HED (e.g., skin, sparse hair and difficulty in sweating in patient 4 and her father, patient 15).

Clinical diagnosis of HED is difficult because the identification of the precise syndrome could be a challenge (9,10) without collaboration between the patient and the different specialties concerned. Without this, a diagnosis of HED, without any other diagnostic precision, would be difficult at best.

Steiner analyses revealed a facial height reduction and concavity in eight patients (patients 4–7, 9–11, and 13), compared with routine values of Turkish persons (11,12). Also found were maxillar reduction, labial retrusion, chin prominence and nasolabial and chin reinforcement. In agreement with preceding research (13), investigators should be aware that these measures may be unreliable because they vary according to tooth ageneses and severity of HED.

In agreement with previous research, sagittally underdeveloped maxillary retrusion and vertical dentoalveolar development are related to severe hypodontia (14) (Table 3). Maxillary retrusion, mandibular protrusion, and class III were found in most of our cases (eight cases, according to Steiner's cephalometric analysis). Teeth support bone formation because of the resorption-apposition process created by dentoalveolar ligaments (10). The consequence of this is that dental ageneses could curb bone growth, such as shown in the studied cases.

In this study, more severe dental ageneses presented a greater evidence of the maxillar abnormalities, specifically, maxillary hypotrophy, maxillary retrusion and forward-upward-displaced-protused mandible for a global osseous, as shown by teleradiographs and Steiner's cephalometric analysis (Figure 8).

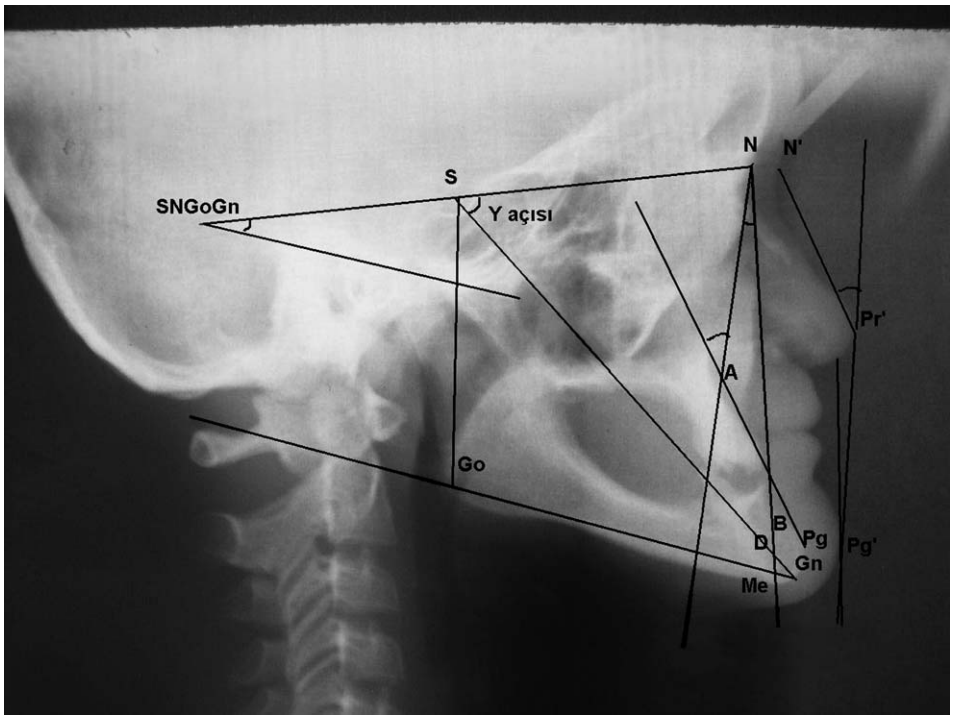

Figure 8. The more severe the dental ageneses, the more evident the maxillar abnormalities: maxillary hypotrophy and retrusion and forward-upward-displaced-protused mandible for a global osseous class III shown by teleradiographs and Steiner's cephalometric analysis (patient 6).

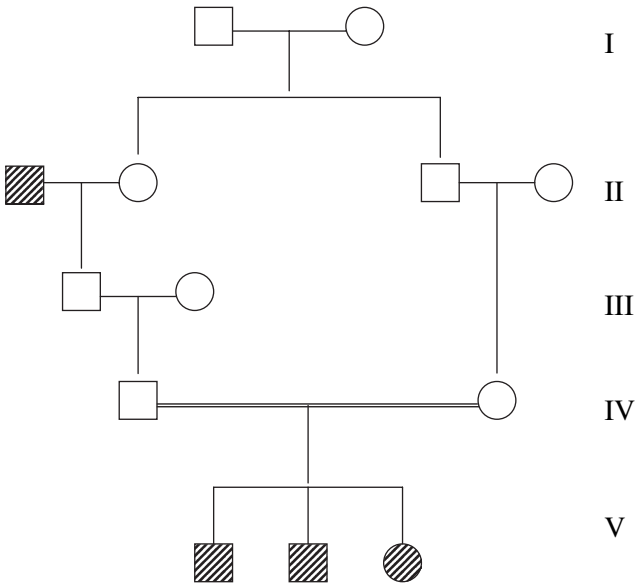

Figure 9. Pedigrees of patients 5, 7, and 9.

All of the jaws were retrusive, according to the cranial base (S–N); however, they were more in the maxilla. As a result of retrusion maxilla and mandible, the soft tissues showed retrusion at the same time. Skeletal class III patients generally showed a high angle and big gonium angles, although our patients showed low angles because of missing teeth.

HED patients typically have affected hair, teeth, nails, and/or skin (Figures 1–6). HED is primarily characterized by partial or complete absence of certain sweat glands (eccrine glands), causing a lack of or diminished sweating (anhidrosis or hypohidrosis: all patients), heat intolerance, and fever; abnormally sparse hair (hypotrichosis: patients 1–8, 12–15) (Figure 1), and an absence and/or malformation of certain teeth (hypodontia: all patients) (Figures 2, 7, and 8). Many individuals with HED also have characteristic facial abnormalities, including a prominent forehead, a sunken nasal bridge (so-called ''saddle nose''), unusually thick lips, and/or a reinforcement chin. The skin on most of the body may be abnormally thin, dry, and soft with an abnormal lack of pigmentation (hypopigmentation: patients 4, 6, 7, 12) (Figures 4–6). However, the skin around the eyes (periorbital) may be darkly pigmented (hyperpigmentation: patients 1, 6, 7, 11, 12, 15) (Figure 1) and finely wrinkled, appearing prematurely aged (Tables 1 and 2). This study agrees with past research (1,2,4,8–10,13,15–20).

Fifteen cases in these studies had hypodontia, six patients with fewer than ten teeth (patients 1, 2, 6, 11–13), and nine patients with more than ten teeth (patients 1, 3–5, 7–10, and 15). Till and Marques reported that approximately 25% of HED patients present anodontia, whereas 75% present oligodontia (Figures 7 and 8) (18).

In many cases, affected infants and children may also exhibit underdevelopment (hypoplasia) or absence (aplasia) of mucous glands within the respiratory tracts and, in some cases, decreased lung capacity and function, potentially causing an increased susceptibility to certain infections and/or allergic conditions. Many affected patients experience recurrent attacks of wheezing and breathlessness (asthma), and respiratory infections (patients 1, 4, 6, 12, and 15).

HED is usually inherited as an X-linked recessive genetic trait; in such cases the disorder is fully expressed in males only. However, females who carry a single copy of the diseased gene (heterozygote carriers) may exhibit some of the signs and findings associated with the disorder. These may include absence and/or malformation of certain teeth, sparse hair, and/or reduced sweating (such as mother of

Table 2. Report of dentomaxillofacial clinical characteristics for each of the 15 cases

Patient no.	Age	Sex	Siblings/ affected	Difficulty in breathing	Dental capital (# teeth)	Prosthetic treatment	Peg-shaped conical teeth	Abnormal root shape	External root resorption	Enclose tooth
1	5	M	2/2	Yes	16	Removable prostheses	Yes	No	No	No
2	5	M	1	Yes	3	Removable prostheses	Yes	No	No	Yes
3	6.5	F	2/2	No	14	No	No	Yes	No	No
4	9	F	2/1	Yes	20	Fixed prostheses as separated	Yes	Yes	Yes	No
5	10	M	3/3	No	18	No	Yes	Yes	No	No
6	12	M	5/2	Yes	5	Removable prostheses	Yes	No	No	Yes
7	14	F	3/3	No	21	Removable prostheses	Yes	Yes	No	No
8	15	F	10/1	Yes	17	Fixed prostheses as separated	Yes	No	No	No
9	17	M	3/3	No	16	Removable prostheses	Yes	Yes	No	No
10	17	M	10/2	No	15	Fixed prostheses as separated	Yes	No	No	No
11	18	M	9/3	No	8	Removable prostheses	Yes	No	No	No
12	18	F	4/1	Yes	1	Removable prostheses	No	No	No	No
13	21	F	9/3	No	9	Removable prostheses	Yes	No	No	No
14	24	F	9/3	No	7	Removable prostheses	Yes	No	No	No
15	45	M	7/1	Yes	17	Removable prostheses	Yes	No	No	No

Table 3. Results report of cephalometric analyses performed on affected patients

Kind of angles	Case 4	Case 5	Case 6	Case 7	Case 8	Case 10	Case 11	Case 13
SNA angle 81.0 ± 3.5	78.5	76	72	73.5	73	73.5	77	76.5
Skeletal class	III	III	III	III	III	III	III	III
SNB angle 78.0 ± 3.5	77.5	74.5	87	72	75	77.5	80.5	78.5
ANB angle 3 ± 2	+1	+1.5	−15	1.5	−2	−4	−3.5	−2
SND angle 74 ± 3.5	78	74.5	89	73	77	78	83	81.5
SN/GoGn angle 31.5 ± 5	28/5	28	19.5	31.5	18.5	28.5	19.5	26
NSGn angle 69 ± 3.5	64	69	53	68	65	68	60.5	61.5
Upper lip/lower lip/S line 0.5 ± 1.5	−2/5	−5.5	−3.5	−3.5	−7	−8	−6	−9
Lower lip/S line 0.0 ± 2.0	−4	−1.5	−3.5	−3	−7	−6	−4	−7
Pg-NB (mm) 2.0 ± 1.5	5	6	8	7.5	9.5	10	12	11.5
SGo:NMe 68%	67.9	71.5	71.2	66.6	79.4	68.5	76.4	70.6
Total concavity angle N′-Pr′-Pg′	43.5	48	28	50	49.5	42	37.5	35
Skeletal concavity angle N-A-Pg	−4.5	−4.5	−41	−7	−16.5	−19	−24	−20.5

S, sella; N, nasion; A, point of Downs A; B, point of Downs B; D, image of symphysis; Go, gonion; Gn, gnathion; Pg, pogonion; Me, menton; N, soft tissue of the nasion; Pr, paranasale; Pg, soft tissue of the pogonion.

patients 5, 7, and 9). Researchers have also reported cases in which HED appears to be inherited as an autosomal recessive genetic trait. In such cases, the disorder is fully expressed in both males and females (16,17) (Figure 9).

All of our cases are fully discernible in both males and females with no differentiation between sexes.

Despite the great number of ED cases described so far, less than 30 have been explained at the molecular level with identification of the causative gene. ED may be inherited by autosomal dominant, autosomal recessive, or X-linked genetic transmission (1–3).

In light of what is currently known about the molecular basis and biological functions in EDs, Priolo and Lagana propose a new classification that is an attempt to integrate both molecular genetic data and corresponding clinical findings. They basically propose two different groups, each likely to result from mutations in genes with similar function and possibly involved in the same mechanisms of regulation of development and/or pathogenesis (6).

These findings give the clinicians the chance to redefine HED, not simply as a result of a general 'ectodermal' abnormal development, but more precisely as systemic pathologic conditions.

At this point, scientists should have a molecular and biochemical background with a scientific multidisciplinary approach and equipment. These conditions are what make clinical diagnosis of HED difficult.

A multidisciplinary approach is required in modern dentistry for diagnosis and treatment. This study has enabled us to demonstrate a relationship among all major symptoms of HED, including hypodontia, thin hair (hypotricosis) and smooth skin (hypohidrosis). Furthermore, results support previous findings of an association among all major symptoms.

A younger age of the study participants was more common. Young oligodontia patients are usually referred to a specialized pediatrician, prosthodontics, orthodontics, pediodontist and caries manager, incorporating a multidisciplinary approach to treatment planning at an early age in this study, while also regularly seeing a specialized dentist. Older persons with oligodontia have, in most cases, received final prosthetic rehabilitation treatment and no longer feel a need to see specialized dentists. Furthermore, in older persons it may be more difficult to determine whether a tooth is congenitally missing or has been lost or whether the patient suffers from oligodontia or sequelae of caries or periodontitis.

In most children, all permanent teeth are visible on X-rays at the age of 5 years. Late mineralization of teeth is associated with oligodontia, so it is therefore possible that the number of missing teeth is overestimated in younger participants in studies (patients 1 and 3). The mean delay in tooth mineralization increases with an increasing number of missing teeth. However, many of the youngest participants were diagnosed on the basis of agenesis in the deciduous and permanent dentition.

The high prevalence of HED found in the present study is confirmed as many of the study participants had an agenesis of eight teeth or more. In the present study, the signs and symptoms of dry skin, asthma, and eczema had to be extensive in order to be recorded. Even so, the prevalence of dry and scaly skin (all patients except patient 9) was found to be high in HED patients (Figures 4–6).

The linings of the nose, larynx, trachea and lungs are moistened by various glands, some of which may be defective in HED (14). The prevalence of asthma and difficulty in breathing (patients 1, 2, 4, 6, 12, and 15) was also higher in these HED patients, although not significantly so.

In HED patients, the hair is sparse, dry, thin and light colored, as seen in a high percentage of the patients (all patients except patients 9 and 11). Also in HED patients, odontodysplasia consists of partial anadontia, microdontia, and enamel hypoplasia was found in the studied patients. All study patients had dental caries.

Nails may show dysplasia, with slow growth, transverse ridges, pitting, and varying degrees of concavity (patients 1, 3, 4, 6, 11–15). Hypohidrosis is clinically significant, and most patients had a history of recurrent fevers (all except patient 11).

All patients were referred for management of the oral manifestations of their HED. The principal aim of this study is to determine the amount of support to patients affected by HED such as restoring missing teeth, establishing normal vertical dimensions and providing support for the facial soft tissues. Conventional prosthodontic treatment (complete dentures, overdentures or a combination of fixed and removable partial dentures) is fraught with problems because of the anatomic abnormalities of existing teeth and alveolar ridges (Figure 2). The conically shaped teeth and 'knife edge' alveolar ridges result in poor retention and instability of prostheses (4,18,19). There is usually a need to remake dentures in young patients as they grow.

In conclusion, when confronted with multiple dental ageneses, the clinician should look for an association of HED signs, because HED may also be detected.

The major goal of our dental management was to provide the patient with optimal aesthetics and function so that the patient could develop physically, emotionally, and socially like other healthy individuals.

Dental management allows these patients preventive and supportive aesthetic activity, and as a result avoids social problems associated with partial or full dentures, particularly in young people. Excellent oral hygiene is crucial for the successful treatment of these patients. Patients should use daily topical fluoride for prophylaxis against new caries attacks. We estimate that the patient's age and the findings of their dentomaxillary oral check-up are essential for future management. In our opinion, practitioners and the parents of young children must be aware of the possible consequences of dental loss and the necessity for conserving the dental capital in place.

Finally, we believe that research should continue in order to improve knowledge, treatment and care for HED patients.

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