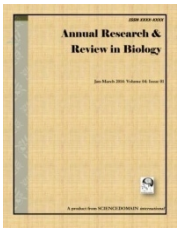

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Ectodermal Dysplasia - A Family Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author VČ designed the study, authors MJ and IŽ performed the statistical analysis. Author GL wrote the protocol. Author DGP wrote the first draft of the manuscript. Author SW managed the genetic analyses of the study. Author AB managed the literature search. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Ectodermal dysplasias (ED) are group of genetically heterogenous conditions that are characterized by abnormal development of ectodermal structures. The most affected structures are teeth, skin and its derivatives (hair, sweat glands) along with other ectodermal structures. The purpose of this work was to present the family with four boys affected with ED. We described the clinical report of male infant (affected twin) aged two months and his older brothers with absence of eyebrows and eyelashes, saddle nose, dry flaky skin, rare thin blond hair, and large number of dental anomalies with pathohistological-skin positive analysis for ectodermal dysplasia. Only a few abnormally formed teeth erupted (microdontia and conical teeth) and at the later then average age. Radiographic examination confirmed previous clinical findings and determined taurodontism of the molar teeth. They also presented pseudoprognathism of the mandible due to micrognathism of the maxilla.

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Based on the positive family history (two older brothers), clinical picture and pathohistological findings of the skin we concluded that the child (and his twin brother) were also affected. EDA gene missense mutation, Ala349Thr (GCA --> ACA), was responsible for the condition of observed family. Hair hypotriyhosis, brittle, scanty hair, absent or scanty eyelashes and eyebrows, blonde, fine scalp hair, as minor clinical signs at grandmother and only scanty eyelashes at mother were observed. Mutation analysis in families with X-linked ED help in genetic counseling, prenatal diagnosis, and confirmation of carrier status.

Keywords: Ectodermal dysplasia; hypodontia; hypotrichosis; hypohidrotic.

1. INTRODUCTION

Ectodermal dysplasia is hereditary condition characterized by the absence or defect of two or more ectodermally derived structures. The signs of hypohidrotic ectodermal dysplasia (HED) are hypotrichosis (sparseness of scalp and body hair), hypohidrosis (reduced ability to sweat), and hypodontia (congenital absence of teeth). Teeth absence is usually classified according to the number of missing teeth. Hypodontia describes a situation where the patient is missing up to five permanent teeth, excluding the third molars. The condition of missing over five (six or more) permanent teeth, excluding third molars, has been called oligodontia. The condition in which all teeth are missing is called anodontia. Erupted teeth are smaller than average and often have conical crowns. Only a few abnormally formed teeth erupt, but later. Oligodontia or anodontia is one of the most severe impairment, since it affects chewing, swallowing, speech, esthetics and social relation. Dental clinicians can be first to diagnose ectodermal dysplasia due to the absence of teeth. Early prosthetic rehabilitation, with partial and complete dentures is essential to improve oral function and reduce the social impairment [1,2]. The cardinal features of HED become obvious during childhood. The scalp hair is thin, lightly pigmented and slow-growing. Sweating, although present, is greatly deficient, leading to episodes of hyperthermia. Physical growth and psychomotor development are delayed. Other signs include: periorbital hyperpigmentation, depressed nasal bridge, decreased sebaceous secretions, large nasal secretions, lack of dermal ridges, asymmetric development of the alveolar ridge, raspy voice, fragile-appearing skin and midface hypoplasia [3].

HED can be transmitted as an autosomal dominant, autosomal recessive, or X-linked manner. Carrier testing is possible for the X-linked and autosomal recessive forms. The most common form of ectodermal dysplasia (ED) is X linked hypohidrotic ectodermal dysplasia, therefore, a male predominance is usually seen [3-6]. Management of affected individuals targets the three cardinal features and is directed at optimizing psychosocial development, establishing optimal oral function, and preventing hyperthermia [1].

2. PRESENTATION OF CASE

The purpose of this study was to present the family with four brothers affected with ED. The parental acceptance for the photographs of the children to be taken and published has been obtained as well as the ethical approval of Ethics Committee of the Split University Hospital Centre, Croatia. We described the male infants (twins) aged two months (Fig. 1) and his older brothers, aged 17 and 20 (Fig. 2), with absence of eyebrows and eyelashes, saddle nose, dry flaky skin, rare thin blond hair, and large number of dental anomalies with

pathohistological-skin positive analysis for ectodermal dysplasia. Clinical examination revealed oligodontia in both older brothers with only a few teeth erupted and anamnestic data showed that eruption occured at later then average age. Intraoral examination revealed absence of major number of the teeth with the thin alveolar crest. Panoramic radiographic examination confirmed previous clinical findings and determined hypotaurodontism of the molar teeth in case of older brother, as well as hypodontia, with no signs of formation of other tooth buds, for both of older brothers (Fig. 3). Taurodontism is a morpho-anatomical change in the shape of the tooth in which the body of the tooth is enlarged and the roots are reduced in size. In 1928., Shaw [7] classified taurodontism as hypotaurodontism, mesotaurodontism and hypertaurodontism based on the relative displacement of the floor of the pulp chamber.

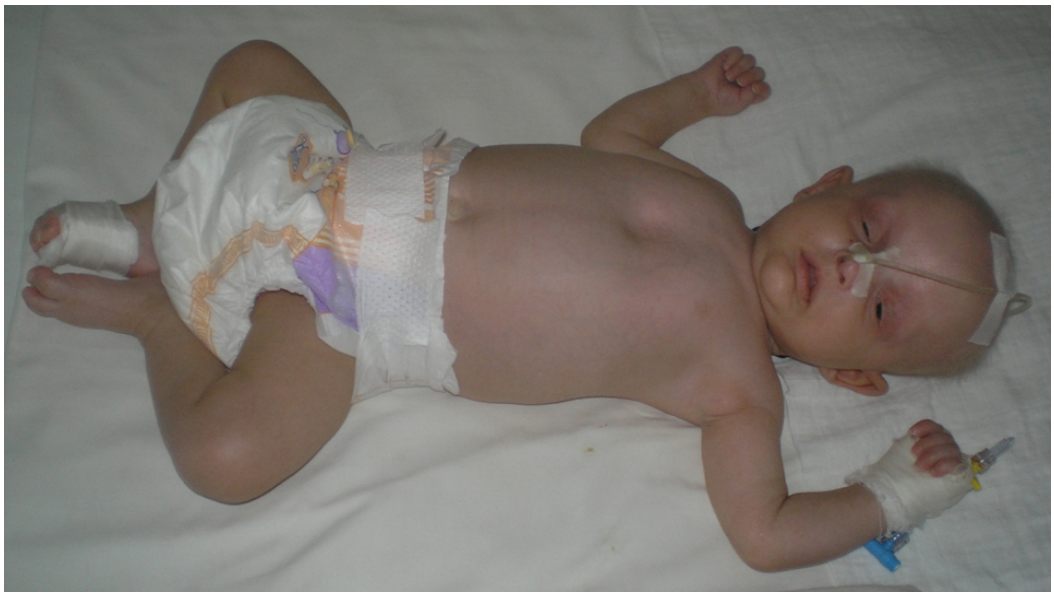

Fig. 1. One twin

The both of them presented pseudoprognathisam of the mandible due to micrognathisam of the maxilla. Reduced vertical dimension of the face was found in the case of middle brother due to hypodontia of the lateral part of upper and lower jaws. Oral mucosa appeared dry; otherwise, no mucosal defects were seen. The tongue and palate appeared normal. Based on the positive family history (two older brothers), clinical picture and pathohistological findings of the skin we concluded that the child was also affected with ED, but without OPG or any other radiographic dental examination performed. Hair hypotriyhosis brittle, scanty hair, absent or scanty eyelashes and eyebrows blonde, fine scalp hair at grandmother (80 years old), and only scanty eyelashes at mother (42 years old), as a minor sings were observed (Fig. 4, Table 1). EDA gene missense mutation, Ala349Thr (GCA --> ACA), was responsible for the condition observed in this family, revealed by polymerase chain reaction test (PCR), (Fig. 5).

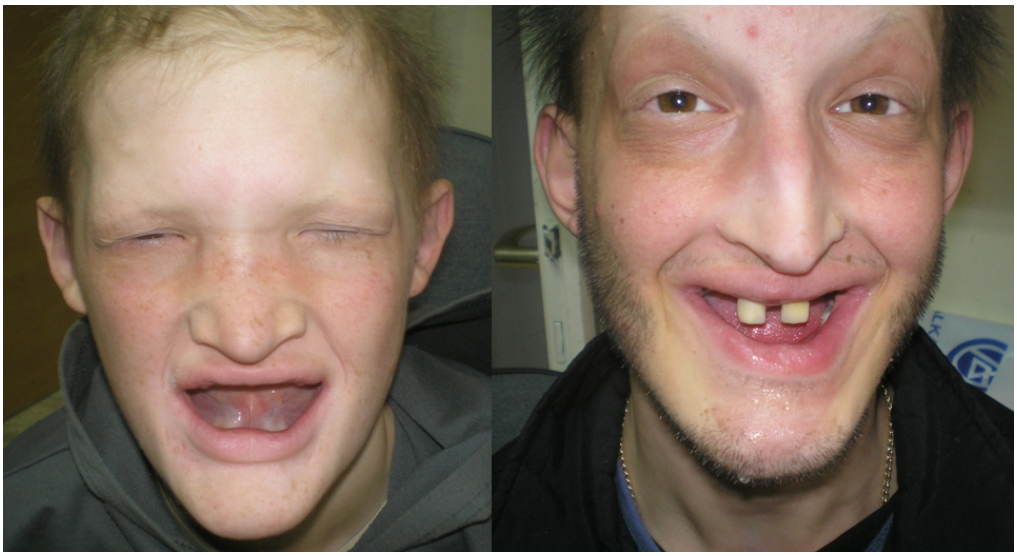

Fig. 2. Two older brothers with EDA aged seventeen and twenty

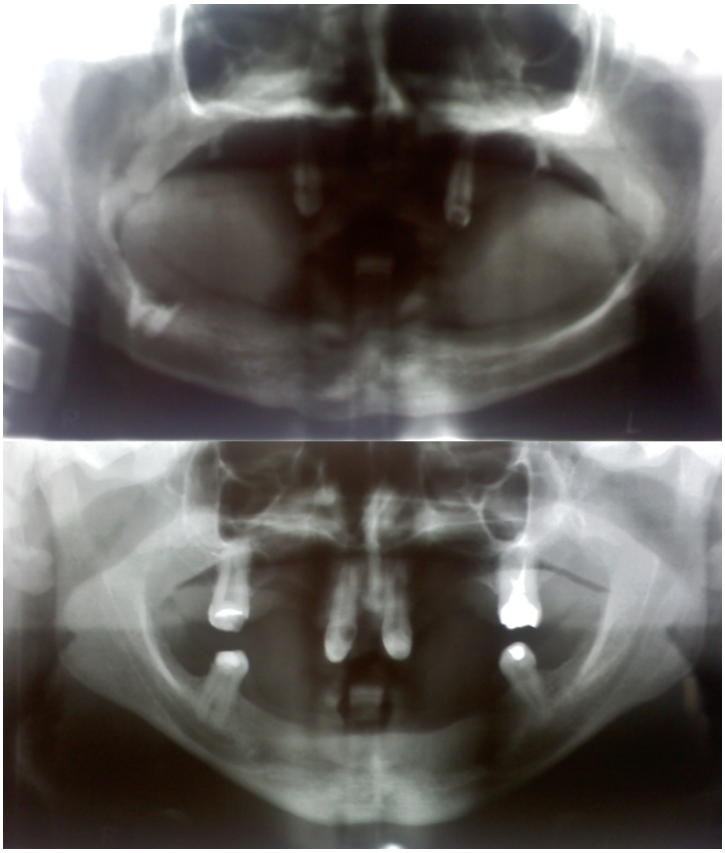

Fig. 3. Orthopan of two older brothers

Fig. 4. Grandmother (80 years old) and mother (42 years old)

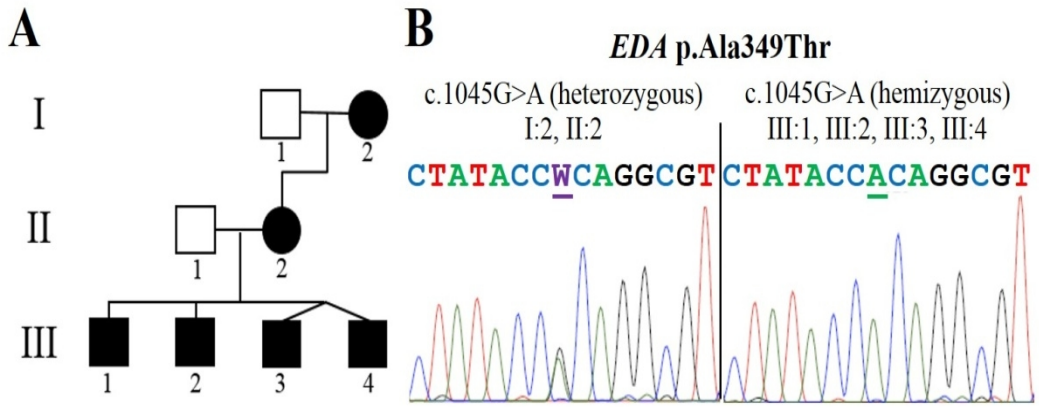

Fig. 5. Pedigree family

Table 1. Clinical synopsis from Mendalian Inheritance in Men (MIM) in comparison with patients

Clinical synopsis	T et T2	B1	B2	G	M
Small cranial length					
Frontal bossing	+	+			
Hypoplastic maxilla	+	+			
Small chin	+	+			
Small facial height	+	+			
Prominent supraorbital ridges	+				
Scand-absent eyebrows	+	+			
Periorbital wrinkles					
Periorbital hyperpigmentation		+			
Absent tears	+	+			
Absent miebomian glands					
Scant-absent eyelashes	+	+			
Small nose	+				
Hypoplastic alae nasi	+				
Nasal mucosa atrophy					
Ozena					
Depressed nasal root and bridge ('saddle nose')	+				
Mouth Decreased palatal depth					
Prominent lips	+	+			
Teeth Hypodontia		+	+		
Adontia, microdontia, conical teeth, taurodontism		+	+		
Respiratory difficulties	+	+			
Nasopharynx atrophic rhinitis					
Atrophic pharyngeal mucosa					
Hypoplastic or absent mucous glands -> lead to dried secretions and obstruction	+	+			
Larynx atrophic mucosa causing dysphonia					
Breasts hypoplastic-absent mammary glands and nipples	+	+	+		
Skin hypohidrosis	+	+	+		
Anhidrosis, sweat pore aplasia	+	+	+		
Soft, thin skin , dry skin	+	+	+		
Mild localized pigmentation abnormalities					
Skin peeling/scaling (newborn) Eczema	+				
Periorbital wrinkling, periorbital hyperpigmentation		+			
Hypoplastic-absent sebaceous glands					
Hypoplastic-absent eccrine and sweat glands	+	+	+		
Nails spoon-shaped nails					
Hair hypotrichosis	+	+			+
Fine, brittle hair	+	+	+		+
Scanty hair, absent or scanty eyelashes and eyebrows blonde, fine scalp hair	+	+	+	+/-	+
Hoarse voice due to dry laryngeal mucosa					
Intolerance to heat and fevers		+	+		
Susceptible to hyperthermia		+	+		

Notice: T1 and T2 refear to twins, B1 et B2 to two older brothers, G to grandmother and M to mother

3. DISCUSSION

HED can usually be diagnosed after infancy in the most affected individuals by the presence of three cardinal features that includes hypotrichosis, hypohydrosis and hypodontia [8]. In this case study we presented typical findings in a single twin and his two older brothers which show a great correlation with typical findings in this disorder. Paramkusam et al. [9] reported patient with very similar presentation of 19 years female with classic features of this condition.

Ohno and Ohmori [10] described case report of five years old girl with absence of all teeth of both primary and permanent dentitions. She also showed hypotrichosis and hypohidrosis [10].

Puttaraju and Visveswariah [11] described typical characteristics of HED in identical adult male twins. There were also other case reports which findings were similar to our findings [12].

As well as typical presentation of this disorder, in our case report we also described two other close relatives (mother and grandmother). Both of each were presented with aberant expression (minor clinical signs) of this disorder. Hair hypotrihosis, brittle, scanty hair, absent or scanty eyelashes and eyebrows, blonde, fine scalp hair, as minor clinical signs at grandmother and only scanty eyelashes at mother were observed. Daniel et al. [13] also reported 12 patients with rare presentation of ED. All of these patients had confirmed ED by genetic evaluation with strong familiar manifestations of the spectrum. They had variable expression of disorder and common manifestation included eczematoid skin changes, unusual facies, hypodontia, sparse scalp hair, ocular drying with corneal injury, dysphagia, hearing loss, dysphonia and even nasal cilia deficiency [13]. Prasun et al. [14] presented unusual physical features and heat stroke-like in infant in extreme winter months of Michigan. Alcon Saez et al. [15] described amastia and athelia as an exceptional presentation of HED in an adolescent female. The diagnosis of ED is based upon typical clinical signs and presence of genetic abnormalities recognised in most cases as X-linked EDA gene abnormalities (minority of cases with autosomal abnormalities). Considering the variability in penetrance of EDA genes, typical phenotype of disease is not always presented (as in some family members in this case study). Another study also described an aberant presentation of this disorder with isolated hypodontia as only presentation od disease [16].

Dental treatment for individuals affected by ED should provide them with dentition which enables chewing action and nutrition, speech, oral development and aesthetics. In order to protect the remaining teeth, good oral hygiene is essential as well as the restricted intake of cariogenic food and use of remineralizing agents (fluoride, derivates of caseine). Options for dental treatment depend on the age of the patients. For children with ED, removable or non-rigid fixed prostheses can be considered or complete dentures or over-dentures [17]. For adults, fixed restorations are preferred to provisional or removable alternatives to restore function [18]. Enamel dysplasia in patients with ED can be treated with composite restorations, veneers or full crowns. If conical shaped incisors are present, they can be extremely sharp and to avoid trauma of lips or other soft tissues, these teeth can be rounded or reshaped with restorative materials. Orthodontic therapy and selective extractions of teeth are often needed to allow prosthetic treatment. Therefore, dental treatment of patients with ED is always multidisciplinary.

4. CONCLUSION

As presented above, there is an importance of early recognising of this disease due to timely start of dental treatment for providing optimal care (and therefore prevent negative medical and social consenquences) of affected individuals. The role of recognising of minor signs of disorder can help in diagnostic evaluation and genetic consultation of family, due to already aforementioned social and medical disturbance of affected individuals.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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