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CASE REPORT

Report of two sibs with cleft lip/palate, one in combination with syndactyly and ectodermal dysplasia

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ABSTRACT

An Iranian girl with ectodermal dysplasia, cleft lip/palate, and syndactyly is reported here whose mental status was briefly impaired. The case was born in the fourth pregnancy from a first cousin marriage. The family's first offspring was aborted in the first pregnancy. The case has an 11-year-old brother with cleft lip and palate without other signs and symptoms. The third child had died just several hours after birth with unknown reason. In this report the clinical and genetic findings and the inheritance pattern of the disease is discussed.

Key words: ectodermal dysplasia, cleft lip, cleft palate, syndactyly

INTRODUCTION

The case is a six-years-old girl who was referred to the Oral Medicine Department of Dental Faculty, Shahid Sadoughi University of Medical Sciences for dental check up. In her physical examination there were signs and symptoms suggesting a rare syndrome. The phenotypes of her parents were normal and the physical examination revealed no congenital malformations in them. In their medical history, hypothiroidism was reported in the mother. The parents were first cousins which suggested an autosomal recessive mode of inheritance in their daughter. The mother's first pregnancy was ended with spontaneous abortion. The second pregnancy was a boy who had died just several hours after birth with unknown reason. The third pregnancy resulted to a boy who is 11 year-old now and after birth had cleft lip and palate without other signs and symptoms. The case present here had been delivered from the fourth pregnancy. The case's father has 2 sisters and 6 brothers. Their parents were first cousins. Two of the father's brothers had cleft palate without any other signs and symptoms (Fig. 1).

CASE REPORT

The current case is a 6-year-old girl with normal growth. Her compliance during taking history was poor suggesting low IQ. In physical examination, she was well grown, her gait was normal, but she had speech disturbances. She had the positive history of surgery contributed to her bilateral lip and palate cleft.

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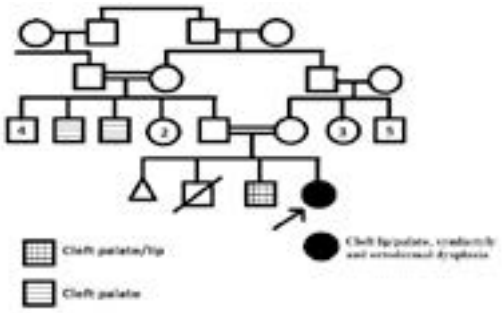

Figure 1, The pedigree of the case family

For this reason she was the subject of two different operations. In clinical examination, she had hypernasal speech and velopharyngeal incompetence which was related to the cleft palate problem and their operation side effects and scars in parts related to speech. The first operation (lip closure) had been done when she was just 10 months old while the second surgery (palatal closure) was performed when she was 3 years old. As her father claimed, she had problems in pronunciations of some consonant sounds. In addition she had congenital syndactyly of the both feet. The signs and symptoms of ectodermal dysplasia were prominent. The symptoms were reviewed in different parts as follows:

In extraoral examination from the craniofacial part, an oval shape face and sparse coarse short hair, with some structural changes called "pilli torti" or "kinky hair" was detected. The eyebrows were laterally sparse. She had reduced eyelashes. The nasal bridge was broad and the eyes were quite prominent. The scar of bilateral lip closure was also evident (Fig. 2). Her skin was dry, scaly and somehow thick especially in palmar and plantar regions. As her father said, she couldn't perspire. She couldn't make complete lipseal according to the lip scars and prominent mandible.

In intraoral examination, she had missed the teeth

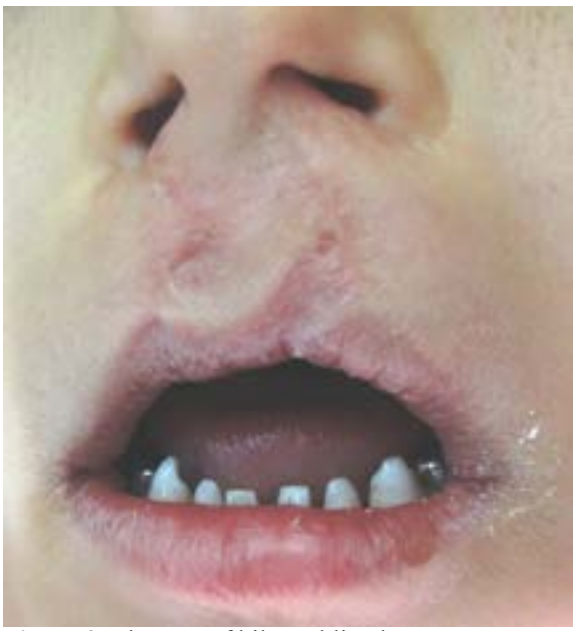

Figure 2, The scar of bilateral lip closure.

involved in the palatal cleft. The scar formation had been remained from cleft closure. The periodontium status was normal but caries evaluation revealed different types of caries which were all treated by SSC (Stainless Steel Crowns) and Amalgam fillings. Delayed eruption and hypodontia of the permanent teeth was obvious (Fig. 3).

There wasn't any syndactyly in fingers but in toes syndactyly was present between toes 2 and 3. A diskeratosis was seen in plantar surface. On her toenails, some parallel horizontal lines were obvious. Discoloration and dystrophic forms were also present in her thick nails. The skin was dry and thick, especially in the palms and soles. Plantar hyperkeratosis with dyskeratosis was seen (Fig. 4).

In her panoramic view of the jaws, enamel hypoplasia (hypocalcified and hypoplastic) was obvious. The mandibular permanent incisors showed changes in crown form, they were conic shaped with pointed or tapered incisal edges. Crown malformations were seen in molar teeth too. Her maxillary lateral incisors were missed contributed to her bilateral cleft palate (Fig. 5).

Based on the above findings, the case is more compatible with OMIM number #225060 (Cleft lip/palate-Ectodermal Dysplasia Syndrome; CLPED1). It is assumed that this condition is related to ED4 gene which is localized to an approximately 1- to 2-Mb interval on 11q23. Despite this fact, the chromosomal condition was tested by karyotype to see if she had any chromosomal abnormalities such as anupleoidy or translocations. Peripheral blood cultures and the chromosome preparations were subjected to GTG-banding using standard procedure. For the case, 30 metaphase plates were counted and at least five cells were analyzed under microscope according to ISCN 2009. The karyotype result revealed normal 46 XX results indicating a normal girl with no anupleoidy.

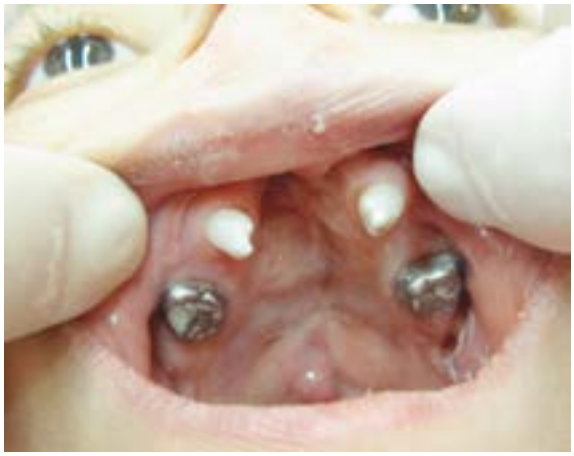

Figure 3, Intraoral examination of the case showing missed teeth involved in the palatal cleft, the scar formation from cleft closure and hypodontia of the permanent teeth.

DISCUSSION

Ectodermal dysplasia (ED) is related to a group of syndromes all derived from abnormalities of the ectodermal structures.[1] Worldwide around 7000 people have been diagnosed with an ED condition. ED can occur in any race but they are much more prevalent in Caucasians than any other group. Some ED conditions are only present in single family units and derive from very recent mutations. The various types of this disorder may be inherited in any one of several genetic patterns, including autosomal dominant, autosomal recessive, and X-linked.[2]

Even though by some accounts over 170 different subtypes of ED can be defined. These disorders are considered to be relatively rare, with an estimated frequency of 1 case occurring in every 10,000 to100,000 births. For a few of these conditions, the specific genetic mutations and their chromosomal locations have been identified.[1, 2]

In other word, this syndrome represents a group of inherited conditions in which two or more ectodermally derived anatomic structures fail to develop. Thus, depending on the type of ED, hypoplasia or aplasia of tissues, such as skin, hair, nails, teeth, or sweat glands may be seen.[2]

Perhaps the most common form of the ED syndromes is hypohidrotic ectodermal dysplasia. Most of the time, this disorder seems to show an X-linked inheritance pattern; consequently, a male predominance is often seen. However, a few families have been detected that reveal autosomal recessive or autosomal dominant patterns of inheritance.[3]

Affected individuals typically show heat intolerance as a result of reduced number of sweat glands. Uncommonly, death results from the markedly elevated body temperature. Sometimes, as a diagnostic aid, a special impression can be made of the patient's fingertips and then examined microscopically to count the density of the sweat glands.[4] Other signs of this syndrome include fine, sparse blonde hair, including

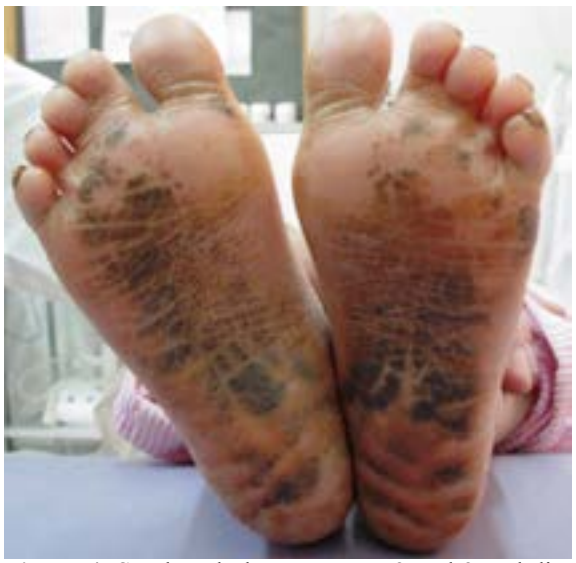

Figure 4, Syndactyly between toes 2 and 3 and diskeratosis of plantar surface

a reduced eyebrow and eyelash hair density. The nails may also appear dystrophic and brittle.[5]

The teeth are usually markedly reduced in number (oligodontia or hypodontia), and their crown shapes are characteristically not normal. The incisor crowns usually appear tapered, conical, or pointed, and the molar crowns are reduced in diameter. Complete lack of tooth development (anodontia) has also been reported, but this appears to be uncommon.[6]

Female patients may show partial expression of the abnormal gene; that is, their teeth may be reduced in number or may have mild structural changes. This incomplete presentation can be explained by the Lyon hypothesis, with half of the female patient's X chromosomes expressing the normal gene and the other half expressing the defective gene.[7]

There are some other abnormalities seen in ED described separately by the abnormal ectodermal structure. Individuals affected by an ED, frequently have abnormalities of the hair follicles. Finger nails and toe nails may be thick, abnormally shaped, discolored, ridged, slow-growing, or brittle. Infections are very common in the cuticles.[8] There may be lightly pigmentation of skin. Skin sustaining injury may grow back permanently hypo-pigmented. In some cases, red or brown pigmentation may be present. Skin can be prone to rashes or infections and can be thick over the palms and soles. Care must be taken to prevent cracking, bleeding, and infection.[9]

The enamel may also be defective. Cosmetic dental treatment is almost always necessary and children may need dentures as early as two years of age. Multiple denture replacements are often needed as the child grows, and dental implants may be an option in adolescence, once the jaw is fully grown. Nowadays this option of extracting the teeth and substituting them with dental implants is quite common. In other cases, teeth can be crowned. Orthodontic treatment also may be necessary. Because dental treatment is complex, a multi-disciplinary approach is best.[10]

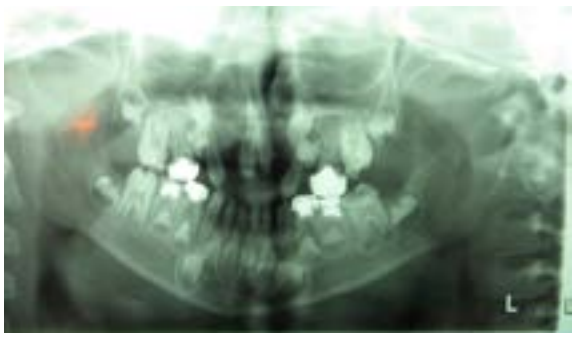

Figure 5, Panoramic view of the jaws showing enamel hypoplasia, conic shaped mandibular permanent incisors with pointed or tapered incisal edges, crown malformations of molar teeth and missed maxillary lateral incisors.

People with ED often have certain cranial-facial features which can be distinctive, frontal bossing is common, longer or more pronounced chins are frequent, broader noses are also very common.[11] In some types of ED, abnormal development of parts of the eye can result in dryness of the eye, cataracts, and vision defects. Similarly, abnormalities in the development of the ear may cause hearing problems.[12] Respiratory infections can be more common because the normal protective secretions of the mouth and nose are not present. Precautions must be taken to limit infections.[13]

In 1988 a very similar case to our case was described in which three symptom associations of cleft lip and palate, ectodermal dysplasia and syndactyly had been reported by Ogur et al. in Istanbul, Turkey.[7] Later, Bowen et al. reported three patients with mental retardation, cleft lip and palate, and syndactyly of the toes with synostosis in one of them. The adhesion of the eyelids and skin defects in two patients indicates that they are affected by a different syndrome.[9] In addition Martinez et al. reported a child with cleft lip and palate, syndactyly of fingers 1 and 2, and structural defects of the hair. However, the coarse and abundant hair with microcephaly, hypertelorism, and prominent eyes make the appearance of this child very different from the one described in the present syndrome.[13]

Among the other syndromes with ED, cleft lip/palate, and limb malformations, Roselli et al. reported four patients with cleft lip and palate, hypohidrotic ectodermal dysplasia, nails and teeth changes and mental retardation. However, some of these children had, in addition, dystrophic face skin desquamation, hypoplasia or aplasia of the thumb, and popliteal and perineal pterygium.[4]

Overall, EEC syndrome which is stands for Ectrodactyly, Ectodermal dysplasia, and Cleft lip/palate is a relatively common syndrome which includes most of the manifestations of the syndactyly, ectodermal dysplasia, and cleft lip/palate. The major differences are the mode of inheritance, as the EEC syndrome is an autosomal dominant trait, and the limb malfor-

mations, which are usually ectrodactyly in the EEC syndrome (65% of patients) but in this case it is an autosomal recessive trait and some other symptoms can be seen. Also syndactyly is evident instead of actrodactyly as seen in EEC.

However, in an isolated patient the differential diagnosis may be difficult; the presence of palmar and plantar hyperkeratosis in older patients may be particularly useful to distinguish between the two syndromes. In conclusion, it is suggested that gene mapping is performed to find the gene related to this condition as there is little published data in this regards.[14, 15]

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