Volume 21 Number 1
January 2015

Case Presentation

Unusual manifestations of ectodermal dysplasia-syndactyly syndrome type I in two Yemeni siblings

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Dermatology Online Journal 21 (1): 7

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Abstract

Ectodermal dysplasias (EDs) are a group of genodermatoses characterized by malformations of tissues derived from the ectoderm, including the skin, its appendages (hair, nails, sweat glands), teeth, and the breasts. Ectodermal dysplasia syndactyly syndrome (EDSS) is a rare, newly described type of ED involving syndactyly. We report 2 Yemeni siblings with typical EDSS manifestations, including bilateral, partial cutaneous syndactyly of the fingers and toes; sparse, coarse, brittle scalp hair, eyebrows, and eyelashes; and conical, widely spaced teeth with enamel notches. In addition, the siblings presented with other features hitherto not described for this syndrome, such as adermatoglyphia, onychogryphosis, hypoplastic widely spaced nipples, hypoplastic thumbs, and red scalp hair.

Keywords: ectodermal dysplasia, syndactyly, adermatoglyphia, conical teeth, blond hair, onychogryphosis.

Introduction

Ectodermal dysplasia (ED) constitutes a large family of congenital disorders affecting at least two ectodermal structures, including the hair, teeth, epidermis, and sebaceous glands [1]. Among them, ectodermal dysplasia syndactyly syndrome (EDSS) is a rare, newly described type of ED associated with syndactyly, whereby two or more fingers or toes are fused together. Ectodermal dysplasia syndactyly syndrome I (EDSSI) is characterized by partial cutaneous syndactyly, sparse hair, conical, widely-spaced teeth, and hypoplastic, widely spaced nipples. The syndrome is caused by a mutation in the *PVRL4* gene that encodes nectin-4, a cell adhesion molecule implicated in the formation of cadherin-based adherens junctions [2]. In contrast, EDSSII (also called ectodermal dysplasia cutaneous syndactyly; EDCS) is characterized by prominent ear pinnae, tooth enamel hypoplasia, hypoplastic nails, bilateral partial cutaneous syndactyly, hypotrichosis, palmoplantar keratoderma, and hyporhidrosis [3]. We describe the first cases of EDSSI in Yemen, involving two siblings who presented with the typical manifestations of EDSSI, in addition to characteristics not previously reported for this congenital disorder.

Case synopsis

A. Case 1

The first patient was an 18-year-old boy who was born to consanguineous parents. At birth, the child was healthy, except for sparse eyebrows, eyelashes, and scalp hair, and cutaneous syndactylies of fingers 3 and 4 and toes 2 and 3 (Figure 1 A–J). The first EDSSI symptoms were detected when the patient was 2-years-old. At that time, his teeth were noted to be conical and widely spaced, and his sweating appeared to be reduced.

At 15-years-old, the patient was detected to have symptoms not previously reported in EDSSI patients, including the absence of fingerprints (adermatoglyphia), absent axillary hairs, sparse pubic hair, and progressive alopecia of the scalp. A skin punch biopsy revealed a decreased number of sweat glands, consistent with a diagnosis of ED. A radiograph of his hands and feet proved that the syndactyly was purely cutaneous (Figure 1F). An otological examination also revealed impaired conductive hearing. Other laboratory tests did not detect other health issues, based on an examination of hematological and urinary markers of inflammation. Genetic testing is unfortunately not available in Yemen.

At 18 years of age, the young man faced difficulties that included an inability to obtain an identification card owing to the adermatoglyphia. In addition, the syndrome had a negative cosmetic impact, specifically related to his progressive scalp alopecia and small, crumpled ears.

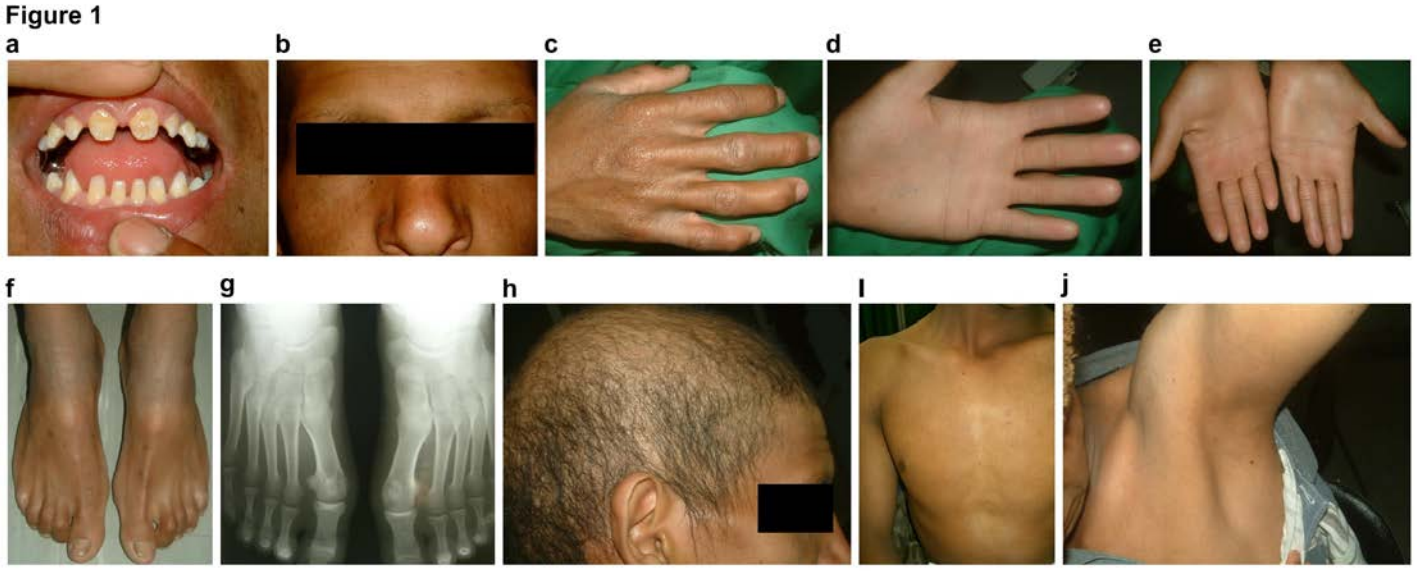

Figure 1. Patient 1. A) Peg-shaped, pointed, spaced teeth, with enamel defects. B) Sparse to absent eyebrows, and eyelashes; note the prominent sebaceous gland over the lateral nasal wall and the broad nasal bridge. C) Mild cutaneous syndactyly of fingers 2 to 5. D) Palmar diffuse keratoderma and cutaneous syndactyly of fingers 2–5; note the absence of fingerprints. E) Diffuse palmar keratoderma; note the double-grooved hand lines and creases. F) Cutaneous bilateral syndactyly of toes 2 and 3, pachyonychia congenital-like changes of the nails of toes 1 and 5. G) X-ray of the feet proved that, the syndactyly of 2nd, and 3rd toes is pure cutaneous. H) Misshapen ears, brittle hair, and diffuse alopecia. I) Hypoplastic, laterally displaced and widely spaced nipples. J) Absence of axillary hairs.

B. Case 2

The second patient was the 12-year-old sister of the first patient, born to the same parents. At birth, the patient presented the same common EDSSI symptoms manifested in her brother, namely, syndactyly, small crumpled ears, and sparse eyebrows, eyelashes, and scalp hair (Figure 2 A–H). In addition, she exhibited the unusual manifestation of wiry, red, scalp hair and hypoplastic thumbs. Further investigations revealed traits similar to those manifest in her brother.

At 12-years-old, the child is facing nutritional complications owing to her dental condition and is undergoing dental treatment for her caries. Additionally, she is facing cosmetic problems because of the appearance of her red, wiry, sparse scalp hair, hypoplastic thumbs, crumpled ears, and webbed fingers and toes.

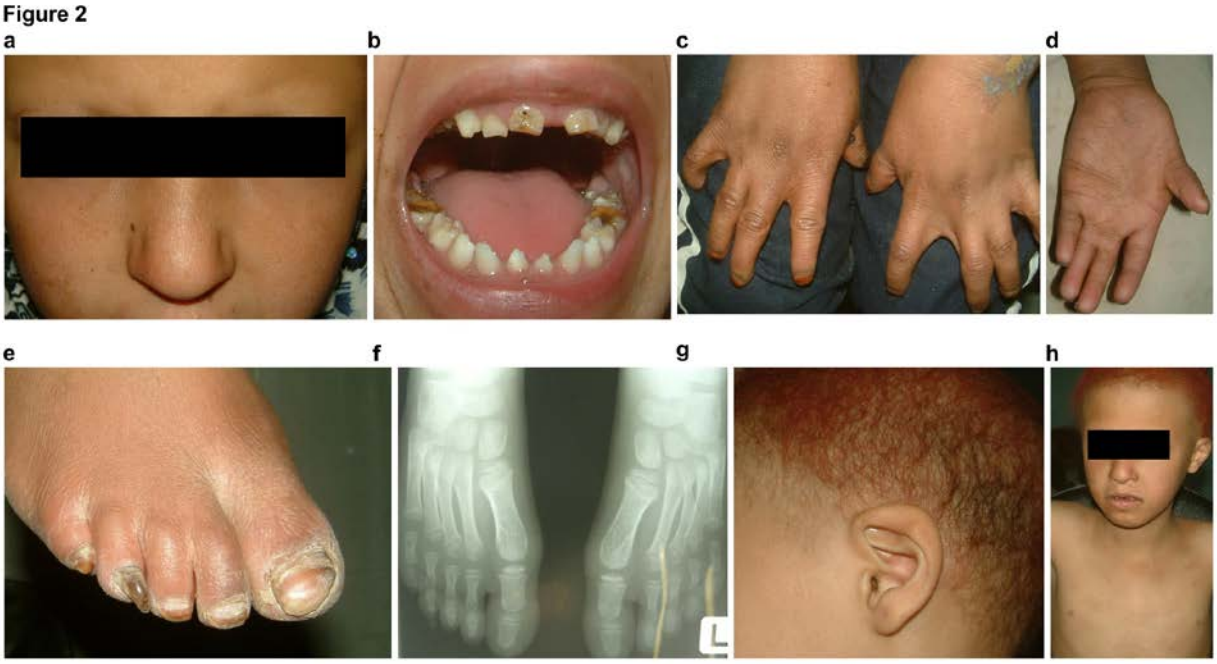

Figure 2. Patient 2. A) Sparse to absent eyebrows and eyelashes, broad nasal bridge. B) Conical, pointed, and peg-shaped teeth with caries. C) Hypoplastic thumb and bilateral, cutaneous syndactyly of fingers 3 and 4. D) Hypoplastic thumb, cutaneous syndactyly of fingers 3 and 4, with diffuse palmar keratoderma. E) Dystrophic toe nails and cutaneous syndactyly of toes 2 and 3; note the peg-shaped, brown nail on toe 4. F) X-ray of the feet showed that, the syndactyly of 2nd, and 3rd toes is pure cutaneous. G) Misshapen ear and brittle, sparse, red, scalp hair. H) Laterally displaced, hypoplastic, and widely spaced nipples.

Discussion

Very few cases of EDSS have been described in the literature, which seriously impairs the diagnosis of these patients. However, more than 170 different types of ED, with overlapping clinical features, have been reported in the literature, further complicating a differential diagnosis. The two siblings described in the present study exhibited the typical, previously reported, symptoms of EDSSI [2, 3, 4], namely partial cutaneous syndactyly; sparse, coarse, brittle, scalp hair, eyebrows, and eyelashes; and conical, widely spaced teeth with enamel notches. A diagnosis of EDSSII was ruled out because neither child manifested prominent ear pinnae, tooth enamel hypoplasia, hypoplastic nails, or hyperhidrosis. On the other hand, our patients exhibited features not previously reported in cases of EDSSI, namely adermatoglyphia, hypoplastic, widely spaced nipples, onychogryphosis, and red scalp hair (in one patient). Table 1 summerizes and compares the clinical features of two syndromes, EDSSI and EDSSII. We considered a possible diagnosis of ankyloblepharon-ectrodactyly ED syndrome because of the presence of syndactyly, crumpled ears, and adermatoglyphia [5]. However, the absence of scalp erosions, ankyloblepharon, and cleft lip/palate made the diagnosis less plausible. These patients also presented manifestations typical of acro-dermato-ungual-lacrimal-tooth [ADULT] ED syndrome; specifically including small malformed auricles, sparse hair, syndactyly, small widely spaced nipples, adermatoglyphia, blond hair, and sparse axillary hair [6,7]. However, the absence of the cleft lip/palate again ruled out this possibility. Therefore, the most plausible diagnosis was EDSSI, with unusual clinical manifestations.

Studies of rare congenital diseases involving siblings are particularly important because common manifestations are likely linked to genetic defects. The two, related patients described in this report were diagnosed with atypical EDSSI owing to the presence of hypoplastic, widely spaced nipples, onychogryphosis, and adermatoglyphia.

Table 1. Clinical features of the two syndromes

TYPE	EDSSI	EDSSII
Ears	small, crumpled	large prominent pinna
Nose	normal	pointed nose
Teeth	conical, widely spaced	enamel hypoplasia

Fingers	partial cutaneous syndactyly	partial cutaneous syndactyly
Toes	partial cutaneous syndactyly	partial cutaneous syndactyly
Nipple, breast	hypoplastic breast, widely spaced nipple	not affected
Hairs	sparse blond scalp, brows, lashes, pubic, and axillary hairs	thin body hairs, hypotrichosis
Pili torti (twisted hairs)	present only in subset of patients	absent
Palmoplantar keratoderma	absent	present
Nails	dysplastic nails, nail pits	hypoplastic flat, yellowish fingernails and toenails
Adermatoglyphia	present	not present
Heart	not affected	cardiomegaly
Mouth	normal	thin upper lip
Freckling	present	absent
Hyperhidrosis	absent	present
Follicular hyperkeratosis	absent	present

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