Hypohidrotic (anhidrotic) ectodermal dysplasia in female twins

GO Ogunrinde, RO Zubair, SO Ajike, SO Ige

Departments of Paediatrics, Oral and Maxillofacial Surgery, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

Abstract

Autosomal recessive hereditary ectodermal dysplasia (HED) has not been described in sub-Saharan Africa. It is acknowledged to be rarer than the occasionally reported x-linked and autosomal dominant variants. We report a pair of Nigerian female twins with family history and clinical features suggestive of recessive HED, thereby showing the existence of this rare form in sub-Saharan Africa.

Key words: Anhidrotic, dysplasia, ectodermal, female, hypohidrotic

Date of Acceptance: 12-Feb-2011

Introduction

Hypohidrotic/anhidrotic ectodermal dysplasia (HED) is rare. Since the first cases reported in Africa by Familusi et al. in 1975 and Denloye et al. in 1996,[1,2] a few other reports have emanated from Africa.[3‑5] It is characterized by a triad of cardinal signs (hypotrichosis, hypodontia, and anhidrosis). HED is most commonly an x-linked recessive disorder and rarely inherited via the autosomal recessive or dominant routes.[6] The male proband in Familusi et al.’s report had an affected mother, suggesting the x-linked variant of HED.[1] Also, there was no history suggestive of consanguinity from these reports.[1,2] Reports of autosomal dominant traits have been made.[1] We, therefore, describe a set of female twins aged 3 years and 5 months with HED, most likely recessively inherited, the first of such cases to be reported in Nigeria.

Case Report

HAA and HUA are identical female twins delivered via elective cesarean section following a 36-week supervised pregnancy to a 37-year old trained, but not practicing, nurse and a 52-year old accountant father, both being cousins. The twins were two of the three surviving children of the family; a male sib died at the age of 4 months of a “fébrile” illness. The twins presented to our hospital at the age of 41 months with persistent hotness of the body since birth.

At birth, both babies were said to be small with no hair on their scalps, but otherwise normal. They were treated for neonatal sepsis at a secondary level health institution. There was history of occasional fainting attacks in both girls, especially during hot weather. They were easily revived by the pouring of tepid tap water on them. They both enjoyed frequent cold baths, preferring air-conditioned environment and had little or no clothing on most of the time. They had delayed and abnormal dentition; however, their growth and development were essentially normal. At the time of presentation, they were in a play school. The second twin (HUA) had recurrent purulent, foul-smelling nasal discharge since birth.

Family history revealed that the first child, a male, had similar presentation at birth with absence of hair on his scalp. He had intermittent fever from birth. There were no other family members with similar abnormalities.

Address for correspondence:
Dr. GO Ogunrinde,
Department of Paediatrics, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.
E-mail: femiogunrinde@hotmail.com
Table 1 shows some anthropometric and clinical features of both girls. Both were of normal nutritional status in terms of height and weight. They both presented with normal body temperature, but also had evidence of recent bath with drops of water scattered all over their bodies. Their heads and facial appearances were similar with frontal and occipital bossing, hypopigmented, scanty and silky hair, sparse eyebrows and lashes. In addition to the hyperpigmentation and wrinkling around their periorbital region, twin 2 also had a generalized hypopigmentation of her face. Both girls had depressed nasal bridges, poorly developed malar bones, well-formed but low-set ears and thickened and everted lips. Their skins, palms and soles were dry. There were no significant skin rashes or abnormal dermal patterns anywhere on their bodies including their backs. The starch-iodine test was not carried out on their backs. Their nails were normal. Their eyes were also normal and not dry.

Intraoral examination revealed hypoplastic gums with only two conical/peg-shaped upper incisors and edentulous mandibles in the two girls [Figure 1]. The orthopanthomogram of twin 1 showed peg-shaped deciduous incisors and erupting ED|DE in the maxilla, while in the mandibular incisal region there were two teeth like structures in the erupting follicle [Figure 2]. In the orthopanthomogram of the second twin were two erupting buds in the mandible, and erupting ED|DE and erupted deciduous incisors in the maxilla [Figure 3]. The image also revealed two unerupted teeth in the canine region on both sides of the maxilla.

Skin biopsies taken over the left palm of each girl showed marked hyperkeratosis of the epidermis with acanthosis and broad, elongated rete pegs. The dermis in each girl showed collagen bundles with few thin blood vessels. No sweat glands were seen in either of the specimens.

**Discussion**

Ectodermal dysplasias (EDs) constitute a heterogeneous group of inherited conditions characterized by a constellation of findings involving a primary defect in at least two ectodermal-derived tissues including teeth, skin appendageal structures, including hair, nails, eccrine and sebaceous glands.\[1,7,8\]

<table>
<thead>
<tr>
<th>Table 1: Clinical data in the twins with HED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Twin 1</strong></td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight-for-height z-score</td>
</tr>
<tr>
<td>Height-for-age z-score</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
</tr>
<tr>
<td>Chest circumference (cm)</td>
</tr>
<tr>
<td>Mid-upper arm circumference (cm)</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
</tr>
</tbody>
</table>

Since the first report of HED in Nigeria in 1975, the issue of survival of affected individuals with impaired sweating and predisposition to hyperthermia, especially in a tropical region, was raised.\[1,7\] In the family that Familusi et al. studied, there were six childhood deaths among the nine children the mother had.\[1\] Three of the deaths occurred in males with facial features suggestive of HED; three
occurred in two females and a male who apparently did not have the disorder. In a Moroccan report, 5 (35.7%) of 14 affected family members died. The brother of the twins in our report with features of HED had demised at the age of 4 months.

There are two broad groups of EDs and these include the anhidrotic/hypohidrotic and hidrotic types. Under these groups, there are more than 170 clinically and genetically distinct EDs. The anhidrotic/hypohidrotic EDs are commoner than the hidrotic type and are mostly inherited x-linked traits; the autosomal dominant and recessive variants are being described as very rare. It had been proposed that the recessively inherited HED probably did not exist and that females with full-blown manifestations of the normal x-chromosome or represent balanced x:Autosome translocation. However, loci for autosomal recessive and dominant HED have subsequently been localized to chromosome 2q11-q13. In addition, Munoz et al. studied five families with possible autosomal recessive HED and were able to demonstrate the non-affectation of the EDA (ectodermal dysplasia, anhidrotic) gene on the x-chromosome in all affected individuals. They concluded, like other authors, that equally affected males and females in single sibships, unaffected parents, and consanguinity — all support the recessive mode of inheritance. Therefore, the twins in our report most likely represent autosomal recessive mode of inheritance in view of the gender, the first-degree relationship between their apparently normal parents, and the affectation of a male sib. In addition, the lack of skin “rashes” or dermal patterns does not favor mosaicism. The absence of dystrophic nails and hyperkeratotic palms and soles in either of the girls would also argue against the autosomal dominant variant. To the best of our knowledge, the twins in this study are the first cases of recessively inherited HED reported in Nigeria, the unavailability and absence of molecular analysis notwithstanding.

The hereditary pattern in Familusi’s report is likely to be x-linked recessive as the mother, but not the father, had features of HED, and there was no history of consanguinity. In addition, there was affectation of only males in the family they studied. Similarly, the twins reported by Denloye et al. were both boys, suggesting an x-linked pattern of inheritance. In the latter cases, a highly skewed random x-chromosome inactivation in the mother may explain her apparent normal appearance and lack of symptoms. The arguments may apply to our report, but the fact that both patients were females and both parents were related would strongly suggest a recessive pattern of inheritance.

One of the twins in our report suffered from recurrent respiratory infections, such as rhinitis, may be responsible for this. Some cases of HEDs have been associated with specific immune deficiencies. We did not assess the immunoglobulin status in our patients. The proband reported by Familusi and co-workers was shown to have moderately elevated level of immunoglobulin A and markedly reduced level of immunoglobulin G, indicating immune dysregulation. The knowledge of the mode of inheritance described in this study would be of vital importance in effective and accurate genetic counseling. This is more so, when as in HED, non-allelic genes produce phenotypically indistinguishable disorders.

The twins were referred to the oral and maxillofacial surgeon on account of their dentition, but the parents later decided to seek treatment elsewhere.

Acknowledgment

We thank the twins and their parents for permitting the use of their photographs in this report.

References


Source of Support: Nil, Conflict of Interest: None declared.