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V-Shaped Hyperpigmented Linear Lesions, Patchy Hypotrichosis, and Teeth Abnormalities in a Young Girl

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CASE REPORT

A 22-year-old woman presented to our Department complaining of linear hypopigmented lesions on the trunk and extremities as well as mild patchy hypotrichosis on the occipital area since infancy. Her medical history was significant for congenital dental abnormalities (hypodontia with conical-shaped teeth) that had been treated with orthodontic management and dental implants (Fig. 1). No consanguinity or similar abnormalities were recorded in the family.

The patient described generalized xerosis and was aware of having hyperpigmented linear areas that were more visible after suntanning. She did not complain of reduced sweating.

Physical examination revealed a fair-haired woman with scanty fine hair and an irregularly shaped occipital area of hypotrichosis. In the abnormal zone, the hair was thin and brittle with a whorly implantation (Fig. 2). Discrete eyebrow hypotrichosis was also noted. Linear hypopigmented streaks following a V-shaped pattern, intermingled with areas of normal skin, were observed on her back (Fig. 3). In addition, after a close examination, a patchy absence of vellus hair and stripes of hypotrichosis along the limbs were noted. No associated nail abnormalities were detected. A skin biopsy specimen taken from the transitional lines showed a segmental loss of eccrine sweat glands.

WHAT SYNDROME IS THIS?

Expression mosaicism of X-linked hypohidrotic ectodermal dysplasia.

ADDITIONAL STUDIES

A starch-iodine test was performed on the patient’s back, demonstrating a linear distribution of nonfunctioning sweat glands along Blaschko lines (Fig. 4). Active sweat pores were evidenced by the appearance of minute dark spots.

Genetic Study

Mutation analysis of the ED1 gene from genomic DNA was performed in our patient. After direct DNA sequencing, a 8-bp duplication in exon 1 of ED1 gene [c.64_71dup8] resulting in a frameshift and premature stop codon [p.Cys25AlafsX34] was demonstrated.

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DISCUSSION

Hypohidrotic ectodermal dysplasia (HED) is a genetic disorder characterized by absent or reduced skin appendages and defective dentition. Affected individuals show distinctive clinical features: frontal bossing, a depressed midface, prominent chin, thick lips, sparse hair, hypodontia, and hypohidrosis. The eccrine sweat glands are absent (anhidrotic) or greatly reduced (hypohydrotic) resulting in heat intolerance. The inability to sweat is responsible for the most dangerous consequences of the disorder, consisting in life-threatening and brain-damaging episodes of hyperthermia.

The disease is most frequently inherited as an X-linked semidominant trait (XLHED) mapped to the X-linked ectodermal dysplasia locus, ED1, at Xq12-q13.1 (1). Typically, affected patients are hemizygous male subjects showing all the characteristic clinical signs. In female carriers, the presence of two different cell lines due to inactivation of one X chromosome during embryogenesis is reflected by the presence of normal and abnormal skin areas following Blaschko lines. Random inactivation, depending on tissues, explains most of the clinical variability of the disease in females.
Female carriers of XLHED may present with only mild involvement, easily overlooked. However, discrete clinical manifestations are present in approximately two-thirds of female carriers and may consist of dental abnormalities, mild hypohidrosis, and hypotrichosis (2). Peg-shaped incisors, conical-shaped teeth or delayed eruption are seen in more than 70% of female carriers and are the most frequently observed dental abnormalities (3).

Diminished sweating, especially during childhood, or feeling uncomfortable in a warm climate is sometimes reported by female carriers. However, in many instances the patients are not aware of having a sweating disorder. Normal skin containing pilosebaceous units is lighter and slightly elevated in contrast to xerotic, slightly darker, and depressed skin containing no adnexal structures. These areas of adjacent normal and abnormal skin follow the Blaschko lines with a characteristic V-shaped pattern on the skin of the back and in a whorled pattern on the vertex or occipital area of the scalp. Some patients are aware of having tree-prints or bizarre patterns on their back, while many are unaware of this (2). Patchy absence of vellous hair and stripes of hypotrichosis along the limbs can also be observed.

These patchy manifestations can be discovered with a thorough examination in most patients, without the help of specific tests. Generally, the starch-iodine test detects heterozygous carriers with mild manifestations (4). However, the mutation search has to be considered a first-line diagnostic test to detect asymptomatic carriers (5).

Mild facial signs of the disorder such as everted lips, mild periorbital ridging, or a prominent chin are also frequently noted. Other clinical manifestations include poor breast development and hollow nipples.

Less frequent autosomal recessive and dominant modalities of HED have also been demonstrated. A gene implicated in these forms of HED, namely EDAR, has been cloned on chromosome 2q11-q13, and encodes the EDA-A1 receptor (6,7). The phenotype is identical to that of XLHED (8).

In conclusion, an increased awareness regarding the clinical manifestations of XLHED female carriers seems important to identify families with this rare genetic disorder. This diagnosis should always be considered when hypodontia and patchy areas of hypotrichosis or hypohidrosis that follow Blaschko lines are observed in a female patient. A careful examination may permit the visualization of V-shaped stripes on the back that will allow easy differentiation between carriers of X-linked and autosomal forms of HED, thus permitting the correct application of molecular studies.

REFERENCES

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