Autosomal recessive anhidrotic ectodermal dysplasia in a large Moroccan family

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Abstract

We studied a large Moroccan family in which anhidrotic ectodermal dysplasia is transmitted as an autosomal recessive trait. Fourteen family members, both males and females, were affected and they all had a common ancestor. Linkage analysis by homozygosity mapping in this family will permit the gene localisation of this rare form of anhidrotic ectodermal dysplasia.

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Anhidrotic or hypohidrotic ectodermal dysplasia (AED) is a disease characterised by total or partial anodontia, absent or reduced sweating (anhidrosis or hypohidrosis), and sparse hair (atrachosis or hypotrichosis).¹ X linked recessive AED (MIM 305100), the most frequent form of this disorder, was first described by Thurnam in 1848² and then by Charles Darwin in 1875.³ A clinically indistinguishable autosomal recessive variant of AED (MIM 224900) has been described in a few cases.⁴

In this paper, we present a very large inbred family, which includes five generations with eight women and six men all affected with AED. An autosomal recessive mode of inheritance is suggested by the consanguinity of the healthy parents who had affected sons and daughters.

Case report

The proband was an 8 year old girl at the time of initial examination (fig 1). She was born in 1985 to a consanguineous couple. She had an uncomplicated prenatal period and a normal birth. The neonatal period was complicated by episodes of hyperthermia and recurrent chest infections and she failed to thrive. In addition, she had few conical shaped teeth with two maxillary canines, four molars, and two mandibular canines (fig 2). It was also noted that she had thin and sparse hair and she was unable to sweat because of the lack of sweat glands. Furthermore, she had a distinctive face with a depressed nasal bridge, prominent lips, periorbital wrinkles, and pigmentation. An X;autosomal translocation associated with the AED phenotype was excluded by cytogenetic analysis.

Family study

The family survey showed that 13 other patients were affected with AED. They all had consanguineous parents and lived in Shoul,

Figure 1 Facial appearance of the proband.

Figure 2 Appearance of teeth in the proband.

about 50 km from Rabat. Seven patients were still living and we examined them. The other six had died from severe episodes of hyperthermia. They all had hypotrichosis, hypodontia, and anhidrosis as the most striking features. This triad is sufficient for the diagnosis of anhidrotic ectodermal dysplasia. The pedigree (fig 3) and the family history suggest autosomal recessive transmission of this disease.

Discussion

Anhidrotic (or hypohidrotic) ectodermal dysplasia is a heterogeneous condition which includes different clinically indistinguishable genetic variants.¹ Thurnam² reported the first description of the clinical features of ectoder-

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Figure 3 Pedigree of the family. The arrow indicates the proband.

mal dysplasia involving skin, hair, and teeth. The X linked recessive form is the most frequent and widely documented variant. A clinically identical autosomal recessive form has also been described, but little is known about it. Females with sporadic AED have been reported with a translocation between the X chromosome and other chromosomes.⁵⁻⁷ The breakpoint was in Xq13 in all cases, which has allowed the mapping of the gene for X linked recessive AED. Recently, the AED gene on the X chromosome was cloned and had, as a product, a novel and small transmembrane protein.⁸ Some very rare families, in which males and females were similarly affected with AED, have been reported. This form of the disease was reported in 1966 by Passarge *et al*⁹ in inbred subjects from eastern Kentucky.

Our report of this consanguineous Moroccan family in which AED is transmitted as an

autosomal recessive trait supports these findings. The localisation and identification of the gene involved in this family by homozygosity mapping and positional cloning should open the field for the molecular study of many other ectodermal dysplasias.

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