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Hair-nail dysplasia – a new pure autosomal dominant ectodermal dysplasia

Pinheiro M, Freire-Maia N. Hair-nail dysplasia – a new pure autosomal dominant ectodermal dysplasia.
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An apparently hitherto undescribed pure ectodermal dysplasia of the tricho-onychic subgroup is described. Its cause is an autosomal dominant gene with complete penetrance and variable expressivity. Differential diagnosis considered 18 conditions belonging to the same subgroup, as well as Clouston syndrome. This report increases the number of conditions of the tricho-onychic subgroup to 19, and the total number of ectodermal dysplasias to 155.

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Key words: autosomal dominant inheritance – dysplasia – ectodermal dysplasia – hypotrichosis – onychodysplasia – trichodysplasia

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Ectodermal dysplasias may be *pure* (when only ectodermal tissue derivatives are affected) as well as compose *syndromes* (when malformations are also a part of the clinical feature). In this case, dysplasias (disturbances of histogenesis) – only ectodermal or including other embryonic layers – are present side by side with disturbances of organogenesis. Pure ectodermal dysplasias are not common members of the whole nosologic group; the majority of the conditions belonging to this group are much more complex, many of them being syndromes.

This paper will describe an extremely simple pure ectodermal dysplasia of the 1–3 (tricho-onychic) subgroup of Freire-Maia's (1971, 1977) classification. The simplicity of this condition stems from the fact that the description of the signs permitting it to be classified as a member of the 1–3 subgroup is the same as the description of its whole spectrum of clinical signs.

Family study

Fig. 1 shows the pedigree of the Brazilian family under study. Both of its founders (generation I) have a German origin: the affected wife was born in Curitiba, PR, to a German family, whereas the unaffected husband was born in Hanover, Germany, and came to Brazil at the age of 8 years.

The members of this family did not permit us to photograph them.

Hair alterations

Hair alterations are present not only on the scalp but on the whole body, including the axillae and pubis. Hairs are thin, fragile, straight, slow-growing and sparse. The degree of hypotrichosis is variable. It varies from severe (almost total absence of scalp and body hair, with sparse eyebrows and normal eyelashes in one, III-10), to mild (only sparse scalp hair) in the other four examined patients.

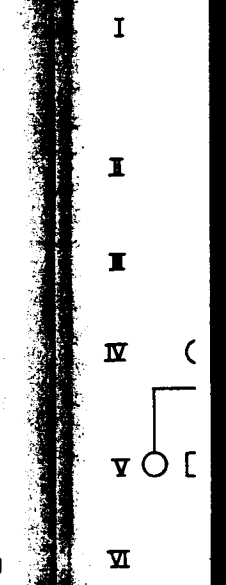
Two deceased patients have been described as having rather severe hypotrichosis similar to III-10 (II-4 and III-12). SEM analysis of hair shafts of different patients (Fig. 2) showed marked structural changes, such as different diameters along the hair shaft as if monilethrix hair shafts were stretched.

Nail alterations

The nails are short, fragile, and spoon-shaped. The fingernails are more affected than the toenails. Onychodystrophy is always mild, even in the patients with severe hypotrichosis.

Differential diagnosis

The simplicity of this pure ectodermal dysplasia makes its differential diagnosis easy. Subgroup 1–3 had 11 conditions in the book by Freire-Maia & Pinheiro (1984). This number increased to 14 in the review by Freire-Maia & Pinheiro (1987), and now (September, 1991) the number is 19, including the present condition. An analysis of the differential diagnosis with these 18 previously described conditions showed that the present hair-nail dysplasia is completely different from all of them. The



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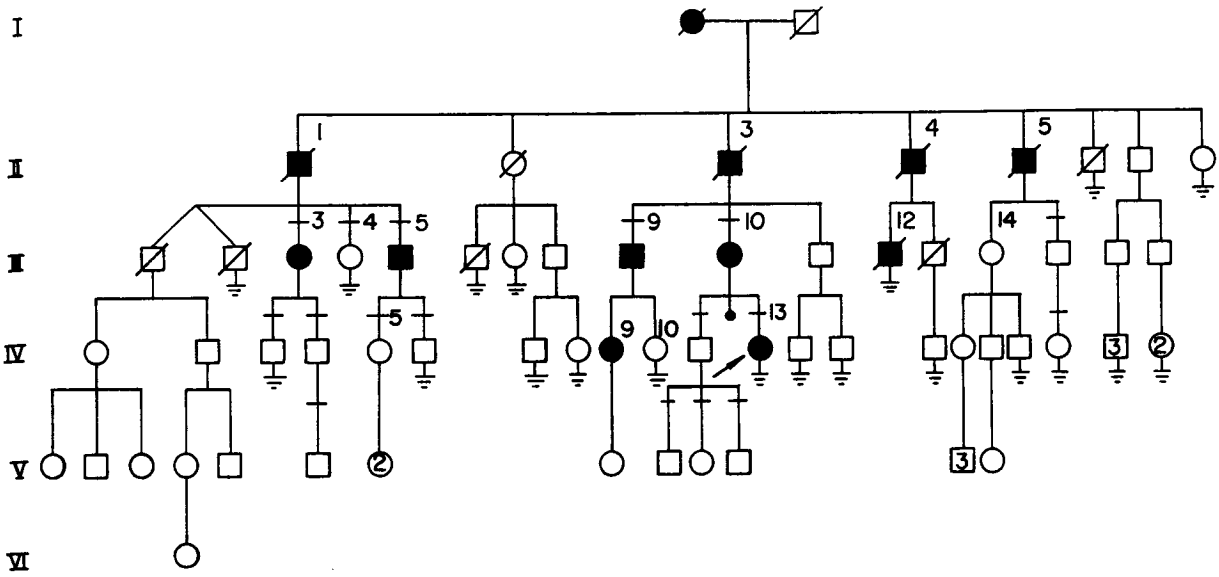

Fig. 1. Pedigree of the family. A few members of generation IV and most of the members of generation V are very young and therefore have no children.

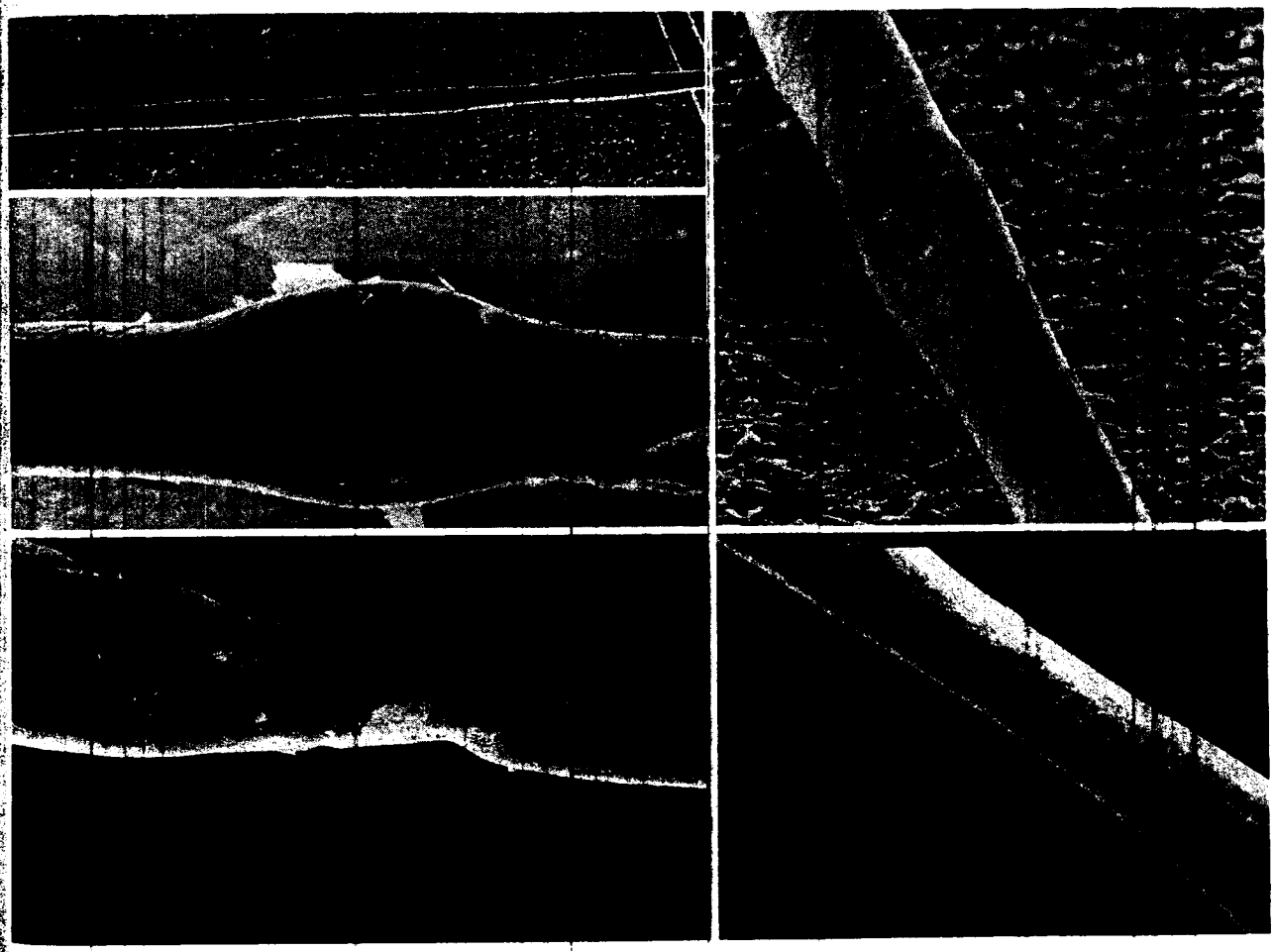

Fig. 2. SEM analysis of hair shafts from different affecteds showing multiple structural changes. (For details, see text). The two lower left photographs show different views of the same hair shaft region.

conditions not referred to in our previous reviews (1984 and 1987) are the following: Oliver-McFarlane syndrome (McK 27540), ichthyosis with alopecia, eclabion, ectropion and mental retardation (McK 24251), alveolar synechia, ankyloblepharon, and ectodermal disorders (McK – not listed; Ohishi et al. 1991) and Halal-Setton-Wang syndrome (McK – not listed; Halal et al. 1991) (cf. McKusick, 1988). All four conditions are caused by autosomal recessive genes. In spite of Clouston syndrome (McK 12950) not being a member of the subgroup (1–3), it was also considered in the process of differential diagnosis.

Genetic analysis

Analysis of the pedigree (Fig. 1) revealed a pattern of distribution of normal and affected members consistent with an autosomal dominant mode of inheritance:

1. Every affected person has an affected parent.
2. The 37 children (22 males and 15 females; $\chi^2 = 1.32$; $P > 0.20$) of normal parents (18) are normal.
3. Sons and daughters of affected persons are equally affected (7 males and 4 females; $\chi^2 = 0.82$; $P > 0.30$).
4. In the offspring of the affected men (6), the proportion of normal and affected is equally verified among both sexes (3 affected men, 6 normal men, 3 affected women and 4 normal women; $\chi^2 = 1.50$; $P = 0.50$).
5. In the offspring of the affected women (4), the same proportion holds true: 4, 5, 1, 3, respectively ($\chi^2 = 2.69$; $P > 0.30$).
6. The total of the two above distributions is 7, 11, 4 and 7 ($\chi^2 = 3.41$; $P > 0.30$).
7. The dysplasia is transmitted from fathers to sons (II-1 to III-5; II-3 to III-9; II-4 to III-12).
8. There are normal daughters (III-4, III-14, IV-5, IV-10) of affected fathers (respectively, II-1, II-5, III-5, III-9).

Some of these items overlap others. Items 1–6 corroborate the hypothesis of an autosomal dominant mode of inheritance, and items 7–8 falsify the hypothesis of a sex-linked dominant gene. Since, according to the first hypothesis, the proband (IV-13), one of her parents (III-10) and one of her grandparents (II-3) should obligatorily be affected, a correction would exclude them from the total data shown in item 6. With this exclusion, the distribution turns out to be 6, 11, 2 and 7, respectively ($\chi^2 = 6.31$; $P > 0.05$). The hypothesis of an autosomal dominant gene (with complete penetrance) is therefore supported by all the data, which also show that this gene has variable expressivity.

Discussion

The present description brings the number of ectodermal dysplasias belonging to the tricho-onychic (1–3) subgroup to 19, the total number of ectodermal dysplasias being 155. These numbers contrast with the generally held view of about two decades ago, that the number of ectodermal dysplasias varied from one (the Christ-Siemens-Touraine syndrome, McK 30510) to a few (less than ten), according to different authors (see a review of this situation in Freire-Maia & Pinheiro 1984). Now we have a totally different picture of this nosologic group, on the basis of clinical data; and we hope that pathogenetic investigations will supply a new and better way of classifying ectodermal dysplasias.

With the present hair-nail dysplasia (as we suggest it should be called), the number of autosomal dominant ectodermal dysplasias reached 44 (28%), against 46 (30%) with an autosomal recessive mode of inheritance and 7 (5%) with an X-linked mechanism, besides 58 (37%) with a poor or no suggestion at all of genetic etiology (Pinheiro & Freire-Maia, unpublished).

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