

# Odonto-ungueal dysplasia: an apparently new autosomal dominant ectodermal dysplasia

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## ABSTRACT

We describe 27 subjects (11 women) from five generations of a family with an apparently hitherto undescribed ectodermal dysplasia. All of them presented dental and/or nail alterations only. A genetic analysis of the family suggests an autosomal dominant gene. Differential diagnosis considered eight conditions belonging to the same odonto-onychic (2-3) subgroup, as well as Fried's tooth and nail syndrome and hypodontia and nail dysgenesis (both in 1-2-3 subgroup).

## INTRODUCTION

Ectodermal dysplasias form a large group of conditions in which the Christ-Siemens-Touraine syndrome (also known under other designations such as X-linked hypohidrotic ectodermal dysplasia) is the most prevalent of all.

As defined and classified by Freire-Maia (1971, 1977), ectodermal dysplasias may be subdivided into two groups. Group A contains the conditions with at least two signs related to hair, teeth, nails, and sweat glands, mnemonically labelled 1, 2, 3, and 4, respectively. A total of 11 subgroups (1-2, 1-3, 1-4, 2-3, 2-4, 3-4, 1-2-3, 1-2-4, 1-3-4, 2-3-4, and 1-2-3-4), previewed in the 1971 paper, are now known to contain 154 conditions. The number of ectodermal dysplasias in each subgroup varies from 1 to 43, and the number of conditions due to autosomal dominant, autosomal recessive, and X-linked genes are 41 (26.6%), 52 (33.8%), and 8 (5.2%), respectively. In 53 (34.4%) conditions cause is unknown: 35 (66.0%) of them present some causal suggestion (Pinheiro and Freire-Maia, 1994). Group B encompasses

those conditions with signs in only one of the above mentioned structures (hair, teeth, nails, and sweat glands) plus at least one sign in another ectodermal structure.

## FAMILY STUDY

Figure 1 shows the pedigree of the Brazilian family under study. The origin of the mutation is ascribed to the man in generation I. He was born in Oporto, Northwestern Portugal, and came young to Brasil.

All the affected (N = 27; 11 women) have dental and/or nail alterations that exhibit a large clinical variability. Figure 2 shows dental changes of the proband (IV-57 in Figure 1).

## Dental defects

Dental defects may involve both jaws and included persistence of deciduous teeth, hypoplastic enamel, microdontia, peg-shaped incisors and/or canines, widely spaced teeth, tendency to erosion up to the gingival surface, and hypodontia (absence of one to

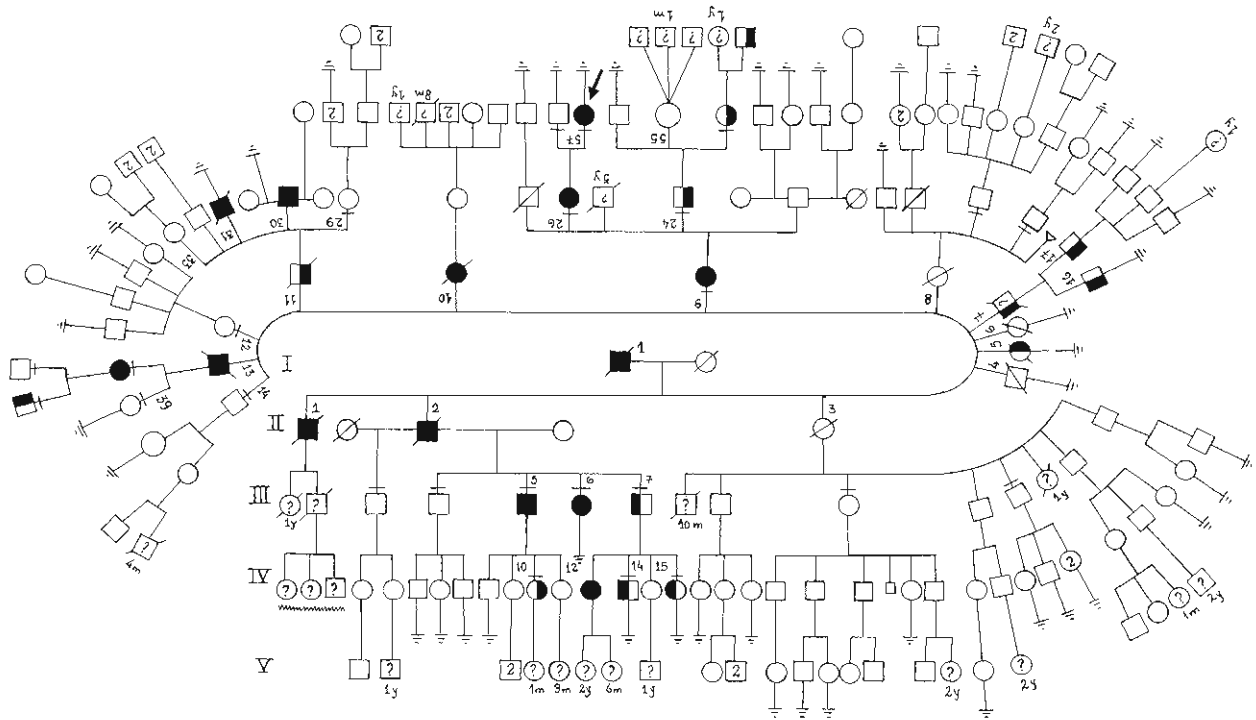


Figure 1 - Pedigree of the family. A few members of generation IV and most of the members of generation V are very young and therefore have no children. Dental alterations: symbols with the left half in black. Ungueal alterations: symbols with the right half in black.

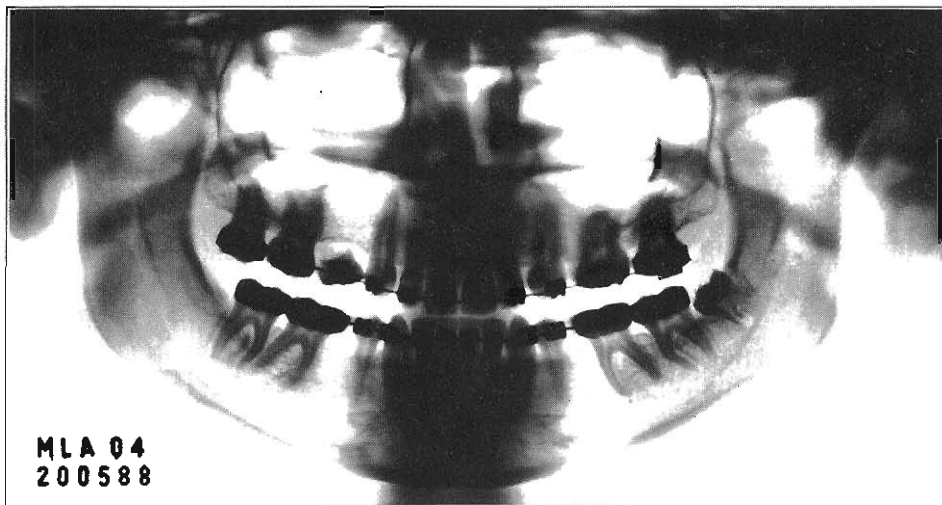


Figure 2 - Orthopantomogram of the proband (IV-57 in Figure 1) at 20 years of age. Note persistence of one deciduous tooth and absence of nine permanent teeth.

nine teeth, mainly premolars and molars). Each subject with dental defects (total = 25) is represented in Figure 1 by a left half black symbol. There were 11 subjects with dental defects only.

### Ungueal alterations

Both fingernails and toenails may be involved, but the fingernails were more affected. The alterations may include: tendency toward longitudinal breaks, short nails (childlike), slow growth, thin, fragile and

brittle, and tendency to scale off. Each subject with onychodysplasia (total = 16) is represented in Figure 1 by a right half black symbol. There were two subjects with ungueal defects only.

Fourteen patients had both dental and ungueal alterations.

### GENETIC ANALYSIS

The pedigree (Figure 1) reveals a pattern of distribution of normal and affected members consistent

with the hypothesis of an autosomal dominant mode of inheritance:

1. Every affected person (excepting I-1) had an affected parent.
2. The 93 children (54 males and 39 females;  $\chi^2 = 2.42$ ;  $P > 0.10$ ) of normal parents ( $N = 37$ ) were all normal.
3. Sons and daughters of affected parents were equally normal or affected (27 normal and 26 affected;  $\chi^2 = 0.02$ ;  $P > 0.80$ ).
4. Sons and daughters of affected parents were equally affected (15 males and 11 females;  $\chi^2 = 0.62$ ;  $P > 0.30$ ).
5. In the offspring of affected men ( $N = 10$ ), the proportion of normal and affected was equal among both sexes (10 normal males, 12 affected males, 12 normal females, 9 affected females;  $\chi^2 = 0.63$ ;  $P > 0.80$ ).
6. In the offspring of the affected women ( $N = 5$ ), the same proportion held true: 4, 3, 1, 2, respectively ( $\chi^2 = 2.00$ ;  $P > 0.50$ ).
7. The total of the two above distributions (items 5 and 6;  $N = 15$ ) was 14, 15, 13, and 11, respectively ( $\chi^2 = 0.66$ ;  $P > 0.80$ ).
8. The condition was transmitted from five fathers to 12 sons (I-1 to II-1, II-2, II-7, II-11 and II-13; II-2 to III-5 and III-7; II-7 to III-16 and III-17; II-11 to III-30 and III-31; III-7 to IV-14).
9. There were 11 normal daughters (II-3, II-6, II-8, II-12; III-29, III-33; III-39; IV-10, IV-12, IV-15; IV-55) from six affected fathers (respectively, I-1, II-11, II-13, III-5, III-7, III-24).

Some of these items overlap others. Items 8 and 9 corroborate the hypothesis of an autosomal dominant mode of inheritance, and also falsify the hypothesis of an X-linked dominant mode of inheritance. Since, according to the first hypothesis, the proband (IV-57), one of her parents (III-26) and one of her grandparents (II-9) should obligatorily be affected, a correction would exclude them from the total data shown in item 7. With this exclusion, the distribution turns out to be 14, 15, 13, and 8, respectively ( $\chi^2 = 2.32$ ;  $P > 0.50$ ).

The hypothesis of an autosomal dominant gene (with complete penetrance and variable expressivity) is supported by all the data.

## DIFFERENTIAL DIAGNOSIS

The odonto-onychic (2-3) subgroup of ectodermal dysplasias had six conditions in the book by Freire-Maia and Pinheiro (1984). This total increased to eight in the most recent review by Pinheiro and Freire-Maia (1994). An analysis of the differential diagnosis with

these eight conditions showed that only one has some similarities with the dysplasia here reported. It is named odontoonychodysplasia (POSSUM number - POS 4102; Freire-Maia and Pinheiro, 1984 - FMP 5) and was described by Murray (1921) in seven subjects (five women) from three generations. However, although these patients had dental and nail alterations only, like ours, the clinical signs (respectively, natal teeth and hypertrophy of nail beds) are different. On the other hand, according to McKusick's Catalog (1994), the patients described by Murray (1921) really have pachyonychia congenita (Jadassohn-Lewandowsky syndrome; MIM 167200).

In spite of Fried's tooth and nail syndrome (FMP 10) and hypodontia and nail dysgenesis (MIM 189500; POS 3261; FMP 11) being members of the 1-2-3 subgroup, they were also considered in the process of differential diagnosis. The first condition is probably due to an autosomal recessive gene; in both, the alterations are not limited to teeth and nails. So, it is highly probable that the ectodermal dysplasia reported here is a new one.

## CONCLUSION

The presently described ectodermal dysplasia (for which we suggest the name odonto-ungueal dysplasia) brings the number of conditions belonging to the odonto-onychic (2-3) subgroup to nine, and the total number of ectodermal dysplasias of group A to 155. The number of conditions due to autosomal dominant, autosomal recessive, and X-linked genes turns out to be 42 (27.10%), 52 (33.55%), and eight (5.16%), respectively.

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## RESUMO

Os autores descrevem 27 pessoas (11 mulheres) pertencentes a cinco gerações de uma mesma família, com uma displasia ectodérmica aparentemente nova na literatura. Todos os afetados têm apenas alterações dentárias e/ou

ungueais. A análise genealógica sugere que a causa é devida a um gene autossômico dominante. O diagnóstico diferencial considerou oito afecções pertencentes ao mesmo subgrupo odonto-oníquico, assim como também as afecções hipodontia e disgenesia ungueal e síndrome dente e unha de Fried (ambas pertencentes ao subgrupo 1-2-3).

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