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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
Pili torti and Onychodysplasia

Report of a Previously Undescribed Hidrotic Ectodermal Dysplasia

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Abstract. Ectodermal dysplasias are a large and heterogeneous group of clinically and genetically distinct syndromes. We studied a family suffering from dystrophies of the distal part of the nails and trichodysplasia. Scalp, beard, pubic and axillary hair were broken off leaving a stubble 1–10 mm in length. Eyebrows, eyelashes and body hair were completely absent. Serum levels of copper and plasma levels of amino acids were within the normal range. Inheritance was autosomal recessive. Previous reports of ectodermal dysplasias and other complex syndromes with pili torti are reviewed.

Introduction

Hereditary developmental deficiencies of tissues of ectodermal origin cause a large and heterogeneous spectrum of clinically and genetically distinct syndromes. In 1977 ectodermal dysplasias were reviewed and classified in two groups [1]. Group A includes conditions with at least two anatomical or functional anomalies of nails, hair, teeth and/or eccrine sweat glands. It is subdivided in 11 subgroups on the grounds of the various associations of these signs. Group B includes conditions with at least one of these signs plus another ectodermal manifestation. Furthermore both groups can include abnormalities in structure of nonectodermal origin and other malformations. In 1984, 117 different syndromes were classified in group A [2] but their number is increasing [3, 4]. We report a previously undescribed hidrotic ectodermal dysplasia with pili torti and onychodysplasia.

Patients and Methods

Case 1. A 54-year-old man (fig. 1; III–3) came to us in September 1988 with the chief complaint of alopecia and dystrophic nails. Both conditions had been present since birth without any variation after puberty. Sweating had always been normal and there was no history of unexplained pyrexia or heat intolerance although he was a manual laborer. He denied photosensitivity. He had always been in good health. Examination of the scalp (fig. 2), beard, pubis and armpits revealed that all the hairs were broken off leaving a stubble 1–10 mm in length. Eyebrows, eyelashes and other body hairs were completely absent. Nails showed marked dystrophies of the distal part of the plate and onycholysis (fig. 3). Teeth appeared normal in number and shape and without enamel defects. There was a mild facial dysmorphism with a long philtrum. Results of internal medicine, ophthalmologic, otolaryngologic and neurological examinations were normal. Complete blood cell count, blood chemistry, blood protein electrophoresis, immunoelectrophoresis and serum levels of copper were within the normal range. Extensive evaluation of plasma amino acid levels was performed and proved normal. Karyotype of the peripheral lymphocyte was normal. A Wechsler Adult Intelligence Scale test for assessment of brain development gave normal results. Electrocardiogram, chest and gastrointestinal X-rays did not show any abnormalities. Results of multiple potassium hydroxide examinations of the nails were negative. Scanning electron microscopy (JEOL, JSM-T100 scanning microscope) revealed focal flattening and rotations through 180° along the long axis of hair shafts at irregular intervals (fig. 4). The cuticle appeared normal. Hairs fractured within the twists. Polarized light microscopy did not show

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Fig. 1. Family pedigree. Recessive transmission mimicking dominant transmission (pseudodominance) because of consanguinous marriages (I–1 and I–2 were first cousins; II–2 and II–5 married third cousins).

Fig. 2. Case 1. Coarse stubbles 1–10 mm in length on the scalp.

Fig. 3. Case 1. Dystrophies of the distal part of the nails.

Fig. 4. Focal flattening and rotations of hair shafts fractures are at the point of twisting. SEM. ×150.
phy. Sweating had always been normal. Dermatological examination showed brittle hairs 0.5-1 cm in length. Eyebrows, eyelashes and body hair were all absent. Nails were distally dystrophic but several nail plates were partially or completely missing and substituted by pterygium unguis. The internal medicine and dental consultants failed to identify other clinical abnormalities. Routine blood and urine analyses, serum levels of copper and plasma amino acid levels were unrevealing. Histologic examination of horizontal and transverse sections of the skin of the scalp revealed a normal number of well-shaped hair follicles.

Other Relatives. The family pedigree is shown in figure 1 and includes 49 subjects. Besides the 3 probands, we examined 20 other family members including the 2 children of patient I and the 4 children and the 2 grandchildren of patient 2 (II-V; III-5; III-7; III-14; IV-2; IV-4; IV-5; IV-6; IV-7; IV-8; IV-9; IV-10; IV-11; IV-12; IV-13; IV-14; IV-15; IV-18; V-4; V-5). These showed no anomalies of sweating and presented clinically normal hair, nails and teeth. Many hairs were pulled from each from different areas of the scalp and were examined by light microscopy. We found no anomalies in the root or shaft of the hair. About the other family members we know only what our patients have referred to us or seen in photographs. Of particular interest were the photographs of 2 patients (II-1; II-2; IV-19) who were said to be suffering from alopecia and onychodystrophy. All the married members of this family married people who were clinically unaffected. Consanguineous marriages were between I-1 and I-2 (first cousins) and II-2 and II-5 married third cousins. These patients came from a mountain village of Northern Italy where consanguineous marriages were commonplace until a few years ago.

Results and Discussion

These patients show alopecia with scalp, beard, axillary and pubic hairs 1-10 mm in length. Eyebrows, eyelashes and other body hairs are completely absent. Scalp biopsies revealed a normal number of well-shaped hair follicles and sebaceous glands. Scanning electron microscopy studies of the plucked hairs revealed flattening and 180° twisting at irregular intervals. They fracture at the point of twisting. We did not find other anomalies of the hair shaft. Nails are distally dystrophic and occasionally the deformity may lead to complete destruction of the lamina with pterygium unguis. Sweating is normal and teeth abnormalities are not found. The physical examination is unremarkable and patients present a normal brain. Inheritance is autosomal recessive and in heterozygous subjects there are no hair or nail abnormalities. The etiopathology of these lesions is unknown but it is not related to abnormalities in metabolism of amino acids or copper. Regrettably no analysis of the overall composition of the hair proteins was performed. In Freie-Maia and Pinheiro’s [2] classification this family can be classified as belonging to ectodermal dysplasias of the trichoonychic subgroup of group A. In this subgroup reports similar in some respects to the syndrome described here are included. In 2 cases recently described by Vogt et al. [3], as well as in our patients, trichodysplasia, distal atrophy of the nails and facial dysmorphism with autosomal recessive inheritance were observed. By contrast, two important differences were shown: atrichia and retardation of psychomotor development were found. Some authors include Clouston’s hidrotic ectodermal dysplasia in this subgroup [4] because dental anomalies are usually minimal or absent. This syndrome is characterized by a marked variability in clinical expressivity of hair and nail dystrophies that may be quite similar to those described in our patients. It can be differentiated on the basis of its genetic characteristics: the pattern of inheritance is autosomal dominant.

Pili torti (Beare type) syndrome [5] shows pili torti and onychodysplasia but typically these anomalies appear only after puberty and it is autosomal dominant. On the basis of the complete absence of sweating and dental anomalies we can rule out all other forms of ectodermal dysplasia. In particular, even if twisted hair is a rather unpecific finding, we have distinguished those syndromes where they were often or always reported, i.e. ectodermal dysplasia with syndactyly [2], trichodontoonychdysplasia with pili torti [2], arthrogryphosis and ectodermal dysplasia [2], twisted hair and enamel hypoplasia syndrome [6], Salamon’s syndrome [7], and Rapp-Hodgkin’s syndrome [8]. Later, we evaluated possible relationships with other complex genetic syndromes, beside ectodermal dysplasia, often featuring pili torti like Bjornstad’s syndrome [9], Crandall’s syndrome [10], Menkes’ kinky hair disease [11], trichothiodystrophy [12], pseudonilethrix [13], citrullinemia [14] and arginosuccinic aciduria [15]. The absence of lesions other than pili torti and onychodysplasia and the normal findings in blood copper and amino acid determinations enabled us to exclude this diagnosis. We therefore conclude that we may be dealing with a previously undescribed ectodermal dysplasia and that our findings emphasize the clinical heterogeneity of these genetic diseases.

References


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