Familial Uncombable Hair Syndrome: Ultrastructural Hair Study and Response toBiotin

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Familial Uncombable Hair Syndrome: Ultrastructural Hair Study and Response to Biotin

V. Boccaletti, M.D.,* E. Zendri, M.D., Ph.D.,* G. Giordano, M.D., Ph.D.,† L. Gnetti, M.D.,† and G. De Panfilis M.D.*

**Section of Dermatology, Department of Surgery and †Section of Pathology and Histology, Department of Pathology and Laboratory Medicine, University of Parma, Parma, Italy*

Abstract: **We report a family affected to the fourth generation by uncombable hair syndrome. This syndrome is characterized by unruly, dry, blond hair with a tangled appearance. The family pedigree strongly supports the hypothesis of autosomal dominant inheritance; some members of the family had, apart from uncombable hair, minor signs of atopy and ectodermal dysplasia, such as abnormalities of the nails. The diagnosis was confirmed by means of extensive scanning electron microscopy. A trial with oral biotin 5 mg/day was started on two young patients with excellent results as regards the hair appearance, although scanning electron microscopy did not show structural changes in the hair. After a 2-year-period of follow-up, hair normality was maintained without biotin, while nail fragility still required biotin supplementation for control.**

Uncombable hair syndrome (UHS), first described by Duprè et al (1), is a dysmorphic hair disorder of unknown origin. Both sporadic and, not exceptionally, familial occurrences have been reported, indicating a probable dominant inheritance with incomplete penetrance in the latter (2).

Although most disorders of the hair shaft can readily be visualized and diagnosed by light microscopy, UHS requires scanning electron microscopy (SEM) evidence for diagnosis. Indeed, UHS is also named pili canaliculi et trianguli because of the SEM-detectable longitudinal depressions affecting the hair shaft, giving a triangular shape to the transversal section of the shaft itself. We describe a family with UHS, and discuss extensive SEM study and therapeutic considerations.

CASE REPORT

A 2-year-old boy had dry, unruly, blond hair (Fig. 1), atopic dermatitis, and onychoschizia of some nail plates of hands and feet. He had never had a hair cut. The hair changes began when he was 18 months-old. His younger sister, a 12 month old, showed similar nail defects but no hair changes. When asked, the mother, who had normal-looking hair, replied that during childhood she also had uncombable hair that grew in all directions; moreover, her mother and her uncle were affected by the same disorder in childhood. She also hypothesized that her grandmother was probably the first in the family with this "funny hair" defect during childhood (Fig. 2).

Address correspondence to Valeria Boccaletti, Clinica Dermatologica Università di Parma, Via Gramsci, 14, I- 43100 Parma, Italy, or e-mail: valeria.boccaletti@libero.it.

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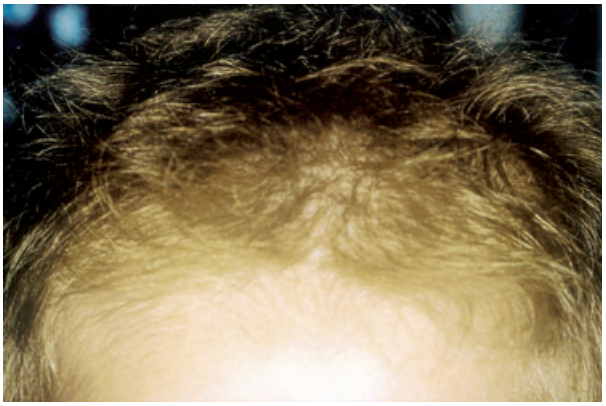

Figure 1. Hair of our 2-year-old UHS patient before biotin therapy.

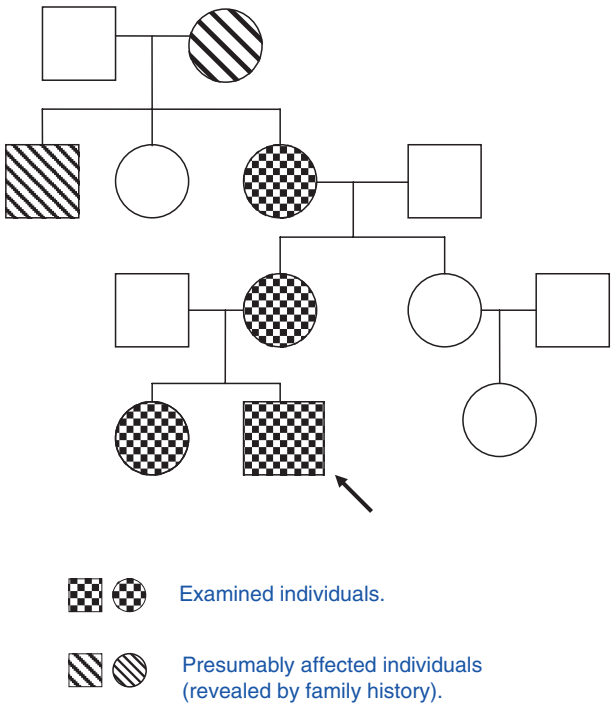

Figure 2. Family pedigree.

A diagnosis of UHS was suspected and screening serum chemistry evaluations were performed on the boy. These included blood cell count, serum zinc and copper, serum antigliadin, antiendomisium, and antithyreoperoxidase antibodies, thyroid hormones, and thyroid stimulating hormone levels. All values were within normal ranges. A light microscopic study of the boy's hair did not show any shaft alterations. Finally, SEM investigation of his hair and that of some members of his family was performed: 50–70 hairs were randomly collected from the whole scalp surface of the child, his sister, his mother, and his grandmother. Scanning electron microscopy of the boy's hair revealed discontinuous, short, longitudinal grooves, and flattenings, giving a faint elliptical or triangular cross-sectional hair shape (Fig. 3), which was unaffected by biotin therapy. It is noteworthy, as had been observed by Hicks et al (3) that these features were seen along the length of the hair and were present in $>70\%$ of the examined hairs. Analogous results came from the samples collected from the relatives, although visually their hair was macroscopically normal.

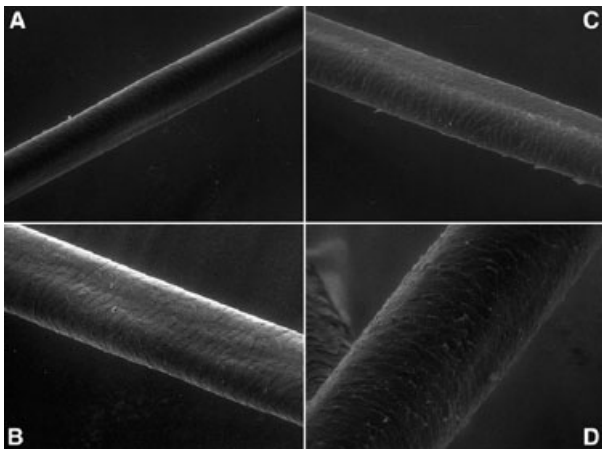

Figure 3. SEM of UHS hair. Our 2-year-old patient before (A) and after (B) biotin therapy; his mother (C) and his grandmother (D).

Once the diagnosis of UHS was established, the boy and his sister were started on oral biotin, as suggested by Shelley and Shelley (4) at a dosage of 5 mg/day and after a 3-month period we observed significant hair and nail improvements (Fig. 4). At 6 months, when the boy's hair was thicker and more combable, SEM was repeated; surprisingly, ultrastructural examination showed the hair unchanged. Moreover, after biotin was stopped by his

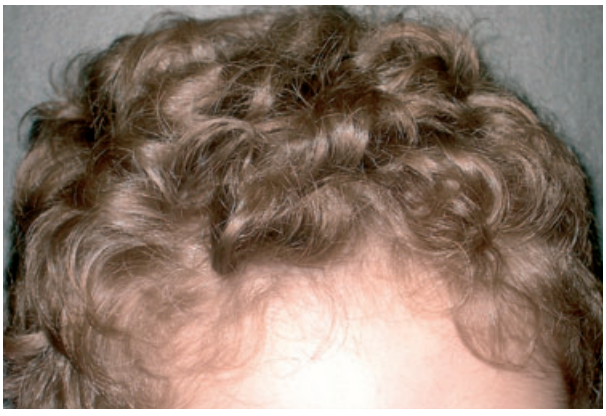

Figure 4. The UHS patient after biotin therapy.

mother because of concerns about drug safety, his hair grew unruly again. Thus a further biotin cycle was instituted, and again improvement was obtained. Now, after 2 years of follow-up, his hair condition is stable clinically, and shows normal combability; his nail fragility, however, still requires biotin supplementation to be controlled. The boy's initial atopy has spontaneously improved during this 2-year period.

DISCUSSION

Pili trianguli et canaliculi is a well-defined hair shaft disorder with the peculiar appearance of spun-glass hair. The clinical spectrum of uncombable hair includes several entities such as diffuse woolly hair, pili torti, and Menke kinky hair that can readily be diagnosed by means of optic microscopy. Based on the observation of Duprè et al (1) we diagnosed UHS not only in our patient, but also in his sister, his mother, and his grandmother. The diagnosis was confirmed by SEM, which showed the typical triangular cross-sections associated with longitudinal grooves in $>70\%$ of the examined hair. The condition had spontaneously improved with age in the two adults and, to a certain degree, their hair became more manageable with longer hair lengths. Of interest, a minimal sign of ectodermal dysplasia, i.e., onychoschizia, was an associated finding.

In early UHS descriptions, the genetics of the disease were uncertain (5), but further clinical evidence and reports of familial occurrences suggested monogenic autosomal dominant inheritance (2). Our family's findings give support to this hypothesis of inheritance, and, moreover, indicates that the condition starts in early life, long before the clinical signs appear, as demonstrated by SEM study of our patient's younger sister.

The pathogenesis of UHS is not clear. Van Neste et al (5) have suggested that misshapen dermal papillae alter the shape of the internal root sheath, which hardens, before the central hair shaft, in a triangular cross-sectional shape. Forslind et al (6) hypothesized a defect in the keratinization process because while, in normal hair, the outer root sheath is a cylinder with constant wall thickness, in UHS the irregularities of the inner root sheath are filled in by the outer root sheath itself.

The physicochemical properties of the hair in UHS that render it uncombable are not clear: stress–strain analysis (5), amino acid analysis, and X-ray diffraction analysis (7) of UHS hair had findings within the normal range. A reduced amount of extractable fibrous protein was shown in some UHS patients (8) but its significance has still to be elucidated. Shelley and Shelley (4) suggested that the matrix proteins are more important than the keratinization process because of the effectiveness of the biotin treatment in increasing the root strength, in making the scaling disappear, and in accelerating the growth rate, hence the hair becomes more pliant and combable.

As no definitive therapy for this disorder has been identified, correct diagnosis is important as it can eliminate repeated evaluations and allay parent's anxiety concerning the etiology and prognosis of UHS. We want also to highlight the undoubted effect of biotin therapy on the hair shaft defect, although the ultrastructural defects remain and combing problems may recur when therapy is stopped. For this reason, and because there seem to be no side effects (9) at least at the considered dosage, we strongly suggest supplementation with biotin in UHS, even for longer periods, in order to relieve young patients from this unpleasant condition.

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