

Congenital hypotrichosis due to short anagen

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Summary

Two children with congenital hypotrichosis are described. Both presented with persistent short, fine hair since birth. Evidence is provided that the short hair observed in these patients is due to a short anagen phase of the hair cycle, with a normal rate of hair growth. Shortening of the anagen phase of the scalp hair cycle leads to a decrease in the maximal hair length and an increase in the number of hairs in telogen, resulting in an increase in hair shedding. Scanning electron microscopy showed a widely spaced cuticular pattern, a finding typically seen in hair of thin calibre. One patient had affected family members with an apparently autosomal dominant mode of inheritance. The disorder appears to resolve spontaneously during puberty and adulthood.

Key words: hypotrichosis, inheritance, short anagen, telogen effluvium, ultrastructural findings

Congenital hypotrichosis and atrichia are among the most complex areas of hair growth disorders, with several apparently distinctive entities. Numerous individuals have so far been described with decreased numbers of hair follicles, smaller follicles and/or fragile abnormal hairs.¹ This may occur as an isolated defect, or as a feature of a hereditary syndrome, usually in association with other ectodermal defects (ectodermal dysplasia). Where a structural hair shaft defect is characteristic, it has given its name to the disorder, as in monilethrix. Among the hereditary forms of isolated hypotrichosis, Marie Unna's hereditary hypotrichosis is the best characterized, and is delineated from hereditary hypotrichosis simplex (HHS) by the presence of wiry hair and development of scarring alopecia.² HHS is a descriptive term for the clinical expression of a variety of phenomena related to diffuse thinning of the scalp hair without any gross abnormality of hair shaft morphology or associated anomalies. Several pedigrees have been published, with autosomal dominant inheritance, but with differences in clinical features, such as age at onset, severity, and involvement of eyebrows and eyelashes.^{3–6}

In his review article on telogen effluvium, Headington⁷ proposed, on the basis of clinical observation, that some individuals may experience a slight but persistent telogen effluvium in association with the

inability to grow long hair due to an idiopathic shortening of the anagen phase of the hair cycle. In a review on congenital hypotrichosis, de Berker¹ described a subset of children where reduced duration of anagen is proposed to be the sole abnormality. However, this has not been quantified. The typical patient is a fair-haired girl presenting between the age of 5 and 10 years, whose hypotrichosis tends to improve with puberty, and there is no specific diagnosis other than a familial tendency to have this hair growth pattern. Scientific evidence for the existence of short hair due to a short anagen cycle was first obtained by Kersey⁸ in a patient with trichodontal syndrome. He described a family in which three members presented with decreased hair length. They all had short, fine hair from birth. By measurement of hairs in a hair growth window and trichogram findings, the short hair was shown to be due to a short duration of the anagen phase.

We present two patients with congenital hypotrichosis in whom we demonstrate, by applying the same methods as Kersey, that a short duration of anagen is the underlying abnormality.

Case reports

Patient 1

A 5-year-old girl was referred with short blond hair that had not been cut since birth (Fig. 1). She was the

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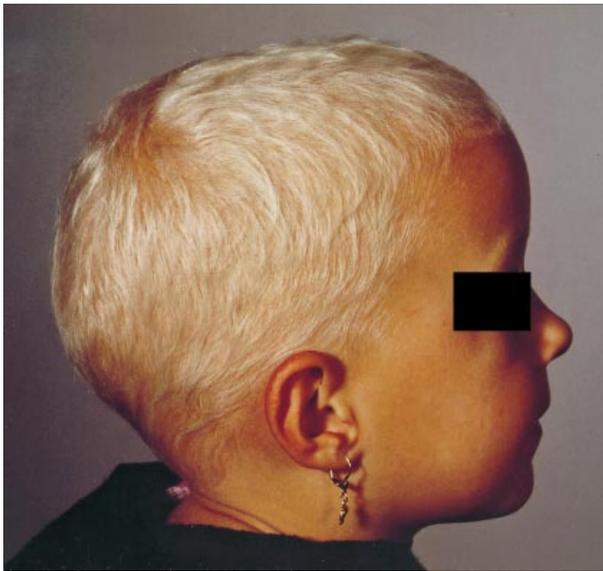


Figure 1. A 5-year-old girl with short, light blond hair that had not been cut since birth (patient 1).



Figure 3. The paternal aunt of patient 1, aged 3 years, with short, blond hair that had not been cut since birth.



Figure 2. The father of patient 1, aged 6 years, with short blond hair that had not been cut since birth.

first child of non-consanguineous parents. Her prenatal, natal and postnatal periods had been uneventful, and physical and psychomotor development was normal. There were no skin abnormalities, and heat- and exercise-induced sweating was normal. No dental or nail abnormalities were noted. Three other family members, namely the father (Fig. 2), his sister (Fig. 3) and their mother (Fig. 4) also had fine blond hair that reportedly did not grow long in childhood. They, too, had no associated abnormalities, particularly of teeth or nails. Although they had short, fine hair as children, the father's and grandmother's condition subsequently normalized in adulthood. The aunt's condition normalized earlier: by the age of 10 years, she had age-appropriate hair length. Other family members reported to have been similarly affected were the great-grandfather, his two sisters and the great-great-grandfather on the paternal side of the family (Fig. 5). The latter family members could not be examined as they were deceased.



Figure 4. The paternal grandmother of patient 1, aged 11 years, with short, blond hair that had not been cut since birth (arrow).

Patient 2

A 6-year-old girl was referred with short blond hair that had not been cut since birth (Fig. 6). She was the first child born to non-consanguineous parents, and had had uneventful prenatal, natal and postnatal periods. Physical examination, including skin, teeth and nails, was normal, and there were no abnormalities related to sweating. Her younger brother and parents had no hair abnormalities, but a cousin on the paternal side was reported to have had very short hair during the first 2 years of life, which had subsequently normalized.

Materials and methods

Two separate samples of approximately 50 hairs each were plucked from the frontal and occipital scalp of

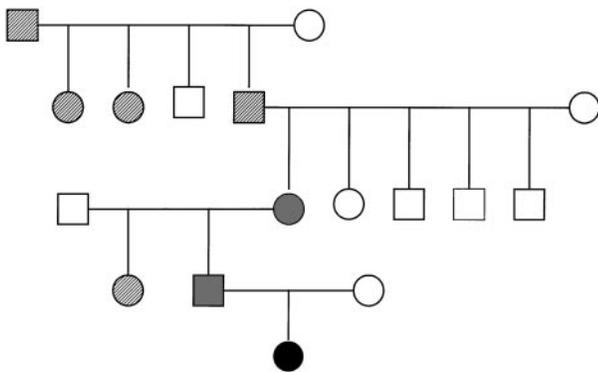


Figure 5. Pedigree of patient 1. Square, male; circle, female; black symbol, short anagen hair (patient 1); grey symbols, probable short anagen hair in childhood; hatched symbols, possible short anagen hair in childhood.



Figure 6. A 6-year-old girl with short, light blond hair that had not been cut since birth (patient 2).

both patients, as well as from the first patient's affected father and grandmother. The roots were examined at $\times 10$ magnification to establish the anagen to telogen ratio (trichogram).⁹ Hair samples obtained from the vertex region were examined by scanning electron microscopy (SEM) to ascertain the hair shaft and cuticular structure.

To determine the rate of hair growth, a hair window was performed by close-shaving an area on the vertex of approximately 4 cm². Six weeks later, the same area was reshaved with a scalpel blade, and the shaved hairs collected and mounted under cellophane tape. The length of each hair that was square cut at both ends was measured. The diameters were measured at $\times 10$ magnification.

The growth rate of the finger nails was measured by marking an area on the nail plate with a carbon dioxide laser, and measuring the distance from the mark to the skin–cuticle interface after a period of 6 weeks.

The urine of both patients, and that of the father and grandmother of the first patient, was examined by electrophoresis to exclude inborn errors of amino acid metabolism. Written statements on dental status were obtained from the patients' dentists, to exclude any dental abnormality. A clinical examination to exclude anaemia was also performed.

Results

Maximal hair lengths were 6 cm (patient 1) and 12 cm (patient 2). Examination of the patients' hair by light microscopy showed fine blond hair with a reduced diameter in patient 1, but no obvious shaft abnormality. The distal end of each hair examined tapered to a fine

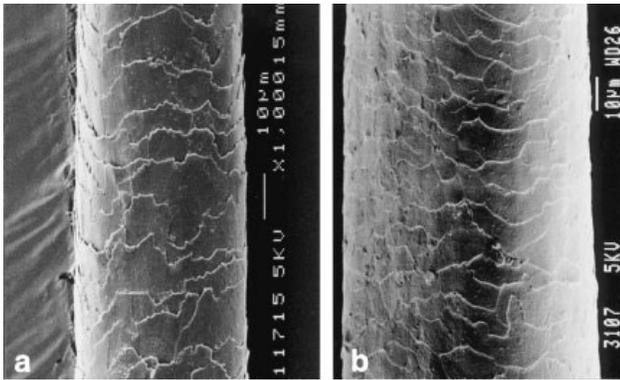


Figure 7. Scanning electron micrographs of scalp hair (a) from patient 1; diameter 36 μm and (b) normal hair; diameter 91 μm . Note the irregular and widely spaced cuticular scales in (a). Scale bar = 10 μm .

point, confirming that it had not been cut. None of the hairs showed any evidence of weathering. Examination of the first patient's father's and grandmother's hair revealed no significant abnormalities of structure. SEM examination of both patients' hair showed a widely spaced cuticular pattern (Fig. 7), without signs of weathering such as saw-toothed margins and fissuring of the cuticular cells, orifices in the cuticular cells, adherence of amorphous material to the cell surface, cuticular detachment or total loss of the cuticular layer.¹⁰

In both patients, anagen to telogen ratios from both the frontal and occipital scalp areas were markedly abnormal, with a high percentage of hairs in telogen (Table 1). Both total anagen counts and anagen to telogen ratios were significantly reduced, even though the many hairs that were incomplete after plucking were assumed to be in anagen. The trichogram findings in the first patient's father and grandmother showed essentially normal anagen to telogen ratios. In both cases the percentage of telogen hairs in the frontal area was higher than that in the occipital area, in keeping with androgenetic alopecia.

Measurement of shaved hairs on the vertex delivered mean \pm SD growth rates of $0.34 \pm 0.08 \text{ mm day}^{-1}$ ($n = 92$) in the first patient, $0.34 \pm 0.08 \text{ mm day}^{-1}$ ($n = 128$) in her father and $0.45 \pm 0.07 \text{ mm day}^{-1}$ ($n = 148$) in her grandmother. Mean growth rate in the second patient was $0.30 \pm 0.04 \text{ mm day}^{-1}$ ($n = 90$). Mean \pm SD hair shaft diameters were $53 \pm 14 \text{ mm}$ ($n = 92$) in the first patient, $70 \pm 15 \text{ mm}$ ($n = 128$) in her father, $80 \pm 18 \text{ mm}$ ($n = 148$) in her grandmother and $100 \pm 20 \text{ mm}$ ($n = 90$) in the second patient. The mean \pm SD rate of nail growth in all the patients was essentially normal ($0.1 \pm 0.01 \text{ mm day}^{-1}$). Both dental records and urine electrophoresis were normal, and there was no clinical evidence of anaemia.

Discussion

Two children are presented, in whom abnormally short blond hair was due to a short anagen phase, as previously proposed by Headington⁷ and de Berker¹ in a subset of patients with persistent telogen effluvium of undetermined aetiology and some patients with congenital hypotrichosis, respectively. Persistently short hair may be due either to slow growth or to a shortened hair cycle. In both patients the measured growth rate on the vertex was in the range reported for normal individuals (females $0.302 \text{ mm day}^{-1}$; males 0.34 mm day^{-1}),^{11,12} suggesting that the short hair was the result of a shortened anagen phase, and not due to slow growth.

This is further substantiated by the results of the trichograms. The normal ratio of anagen to telogen is 9 : 1. This parallels the ratio of the duration of these phases of the hair cycle in normal hair growth.⁹ In children of either sex between 3 and 11 years of age, 90% of the hairs are in the anagen phase.¹¹ If the short hair in both patients was due only to slow growth, then the anagen to telogen ratio should be normal, as the proportion of time spent in each phase of the hair cycle

Table 1. Numbers of hairs in anagen and telogen in samples from the frontal and occipital areas of the scalp (trichograms from patients 1 and 2)

	Number of hairs			Anagen to telogen ratio	% of hairs in telogen
	Telogen	Anagen	Incomplete ^a		
Patient 1					
Frontal	61	19	19	38: 61	63
Occipital	17	3	27	30: 17	36
Patient 2					
Frontal	47	4	0	4: 47	92
Occipital	27	3	4	7: 27	79

^aIncomplete hairs assumed to be in anagen.

would still be normal. However, if the short hair was due to a shortened anagen phase, an alteration of the anagen to telogen ratio would be expected. In the first patient, this ratio was 38 : 61 (frontal region) and 30 : 17 (occipital region). In the second patient, the ratio was 4 : 47 (frontal region) and 7 : 27 (occipital region). These findings are markedly abnormal. On the basis of the patients' histories and clinical findings, alternative causes of decreased anagen roots in the trichogram are excluded, namely: (i) diffuse telogen effluvium due to synchronized premature entry of anagen hairs into telogen as a result of drug-related events or following periods of physiological stress, including high fever, and (ii) progressive shortening of the duration of anagen due to miniaturization of the hair follicle, as in androgenetic alopecia. The trichogram findings are thus consistent with a shortened anagen phase. In contrast, the ratios in the first patient's father and grandmother were consistent with age-related expression of androgenetic alopecia, where the occipital ratio is normal.

The greater proportion of telogen hairs present with a short anagen phase also explains the clinical finding of reduced hair density. On the other hand, dramatic increases in hair shedding are not clinically encountered until the duration of anagen is significantly reduced below a clinically detectable threshold (approximately 500 days). A 50% reduction in the anagen phase results in a doubling of hairs in telogen.⁷ The first patient's hair growth rate was 0.34 mm day⁻¹, and maximum hair length was 6 cm. The duration of anagen was thus 176 days, this being approximately one-quarter of the minimal length of anagen in normal individuals. The second patient's hair growth rate was 0.3 mm day⁻¹, and maximum hair length was 12 cm. The duration of anagen was thus 400 days, this being approximately one-half of the minimal length of anagen in normal individuals. The lack of signs of weathering at the tips of the hair provides further evidence of a shortened anagen phase. Hair that has not been cut for the duration of normal anagen would have cuticular degeneration near the tip. This was not observed in either of our patients. On SEM, the observed widely spaced cuticular pattern is not a feature of weathering,¹⁰ but is typically found in hair of thin diameter.¹³ The reduced hair diameter in patient 1, being at the lower end of the normal range (40–120 µm), confirmed the clinical impression of fine hair.

The condition appeared to be familial in the first patient, with probable autosomal dominant inheritance. Photographs of her father, his sister and their mother in

their childhood (Figs 2–4) show the appearance of their hair to be very similar to that of the patient. Our investigations in the father and grandmother did not demonstrate a shortened anagen cycle other than in the context of clinically evident androgenetic alopecia. However, the historical evidence points to them having had this condition in childhood. With our present knowledge, we can only speculate that short anagen hair may normalize during puberty and adulthood, a phenomenon observed in other hair disorders of childhood, such as loose anagen hair and uncombable hair. In contrast, in the previously reported cases of HHS with autosomal dominant inheritance, the course tends to be progressive, leading to severe hypotrichosis by the early twenties.^{3–6}

As a therapeutic measure, minoxidil may be useful for short anagen hair. It is believed to stimulate mitotic activity and prolong the viability of follicular keratinocytes, resulting in a longer anagen phase.¹⁴ On the other hand, spontaneous normalization can be expected with the onset of puberty.

Short hair due to a short anagen cycle was first demonstrated in 1987 by Kersey⁸ as part of the trichodontal syndrome. To the best of our knowledge, these are the first cases of congenital hypotrichosis due to short anagen without associated abnormalities, documented by the same methods. The ultrastructural findings were identical to those found in the trichodontal syndrome, i.e. widely spaced cuticular pattern and absence of weathering at the tips of the hairs. The pattern of inheritance in one of the patients appeared to be autosomal dominant. On the basis of these findings, we conclude that congenital hypotrichosis due to short anagen is a true entity.

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