Non-Familial Congenital Hypotrichosis: Report of 11 Cases

Hee Chul Eun, M.D., Oh Sang Kwon, M.D.,
Sang Duck Kim, M.D., Dae Hun Suh, M.D.

Department of Dermatology, Seoul National University College of Medicine,
Seoul, Korea

Background: Congenital hypotrichosis is a non-specific, descriptive term for structural abnormalities of hairs showing variable clinical features. We recently have encountered a group of eleven patients exhibiting abnormal hairs showing similar patterns.

Objectives: Our purpose was to clarify the entity of this structural hair disorder.

Methods: Dermatologic examination with routine histopathology, trichograms along with scanning electron-microscopic examination and laboratory studies were undertaken.

Results: All cases except one were female, and hair abnormalities had developed at birth or within a year. Diffuse distribution of thin, sparse, soft and hypopigmented hairs were noticed. On hair mounts, four patients showed tapering of roots. The majority of the patients exhibited cuticular changes, as well as pitting and longitudinal axial twisting by scanning electron-microscopic examination; one case demonstrated trichorrhexis nodosa, and another, transverse fracture.

Conclusion: Although our cases bear some similar points with woolly hair, some differences were noted between this type of congenital hypotrichosis and other previously described syndromes. (Ann Dermatol 12(1) 26–32, 2000).

Key words: Congenital hypotrichosis

Hereditary or congenital hypotrichosis is regarded as a non-specific term to describe the clinical expression of abnormal hairs with variable pattern of inheritance. Its clinical pattern is variable as hypotrichosis is either confined to their hairs in some patients or associated with other ectodermal abnormalities. Features of skeletal, chromosomal or amino acid defects are frequently noticed. A syndrome of congenital hypotrichosis with diffuse, thin, curled and hypopigmented hair with unusual clinical features was encountered in eleven Korean patients. The mode of inheritance was unknown, which may be sporadic or X-linked as female subjects were predominantly affected. Furthermore, associations with anomalous conditions of the teeth and nails were not observed. A search of the literature revealed no records exactly coinciding with this pattern of congenital hypotrichosis. Therefore, it may be a variant of previously described congenital hypotrichosis syndromes.

PATIENTS AND METHODS

All the patients who the visited hair clinic between 1990 and 1997, with complaints of abnormal hairs were evaluated. Various investigative measures including physical examination of hairs and hypoplastic teeth, routine histopathology, trichogram, scanning electron-microscopic examination, and laboratory studies were performed; the studies included a routine laboratory series of com-
plete blood count, liver function tests, urinalysis with microscopic examination and serologic studies, measurement of serum copper and zinc levels, thyroid function test and T cell subset counts. Among those evaluated, eleven patients who did not coincide with the criteria of previously described congenital abnormalities of hair showing similar features were enrolled.

Further analysis of these subjects on clinical history including age of onset, duration, sex, familial tendency, clinical characteristics including development of anhidrosis was performed by interviewing the patients and their parents. As for adults, the pattern of hair loss which was before the puberty was investigated by the interview method. For those who were younger than fifteen, body weights and heights were recorded and were matched with the percentile of the identical age group, as for adults, those whose height was less than 150cm were regarded as suffering from growth retardation. The degree of development was assessed by interviewing the patient - or their parents- with representative scales of Korean DDST (Denver Development Scale Test). Furthermore, any affected relatives within the third degree were investigated by interview. In addition, laboratory results were reviewed retrospectively.

**RESULTS**

Based on their medical and family history, all eleven cases were presumed to be sporadic. However, possibilities of X-linked inheritance could not be ruled out.

**Clinical characteristics (Table 1)**

Five cases presented with structural hair abnormalities at birth while in six, the condition developed within a year. In cases of the adult patients, the pattern of abnormal hair growth was identical to

<table>
<thead>
<tr>
<th>Case</th>
<th>No</th>
<th>Sex/ Age</th>
<th>Age of Onset</th>
<th>Hair loss</th>
<th>Hair breaking</th>
<th>Hair shedding</th>
<th>Other hair involvement</th>
<th>Other disease</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/5</td>
<td>Birth</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Atopic dermatitis</td>
<td>MNX, 6 Months</td>
</tr>
<tr>
<td>2</td>
<td>F/7</td>
<td>Birth</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>MNX, 2 year</td>
</tr>
<tr>
<td>3</td>
<td>F/4</td>
<td>1 Mo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Eye brow with depigmentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F/6</td>
<td>1 Mo</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Atopic dermatitis</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F/5</td>
<td>3 Mo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Eye brow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F/13</td>
<td>3 Mo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Scoliosis, Caf-au-lait spot</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F/9</td>
<td>4 Mo</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Atopic dermatitis</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F/11</td>
<td>11 Mo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Lateral eyebrow</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case</th>
<th>No</th>
<th>Sex/ Age</th>
<th>Age of Onset</th>
<th>Hair loss</th>
<th>Hair breaking</th>
<th>Hair shedding</th>
<th>Other hair involvement</th>
<th>Other disease</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>F/17</td>
<td>Birth</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>MNX, 6 Months</td>
</tr>
<tr>
<td>10</td>
<td>M/20</td>
<td>Birth</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Eyebrow, axilla, pubic hair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>F/34</td>
<td>Birth</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MNX: 3% minoxidil solution
the pattern before their puberty. The sexual predominate was for females with a ratio of 10:1. No patient complained of progressive hair loss but most had experienced retarded hair growth, less hair mass and sparse, hypopigmented, thin hair. One patient complained of brittle hair (Case 3), and two (Cases 7, 10) experienced diffuse hair loss.

Diffuse, abnormal hair over the entire scalp was noticed in all the patients (Figs. 1a, 1b), and in four, there were abnormal findings of their hairs other than on the scalp. Decreased amounts of lateral eyebrow, pubic and axillary hair were observed in one patient (Case 10), and reduction of the eyebrows in two (Cases 3, 5). One patient had hypopigmented eyebrows (Case 3), while another had lost the lateral portions of her eyebrows (Case 8).

Physical examination revealed less hair mass and sparse distribution of thin, smooth, hypopigmented hair, the growth pattern of which was more or less twisted and curled with an average length over 0.5cm in all cases. No other ectodermal abnormalities including teeth and nails were noticed. Neither congenital anomalies nor developmental and growth disorders were observed, and in cases of adults their heights were within 95% percentile of the normal range, but three patients had atopic dermatitis (Cases 1, 4, 7), and in one case, caf-au-lait spot along with scoliosis was observed (Case 6).

Fig. 1. (a)(b) Sparse, thin, short, twisted and light-colored hairs on the scalp (case 2).

Fig. 2. Thin, short, and twisted hairs on hair mount (case 1).

Three patients underwent conventional treatment over 6 months (3% minoxidil solution was applied to the affected scalp), but no beneficial effects were observed.

Laboratory findings (Table 2)

In no cases did the hair pull test demonstrate increased plucking. A trichogram of affected hair obtained during the hair pluck test revealed decreased diameter of affected hairs in eight cases; these included tapered tips of the hair in four cases and longitudinal axial twisting of hair shafts in three (Fig. 2). The test showed no abnormality of anagen/telogen ratio in all the subjects.
Table 2. Laboratory findings of eleven patients

Pre-puberty patients

<table>
<thead>
<tr>
<th>No</th>
<th>Pull test</th>
<th>Trichogram</th>
<th>SEM</th>
<th>Cu/Zn</th>
<th>TFT</th>
<th>T-cell subset</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>Tapered, thin, twisted</td>
<td>Wear &amp; tear, twisted</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>Thinning only</td>
<td>Erosive, poor cuticular development</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>Tapered, thin</td>
<td>Wear &amp; tear, twisted</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>Tapered, thin</td>
<td>ND</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>Thinning</td>
<td>Erosive, twisted</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>Tapered, thin</td>
<td>Erosive, twisted</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>7</td>
<td>-</td>
<td>Tapered, thin</td>
<td>Twisted</td>
<td>ND</td>
<td>WNL</td>
<td>WNL</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>Tapered, thin, twisted</td>
<td>Erosive, twisted</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
</tbody>
</table>

Post-puberty patients

<table>
<thead>
<tr>
<th>No</th>
<th>Pull test</th>
<th>Trichogram</th>
<th>SEM</th>
<th>Cu/Zn</th>
<th>TFT</th>
<th>T-cell subset</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>-</td>
<td>Thinning</td>
<td>Wear &amp; tear, trichorrhexis nodosa, pitting</td>
<td>WNL</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>Tapered, thin, twisted</td>
<td>Erosive, variable diameter, twisted</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>Thinning</td>
<td>Wear &amp; tear, twisted</td>
<td>WNL</td>
<td>WNL</td>
<td>WNL</td>
</tr>
</tbody>
</table>

SEM: Scanning electron-microscopic examination, Cu/Zn: Serum copper/zinc level
TFT: Thyroid function test, WNL: Within normal limits, ND: Not done

Scanning electron-microscopic examination showed cuticular changes of wear-and-tear and erosions, along with 180-degrees rotation of the longitudinal axis at irregular intervals in affected hairs (Fig. 3a). Trichorrhexis nodosa, which correlated well with the complaint of brittle hairs (Fig. 3b) and transverse fractures were found in two patients respectively (Fig. 3c).

Routine laboratory analyses including complete blood count, liver function tests, and urinalysis with microscopic examination showed normal values. The values of serum copper and zinc levels, the thyroid function test including thyroid stimulating hormone test, and T cell subsets were also within the normal ranges. Histopathology revealed decreased number of hair follicles and mild inflammatory infiltrate around these follicles and no evidence of decreased sweat glands.

**DISCUSSION**

Categorising congenital hypotrichosis is very difficult as there are numerous clinical phenotypes reported in the literature, reflecting the heterogeneity of the disease. Nevertheless, as a rule, congenital hair disorders can be primarily classified by their genetic inheritance pattern into autosomal dominant, autosomal recessive, X-linked, sporadic and unknown types. Furthermore, these disorders may be classified by coexisting conditions including various kinds of abnormalities in amino acid metabolism and other chromosomal, ectodermal or skeletal defects. In addition, when the disorder is confined to the hair alone, obvious structural defects such as monilethrix, pseudomonilethrix, pili torti, bamboo hairs, woolly hair, or kinky hairs may be observed.

In identifying the disease exhibited in our subjects, we were able to exclude other types of congenital hypotrichosis showing typical inheritance patterns, such as Marie-Unna hypotrichosis, hereditary hypotrichosis simplex (HHS), or Dominant hereditary alopecia, which shows autosomal dominant trait and later onset. Recessive hereditary alopecia could also be excluded by its different clinical course, showing permanent absence of hair. With regard to the associated ectodermal anomalies including the abnormal changes of teeth, the changes of permanent teeth in younger patients was not definitely clarified as our study was performed in a limited period. However, as most of our patients did not show any signs of combined ectodermal defects for a certain period of follow up, it was inappropriate to concern ectodermal
dysplasia or trichorhinophalangeal syndrome as a differential diagnosis in which other ectodermal tissues are also affected. Moreover, the patients in our study did not demonstrate any notable findings of growth or mental retardation, so hereditary syndromes such as dyskeratosis congenita or pachyonychia congenita were excluded.

In our study, all cases resembled the clinical characteristics of sporadic or autosomal recessive type woolly hair. Especially, clinical characteristics such as sparse hair with reduced hair shaft diameter and color-lightening over the whole scalp were noteworthy findings. Morphologically, affected hair was sparsely distributed, while individual hairs were thin, short and hypopigmented; these findings in our cases coincided with those of previous reported. Occasionally, due to its reduced growth rate, woolly hair grows no more than a few centimeters, and short hypopigmented hairs in the lateral portion of both eyebrows is a frequent associated finding. A trichogram of woolly hair shows significantly reduced hair-shaft diameter, and this explains the hair's fragility. Light microscopic examination reveals longitudinal axial twisting of 180 degree at irregular intervals and occasional findings of trichorrhexis nodosa in woolly hair, which coincided with our cases. In scanning electron-microscopic examination, findings typical of previous studies of woolly hair, such as erosion, irregular rotation of the longitudinal axis and trichorrhexis

Fig. 3. Scanning electron-microscopic examination
(A) Irregular longitudinal axial twisting of the affected hair shaft (case 8)
(B) Erosive hair shaft with pitting and trichorrhexis nodosa. Affected hair showed loss of the cuticular scales (case 3)
(C) Transverse fracture of the hair shaft (case 6)
nodosa were also observed in our cases\textsuperscript{11}. There are no diagnostic findings of woolly hair on scanning electron microscopic examination, but cuticular changes such as those due to wear and tear can be seen. Findings of trichorrhexis nodosa are rarely reported\textsuperscript{19}. However, our cases possess several unique characteristics compared with woolly hair. By definition, the characteristics of woolly hair are sparse, tightly coiled condensed hairs with an average curl diameter less than 0.5cm, but our cases had curly hairs over 0.5cm, which was more or less loose than woolly hair. The natural course of the disease was also unique as the condition persisted throughout adulthood till the fourth decades in adults, in contrast to the fact that woolly hair worsens maximally during childhood and gradually improves during adulthood. Another discriminating point was the difference of the genetic inheritance pattern. Genetic evidence for the familial, or sporadic recessive type of woolly hair is not fully established so far, but the autosomal recessive trait is suggested by the occurrence in a family of consanguinity and by the occurrence of woolly hair in siblings with unaffected parents\textsuperscript{42}. The mode of inheritance in our cases was unknown, which might be sporadic or X-linked. However, female preponderance was significant in our study since one case was male and the rest were female, without evidence of family history or consanguinity. Trichogram of woolly hair shows abnormal anagen and telogen phase (A/T) ratio of hairs, which is regarded as one of the criteria in determining woolly hair. However, the trichograms obtained by forced pluck in our cases showed no abnormality of A/T ratio. In addition, trichogram revealed four cases of tapered roots, a frequency which was significant. Another point to mention is that histopathologic features of woolly hair shows a reduction of hair follicles during the anagen phase and deficient hair root sheaths\textsuperscript{51}, but our cases did not show such findings.

Neither evidence of congenital anomalies nor developmental disorders were observed, but three patients had atopic dermatitis, and in one case, first reported in our study, café-au-lait spot along with scoliosis was present. From the viewpoint of polygenic influence on hair polymorphism and genetic diversity in hair growth rate and characteristics\textsuperscript{2}, these unique findings of our study might be explained by racial or ethnic diversity.

To exclude dystrophic hair changes secondary to systemic disorders and deficient minerals, a full range of laboratory tests is essential. In our study, routine laboratory analysis included hemogram, liver function tests and urinalysis, and values were found to be normal, as were those of serum copper and zinc levels, thyroid function test including thyroid stimulating hormone test, and T cell subsets. Histologically, a reduction of hair follicles could be seen but deficient hair root sheaths were not observed.

In summary, we could not find a similar pattern of hair disorder by searching the literature and the cases presented in our study might bear the possibility of variant of woolly hair or a novel entity of congenital hypotrichosis.

REFERENCES


