Hair Diameter Diversity

A Clinical Sign Reflecting the Follicle Miniaturization

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Background: The degree of androgenetic alopecia is generally evaluated either by global clinical scales or time-consuming methods like phototrichogram or histological studies. We describe a new clinical and reliable scoring method based on hair diameter diversity.

Observations: (1) The clinical macroscopic scoring we propose for hair density was significantly correlated with Hamilton classification and with histological hair density. (2) Diversity in hair diameter was the main and most accurate clinical parameter linked to follicle miniaturization. (3) The anagen-telogen ratio decreased in parallel with the decrease in clinical hair density score.

Conclusions: Considering that hair follicle miniaturization is the key point during androgenic alopecia onset and development, diversity in hair diameter represents an important feature to consider as an accurate clinical sign reflecting hair follicle miniaturization. Moreover, diversity in hair diameter seems to be an easily accessible and reliable parameter that should be taken into consideration for further characterization of hair disorders. By itself, we believe that this clinical feature constitutes a new tool of substantial help for the diagnosis and management of androgenic alopecia.

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Male Pattern alopecia is a common disorder in men, characterized by a progressive miniaturization of hair follicles whereby terminal hair evolves into vellus hair. The distribution and incidence of androgenic alopecia was first documented by Hamilton. Up to now the degree of androgenic alopecia was evaluated using global clinical scales such as those proposed by Hamilton, Ludwig, and Savin, or more accurately with technical methods. Among others, the phototrichogram is a noninvasive technique, well recognized by physicians, and used as a routine examination procedure to assess both the degree of alopecia and treatment efficacy. It is based on the determination of hair cycle duration and anagen-telogen ratio. Other methods such as hair weight, transverse microscopic analysis, and unit area trichogram have also been proposed.

We have recently developed a simple, rapid, and reproducible clinical procedure to describe the scalp semiology during androgenic alopecia. This method was developed by studying 850 scalp macrophotographs taken from a large group of male volunteers involved in a French health national program called “SUVIMAX.” Macrophotograph scoring led us to qualitatively characterize 3 fundamental hair parameters: hair density, hair diameter, and diversity in hair diameter. Furthermore, histological studies were performed to describe follicular features associated with the above clinical hair parameters. Namely, normal and abnormal follicles were identified and counted on horizontal microscopic sections. This work was aimed at evaluating the reliability of this new clinical scoring approach by performing a quantitative histological study on those scalp areas previously scored from macrophotographs. The purpose was to establish a link between macroscopic scores of clinical parameters and microscopic assessment of follicular structures.

RESULTS

Clinical Features

Hamilton Classification vs Local Hair Density on the Vertex Area

High scores of hair density (5 and 6) were mainly represented by very early stages of alopecia (I, II), whereas a decrease to lower scores of hair density (from 4 to 2) was reflected by a gradual worsening of alopecia.
PATIENTS AND METHODS

PATIENTS

After study approval by the ethical committee of the University of Bologna (January 1998), Bologna, Italy, 21 men aged 19 to 51 years (median age, 27 years; mean±SEM age, 29±1.57 years) and with androgenic alopecia gave their informed consent to participate in the investigation. Their demographic characteristics are given in Table 1. The study took place between January 1998 and May 1999.

METHODS

Macrophotographs and Clinical Scoring

Macrophotographs were taken on a delineated area, with a preadjusted macroscopic camera (Dermaphot; Heine Optotechnik, Herrsching, Germany) at an original magnification of ×4. For each subject, the vertex area was delineated at the cross between nose line and ear implantation line, then located by a temporary tattoo. A center parting was made with a comb, and the separated hairs were fixed on either side of the part with an adhesive tape before taking the macrophotograph. From macrophotographs, we assessed the following clinical parameters: hair density, hair diameter, and diversity in hair diameter.

Two photographic scales were used for scoring these clinical parameters. The first scale was established for simultaneous scoring of hair density and hair diameter (Figure 1). The hair density scale was obtained by counting accurately the number of hairs on one side from center parting within a delineated rectangle on the photographed area that corresponded to a scalp area of 1.4×13 mm. The reference scores for hair density area were as follows: 1, baldness (<4 hairs); 2, very low hair density (5-10 hairs); 3, low hair density (11-20 hairs); 4, medium hair density (21-30 hairs); 5, high hair density (31-40 hairs); 6, very high hair density (>40 hairs).

Hair diameter was scored as 1 (thin), 2 (medium), and 3 (thick). The hair diameter clinical scale was checked with micrometer measurements on corresponding hairs: a score of 1 (very thin/thin) corresponds to 30 to 40 µm; 2 (medium), 50 to 80 µm; and 3 (thick), 90 to 110 µm.

The scale used to score diversity in hair diameter (Figure 2) was graded as 0 (<20% in hair diameter diversity) and 1 (>20% in hair diameter diversity).

Handling of Biopsy Samples

For each subject, after administration of local anesthesia, a 4-mm punch biopsy sample was obtained from the photographed area by using the tattoo as a reference area. Samples were formalin fixed and paraffin embedded, and horizontal sections were performed according to the procedure outlined by Whiting.11

Histological Analysis

Sections were stained with hematoxylin-eosin and then examined under a bright-field microscope. On each biopsy sample (4 mm in diameter), the following parameters were evaluated: total number of follicles (anagen plus telogen), number of meaningful anagen follicles,6 number of telogen follicles, and number of miniaturized follicles (defined as follicles measuring less than 0.03 mm in diameter).11 Only meaningful6 anagen hairs were taken into consideration for the calculation of the anagen-telogen ratio.

Data Management and Statistical Analysis

First, the links between clinical and histological findings were displayed as box plots, showing the median and the interquartile range. Second, correlation tests were carried out using the Cochran-Mantel-Haenszel statistics12,13 based on standardized midranks. Descriptive and inferential analyses were performed using SPSS (version 9.0 for Windows; SPSS, Chicago, Ill) and SAS (version 6.2 for Windows; SAS, Cary NC) statistical software.

Table 1. Age of Patients and Hamilton Classification

<table>
<thead>
<tr>
<th>Hamilton Classification</th>
<th>No. of Subjects (N = 21)</th>
<th>Median Age (Range), y</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>2</td>
<td>24.5 (19-30)</td>
</tr>
<tr>
<td>II</td>
<td>10</td>
<td>26.5 (23-32)</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>27 (24-32)</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>32 (23-51)</td>
</tr>
<tr>
<td>VI</td>
<td>1</td>
<td>41</td>
</tr>
</tbody>
</table>

HISTOLOGICAL AND CLINICAL RELATIONSHIPS

Clinical Hair Density and Quantitative Histological Features

Clinical parameters were compared with quantitative histological parameters obtained from the same scalp grading (from III to IV). Interestingly, there was a good correlation (P=.01) between the 2 clinical gradings (ie, global scores of Hamilton classification and macroscopic scores of hair density) (Figure 3A). This led us to further characterize the stage of alopecia according to our clinical macroscopic scale of hair density.

Hair Diameter and Hair Diameter Diversity vs Local Hair Density

To appreciate the score changes in hair diameter and hair diameter diversity in the 21 men involved in the study, we investigated their distribution according to changes in hair density. On the one hand, there was a good correlation between hair diameter diversity and hair density. Figure 3B shows a statistically significant increase in hair diameter diversity associated with a decrease in hair density score (P=.02). On the other hand, no statistical link was found between the distribution of hair diameters and the evolution of the hair density score (P=.70).

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area (Table 2). Clinical hair density scores were significantly correlated ($P=.006$) with hair density as assessed by histological analysis. The total number of anagen plus telogen follicles was higher when hair density increased (Figure 3C). With high hair density scores, the median number of anagen follicles increased significantly ($P=.006$), whereas no change was found in the number of telogen follicles. There was a good trend ($P=.10$) in the reduction of the meaningful anagen-telogen ratio, paralleling the reduction in hair density score (Figure 3D). Nevertheless, the statistical significance could not be reached in this preliminary work.

**Figure 1.** Clinical scoring of hair density and hair diameter using a photographic scale (original magnification $\times 4$).
Figure 2. Hair diameter diversity scale (original magnification ×4). A score of 0 indicates less than 20% hair diameter diversity; 1, more than 20% hair diameter diversity.

Figure 3. Statistical analysis of hair parameters. (For a full explanation of all scores and ratios, see the “Methods” subsection of the “Patients and Methods” section.)

A, There is a significant relationship between global scores of the Hamilton and macroscopic hair density scores (P = .01); B, a significant increase in hair diameter diversity is associated with a hair density decrease (P = .02); C, there is a significant correlation between follicle histological density (total anagen plus telogen) and an increase in hair density score (P = .006); D, there is a correlation between the clinical hair density score and a meaningful anagen-telogen ratio (P = .10); E, a significant increase in the number of miniaturized follicles is associated with a decrease in hair density score (P = .02); F, there is a significant link between hair diameter diversity score and follicle miniaturization (P = .02). Each box represents values between the 25th and 75th percentiles; the horizontal line is the median. Circles mark cases with values more than 1.5 box lengths away from the 75th or 25th percentiles. The upper brackets extend to the largest value not exceeding the 75th percentile plus 1.5 × the height of the box, while the lower brackets extend to the smallest value not below the 25th percentile minus 1.5 × the height of the box.
probably owing to the small number of volunteers and real controls. Furthermore, the number of miniaturized follicles was inversely correlated with clinical hair density \((P = .02)\) (Figure 3E).

**Clinical Hair Diameter and Miniaturization of Hair Follicles**

Finally, we investigated the link of clinical scoring of hair diameter and hair diameter diversity with histological features. Hair diameter diversity was significantly linked to the miniaturization degree of hair follicles \((P = .02)\) (Figure 3F), whereas the link between follicle miniaturization and hair diameter showed a statistical trend \((P = .07)\).

### Table 2. Histological Data on Horizontal Sections of Scalp Biopsy Samples According to Clinical Hair Density Score*

<table>
<thead>
<tr>
<th>Clinical Hair Density Score</th>
<th>Histological Density (Total Anagen Plus Telogen Follicles)</th>
<th>No. of Meaningful Anagen Follicles</th>
<th>No. of Telogen Follicles</th>
<th>Meaningful Anagen-Telogen Ratio</th>
<th>No. of Miniaturized Follicles</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-5 (n = 12)</td>
<td>44.0 (21-52)</td>
<td>38.5 (20-45)</td>
<td>3.5 (1-14)</td>
<td>10.9 (1.9-22.5)</td>
<td>6.0 (2-20)</td>
</tr>
<tr>
<td>4-3 (n = 7)</td>
<td>32.0 (22-43)</td>
<td>26.0 (21-40)</td>
<td>4.0 (1-11)</td>
<td>6.5 (2.6-25)</td>
<td>10.0 (4-24)</td>
</tr>
<tr>
<td>2-1 (n = 2)</td>
<td>22.5 (14-31)</td>
<td>18.5 (9-26)</td>
<td>4.0 (3-5)</td>
<td>5.6 (1.8-9.3)</td>
<td>13.0 (3-23)</td>
</tr>
</tbody>
</table>

*Data are median (range) values. For a full explanation of scores and ratios, see "Methods" section.

Probably results from the fact that hair miniaturization does not equally affect all the hair follicles of the same area, resulting in the simultaneous presence of terminal, indeterminate, and miniaturized hairs. Indeterminate hairs (0.03-0.06 mm in diameter) are rare in the normal scalp.  

Furthermore the link we showed between hair diameter diversity and hair follicle miniaturization strongly suggests that hair diameter diversity was the main and most accurate clinical sign reflecting the follicle miniaturization process. Although hair follicle miniaturization is the key point during androgenic alopecia, hair diameter diversity represents an important feature and should be considered an accurate, easily accessible, and reliable macroscopic clinical sign that could, from now on, be taken into consideration for further characterization of hair disorders. By itself, this clinical feature constitutes a new tool of substantial utility in the diagnosis and management of androgenic alopecia. Further studies, including analysis of scalp biopsy specimens from subjects not affected by androgenetic alopecia, are needed to confirm our clinical-pathological correlations.

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**REFERENCES**

News & Notes

The International Society for Behçet’s Disease, a multidisciplinary society, was inaugurated at the Ninth International Conference for Behçet’s Disease in Seoul, South Korea, on May 28, 2000. The aim of the society is to advance the knowledge of the etiology, pathogenesis, diagnosis, natural history, clinical features, treatment, and management of Behçet’s Disease. The Executive Committee is made up of the following members:

Committee Member
Dr Colin G. Barnes (UK)
Professor Hasan Yazici (Turkey)
Professor Sungnack Lee (Korea)
Professor Dorian Haskard (UK)
Professor Christos Zouboulis (Germany)

Position
President
President Elect and Secretary
Secretary
Vice-President
President of the 10th International Congress, Berlin, June 2002

Owing to the diverse clinical manifestations of Behçet’s disease the founder members of the society include dermatologists, epidemiologists, gastroenterologists, immunologists, internal medicine physicians, neurologists, ophthalmologists, pathologists, and rheumatologists. Colleagues from any interested discipline, including nonmedical scientists, are encouraged to become members. Details are available from the secretary: Professor Hasan Yazici, Safa sok 17/7, Kadikoy, Istanbul 81310, Turkey; phone and fax: +90 216 337 8789 (e-mail: hyazici@attglobal.ne).