

Clinical and Trichoscopic Graded Live Visual Scale for Androgenetic Alopecia

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ABSTRACT **Introduction:** Currently, the mostly used classifications of androgenetic alopecia (AGA) only provide a macroscopic and subjective description of this disorder, without evaluating trichoscopic features. **Objectives:** The aim of this study is to elaborate a graded live visual AGA severity scale including macroscopic and microscopic (trichoscopic) pictures, and to determine the most frequent trichoscopic characteristics associated to each grade. **Methods:** A retrospective observational study was conducted on 122 patients (50 females and 72 males) affected by AGA. Macroscopic and trichoscopic photographs were taken at standardized scalp points. **Results:** Each picture was ranked from AGA stage I to VII, according to Hamilton scale for men and Sinclair scale for women, and the most representative images of each severity degree were collected to produce a graded live visual scale. In males, 2 live visual scales, 1 for the anterior and 1 for posterior region of the scalp were created. In females, only 1 scale of the anterior region was realized. For each stage of severity, the corresponding trichoscopic parameters were statistically analyzed. **Conclusions:** We realized new macroscopic and trichoscopic graded live visual scales for male and female patients affected by AGA, which could help physicians in giving an objective evaluation of the disease and in better managing it.

Introduction

Androgenetic alopecia (AGA) is one of the most common causes of hair loss in both sexes. The development and occurrence of AGA depends on multiple factors, such as genetic predisposition, endocrine and metabolic factors and exogenous causes. AGA prevalence rates in the Caucasian population are around 12% among men younger than 30 years, 50% in the fourth decade and over 90% in individuals older than 80 [1]. In women, prevalence is estimated around 16% under 50 years and 30-40% in subjects older than 70 years [2].

In male patients, hair loss typically involves temporal and vertex regions, sparing the occiput. In women, the process starts with frontal area hair thinning. Then, the parietal regions of the scalp become gradually more visible, leaving the frontal hairline intact. These different hair loss patterns are determined by differences in androgen-sensitivity of the scalp areas. Frontal and vertex regions are characterized by high expression of androgen receptors. On the contrary, occipital and temporal regions contain androgen-insensitive hair follicles [3]. Furthermore, male and female individuals show different expression of enzymes: high expression of aromatase in the anterior region of female scalp and high expression of 5- α R2 in the anterior region of male scalp.

In both sexes, AGA is characterized by progressive miniaturization of hair follicles and evolution of terminal hairs to vellus hairs. This is due to hair cycle dynamics alteration, with progressive anagen phase shortening and telogen phase prolonging [4]. Currently, the most widely used method of measuring the male AGA (MAGA) is the Hamilton–Norwood classification, developed in 1975 and characterized by stages I–VII and special types IIa–Va [5].

In 1977, Ludwig proposed a 3-grade classification for the female AGA (FAGA) [6], which is still in use today. However, in 2004, Sinclair introduced a more detailed scale, consisting of 5 pictures [7].

In 2007, Lee et al proposed a new universal classification of pattern hair loss, independent from gender: the basic and specific classification, which is based on observed patterns of hair loss, including anterior hairline shape and hair density on the frontal and vertex areas [8].

However, all the classifications formulated so far provide a descriptive, macroscopic and subjective assessment of alopecia extent and hair loss patterns.

In the last decade, several studies accumulated evidence about the use of trichoscopy in the daily clinical evaluation of hair disorders, improving the diagnostic capability beyond the simple clinical inspection [9,10]. According to this progress, a new semi-quantitative grading scale was recently proposed by Jin Nie et al. In their study, they considered some objective parameters, such as hair coverage, hair

density, vellus/terminal hairs ratio, and produced a graded visual scale of six macroscopic AGA photographs [11].

Objectives

The aim of this study is to elaborate a graded live visual AGA severity scale including macroscopic and microscopic (trichoscopic) pictures, and to determine the most frequent trichoscopic characteristics associated to each grade.

Methods

We performed a single-center observational study on 122 patients (72 men and 50 women) affected by AGA. Patients were recruited in our “Skin Appendages Physiopathology Center” of Sapienza, University of Rome, from January 2019 to January 2020. AGA diagnosis was formulated through classical clinical and trichoscopic parameters, such as alopecia clinical extension and hair shaft thickness heterogeneity (anisotrichosis).

We took macroscopic photographs of each patient’s scalp using a video-dermoscope (FotoFinder®). The instrument was attached to a rotating arm of a head-positioning device (Canfield Scientific®) in order to take pictures in standardized areas of the scalp: 2 for men (frontal and vertex region) and 1 for women (only frontal region). The scalp of all subjects was combed along the midline to the sides and evaluated using the video-dermoscope. Digital trichoscopic photographs were obtained in standardized scalp areas according to patient sex: in women, photographs were collected in the scalp point corresponding to the intersection between the line connecting the ears and the line connecting the tip of the nose and the vertex (“P point”). In men, photographs were collected at the vertex (“V point”) and 2 centimeters ahead of the intersection point previously described for women (“F point”). These images were taken at 20-fold magnification, which allows high-quality enlargement of a 0.903 cm² area (field of view).

All the 122 trichoscopic pictures were analyzed with Trichoscale Pro® software, which allows to perform accurate automatic measurements of scalp structures, with subsequent manual verification. In our analysis, we considered the following trichoscopic parameters:

1. the percentage of anisotrichosis (determined as the number of not terminal hair divided by total hairs number);
2. the percentage of vellus hairs (defined as hairs with a diameter lower than 0.03 mm and shorter than 30 mm);
3. the number of empty follicles;
4. the percentage of single-hair follicular units (SHFUs);
5. the percentage of follicles with peripilar sign;
6. the presence of honeycomb pigment pattern (HCPP);
7. the presence of fibrosis.

The first 5 parameters were selected as activity indexes, while HCPP and fibrosis were considered as marker of long-lasting disease.

Statistical Analysis

The tests used to produce the graphics of the quantitative variables were a one-way ANOVA corrected with the Sidak method and multiple t-tests, setting 95% confidence intervals. The P values of the ANOVA tests were considered statistically significant when less than 0.05. For the binomial variables we used Fisher Exact Tests with the Baptista-Pike method.

Results

Mean age was 34 (standard deviation [SD] \pm 11.7) years (range: 21-83 years) for men and 52 (\pm 17.8 SD) years (range: 23-82 years) for women. Macroscopic pictures were then ranked by severity (7 degrees for men and 5 degrees for women), and the most representative image for each degree of severity was selected and collected, producing 3 macroscopic graded live visual scales (2 for men, 1 for women)

(Figures 1, 3 and 5). Then, we selected 1 trichoscopic photograph for each grade represented on the macroscopic scale (micro and macro pictures of the same grade were taken from the same patient), producing 3 microscopic graded live visual scales (2 for men, 1 for women) (Figures 2, 4 and 6).

For each AGA and FAGA stage, the number of empty follicles, the percentage of vellus hairs, single-hair follicular units and follicles with peripilar sign were reported as graphs (Figures 7-9). We did not report data for AGA stage VII and FAGA stage V, since patients affected by very severe alopecia only showed fibrosis and HCPP. In MAGA, in both frontal and vertex areas, we observed a statistically significant increase of vellus hairs and empty follicles in relation to the clinical severity of AGA. In addition, a statistically significant increase of SHFUs correlated to the clinical stage was detected in the frontal region of MAGA patients, but not in the vertex (Figures 7, 8). In FAGA, the percentage of vellus hairs, the number of empty follicles and the number of SHFUs showed a significant increase correlated to clinical severity of alopecia (Figure 9). In all cases, the peripilar sign did not show significant variations (Figures 7-9). Prevalence of fibrosis and HCPP for each AGA and FAGA stage are reported in Table 1



Figure 1. Graded live visual scale of male androgenetic alopecia (anterior region of the scalp): stage I, II, III, IV, V, VI and VII.

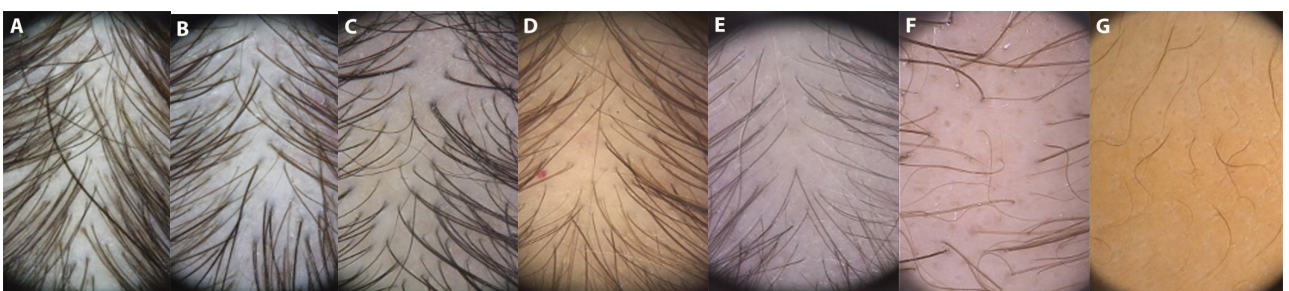


Figure 2. Corresponding trichoscopic photographs of figure 1, taken at 20-fold magnification.

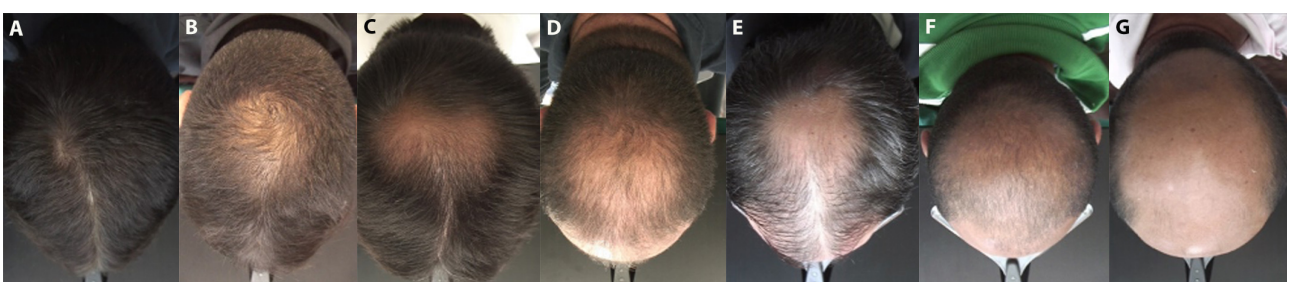


Figure 3. Graded live visual scale of male androgenetic alopecia (posterior region of the scalp): stage I, II, III, IV, V, VI and VII.

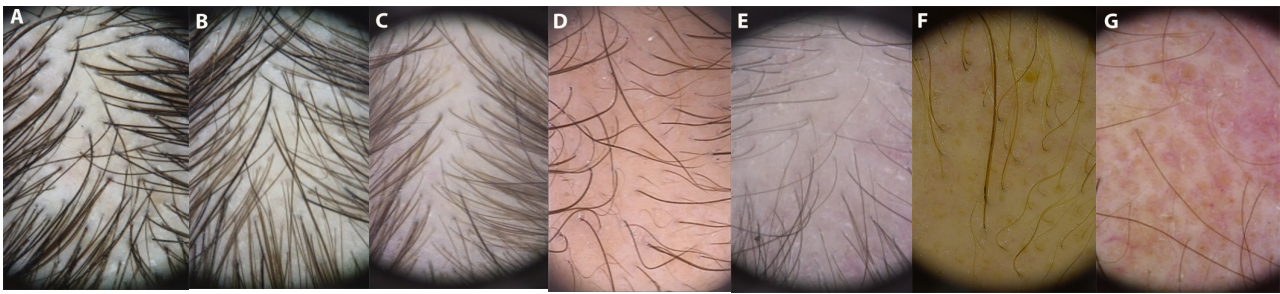


Figure 4. Corresponding trichoscopic photographs of figure 3, taken at 20-fold magnification.



Figure 5. Graded live visual scale of female androgenetic alopecia (anterior region of the scalp): stage I, II, III, IV and V.

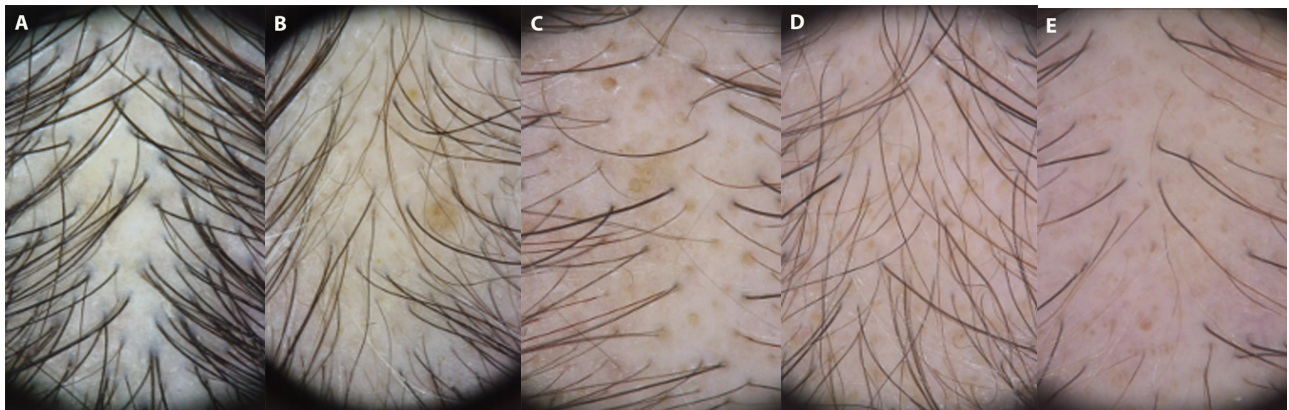


Figure 6. Corresponding trichoscopic photographs of figure 5, taken at 20-fold magnification.

and Table 2. We also evaluated the correlation between HCPP and AGA stages, finding a proportional relation between HCPP and the clinical worsening of AGA (Table 3).

The most widely used methods to classify AGA only give an idea of the extent and pattern of hair loss, without evaluating the actual severity of the disease with objective parameters. The chance to use trichoscopy in the daily clinical practice has revolutionized the approach to AGA in terms of classification and disease management. In our clinical practice, we noted that some cases of alopecia improved visibly after treatment, but their grade of classification did not vary. Moreover, some patients who were assigned the same grade of severity, according to the classic scales, presented important differences in their trichoscopic characteristics,

which lead us to different therapeutic choices. In this study we wanted to underly the importance of trichoscopy in AGA classification, elaborating three macroscopic live visual scales associated to three microscopic ones. In addition, we wanted to evaluate the prevalence of trichoscopic parameters for each AGA stage and if prevalence variations between stages were statistically significant.

Hair shaft thickness heterogeneity (anisotrichosis) is an expression of the terminal hair transformation into vellus hair, suggesting that it might represent an accurate clinical sign reflecting the miniaturization process evolution, which is the basis of AGA pathogenesis [1].

Anisotrichosis higher than 20% is an essential criterion for the diagnosis of AGA [12].

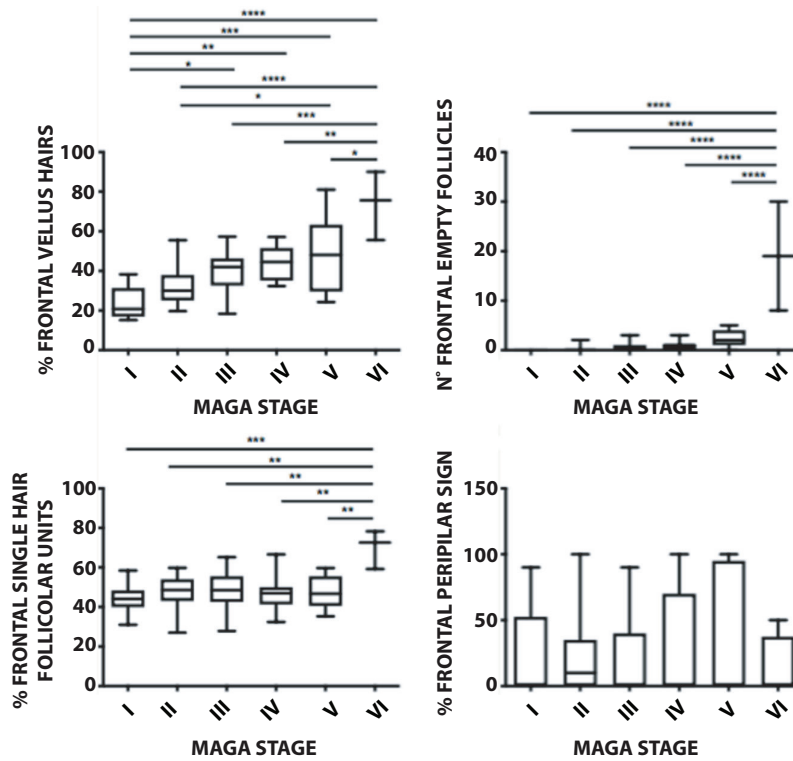


Figure 7. Graphic distribution of the quantitative trichoscopic parameters according to the visual stage of male androgenetic alopecia, evaluated in a standardized area of 0.903 cm² at “F point”, accompanied by the P (* = low statistically significant, ** = mildly statistically significant, *** = highly statistically significant) of the differences observed between the various androgenetic alopecia stages.

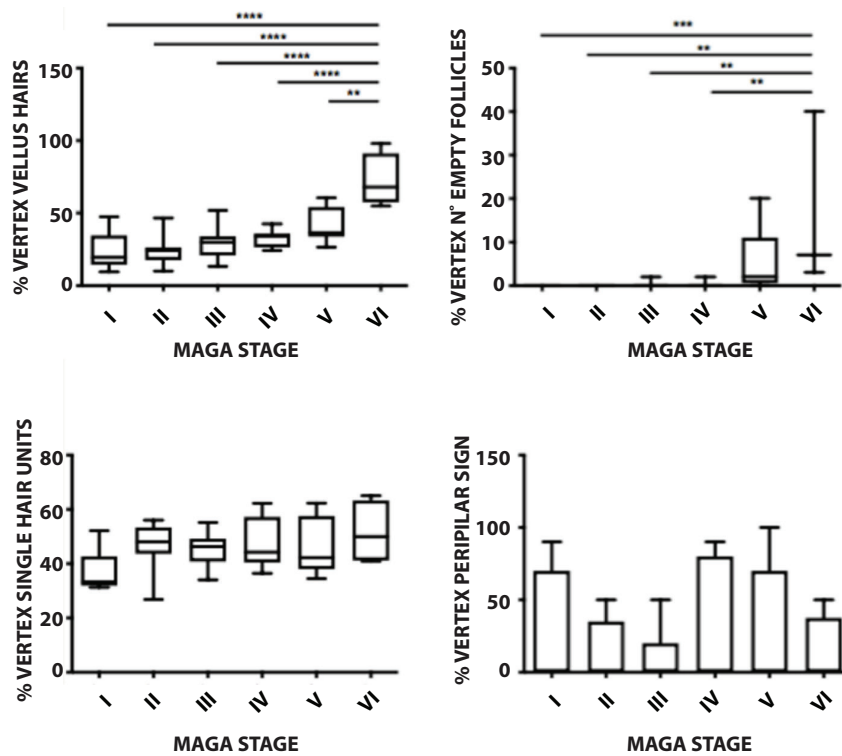


Figure 8. Graphic distribution of the quantitative trichoscopic parameters according to the visual stage of male androgenetic alopecia, evaluated in a standardized area of 0.903 cm² at “V point”, accompanied by P (* = low statistically significant, ** = mildly statistically significant, *** = highly statistically significant) of the differences observed between the various androgenetic alopecia stages.

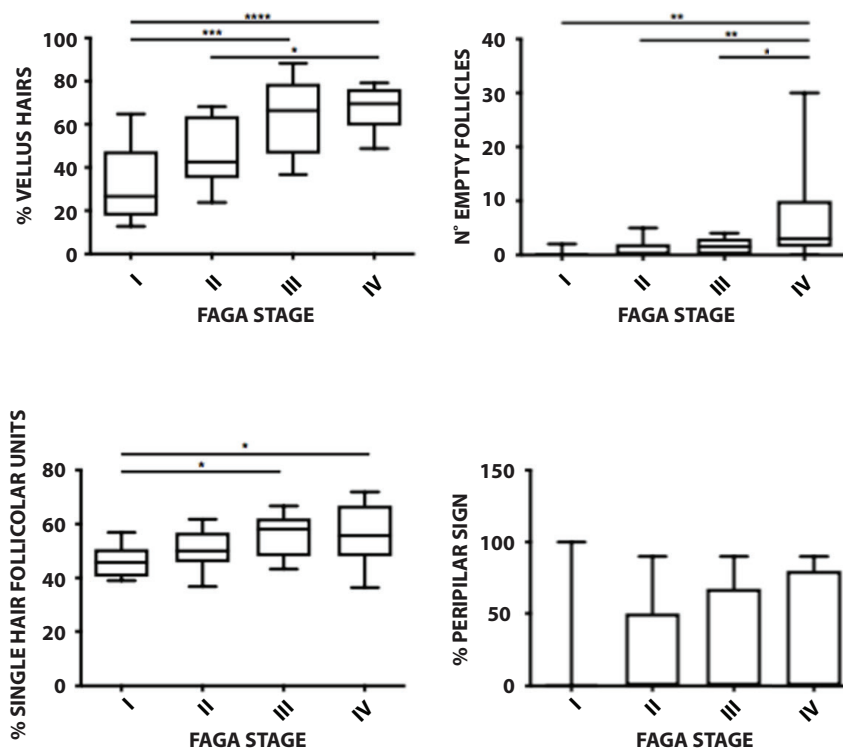


Figure 9. Graphic distribution of the quantitative trichoscopic parameters according to the visual stage of female androgenetic alopecia, evaluated in a standardized area of 0.903 cm² at “P point” accompanied by the P (* = low statistically significant, ** = mildly statistically significant, *** = highly statistically significant) of the differences observed between the various androgenetic alopecia stages.

Table 1. Presence of fibrosis at F, V and P Point, i for each AGA stage (%).

AGA	F point	V point	P point
I	0	0	0
II	0	0	0
III	0	0	0
IV	0	0	33
V	22	22	-
VI	25	25	-

AGA = androgenetic alopecia.

Table 2. Presence of Honeycomb Pigment Pattern (HCPP) at F, V and P Point, for each androgenetic alopecia stage (%).

AGA	F point	V point	P point
I	0	0	0
II	0	0	20
III	11	27	40
IV	63	62	100
V	77	75	-
VI	100	100	-

AGA = androgenetic alopecia.

Table 3. Odds Ratio (OR) for Honeycomb Pigment Pattern (HCPP) Associated to different AGA stages.

HCPP	OR	p
F point	67.5	0.0001
V point	37.1	0.0001
P point	19.5	0.0001

F point: Correlation between MAGA IV-VI and MAGA I-III patients in the frontal area.

V Point: Correlation between MAGA IV-VI and MAGA I-III patients in the vertex area.

P Point: Correlation between FAGA III-IV and FAGA I-II patients.

AGA = androgenetic alopecia;

FAGA = female androgenetic alopecia;

MAGA= male androgenic alopecia.

Indeed, all enrolled patients presented a percentage of anisotrichosis higher than 20%. In our study, male patients, at F and V points, presented a vellus hairs rate of 24% at AGA stage I and 73% at stage VI. In women, the vellus hairs rate ranged from 32% of stage I to 68% of stage IV.

In our study population, the increase of vellus hairs rate is related to the increase of severity stage, in both sexes. These results agree with the concept that vellus hairs rate is a trichoscopic index of disease severity.

Empty follicles have been described in AGA, especially in advanced stages of the disease [13,14]. Trichoscopically they appear as yellow dots (YD), which correspond to empty follicles filled with keratotic material and/or sebum, or follicles containing a completely miniaturized hair or a kenogen hair. If the scalp is exposed to the sun, these follicles can appear as pinpoint white dots. They occur predominantly in the frontal region, have irregular size and distribution, and are less numerous when compared to the amount found in alopecia areata. Moreover, the presence of 4 or more YD in 4 trichoscopic fields in the frontal region is one of the major trichoscopic criteria for the diagnosis of FAGA [15]. In our experience, as expected, we observed that the increase in number of empty follicles significantly correlates with AGA severity.

One follicular unit is able to produce up to 6 hairs, depending on the body region. In the human scalp, follicular units usually contain 2-4 terminal hairs and 1-2 vellus hairs. A decreased number of hairs per follicle is a characteristic feature of AGA [16, 17]. Indeed, this finding is present also in healthy individuals and patients with chronic telogen effluvium, but it is usually limited to the temporal areas.

We observed that differences in number of SHFUs between the lower stages of AGA were very little. This could be the expression of a general shortening of anagen and prolongation of telogen, which is characteristic of AGA pathogenesis, and reaches its peak in the advanced stages of this condition. Actually, in our study, the number of SHFUs correlated with AGA severity in women and in male frontal region, but not in the vertex.

Peripilar sign had been described as significantly more frequent in AGA, if compared with healthy people or patients with chronic telogen effluvium. Rakowska et al observed that the mean percentage of hair follicles with surrounding discoloration was around 32% in the frontal area and around 7% in the occipital area in patients with FAGA. Nevertheless, they documented that healthy subjects presented perifollicular discoloration in less than 25% of the follicles in the frontal area, less than 15% in the occiput and less than 20% in the temporal areas [15]. In our experience, the percentage of follicles involved by peripilar sign ranged from 13% to 43% in women, and from 9% to 37% in men. Interestingly, in our sample size, the peripilar sign did not show statistically significant variations in relation with the severity of alopecia. In fact, this trichoscopic finding corresponds to a not constant sign of inflammation and clinical activity, which may be present in both early and late stages, with no proportional correlation with the stage of AGA. Certainly, in case of peripilar sign, and consequently of inflammation, the progression of alopecia is more rapid.

Although AGA is classified within the nonscarring alopecia, the micro-inflammation involving the follicles (trichoscopically corresponding to the peripilar sign) could slowly induce the development of perifollicular fibrosis. Hence, in severe disease, it is possible for hair follicles to be replaced by connective tissue, leading to fibrous tracts, and finally causing atrophy. These empty follicles appear as white dots, which are usually observed in cicatricial alopecia, or as amorphous white cicatricial area, when the follicular ostia cannot be observed anymore [14]. In our experience, we found the highest prevalence of fibrosis in the most advanced stages of AGA reflecting a previous perifollicular inflammation and a long disease duration.

HCPP corresponds to contiguous brown rings, usually related to chronic actinic damage due to its preferentially presence in sun-exposed areas of the scalp, where hair coverage is reduced. Therefore, this do not correspond to a specific trichoscopic finding of AGA, but it is a marker of chronic and long-lasting disease, much more evident in cases of decreased hair density [18]. In our study, HCPP has been rarely observed in lower stages of AGA, with progressive increase till the 100% in the last stages. Moreover, we found a significant positive correlation between HCPP and AGA worsening. Intuitively, this result expresses the fact that, with the increase of hair thinning and hair loss, the scalp is more exposed to UV lights and cutaneous photodamage, with consequent occurrence of HCPP. Certainly, the extension of the bald area and especially the duration of the disease influence the occurrence and severity of HCPP.

Conclusions

The classification methods currently used for male and female AGA only describe the clinical pattern and the extent of disease. Therefore, they cannot be considered as objective classifications, and, frequently, do not allow to describe the real trend of hair loss because of the wide gap between different stages and since they do not take into account trichoscopic parameters.

Nowadays, trichoscopy is a fundamental tool for the management of hair loss diseases, showing high utility for their diagnosis and follow-up. Thus, trichoscopy should be considered when trying to assess a severity degree, as we performed for AGA.

Thus, we created 6 graded live visual scales, 3 macroscopic and 3 microscopic, which could help physicians in giving an objective evaluation of the disease and in better managing it.

Further studies are needed, but it is evident that only an objective trichoscopic evaluation could guide physicians to the correct management and to an appropriate “phase therapy” for AGA, as we already do for other trichological diseases.

Informed Consent: The patients in this manuscript have given written informed consent to publication of their case details.

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