Underestimated clinical features of postadolescent acne

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Background: Postadolescent acne is usually described as an inflammatory, mild-to-moderate dermatosis, frequently involving the lower third of the face, the jawline, and the neck. However, we have also frequently observed a clinical form predominantly characterized by retention lesions (microcomedones and macrocomedones), with few inflammatory lesions (comedonal postadolescent acne [CPAA]), which appears significantly correlated with cigarette smoking.

Objective: We sought to investigate the clinical features of postadolescent acne in a group of female patients affected by acne and its relationship with cigarette smoking.

Methods: A total of 226 women with acne (25-50 years) attending our department were examined by a team of 3 dermatologists, to assess the age of onset of the disease, and the number, type, and distribution of acne lesions.

Results: In all, 192 of 226 patients (85.0%) were classified as having CPAA and 34 as having papulopustular postadolescent acne. A smoking habit was confirmed in 150 of 226 (66.3%). Remarkably, 72.9% of patients with CPAA were smokers as compared with only 29.4% of those with papulopustular postadolescent acne ($P < .0001$).

Limitations: Possible limitations are related to geographic area or to the prevalence of darker skin types (III and IV) (data about skin types have not been collected). Other possible aggravating factors (ie, stress and diet) have not been investigated.

Conclusions: According to our results, CPAA appears as the most frequent clinical form of postadolescent acne and seems to be strictly correlated with cigarette smoking. (J Am Acad Dermatol 2010;63:782-8.)

Key words: cigarette smoking; clinical features; postadolescent acne.

Acne is generally considered a disorder of adolescence. However, the prevalence of acne among adults, estimated around 12% to 14%, is increasing. Papulopustular postadolescent acne (PPAA) is usually described as an inflammatory, mild-to-moderate form, consisting predominantly of deep-seated, tender inflammatory papules and nodules, frequently involving the lower third of the face, jawline, and neck, with comedonal lesions involving the forehead or side margins of the face and usually not prominent. However, we have previously reported a frequent clinical form characterized by a predominance of retention lesions (microcomedones and macrocomedones) with few inflammatory lesions. We called this form comedonal acne. From the Pediatric Dermatology Department, Department of Clinical Pathology and Microbiology, and Cutaneous Physiotherapy Department, San Gallicano Institute, Istituti Fisioterapici Ospitalieri, Rome; and Departments of Dermatology, Venerology, Allergology, and Immunology, Dessau Medical Center. Funding sources: None. Conflicts of interest: None declared. Accepted for publication November 13, 2009. Reprint requests: Jo Linda Sinagra, MD, Pediatric Dermatology Department, San Gallicano Istituto di Ricerca e Cura a Carattere Scientifico, Via Elio Chianesi 53, 00144 Roma, Italy. E-mail: dermped@ifo.it.

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Abbreviations used:
ACH: acetylcholine
CPAA: comedonal postadolescent acne
PPAA: papulopustular postadolescent acne
postadolescent acne (CPAA). In CPAA, comedones are usually prominent and homogeneously distributed on the whole face with a relative preservation of the lower third and the jawline. In most of these patients, the distribution of lesions is widespread, representing a major clinical feature and giving rise to a characteristic face. This form of acne has a heavy psychosocial impact for the patients, is very difficult to treat, and can be so severe as to be disfiguring.

Several aspects of the pathogenesis of postadolescent acne are still obscure. Because most patients usually have normal hormone parameters, hyperandrogenism (patients with SAHA [seborrhoea, acne, hirsutism and alopecia] syndrome3)/hyperandrogenemia (irregular menstrual cycle and change of the secondary sex signs) should be considered as a pathogenic factor in only a subgroup of patients.2

Several environmental pathogenetic factors (stress, atmospheric pollution, job-related and environmental factors, photoexposure) can contribute to hyperseborrhea and hyperkeratinization that seem to be prevalent in this form of acne. Among them, cigarette smoking seems to be of particular interest, and in a recently published letter, we have proposed a significant correlation with CPAA.4

This study on 226 women of our department affected by acne focuses on clinical features and age of onset of postadolescent acne and its possible correlation with smoking. Our findings indicate that frequency of late-onset acne is higher than previously reported and that CPAA is the more frequent form in our series. Many of these patients are smokers.

**METHODS**

A case series of 269 consecutive female patients (25-50 years) affected by acne attending our department for the first time from November 2007 to April 2008 were included in this study.

Clinical evaluation was performed by a team of 3 dermatologists, to assess the number, type, and distribution of the acne lesions. According to the clinical characteristics, acne was classified as PPAA or CPAA. The identification of PPAA or CPAA was established on the basis of clinical criteria (Table I). Cases were classified as CPAA when the inflammatory lesions (papules, pustules, nodules, or a combination of these) accounted for less than 5% of the total count and retention lesions (open, closed, and macrocomedones) accounted for at least 95%. According to the number and type of lesions, CPAA was classified as mild to moderate (Fig 1) or severe (Fig 2). Conversely, cases with more than 5% inflammatory lesions were classified as PPAA (Fig 3).

According to the age of onset, postadolescent acne was defined as persistent when it began during adolescence, and as late onset when it occurred for the first time after the age of 25 years.2 For each patient a detailed medical history, including age of acne onset, previous therapies, hormonal contraception, and smoking habits were recorded. Smokers were divided into 3 groups according to the number of daily smoked cigarettes: less than 10, 10 to 20, and more than 20.

Patients who underwent a systemic or topical treatment for acne during the 3 months before the study were excluded.

Patients who abandoned smoking at least 5 years before the study were considered as nonsmokers, whereas patients who abandoned smoking less than 6 months before were considered as active smokers. Patients who abandoned smoking between 5 years and 6 months before the study were excluded.

**Statistical analysis**

The Fisher exact test was used to analyze the contingency tables created to compare different clinical conditions and smoking habits or age of disease onset. A P value less than .05 was considered to be statistically significant. Statistical analysis was performed with software (GraphPad Prism, Version 5.00 for Windows, GraphPad Software, San Diego, CA).

**RESULTS**

From the 269 patients examined, only 226 were eligible for assessment in this study because 35 quit smoking between 5 years and 6 months before the examination and 8 underwent a systemic or topical treatment for acne during the 3 months before this study. Characteristics of the sample are summarized in Table II. In all, 192 patients of 226 (85.0%) were classified as having CPAA: 139 of 192 mild-to-moderate CPAA (72.4%) and 53 of 192 severe CPAA (27.6%) (Figs 1 and 2). Patients with CPAA were older than those with PPAA (39.1 vs 32.3 years, P = .08).

**CAPSULE SUMMARY**

- Among women, postadolescent acne is predominantly characterized by retention lesions (microcomedones and macrocomedones), with few inflammatory lesions (comedonal postadolescent acne).
- Comedonal postadolescent acne is frequently of late-onset and seems to be strictly correlated with cigarette smoking.
Late-onset acne accounted for 45.1% (102 of 226) and was more frequent among patients with CPAA (94 of 192, 48.9%) than with PPAA (8 of 34, 23.5%) ($P = .008$). A higher prevalence of smokers was found among late-onset compared with persistent acne (83.3% vs 51.5%) ($P = .04$) (Fig 4).

Smokers represented 150 of 226 (66.3%) of the whole cohort. In all, 140 of 192 (72.9%) patients with CPAA were smokers versus 10 of 34 (29.4%) of those with PPAA ($P < .0001$) (Fig 5). According to the clinical severity, for mild-to-moderate CPAA there were 96 of 139 smokers (69.0%) whereas for severe CPAA there were 44 of 53 smokers (83%) ($P = .068$) (Fig 5).

A positive correlation was found between number of daily cigarettes and CPAA severity ($P = .002$). Data on smoking habits are reported in Table III.

Among the patients with CPAA, 84% (79 of 94) with late-onset acne were smokers versus 62.2% with persistent acne ($P = .03$).

Of the whole sample, 35 patients (15.48%) were using a hormonal contraceptive for a mean period of 6.2 years (range 1-9 years). No differences were found among patients with late-onset and persistent acne or CPAA and PPAA.

**DISCUSSION**

Postadolescent acne affects approximately 14% of women between the ages of 25 and 50 years, and its incidence is increasing.² It is described as a predominantly inflammatory, mild-to-moderate form, characterized by papules and pustules, mainly located on the lower third of the face, jawline, and neck, with rare and not prominent comedonal lesions.⁵

Our data are partially in contrast with this clinical description because we show that most (85.0%) patients with acne have a comedonal form (CPAA). As described in Table I, CPAA differs in several aspects from the papulopustular type of postadolescent acne (PPAA). In fact, it is characterized by a predominance of open and closed comedones tending to small cysts, with few inflammatory lesions, affecting principally the upper third of the face. In patients with acne, retention and inflammatory lesions usually coexist, but in CPAA the retention lesions are abundant and represent the main clinical characteristic of the disease. In contrast, inflammatory lesions are rare, thus reinforcing our conventional adoption of a main clinical parameter to define CPAA as presenting with less than 5% of inflammatory lesions. The striking contrast of our results with the common description of postadolescent acne may be, at least in part, a result of the scarcity of recent scientific publications about this disease. In 1991,
Kligman reported a type of acne that appears quite similar to CPAA. According to Kligman, the lesions are scattered, consisting mainly of diminutive closed comedones, which are easily visualized when the skin is stretched. Among these are sparse papulopustules. Juicy, large, deep seated, long lasting papules are absent, as are nodules and cysts. This report, however, has inexplicably not been followed by any further studies. The most recent reviews also continue to base their description on consolidated findings reported by others, and, to our knowledge, no recent observational or longitudinal studies have been published about the clinical features of postadolescent acne.

Another possible explanation may be related to differences in the study population and geographic area. Indeed, we found that CPAA affects mainly individuals with olive-toned skin and this is consistent with that reported by Kligman, who states that “this condition is more frequent in large-pored, dark complexioned women, than in pale, thin-skinned women with type 1 skin.” Epidemiologic studies on adult acne have been mainly conducted on Nordic (in particular Anglo-Saxon) populations, presumably (even if not specified) characterized by a predominance of fair skin type and by a low-grade ultraviolet exposure. Our study was conducted during the period between November and April to avoid confounding factors related to ultraviolet exposure. However, our patients who live in a Mediterranean area commonly have chronic photoexposure, so we cannot exclude that this may influence the clinical characteristics of acne, particularly in older patients.

Although the figures did not permit a statistical treatment, we noted that patients with PAA had a younger mean age. One possible explanation may involve the immunologic and inflammatory functions of the skin, which tend to decrease with age.

One of the difficulties that we had to circumvent in this study was the absence of a grading system to classify the clinical severity of CPAA. Indeed, the
The most recent classification systems for clinical grading of acne are useful to assess the severity of the inflammatory lesions but do not take into consideration the retention types; they are, therefore, useless to describe those cases in which comedonal lesions are predominant. This forced us to adopt novel classification criteria, which take into consideration not only the number of retention and inflammatory lesions but also their proportion.

Scarring is a well-known consequence of acne, but it is commonly attributed to inflammatory lesions regardless of their severity. Among our patients with CPAA, we also detected the presence of ice-pick scars in patients with late-onset acne who did not experience inflammatory lesions. In the most severe and long-lasting forms, ice-pick scars were so numerous as to lead to a crater effect. This suggests that the retention lesions, and in particular the macromcomedones, can leave scars. This may be a result of the involvement of the extracellular matrix proteins detected in acne lesions.

Postadolescent acne is distinguished—according to the age of onset—as persistent and late onset. Few data have been published about the prevalence of late-onset acne, and Goulden et al reported a percentage of 18.4% of late-onset acne, in a group of 254 patients with acne. In our study, late-onset acne represented 45.1% of the whole sample.

The pathogenesis of postadolescent acne is still obscure. The role of circulating hormones has been extensively investigated but remains controversial and, although hormones can have an influence on acne, most patients do not have an endocrine disorder.

In a previous observational study, we found a strong correlation between CPAA and smoking. On the basis of these preliminary results, we assessed the prevalence of smoking in this study. Our data confirmed a significant association between smoking and CPAA. We found that 66.3% of all patients were smokers, with a statistically significant difference between CPAA (72.9%) and PPAA (29.4%) (P < .0001). However, it is difficult to calculate the exact amount of smoking exposure of an individual, because this parameter is affected by a number of variables (anamnestic difficulties, cigarette size differences, presence or absence of a filter, nicotine content, smoking modalities, passive smoking). Despite these difficulties, we found a positive correlation between CPAA severity and number of cigarettes smoked daily. Smoking seems to be associated with late-onset acne (73.4%, P = .05). These findings suggest a role for smoking both in the induction of acne and in the worsening of the disease.

Data on the correlation between acne and smoking are still controversial. In a study on postadolescent...
acne, smoking has not been taken into consideration among possible pathogenetic factors (hormonal alteration, stress, cosmetic use, occupational). On the other hand, a study by Schäfer et al. showed a higher prevalence of acne among smokers compared with nonsmokers and a linear correlation between the severity of acne and the number of smoked cigarettes. These results seem to be confirmed by a recent study by Chuh et al. Meanwhile, Mills et al. reported an inverse correlation between the incidence of acne and smoking but these authors considered a highly selected population consisting of hospitalized male patients affected by serious inflammatory acne. A recent study by Klaz et al. reported an inverse correlation between the severity of acne and the number of cigarettes smoked, whereas a negative correlation between smoking and the presence of inflammatory lesions in girls has recently been found.

The hyperkeratizing effect of cigarette-smoke compounds has been demonstrated. In particular, nicotine is an agonist of acetylcholine (ACh) and its effects are mediated through nicotinic receptors (ACh receptor). In recent years, the physiologic role of nonneuronal ACh and its receptors in epidermal physiology has been under intense investigation.

Human keratinocytes synthesize, secrete, and degrade ACh. Stimulation of ACh receptor on epidermal keratinocytes results in hyperproliferation and increased differentiation. Thus, nicotine could induce hyperkeratinization, providing the first hints for a causative role of nicotine in promoting infundibular epithelial hyperplasia. Composition or the level of endogenously produced ACh may explain the conflicting results reported for the influence of smoking on the course of acne vulgaris. This, together with the known anti-inflammatory and vasoconstrictive properties of smoking, perfectly fits with the major clinical features of CPAA, the strong retention phase and the scarce inflammatory aspects.

In this study, 33.7% of all patients and 27.1% of patients with CPAA were not smokers. Several factors, other than smoking, can induce or aggravate acne. Kligman considered the form of acne he had described as stress induced. Stress is an exacerbating factor for acne, and its link with smoking is strong and intriguing. Recent experimental studies demonstrated that corticotropin releasing hormone (CRH) has a role in promoting lipogenesis in human sebocytes, and that the CRH system is highly expressed on acne skin, especially on the sebaceous gland. Insufficient sleep is considered a risk factor for acne vulgaris. Recently, several studies have investigated the role of diet on acne exacerbation. Observational studies reported a positive association between milk intake and acne prevalence and severity, and between high glycemic index foods and longer acne duration.

In this study, stress levels, number of night sleep hours, and milk or high glycemic index food consumption were not investigated, but they will be included in future studies.

Our findings suggest that the commonly accepted model for postadolescent female acne should be critically revised for important academic, pathogenetic, and therapeutic reasons. Moreover, recognizing the correlation between CPAA and smoking could contribute to correct information about the effects of tobacco on the skin and to antismoking information programs, especially among adolescents where aesthetic motivation plays an important role.

**REFERENCES**


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**Table III. Correlation of smoking habits and development of postadolescent acne**

<table>
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<th>No. of cigarettes smoked daily</th>
<th>PPAA</th>
<th>CPAA</th>
<th>CPAA1</th>
<th>CPAA2</th>
<th>Total</th>
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</thead>
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<td>&lt;10</td>
<td>3 (30.0%)</td>
<td>49 (35.0%)</td>
<td>41 (42.7%)</td>
<td>8 (18.2%)</td>
<td>52 (34.7%)</td>
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<td>10-20</td>
<td>6 (60.0%)</td>
<td>73 (52.1%)</td>
<td>48 (50.0%)</td>
<td>25 (56.8%)</td>
<td>79 (52.6%)</td>
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<tr>
<td>&gt;20</td>
<td>1 (10%)</td>
<td>18 (12.8%)</td>
<td>7 (7.3%)</td>
<td>11 (25%)</td>
<td>19 (12.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>140</td>
<td>96</td>
<td>44</td>
<td>150</td>
</tr>
</tbody>
</table>

CPAA, Comedonal postadolescent acne; CPAA1, mild-to-moderate comedonal postadolescent acne; CPAA2, severe comedonal postadolescent acne; PPAA, papulopustular postadolescent acne.


