Status Report From the American Acne & Rosacea Society on Medical Management of Acne in Adult Women, Part 1: Overview, Clinical Characteristics, and Laboratory Evaluation

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PRACTICE **POINTS**

- Acne in adult women is common and may persist beyond the adolescent years or may be late in onset with emergence usually during the early to mid-20s.
- Adult women with acne often are frustrated, as they perceive it as a disorder of teenagers and are perplexed by its presence later in life. They often are distressed by unpredictable flares as well as difficulty with covering lesions and associated dyschromia and scarring.
- Clinical patterns of acne in adult women are mixed inflammatory and comedonal facial acne or a *U*-shaped pattern of inflammatory lesions involving the lower face and neck.
- Laboratory testing is not considered mandatory in all cases. The clinician is encouraged to carefully evaluate each case and determine if further evaluation to detect a cause of androgen excess is warranted.

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Acne presenting in adult women is commonly encountered in clinical practice. Many affected women have had acne during their teenaged years, have tried several therapies in the past, and are seeking effective treatment. Others are frustrated by the inexplicable emergence of acne as an adult when they never had it as a teenager. Both groups seek an explanation of why they have acne, are often psychosocially affected by its effects on appearance and self-esteem, and all are wanting effective and safe treatment. Clinicians are encouraged to connect favorably with each patient through careful history and physical examination and to consider underlying causes of androgen excess. Practical approaches to examination and laboratory evaluation are discussed.

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It was not long ago that acne vulgaris (AV) was commonly considered to be a skin disease that affected teenagers with little attention given to preadolescent and postadolescent AV. This perspective has changed, with more attention being given to AV across a broad range of affected age groups, including preadolescent, adolescent, and postadolescent subgroups.[1-5] Earlier onset of adrenarche has led to earlier development of AV in many young girls, with a higher range of dehydroepiandrosterone sulfate (DHEAS) levels observed overall in those with AV as compared to a normal age-matched population.[3,4] At the other end of the age spectrum, AV is a common phenomenon in adult females, with at least half of women estimated to exhibit some form of AV.[1,2,5-8] Based on a large survey of females and males (N=1013), the prevalence of AV in adult females has been reported to be 50.9%, 35.2%, 26.3%, and 15.3% among women aged 20 to 29 years, 30 to 39 years, 40 to 49 years, and 50 years and older, respectively.[2] Acne vulgaris that persists beyond adolescence into adulthood is termed *persistent acne*, or *early-onset acne*, and the development of AV in women 25 years and older who have not previously been affected by AV has been termed *late-onset acne*.[6,8,9] Publications on the management of AV in adult women have focused primarily on systemic hormonal therapies; however, topical therapies more recently have received greater attention in this subpopulation[9-12] and will be discussed in part 2 of this series. Because data on AV in women are limited primarily to involvement of the face and neck region, this article does not address truncal AV unless otherwise specified. Table 1 depicts factors that can influence the management of AV in adult women.

VISIBLE PATTERNS AND CONSIDERATIONS FOR CLINICAL EVALUATION

Clinical Patterns

Although epidemiologic and demographic data are limited in the subpopulation of women with AV, it is reported that females account for up to 82% of adults with AV, with approximately 75% presenting with AV that is clinically similar to their disease course in adolescence.[2,5,13] Among those women with persistent AV, some state that their AV is worse compared to adolescence, while others report it is not as severe. The pattern of AV often is similar to that seen in adolescence, presenting as mixed comedonal and inflammatory papular/pustular lesions diffusely distributed on the face; in other cases, a more selectively distributed *U*-shaped pattern is noted, characterized predominantly by inflammatory papules and/or nodules involving the lower cheeks and jawline margin, with lesions also commonly noted on the anterior and lateral neck.[5,8,9,13-16] A *U*-shaped pattern is believed to be more common in late-onset AV, often with persistence into the mid-40s.[1,15,17] It is important to emphasize the need for additional studies on the demographics and clinical characteristics of AV in adult females, especially correlations between onset, age, and clinical patterns of AV.

An international, prospective, observational study assessed the clinical characteristics of AV in adults (aged ≥25 years) at a dermatology visit for acne (N=374).[16] Participants who were under management for their AV showed severity grades of mild (clear/almost clear) in 47.3% of cases. Involvement of multiple facial sites—cheeks, forehead, mandibular region, and temples—was noted in 89.8% of women, often with both inflammatory and comedonal lesions, which is a pattern similar to adolescent AV. Inflammatory lesions alone were observed in 6.4% of women, 17.1% had comedonal AV only, and truncal AV was present in 48.4%.[16] Additional well-designed studies are needed to determine if this study reflects an accurate qualitative and quantitative depiction of the spectrum of AV in adult females.

Mandibular Pattern

In the observational study of AV in adults, AV localized to the mandibular area was noted in only 11.2% of participants.[16] Women with localized mandibular AV were more likely than women without localized AV to be employed, noted greater daily stress levels, and tended to report more psychologically stressful jobs. Interestingly, the subgroup

Table 1.

Differentiating Factors That Can Impact Management of AV in Women[a]

Factor	Clinical Implications in Women With AV
Prior experience with AV	3/4 have experienced AV as a teenager
	3/10 stated their AV is worse as an adult
	5/10 have used >3 products for AV within the last 12 mo
	5/10 have not seen a dermatologist within the last 3 y
Psychosocial issues	3/4 frustrated with thinking about or seeing their AV
	3/4 feel they will never understand why they have AV as an adult
	6/10 feel others do not understand how it feels to have AV as an adult
	1/3 embarrassed to discuss their AV with a dermatologist, as it is a teen issue
Attitudes and expectations as a woman with AV	Many use makeup to cover up or divert attention from AV lesions
	6/10 would "understand that AV will not clear up overnight"
	3/4 stated they could tell if a prescription medication is working in ≤2 wk; 4/10 stated they could tell within 1 wk
	More than 8/10 stated they would like a dermatologist to recommend prescription therapy for AV when at an office visit unrelated to AV
	1/3 want a discussion of treatment options by the dermatologist
	3/4 indicated they want treatment proven to work for AV in adult women

[a]Sources from European and US publications; surveys completed by women with AV aged >25 y of diverse ethnicities and skin color with >25 "facial pimples" (N=617).
Abbreviation: AV, acne vulgaris.

with mandibular acne alone was much less likely to exhibit a global severity grade of moderate or higher (7.1% vs 50.1%), truncal acne (19.0% vs 51.9%), postinflammatory hyperpigmentation (23.8% vs 51.9%), and erythema (19.0% vs 48.4%), suggesting a unique subset of AV presentation.[16]

Ethnicity/Skin Color

Women of all ethnicities and skin types may be affected by AV.[1,18-20] Earlier age of onset of AV has been suggested in white women; however, earlier onset of adrenarche may be more frequent in black girls, which supports an earlier age of onset of AV in this subpopulation.[15-17] Women with skin of color usually express greater concern with persistent dyschromia at sites where lesions have resolved, and presence of acne scars is a concern among women regardless of skin color, ethnicity, or race.[18,20-22]

Scarring

Acne scarring has been noted to affect up to three-fourths of adult women in one report[17] and often is stated by patients to be a cause of concern and frustration.[1,5,17]

Perimenstrual Flaring

Flaring associated with menses is commonly reported in adult females with AV, with 56%, 17%, and 3% of women in one study (n=230) reporting worsening before, during, or after menses, respectively.[21]

External Factors

Comedogenic products used for skin care, cover-up makeup, or hair care may be important to

consider in selected cases as potential etiologic or exacerbating factors in adult females with AV; they also may be used in the management of AV.[23-25] Adult females often are perplexed and frustrated by the presence of AV after their teenaged years and anxiously wonder about or search for the potential causes. Many women use cosmetic products to cover up facial AV.[5,23-25] Therefore, even if skin care or personal hygiene products or makeup are not believed to be an etiologic factor, many patients appreciate that their dermatologist addressed skin care and cosmetics as a component of AV management and provided appropriate recommendations.[5,13]

Ingestion of dietary supplements containing whey protein have been associated with precipitation of AV.[26,27] Diets with specific content characteristics have been implicated as potential etiologic or exacerbating factors for AV; however, data are limited and specific recommendations remain elusive at present. Individual cases may warrant consideration of dietary factors, especially when treatment resistance is noted.[28] Importantly, progestin-only contraceptives (ie, injectables, intrauterine devices) also can exacerbate or induce AV.[29]

Table 2.

Clinical Signs of Androgen Excess

Acanthosis nigricans (1 or multiple anatomic sites)
Acne vulgaris
Androgenetic alopecia
Cushingoid features
Hirsutism
Increased libido
Insulin resistance states
Irregular menses (including infrequency)
Truncal obesity (central obesity)
Virilization (ie, deepening voice, enlarged clitoris)

Hyperandrogenism

Although most adult females with AV are reported to have normal serum androgen levels when tested, it is important to explore potential signs and symptoms that are suggestive of underlying hyperandrogenism through both the patient's history and physical examination.[9-11,21,29-33] Some investigators have suggested that underlying peripheral hyperandrogenism is the leading cause of AV in adult females, with or without concurrent polycystic ovarian syndrome (PCOS), though it is believed that most women with AV exhibit normal results when undergoing laboratory testing for androgen excess.[10,11,21,29,30] Nevertheless, it is important to consider the possibility of underlying causes of androgen excess (Table 2), the most common being PCOS and late-onset congenital adrenal hyperplasia; an androgen-secreting tumor is less common.[11,29-33] It is suggested that screening for underlying endocrinopathy should be conducted in women presenting with (1) AV recalcitrant to conventional treatment, (2) sudden emergence of severe AV, (3) concurrent signs/symptoms of androgen excess, and/or (4) AV relapse shortly after isotretinoin therapy.[7,11,16,33]

Hirsutism and acanthosis nigricans have been reported to be more reliable predictors of hyperandrogenism than androgenic alopecia.[21] Although it may be subtle in some cases, acanthosis nigricans is harder to camouflage, so the clinician can usually detect it if a thorough physical examination is performed. However, a patient may not voluntarily report to the clinician and their staff that she has hair removed, so despite a thorough examination, the clinician may not detect hirsutism. Therefore, it is important to inquire directly about the presence of hairs (pigmented terminal vs "peach fuzz" hairs), their anatomic location, and any hair removal practices the patient has used. The absence of androgenic alopecia does not exclude underlying hyperandrogenism; however, its presence, especially in younger women, may serve as a clinical marker for underlying hyperandrogenism.[5] Some women may camouflage more subtle alopecia through hairstyling, but obtaining this history usually is not problematic, as most women are distressed by any degree of hair loss.

Laboratory Evaluation—A relatively straightforward approach to the workup of androgen excess includes assessment of serum DHEAS, free testosterone, and total testosterone levels.[10,30] Elevation of serum DHEAS levels indicates an adrenal source of androgen production. Elevation of testosterone is associated with excess androgens produced by the ovaries. Modest elevations of DHEAS are most commonly associated with late-onset congenital adrenal hyperplasia that may not have been previously diagnosed. Modest elevation of testosterone is most commonly associated with PCOS, which also can be accompanied by an elevated luteinizing hormone:follicle-stimulating hormone ratio of 2.5:1 to 3:1.[10,30] Marked elevations

of DHEAS or testosterone can be indicative of adrenal or ovarian tumors, respectively.[30]

In some cases, a woman might have elevated DHEAS and testosterone levels. A 17-hydroxyprogesterone test can help discriminate between an adrenal or ovarian source of androgen excess in these cases, as elevated 17-hydroxyprogesterone levels indicate that the androgens are coming from the adrenal gland.[10,30]

It is important that laboratory evaluation be performed when ovulation is not occurring. Blood tests can be drawn just prior to or during menses. It is important that a woman is not taking an oral contraceptive at the time of testing, which can mask an underlying endocrine abnormality.[10,11,29,30] Generally, testing can be performed at least 4 to 6 weeks after stopping the oral contraceptive.

Psychosocial Impact

Facial AV exhibits a broad range of adverse psychological and social effects on many adult females.[2,5,13,18] It can be associated with depression, anxiety, psychological stress, and suicidal ideation; therefore, thorough screening for these comorbidities may be warranted in some patients.[2,18]

CONCLUSION

The epidemiology, clinical presentation, and clinical and laboratory evaluation of AV in adult females was reviewed in part 1 of this 3-part series. It is important for the clinician to assess the clinical presentation, psychosocial effects, and the possibility of underlying causes of androgen excess. In part 2, skin care and topical management of AV in adult females will be discussed.

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