Endocrinologic Aspects of Hidradenitis Suppurativa

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KEYWORDS

• Hidradenitis suppurativa • Acne inversa • Endocrinology • Androgens • Apocrine glands • Obesity • Metabolic syndrome • Hyperandrogenism

KEY POINTS

- Although the pathophysiology of hidradenitis suppurativa (HS) remains controversial, it is likely that endocrinologic factors play some role in its pathogenesis and maintenance.
- The exact association between sex hormones and occurrence of HS remains unclear.
- Despite normal androgen profiles in most patients, an abnormal peripheral conversion of androgens by the apocrine glands may induce a hormonal dysregulation in situ.
- Obesity is a well-known trigger factor of HS.
- Diabetes, dyslipidemia, polycystic ovarian syndrome, and thyroid disease are among the commonest comorbid disorders.

INTRODUCTION

The occurrence of hidradenitis suppurativa (HS) in a narrow age spectrum after puberty and predominantly in obese patients suggests that endocrinologic factors may be involved in the pathogenesis of HS. Although its pathophysiology is still not elucidated, HS, similar to acne, is a disease of follicular plugging and subsequent inflammation.[1,2] Based on this fact, endocrinologic disorders associated with follicular diseases could be proposed to be involved in the pathophysiologic pathway of HS. In a large, retrospective, case-control study including 2292 patients with HS, comorbid endocrinologic/metabolic disorders such as dyslipidemia, polycystic ovarian syndrome, diabetes, and thyroid disease were among the commonest group reported.[3,4]

HIDRADENITIS SUPPURATIVA AND SEX HORMONES

Association with acne vulgaris, irregular menses, hirsutism, and higher concentrations of total testosterone and free androgen index has been documented in a study.[5] Exacerbations of the disease have also been reported with menses.[1] Shorter menstrual cycles and longer duration of menstrual flow are correlated with the disease[6] and absence of a premenstrual flare of the disease is associated with anovulatory or irregular menstrual circles.[7] Decreased progesterone levels were documented in female patients without premenstrual flares.[7] Onset after menopause is rare.

Interestingly, further studies provided contradictory data: basal levels of major sex hormones, such as estrogens, progesterone, testosterone,

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dehydroepiandrosterone sulfate in serum were not found significantly altered in comparison to controls.[8] Moreover, signs of virilization are not common in HS patients.[2] A prospective study with 70 females with HS failed to show a significant difference in acne, hirsutism and irregular menstruation.[6]

Because the majority of HS patients exhibit normal androgen levels, it has been suggested that the pathophysiology of the disease correlates with an enhanced peripheral conversion of androgens,[9,10] introducing for the first time the idea of HS being a disease based on in situ hormonal dysregulation. However, the activity of three peripheral androgen-converting enzymes in apocrine glands of the axilla of HS patients showed no differences in comparison with those of the controls.[10] An interesting immunohistologic analysis from axillary, inguinal, and perianal skin biopsies deriving from 16 women and 8 men suffering from HS tried to provide evidence for a difference in apocrine gland androgen receptor and estrogen receptor expression. In accordance with previous findings, no alterations in androgen receptor or estrogen receptor expression were reported in biopsies deriving from lesional HS skin in comparison with controls.[11]

Increased free androgen levels may be a result of low levels of sexual hormone–binding globulin as reported in patients with increased body weight.[2,12] In these cases, an increased free androgen index does not necessarily indicate hyperandrogenism. Although the majority of HS patients have normal androgen profiles, there are reports of significant remission after antiandrogen therapy.[13–16] In a double-blinded study conducted by Mortimer and colleagues,[17] the antiandrogen cyproterone acetate (50 mg) in conjunction with ethinyl estradiol (50 μg) led to complete or partial clearance in 50% of 24 female patients after 18 months of treatment.[17] Kraft and Searles[13] studied retrospectively a case series of 64 female patients with HS. In this group of patients, the antiandrogen therapy was superior to oral antibiotic therapy (55% vs 26%), although the *P* value was marginal (<0.04). In contrast, the use of oral contraceptives containing progestogens may worsen the course of the disease or even induce it, because of their proandrogenic properties.[15] In the recently published S1 guideline for HS,[18] the use of oral contraceptives with antiandrogenic potential is suggested for female patients with menstrual abnormalities, signs of hyperandrogenism (seborrhea, acne, hirsutism, androgenetic alopecia syndrome[19,20]), and upper normal or increased serum levels of dehydroepiandrosterone, androstenedione and/or sexual hormone–binding globulin.

The antiandrogenic diuretic spironolactone was also reported to have beneficial results in the treatment of HS.[21] HS is rarely a feature of premature adrenarche, supporting the aspect of an androgen-dependent disorder.[22,23] Interestingly, the disease frequently improves during pregnancy.[2,24] Inhibitors of type II 5α-reductase can also be a therapeutic option in HS, especially in recalcitrant cases. Joseph and colleagues[25] used the type II 5α-reductase inhibitor finasteride (5 mg/d) in a pilot study with 7 patients, who did not respond well to antibiotic treatment. Six of the 7 patients showed a significant clinical improvement and 2 of the 6 showed complete remission of the lesions.

HIDRADENITIS SUPPURATIVA AND METABOLIC DISORDERS

HS is considered as one of the skin comorbid disorders of obesity.[4,26] It primarily affects obese women in the third to fourth decade,[27] about 3.3 times more often than men of the same age.[28–31] In 2 recent, large, cross-sectional studies including 3207 patients and 326 patients, there was a clear association between HS and the metabolic syndrome.[32,33] HS patients present almost all metabolic syndrome criteria, including hypertriglyceridemia, central obesity, hypo–high-density lipoprotein cholesterolemia, and hyperglycemia.[18,34] The clinical efficacy of metformin in treating cases of HS that have not responded to standard therapies supports further this association.[25] A retrospective chart review was conducted by Gold and colleagues[35] investigated the correlation of HS and the metabolic syndrome. This study, which included 366 patients with HS, showed a clear correlation of disease with the prevalence of the metabolic syndrome (50.6% in the HS group in comparison with only 30.2% in the control group).[35]

Metformin has been proposed as an effective HS treatment in patients who have not responded to standard therapies in case reports and in a clinical study.[16,36,37] In the clinical study, 25 patients were treated with metformin over a period of 24 weeks, and 18 clinically improved with a significant average reduction in their Sartorius score of 12.7 and number of monthly work days lost reduced from 1.5 to 0.4.[37] The Dermatology Life Quality Index also showed a significant improvement in 16 cases, with a decrease in the Dermatology Life Quality Index score of 7.6.

HIDRADENITIS SUPPURATIVA AND THE HYPOTHALAMUS–PITUITARY AXIS

A functional disorder of the hypothalamus pituitary axis was found in 13 patients with HS when