Hidradenitis suppurativa in a patient with hyperandrogenism, insulin-resistance and acanthosis nigricans (HAIR-AN syndrome)

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Abstract

The author reports a rare presentation of hiradenitis suppurativa (HS) in combination with hyperandrogenism, insulin-resistance and acanthosis nigricans (HAIR-AN syndrome) in a female patient. Recently many clues have improved the understanding of HS as a systemic disease rather than a disease only with dermatological manifestation. This report might give another hint emphasizing the endocrinological and hormonal role in HS.

Case Report

An 18-year-old female patient presented to the dermatology clinic with recurring painful and tender boils on her axillae, groin and neck. She had been suffering from these boils for two years. Her family history was unremarkable for hidradenitis suppurativa (HS). Previous therapy included local antimycotic treatment (clotrimazole, econazole and ketoconazole), local anti-inflammatory treatment with corticosteroids and systemic antibiotic treatment (doxycycline, clindamycin, rifampicin and azithromycin). The patient is a known case history was unremarkable for hidradenitis suppurativa (HS). Previous therapy included local antimycotic treatment (clotrimazole, econazole and ketoconazole), local anti-inflammatory treatment with corticosteroids and systemic antibiotic treatment (doxycycline, clindamycin, rifampicin and azithromycin). The patient is a known case endocrinology clinic where congenital adrenal hyperplasia (CAH) is a systemic condition that affects mostly the adrenals, hypothesizing a role in the inflammatory background of HS and might be a marker of its severity on the insulin resistance HS patients. On the other hand, the role of hyperandrogenism in terms of high free androgen index and high DHEA-serum and the sexual hormones and the definitive improvement effect under antiandrogen therapy are still in different studies conflictual. It may play a role in the inflammatory background of HS. Nevertheless, Elmer et al.4 mentioned the possibility for underlying endocrine conditions that may associate HAIR-AN-syndrome.

Discussion

HAIR-AN-syndrome is an acronym for a multi-systemic condition that affects women and consists of hyperandrogenism (HA), insulin-resistance (IR) and acanthosis nigricans (AN). It is understood as a subtype of PCOS, however it differs from the PCOS by the presence of insulin resistance. It is associated with psychological distress, depression and low self-esteem.4 The hyperandrogenism manifests with male body habitus, acne, menstrual irregularities, hirsutism and seborrhea. AN develops due to long-term sensitization to elevated insulin, which binds to IGF-1 receptors on the keratinocytes, thereby stimulating the proliferation of the epidermal keratinocytes and dermal fibroblasts.3 Hyperinsulinemia and Insulin resistance have often an impact on each other and they may induce one another.4 Monfrecola et al.3 suggested that the mTOR dysregulation (conserved serine/threonine kinase mammalian target of rapamycin) may play a role in the inflammatory background of HS and might be a marker of its severity on the insulin resistance HS patients. On the other hand, the role of hyperandrogenism in terms of high free androgen index and high DHEA-serum and the sexual hormones and the definitive improvement effect under antiandrogen therapy are still in different studies conflictual. Under these complicated loop effects of obesity, androgen production and insulin resistance manifest the symptoms of HS further. Nevertheless, Elmer et al.4 mentioned the possibility for underlying endocrine conditions that may associate HAIR-AN-syndrome.

Hidradenitis suppurativa (HS) is a chronically recurring inflammatory disease that affects mostly the axillae, groin, perineum, anogenital and inframammary regions. Women seem to be affected more often by HS than men with the course of disease being more severe in men than women.4 Genetic predisposition appears to be a risk factor for HS with a positive fam-

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ily history for the disease in about a third of all patients. Mutations of the γ-secretase gene and its a cofactor subunit: nicastrin (NCSTN) and High Copy Numbers of β-defensin Cluster on 8p23.1 have been allocated in patients with severe forms family-associated HS. Several modifiable behavioral risk factors are known for HS, in particular cigarette smoking and obesity. Since a number of comorbid conditions like the metabolic syndrome, chronic inflammatory bowel disease and psychosomatic disorders have been strongly associated with HS, the disease is today understood as a systemic disorder. Nevertheless its etiology is still not completely understood.

Earth et al. studied 13 cases with acanthosis nigricans (AN) who have presented with features of cutaneous virilism, he examined 5 patients in that group suffered from HS without any further written clarifications in regard of any relationship between their symptoms, and it was shown in another study on 70 females by Jemec et al. that HS is not associated with other signs of androgenization. Therefore, It is unclear, if our patient and those patients in the study by Earth et al. developed HS because of the elevated risk factors for HS (being overweight, insulin resistance and hyperandrogenism), but since in Earth’s group of 13 patients 5 were suffering from HS, HAIR-AN seems to be an independent risk factor for HS. Stone et al. reported in 1976 another association between HS and AN in male patients was reported in a case. Mostly, this association was explained by the common cause for both disorders being obesity. Whether the etiology in our case is due to obesity or insulin resistance or to unclear pathological association between to AN or secondary to all of them, is still unclear. Many characteristics such as its postpubertal onset, female predominance, pre-menstrual flare ups and perigestational improvement, indicate that hormonal disturbance with or without the endocrinological abnormalities play an unclear provoking role in the emergence of HS. Thus it has not been mentioned in the literature any previous presentation with these manifestations of HAIR-AN and HS together rather in male or female patients, this case reports the first association between HAIR-AN syndrome and HS in a female patient. However, it stays unclear which etiological background provokes the other manifestations. Nevertheless, this case strengthens the indications of possible associations with HS to hormonal dysregulation.

Conclusions

Hidradenitis suppurativa showed itself with multifactorial presentations and often with different systemic relations. Definitely, more studies are needed to evaluate the endocrinological and hormonal role in the emergence of HS. This case might suggest a new association that requires further investigation. It is still unclear if an etiological association presents between HS with HAIR-AN-syndrome as a whole or in part. Nevertheless, it is important for physicians treating patients with HAIR-AN syndrome to pay attention to early symptoms of HS to improve diagnostic accuracy and disease management.

References

13. Xiao X, He Y, Li C, et al. Nicastrin mutations in familial acne inversa impact keratinocyte proliferation and differentiation through the Notch and phosphoinositide 3-kinase/AKT sig-

Figure 1. Acanthosis nigrians on different body folds (photo was taken post operative).


