Hidradenitis Suppurativa in a Patient Affected by Mayer-Rokitansky-Küster-Hauser Syndrome: Insight into the Role of Hormones in HS

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Established Facts

- Hidradenitis suppurativa (HS) is an inflammatory skin disease, which usually occurs after puberty.
- HS exhibits premenstrual flares in women, improves in pregnancy, and worsens postpartum.

Novel Insights

- An ovarian stimulation for in vitro fertilization (IVF) could be a trigger factor for the onset of HS manifestations.
- Hormones could play a central role in the onset and worsening of HS manifestations.

Keywords

Hidradenitis suppurativa · Mayer-Rokitansky-Küster-Hauser syndrome · Hormones

Abstract

Introduction: Hidradenitis suppurativa (HS) is an inflammatory skin disease, which usually occurs after puberty. Even if the pathogenesis of HS is still unproven, numerous studies hypothesized that the disease is triggered by genetic and environmental factors, with hormones playing a central role. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital malformation in which a failure of Müllerian duct development results in absent uterus and fallopian tubes and malformations of the vagina. **Case Presentation:** A 38-year-old Caucasian female referred at our outpatient clinic affected by HS. Before the appearance of HS manifestations, the

patient referred to a gynecologist due to difficulties in getting pregnant. The sonographic findings were consistent with MRKH syndrome. An ovarian stimulation for in vitro fertilization was started. However, after 3 months the patient showed the first HS onset. After the hormonal treatment ended, a combined treatment with rifampicin and clindamycin was started, showing a great clinical improvement at week 10. **Discussion/Conclusion:** HS usually appears after puberty, exhibits premenstrual flare, improves in pregnancy, and worsens postpartum, which indicates a role of hormones and particularly of androgens in its pathophysiology. Contrasting data are reported in the literature. Our case wants to strengthen the idea that hormones could play an important role, probably with other endogenous or exogenous factors. Multidisciplinary investigations will clarify which part is played by each factor in the pathogenesis of HS.

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Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, and debilitating skin disease, which usually occurs after puberty with painful, deep-seated, inflammatory lesions in the apocrine gland-bearing areas of the body [1, 2]. The exact pathogenesis of HS is still unproven. In the last few years, numerous studies hypothesized that the disease is triggered by genetic and environmental factors [3]. The primary defect in HS pathophysiology involves occlusion and subsequent inflammation of the hair follicle; these conditions, together with both innate and adaptive immune dysregulation, are necessary to initiate the development of clinical HS [4]. A recent theory hypothesizes that the disease is triggered by an environmental insult in a genetically predisposed individual, which explains why HS can present as sporadic or familial [5]. Several exogenous and endogenous factors are associated with HS. Hormones could play a key role given its post-pubertal and premenopausal pattern of onset and the efficacy of antiandrogen treatments [6]. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital malformation in which there is failure of the Müllerian ducts to develop, resulting in absent uterus and fallopian tubes and variable malformations of the vagina. Ultrasonography reveals absence of uterus with normally visualized ovaries [7]. Herein, we report the case of a 38-year-old Caucasian female affected by MRKH syndrome which developed for the first time HS manifestations after starting an ovarian stimulation to perform in vitro fertilization (IVF).

Case Presentation

A 38-year-old Caucasian female referred at our outpatient clinic affected by HS. Lesions started 6 months before our consultation. Her medical history was insignificant except for menstrual cycle disorders, particularly with the absence of menstruation after age of puberty and lower abdominal pain occurring almost at the same period every month. However, these symptoms have never been investigated or treated until 1 year ago, when the patient referred to a gynecologist due to difficulties in getting pregnant. The sonographic findings of this patient were consistent with MRKH syndrome. Patients with MRKH syndrome could become mothers through IVF and surrogacy. Therefore, an ovarian stimulation for IVF was started. However, after 3 months of treatment the patient showed the new onset of papules and nodules in the groins and genital area that were worsening during the treatment. When referred at our outpatient clinic, the dermatological examination revealed inflammatory papulopustules and nodules and sinus tracts with malodorous discharge in the axillary and inguinal regions (Fig. 1). An ultrasound examination of the groin

Fig. 1. Manifestations of hidradenitis suppurativa at axillary (a) and inguinal (b) regions.

region was performed, showing hypoechoic band-like structures across skin layers in the hypodermis connected to the base of widened hair follicles compatible with fistulous tracts (Fig. 2). However, she decided to continue the ovarian stimulation treatment until the oocyte aspiration for IVF was performed. The patient started the treatment with oral rifampicin 300 mg twice a day for 7 days, and after the first week, oral clindamycin at a dose of 300 mg twice a day was added [8]. After 10 weeks of treatment, HS showed a great clinical improvement. The patient achieved HiSCR at the end of the treatment and maintained it at last follow-up visit (week 24).

Discussion/Conclusion

Even if the exact pathogenesis of HS is still unproven, in the last few years numerous studies hypothesized that the disease is triggered by genetic and environmental factors, with an important role being played by hormones [3–6]. Observational findings demonstrate that the disease usually appears after puberty, exhibits premenstrual flares in women, improves in pregnancy, and worsens postpartum, which indicates a role of hormones and particularly of androgens in its pathophysiology [9]. This association is also suggested from the increased incidence of polycystic ovary syndrome in patients with HS (reported in 8 of 21 patients in one study) and the thera-

Fig. 2. Ultrasound examination of the groin region showing hypoechoic band-like structures across skin layers in the hypodermis connected to the base of widened hair follicles compatible with fistulous tracts.

peutic efficacy of antiandrogens [10, 11]. Premenstrual flares in women with HS are frequently reported, with occurrence rates between 44 and 63% [12]. Particularly, the flare-up of the disease in the luteal phase of the menstrual cycle occurs after a boost in ovarian androgens, indicating that androgens might play a role in the pathogenic process. Also, it has been showed that obesity and metabolic syndrome are more frequent in HS patients than in non-HS patients. Obesity and metabolic syndrome are well known to be associated with hyperinsulinemia and other hormonal alterations that include hyperandrogenism and polycystic ovary syndrome which have been found with a higher prevalence in female HS patients [11, 13]. However, in contrast with these evidences, it has been showed that patients with HS do not seem to have increased levels of sex hormones and that their hormone levels lie within the normal range, while decreasing levels of progesterone and estrogens seem to coincide with disease flares in premenopausal women [12]. Despite the normal androgen levels in serum of HS patients, it has been previously proposed that the pathophysiology of HS is related to an increased peripheral conversion of androgens by the apocrine glands [14, 15], introducing the idea of HS being a disease based on an end-organ or receptor dysregulation [16]. Indeed, the apocrine glands represent a source of androgen-converting enzymes, such as 5α -reductase which converts testosterone into its metabolically most active form (dihydrotestosterone) [16]. However, no difference in apocrine gland hormone receptor expression was found between patients and HS controls [17]. In addition to all

these evidences, the association between HS and hormones is also suggested by the efficacy of antiandrogens [18]. Indeed, the use of oral contraceptives with antiandrogenic potential, such as cyproterone acetate with ethinyl estradiol, is suggested by the European S1 guideline for HS for female patients with menstrual abnormalities, signs of hyperandrogenism, or upper normal or increased serum levels of DHEA, androstenedione, and/or SHBG [19]. As regards the MRKH syndrome, Henes et al. [20] reported that the proportion of hyperandrogenemia without clinical symptoms was significantly high in MRKH syndrome patients when compared to age-matched controls. Herein, we reported the case of a Caucasian female affected by MRKH syndrome which developed for the first time HS manifestations after starting an ovarian stimulation to perform IVF. In agreement with the literature, this case report suggests that hormones could play a role in the pathogenesis of HS. However, despite the evidences reported to date, the exact role that hormones play in the pathogenesis of HS is still not clarified. The role of androgens and in general of hormones in the pathogenesis of HS is not so far clarified. Our case report wants to strengthen the idea that hormones could play an important role, probably in association with other endogenous or exogenous factors. Further understanding of HS pathogenesis will come from multidisciplinary investigations to understand which part is played by each factor in the pathogenesis of this complex disease.

Statement of Ethics

Informed consent for the study and for the publication of the photos was obtained from the patient. The study complied with the Declaration of Helsinki. Internal board review number is not required since we present a case report that does not need to be approved by the local ethical committee as it is not an experimental or an observational study.

Conflict of Interest Statement

None of the authors have any conflict of interest, including specific financial interests of relationships and affiliation relevant to the subject matter or discussed materials in the manuscript.

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Author Contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of the manuscript, take responsibility for the integrity of the work as a whole, and gave final approval of the version to be published.

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