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CASE REPORT

Autoimmune progesterone dermatitis diagnosed by intravaginal progesterone provocation in a hysterectomised woman

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Abstract

We report the case of a 39-year-old Hungarian woman who cyclically experienced painful, erythematous, patchy skin lesions on her face and chest. Because of her irregular menses and hysterectomy performed later on to manage endometriosis, it was difficult to link her symptoms to the menstrual cycle. But on the basis of the cyclic nature of the rash and the previous negative results – acne vulgaris, psoriasis, atopic dermatitis, lichen planus, systemic lupus erythematosus and infections were ruled out – autoimmune progesterone dermatitis was suspected. As progesterone is not available in aqueous solution for intradermal allergen test in Hungary, we performed progesterone provocation vaginally. The patient developed the usual skin lesions to vaginal progesterone exposure, which confirmed the diagnosis. The patient became symptom free to gonadotropine-analogue treatment and remained so even after the cessation of the therapy after 6 months. To our knowledge, this is the first case in the medical literature, in which autoimmune progesterone dermatitis was proved by vaginal progesterone provocation.

Keywords: Progesterone, dermatitis, vaginal provocation, gonadotropine-analogue, ovulation suppression

Introduction

Autoimmune progesterone dermatitis is a rare condition, which usually occurs in fertile females because of an autoimmune response to endogenous progesterone. The patients cyclically develop variable cutaneous and/or mucosal lesions in the luteal phase of the menstrual cycle, when the progesterone level is elevated. The symptoms usually start 3–10 days before and resolve 1–2 days into the menses [1]. Women with irregular menstrual cycle may not have this clear correlation, which makes those cases difficult to diagnose.

A 39-year-old Caucasian female was previously treated for allergic asthma and has taken oral contraceptive pills for 3 years. Later on, she bore one healthy child from an uncomplicated pregnancy. She had irregular menstrual cycles. Her gynecologist performed hysterectomy because of endometriosis without removing the ovaries.

The patient has experienced painful, erythematous, patchy skin eruptions on her face and chest for 6 years (Figure 1). The lesions recurred cyclically, once in every month. Each flare lasted for 5–7 days and the eruptions healed with residual pigmentation. The rash was accompanied by malaise, headache and low-grade fever. The patient was asymptomatic between the outbreaks. She consulted a dermatologist, an infectologist and an immunologist. Detailed examination was carried out without reaching a definite diagnosis. The complete blood count, serum levels of immunoglobulins and autoantibodies were in normal range. Herpes simplex, human immunodeficiency virus and varicella infections were ruled out. Skin biopsy revealed perivascular mononuclear cell infiltrate in the superficial dermis.

At that point, she presented herself at our institution for further evaluation. The cyclic nature of the symptoms was suggestive of autoimmune sex hormone dermatitis even though we were not able to



Figure 1. Erythematous, patchy skin eruptions on the forehead of the patient.

establish a relationship between the rash and the menstrual cycle because of the previous hysterectomy. Negative estrogen skin test ruled out autoimmune estrogen dermatitis. To intravaginal provocation with progesterone pills after 12 h, the patient developed the usual skin lesions and general symptoms, which confirmed autoimmune progesterone dermatitis. We started triptorelin, a gonadotropine-analogue to suppress ovulation. As a result, the patient stopped producing flares and remained symptom free even after the cessation of the treatment after 6 months.

So far, approximately 50 cases of autoimmune progesterone dermatitis have been reported in the medical literature [1]. Patients can present a variety of symptoms, such as eczema, urticaria, erythema multiforme, angioedema, pruritus and even anaphylaxis [2]. The skin lesions frequently occur on the face and torso. Mucosal manifestations include ulcerative and erosive stomatitis [3]. The patients may experience malaise, headache and fever. The symptoms can spontaneously diminish, continue to appear cyclically, or progress by time, even to anaphylaxis [4].

The exact pathogenesis of autoimmune progesterone dermatitis is unknown. Most of the patients have previously taken an exogenous progestin, such as an oral contraceptive pill, which could have resulted in antibody formation. The antibodies would cross-react with the endogenous progesterone [5]. However, several cases exist, in which the affected women have never been exposed to exogenous progestins [4]. In those cases, potential viral antigens or food proteins could have triggered the antibody formation [3,6].

According to Warin, there are three main criteria to diagnose autoimmune progesterone dermatitis, such as a cyclic rash in the luteal phase of the menstrual cycle, a positive intradermal skin test with

progesterone, and the prevention of the symptoms by suppressing ovulation [7]. Serologic markers of the disease, like autoantibodies to progesterone, basophil degranulation test and *in vitro* interferon- γ release were not routinely checked in the published cases, and when examined, have not been found to be always reliable [1]. There are no specific histologic findings in the disorder. In several cases, the intradermal progesterone test proved to be negative [3]. Before diagnosing autoimmune progesterone dermatitis, other more common skin conditions like acne vulgaris, psoriasis, systemic lupus erythematosus, atopic dermatitis, lichen planus and dermatitis herpetiformis have to be ruled out [5].

The main goal of the therapy is to suppress ovulation and therefore prevent the postovulatory rise of the progesterone level. Patients have been successfully treated with conjugated estrogens, gonadotropine-releasing hormone analogs, tamoxifen, danazol and bilateral oophorectomy. Oral contraceptives usually had limited effect because of the progesterone component of the pills [1]. The disease is usually resistant to antihistamines and glucocorticoids, but there are exceptions [8,9].

Our patient had irregular menstrual cycles and no menstrual flow after hysterectomy, which made it difficult to connect the symptoms to the menstrual cycle. This hindered the establishment of the diagnosis and required the detailed reconstruction of the patient's history. As progesterone is not available in aqueous solution for intradermal allergen test in our country, we performed progesterone provocation vaginally with positive result. Jenkins et al. also experienced that intravaginal administration of progesterone in their patient with autoimmune progesterone dermatitis during infertility treatment provoked the appearance of the symptoms [8]. So, in our opinion intravaginal progesterone provocation test is a feasible method to prove progesterone sensitivity. In this case, after 6 months the gonadotropine-analogue treatment could be stopped without returning of the flares, so it was possible to avoid the long-term side effects of estrogen depletion. Beside the treatment, the natural history of the disease, that the symptoms can improve or disappear by time in some patients, could have contributed to the fortunate outcome of this case.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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