

BRIEF REPORTS

Autoimmune progesterone dermatitis: Case report of an unexpected treatment reaction

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ABSTRACT

Autoimmune progesterone dermatitis (APD) is a rare skin condition with a varying morphology, which appears on a monthly basis during the luteal phase of the menstrual cycle and resolves spontaneously with the endogenous decrease in progesterone during menses. We present the case of 39-year-old multiparous Caucasian woman with generalised, self-limited urticaria in her perimenstrual period. APD was diagnosed in light of the cyclical nature of the symptoms. An intradermal test with the administration of 0.5 mg/mL of medroxyprogesterone acetate showed a positive result. She started using vaginal hormonal contraceptive that paradoxically exacerbate the symptoms, which ceased after the removal of the device. An oral combined contraceptive was initiated instead, with complete resolution of the symptoms.

We share the case because of the rarity of the situation, emphasising the importance of a multidisciplinary team for differential diagnosis and patient follow up.

Key words: allergy and immunology, autoimmune dermatology, progesterone dermatitis, urticaria.

INTRODUCTION

Autoimmune progesterone dermatitis (APD) is a rare skin condition with a varying morphology, appearing on a monthly basis during the luteal phase of the menstrual cycle. Progesterone levels gradually rise after ovulation, reaching a peak concentration about 7 days before menstruation, then decreasing 1 to 2 days after menses, when there is a spontaneous resolution of APD.^{1,2}

Although there is a variable spectrum of the disease, ranging from rash to anaphylaxis, urticaria with angioedema are the most common manifestation of APD.³

Symptoms may appear during or shortly after pregnancy, or after the administration of exogenous progesterone. In some pregnant women the disease is resolved, as pregnancy mimics a natural desensitisation process.^{3,4}

The pathogenesis of APD remains unclear. Sex hormones modulate the immune and inflammatory functions of cells, including mast cell degranulation.⁵ Several studies point to an autoimmune mechanism mediated by Th1 lymphocytes targeting endogenous progesterone, as in delayed hypersensitivity reactions.^{2,4} In women undergoing exogenous progesterone prior to APD diagnosis, Th2 cells and immunoglobulin IgE may also play a role.¹

CASE REPORT

The patient was a multiparous, 39-year-old Caucasian woman with a history of allergic asthma and recurrent migraine, exacerbated during her premenstrual period. She was referred for an allergy, immunology and dermatology consultation after an episode of generalised urticaria associated with the swelling of hands and face, as shown in Figure 1, after taking ibuprofen to relieve the migraine. Reviewing medical past history, it was found that

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Abbreviations:

APD	autoimmune progesterone dermatitis
Ig	immunoglobulin
NSAID	nonsteroidal anti-inflammatory drug



Figure 1 Urticaria associated with swelling of the hand.

our patient had been presenting with cyclic hives in the premenstrual period for the previous 6 years, 4 months after her second and last pregnancy, which had been initially associated with an allergy to nonsteroidal anti-inflammatory drugs (NSAID) due to the temporal relationship between the two events. Her skin lesions had varying morphology, sometimes with a vasculitic aspect, as shown in Figures 2 and 3. She was prescribed oral antihistamines (levocetirizine i.d. to b.i.d.), resulting in a relief in symptoms, although they recurred after the oral antihistamines were stopped. An immunological study failed to show antinuclear and anti-neutrophil cytoplasmic antibodies, she had a negative rheumatoid factor, with normal IgA, IgG and IgM, C3 and C4. Her IgE level was 990.2 UI/mL, serum eosinophils varied from 0 to 7.5% (400/ μ L) and basophils from 0.4 to 0.8% (400/ μ L). No other autoimmune manifestations occurred.

The diagnosis of APD was considered. Prick and intradermal tests with 0.5 mg/mL of medroxyprogesterone acetate showed positive results, confirming the suspected diagnosis. She started a combined hormonal contraceptive vaginal ring (etonogestrel 0.120 mg and ethinyl estradiol 0.015 mg), but 24 h afterwards developed urticaria, shivering and generalised arthralgia that remitted after the removal of the device. At this time, she was taking no concomitant drug such as NSAID. The anovulatory treatment was changed to drospirenone 3 mg and ethinyl estradiol 0.02 mg, p.o. with complete resolution of the condition. There was no record of new episodes despite her continued use of NSAID for migraine in 2 years of follow up.



Figure 2 Vasculitic aspect of an urticaria rash on thigh.



Figure 3 Papular aspect of an urticaria rash on thigh.

CONCLUSION

Diagnostic criteria for APD were proposed by Warin in 2001,⁶ including the presence of a premenstrual flare, positivity in the i.m. administration of progesterone test and the prevention of symptoms with inhibition of ovulation. Intradermal administration of medroxyprogesterone can be used instead (0.2–20 mg/mL to avoid false positive results).^{5,4}

Differential diagnosis with other skin diseases characterised by premenstrual flare as acne, dermatitis herpetiformis, erythema multiforme and systemic lupus erythematosus should be considered.⁴

There are no published guidelines for treating APD. The aim is to prevent ovulation, suppressing the increase of endogenous progesterone during the luteal phase of the cycle. Antihistamines and corticosteroids establish symptomatic control. Combined anovulatory drugs are recommended as opposed to isolated oestrogen therapy that requires high doses which is currently discouraged due to its possible side-effects.¹ In refractory cases, tamoxifen, danazol or GnRH analogues can be used, with case reports suggesting they are efficacious.^{1,4,7} Bilateral oophorectomy can be an option.^{4,7}

Regarding the pathogenesis of this particular case, it seems to be IgE mediated, due to urticaria manifestations, but is also T-cell driven in light of the vasculitic aspect of some lesions and the inflammatory systemic reaction after contact with a vaginal ring. Some authors have described a process of desensitising patients by using vaginal suppositories with incremental doses of progesterone.⁸ Nevertheless, there are no published data on the use of the hormonal vaginal ring in this setting. We can speculate that the sudden contact of vaginal mucosa with high quantities of progestative hormones acted as a trigger, potentiating a hypersensitive immunological reaction. The development of other *in vitro* immunological studies as basophil activation tests should be considered to improve knowledge of this complex pathology.

We share this case not only because of its rarity, but also because of the unexpected reaction to vaginal hormonal contraceptive, of which doctors dealing with this pathology should be aware.

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