

Case report

Autoimmune progesterone dermatitis. Case report with histologic overlap of erythema multiforme and urticaria

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Abstract

Background Autoimmune progesterone dermatitis is a rare eruption that recurs monthly as progesterone levels peak during the menstrual cycle. Clinical and histologic features are variable, and the eruption is thought to represent a hypersensitivity response to endogenous progesterone.

Methods We present the case of a 38-year-old woman with a pruritic intermittent facial eruption of 18 months' duration that recurred predictably in the days surrounding menses.

Results The histology showed interface dermatitis with features of both erythema multiforme and urticaria. Intradermal injection of medroxyprogesterone acetate was positive. Her symptoms responded to antihistamine therapy.

Conclusion This unusual case is particularly distinctive both in terms of the histologic findings and the response to therapy.

Introduction

Autoimmune progesterone dermatitis is a cyclic eruption with variable clinical presentation. Cutaneous eruption occurs during the luteal phase of the menstrual cycle as serum progesterone levels peak, and then remits shortly after menses. We present the case of a 38-year-old woman with autoimmune progesterone dermatitis presenting as a recurrent urticarial eruption on the face and neck. Biopsy showed simultaneous histologic features of urticaria and erythema multiforme. Her symptoms responded rapidly to antihistamine therapy. Both the histologic overlap and the dramatic therapeutic response to nonhormonal therapy are exceedingly unusual in this rarely reported dermatosis.

Case Report

A 38-year-old woman was seen for a pruritic facial eruption that had occurred monthly for the last 18 months. The onset was associated with the discontinuation of an oral contraceptive pill containing estrogen and progesterone. The eruption occurred predictably about 5 days prior to menses, and resolved spontaneously about 3 days after completion of menses. She was otherwise healthy and had no history of dysmenorrhea or menstrual irregularity. She was at day 2 of her menstrual cycle on the day of presentation. On examination, well-demarcated, symmetric, urticarial-appearing erythema and edema were present on the cheeks, chin, and forehead, as well as the submental chin and superior neck, sparing the eyelids and lips (Fig. 1). Autoimmune progesterone



Figure 1 Fixed urticarial plaque on the cheek of a 38-year-old woman with autoimmune progesterone dermatitis

dermatitis was suspected. A 4-mm punch biopsy was performed and she was prescribed cetirizine 10 mg every morning and hydroxyzine 10 mg at bedtime. A complete blood count was normal, and an antinuclear antibody titer was < 1 : 40. Biopsy showed spongiosis, interface dermatitis with keratinocyte necrosis, and lymphocyte exocytosis in both the epidermis and follicular infundibula (Fig. 2a). Interstitial mixed inflammation with mononuclear cells, neutrophils, and eosinophils was present in a background of edema (Fig. 2b). Sparse mucin deposition was demonstrated

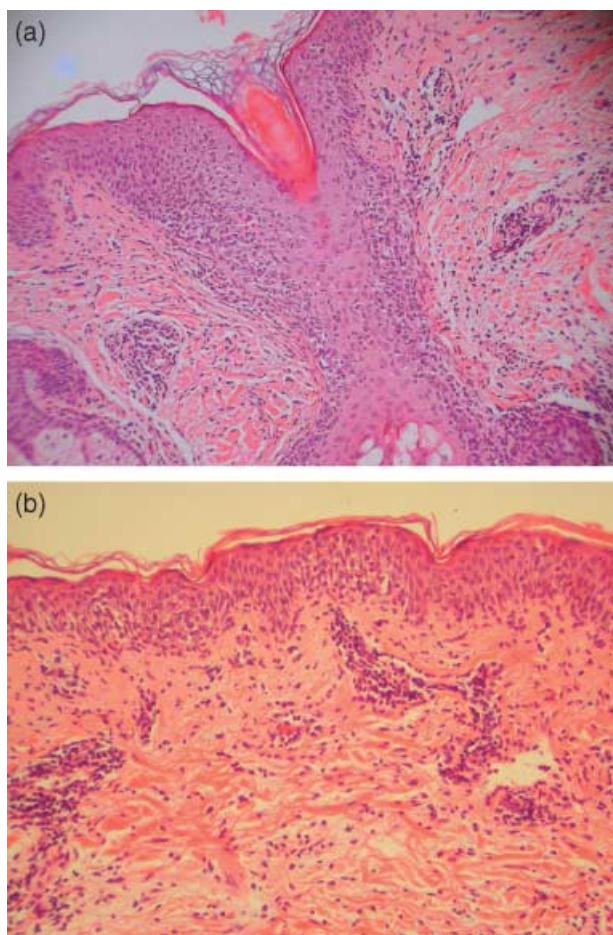


Figure 2 (a) Hematoxylin and eosin-stained histologic section demonstrating prominent erythema multiforme-like features of interface dermatitis along the follicular epithelium (original magnification, $\times 40$). (b) Hematoxylin and eosin-stained histologic section displaying necrotic keratinocytes, spongiosis, and lymphocytic exocytosis with pronounced urticarial edema and a mixed inflammatory infiltrate in the dermis (original magnification, $\times 20$)

on colloidal iron staining. This histologic pattern had features of spongiotic dermatitis, erythema multiforme, and urticaria.

The patient returned 3 days later and reported excellent improvement of the eruption on the above antihistamine therapy. Intradermal testing with medroxyprogesterone acetate (25 mg) was performed, with a wheal-and-flare reaction occurring over the next 24 h, and also triggering a recurrence of her facial eruption. The diagnosis of autoimmune progesterone dermatitis was confirmed. Given her dramatic response to oral antihistamines, she was instructed to take these medications on the days of her menstrual cycle that had previously been associated with her eruption. She has remained asymptomatic on this regimen during the ensuing 8 months.

Discussion

Autoimmune progesterone dermatitis is a rare disorder characterized by cyclic eruption of varying morphology and distribution. The eruption is induced by hypersensitivity to endogenous progesterone, and typically occurs during the luteal phase of the menstrual cycle as serum levels of this hormone increase.¹ Partial to complete resolution occurs within days of menstruation, with recurrence during the next menstrual cycle. The eruption may be localized or generalized. Sensitization with exogenous estrogen in oral contraceptives may be an inciting factor in some cases. Pregnancy may either worsen or improve the condition.¹

A variety of cutaneous manifestations have been reported, most commonly urticaria^{1–3} and erythema multiforme.^{4–8} In a comprehensive review, 11 of 42 reported cases described the clinical presentation of urticaria, four described erythema multiforme, and one described both urticaria and erythema multiforme.¹ Presentations such as erythema annulare centrifugum,⁹ eczematous, fixed drug-like eruption, and papulovesicular eruption^{1,10} have also been described. The histologic findings are variable, and only some of the reported cases have had cutaneous biopsies. Superficial perivascular mixed inflammation may be the most consistent histologic finding.¹¹

The diagnosis of autoimmune progesterone dermatitis is generally suspected by the clinical context, although women with irregular menses may pose a diagnostic challenge because of variable temporal correlation between the eruption and menses.³ The diagnosis may be confirmed with intradermal testing with progesterone. Both immediate (30-min) and delayed (24–48-h) hypersensitivity reactions have been described.¹ Provocative testing with intramuscular or oral progesterone may also be performed.¹

A variety of treatment options have been described, including hormone-based therapy with oral contraceptives,^{4,12} conjugated estrogens or ethinyl estradiol,¹¹ tamoxifen,^{8,10,13,14} and danazol,¹⁵ administered either daily or intermittently around the time of the expected flare. These medications presumably are effective by suppressing ovulation and therefore preventing the production of progesterone by the corpus luteum. Oophorectomy has been performed for refractory cases and is curative.^{6,7,16} Spontaneous resolution has been reported.^{1–17}

Although antihistamine therapy has shown some benefit for cases presenting as urticaria, we are not aware that this medication has resulted in complete resolution in previously reported cases, particularly with erythema multiforme-like histology. Given its excellent safety profile, antihistamine therapy would be a reasonable first step in therapy.

In conclusion, we report a case of autoimmune progesterone dermatitis with a positive intradermal test to progesterone and histologic overlap of urticaria and erythema multiforme. The response to antihistamine therapy was prompt and

dramatic in this case, and warrants consideration in other patients presenting with this rare dermatosis.

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