

BRIEF REPORT

A case of autoimmune progesterone dermatitis diagnosed by progesterone pessary

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ABSTRACT

Autoimmune progesterone dermatitis is a rare, cyclical eruption that occurs in the luteal phase of the menstrual cycle and during pregnancy. Many manifestations have been reported including cyclical eczema, urticaria, erythema multiforme, stomatitis and even anaphylaxis. The condition spontaneously resolves after menopause. As histopathology is non-specific, the diagnosis rests on history with precipitation of the eruption by a progesterone challenge, usually by the intradermal, intramuscular or oral route. We present the case of a 34-year-old woman with a premenstrual papular and eczematous eruption that was exacerbated after pregnancy. Biopsy showed subacute spongiotic dermatitis. To confirm the diagnosis, we used an intravaginal progesterone pessary as a provocation challenge. There was recurrence of the rash 12 h after insertion of the pessary with spontaneous resolution thereafter. We propose that use of a progesterone pessary is an effective tool in the diagnosis of autoimmune progesterone dermatitis.

Key words: autoimmune, danazol, dermatitis, luteinising hormone releasing hormone analogue, oophorectomy, ovulation, pessary, progesterone, tamoxifen.

INTRODUCTION

Autoimmune progesterone dermatitis (APD) is characterised by cyclical skin eruptions, typically occurring in the luteal phase of the menstrual cycle with spontaneous resolution after menses. The diagnosis is primarily made on

demonstration of a skin reaction to progesterone provocation and treatment involves suppression of ovulation.

CASE REPORT

We present a 34-year-old woman with a 2-year history of a papulovesicular eruption initially occurring several days after the delivery of her first child. The eruption initially affected the inner forearms and palms bilaterally. At the time this was treated as scabies and eczema with improvement of her symptoms. However, she subsequently developed recurrent flares of the rash, with premenstrual onset and spontaneous resolution after several days. There was also recurrence of the rash several days after the delivery of her second child. She presented 2 years after the onset of the rash for diagnosis and management.

The patient's background was unremarkable except that she had been on the oral contraceptive pill containing ethinylloestradiol and cyproterone acetate as a teenager until her first pregnancy. She took no other medications. On examination there were excoriated papules and vesicles on the palms and volar aspect of the forearms bilaterally. The clinical appearance and cyclical nature of the eruption lead to a provisional diagnosis of APD.

Initial investigations are shown (Table 1). To confirm the diagnosis of APD, we undertook a progesterone challenge. After discussion with obstetricians at our hospital, we elected to use a 100 mg progesterone pessary. In Australia progesterone pessaries are listed in the Pharmaceutical Benefit Scheme for use in *in vitro* fertilisation (IVF) or the gamete intra-fallopian transfer program. We obtained a 100 mg progesterone pessary for use in our patient from the IVF Australia closest to our hospital (Maroubra branch). We performed the progesterone challenge in the first week of

Abbreviations:

APD	autoimmune progesterone dermatitis
ANA	antinuclear antibodies
ENA	extractable nuclear antibodies
IVF	in-vitro fertilisation
LHRHa	luteinising hormone releasing hormone analogue

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Submitted 5 November 2010; accepted 10 January 2011.

Table 1 Investigations undertaken in our patient

Investigation	Results
Skin biopsy	Subacute spongiotic dermatitis, mild perivascular dermal infiltrate
ANA, ENA	Normal
Thyroid function tests	Normal
Anti-progesterone antibody assay	Unsuccessful attempt to formulate assay in our institution

ANA, antinuclear antibodies; ENA, extractable nuclear antibodies.

**Figure 1** Erythematous papule, inner forearm 24 h after progesterone pessary challenge.

the menstrual cycle, when progesterone levels are minimal. The patient was observed in our clinic for 2 h after the insertion of the pessary to monitor for anaphylactic reactions. Erythematous papules were evident on the inner forearms and palms on 24 h follow up, confirming the diagnosis of APD (Fig. 1). The rash spontaneously resolved several days after onset.

At the time of writing our patient continues to have premenstrual flares of her eruption. For more severe episodes she applies topical betamethasone dipropionate 0.05%. The rash once again recurred after the delivery of her third child (Fig. 2). Given that her symptoms are controlled with simple measures, no further treatment was pursued.

DISCUSSION

APD is thought to be a hypersensitivity reaction to progesterone, although exact pathogenesis is unknown. The hypersensitivity response may be induced by earlier exposure to exogenous progesterone,¹ most commonly in the form of the oral contraceptive pill. Our patient had been taking the combined oral contraceptive pill during her twenties and this may have been a precipitating factor. Previous exposure to progesterone is not always found in patients with APD. APD in pregnancy has been reported and can occur in the first week¹ to several months after delivery.²

**Figure 2** Erythematous papules on the palm in the first week after delivery of the patient's third child.**Table 2** Clinical manifestations of autoimmune progesterone dermatitis

Eczema, pruritus, pompholyx ¹
Stomatitis ¹
Erythema annular centrifigum ²
Fixed drug eruption ³
Cyclical fixed facial plaque ⁴
Urticaria ⁴
Erythema multiforme ⁴
Anaphylaxis ^{1,5}

The clinical presentation of APD is variable (Table 2).

Diagnosis of APD depends on the history of a cyclical eruption, induction of the rash after a progesterone challenge and resolution of the rash with ovulation suppression. Histological findings in APD are not diagnostic.

Progesterone challenge tests have mainly involved intradermal injections of aqueous progesterone at varying concentrations (0.01%, 0.1% and 1%⁵ and 0.05%¹ of aqueous progesterone diluted with normal saline). Immediate urticaria has occurred after intradermal injection in some patients^{2,5} with others experiencing a delayed reaction, peaking at 24 to 96 h.¹

The detection of autoimmune progesterone antibodies has been reported in the literature.¹ Interferon- γ release assays have been reported to successfully aid in the diagnosis of APD.^{2,6}

In our patient, we elected to use a vaginal progesterone pessary for the progesterone challenge as it was relatively painless and convenient. Reports of the recurrence of APD in patients receiving intravaginal progesterone for luteal phase support in infertility treatment⁷ further support the use of a progesterone pessary. Since performing the test on our patient, the diagnosis of APD through intravaginal progesterone provocation has been described in the gynaecological literature.⁸

The treatment of APD involves ovarian suppression, which in turn suppresses progesterone release. Conjugated oestrogen 0.625–1.25 mg/day in a 21 day cycle has been used with success.⁸ In patients naive to the oral contraceptive pill, a regimen of ethinyloestradiol and levonorgestrel may be effective.⁹ Luteinising hormone releasing hormone (LHRH) analogues (LHRHa) suppress ovulation through continuous occupation of LHRH receptors and desensitisation. LHRHa were used successfully to treat recurrent premenstrual anaphylaxis.⁵ The main side effect of therapy with LHRHa is the induction of menopause, which precludes its use in a large proportion of patients with APD. Danazol has been used prophylactically with success at a dose of 200 mg twice daily commencing 3 days prior to menstruation and continuing for 3 days thereafter.¹⁰ The adverse effects of danazol include hepatocellular derangement and hyperandrogenism. Tamoxifen has been used with success to suppress ovulation in APD¹ at a dose of 10 mg twice daily. The effects of bone demineralisation limit the long term use of tamoxifen in younger women. When conservative treatment has failed and symptoms are disabling, oophorectomy has lead to cure in APD.¹

For some patients, including the case we present, symptoms are mild enough to allow explanation and symptomatic treatment only. However, regular antihistamines and topical corticosteroids do not result in long-standing improvement in the majority of patients.¹ For patients with more severe manifestations management includes short course adrenaline and oral corticosteroids.⁵ Complete resolution of APD without treatment has also been reported.

Our case demonstrates that APD should be considered in premenopausal women who have cyclical skin symptoms. The use of a progesterone pessary in our patient confirmed the diagnosis. To the best of our knowledge, this is the first

report of the use of a progesterone pessary to diagnose APD in the dermatological literature.

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