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Case Report
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Autoimmune Progesterone Dermatitis Treated with Gonadotropin Releasing Hormone Analogue a Case Report

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Abstract

Autoimmune progesterone dermatitis (AIPD) is a rare condition due to hypersensitivity reaction to own endogenous progesterone produced during second half of menstrual cycle with varieties of dermatological manifestations including urticaria, eczema and vesiculobullous eruptions.

This is a case report of 22 years old Caucasian female with history of eczema since age of 3 years. She presented initially to dermatologist with a history of recurrent cyclical rash. She reported her dermatological symptoms flared up at the time of her period and settled in between periods for last 2 years. She had used tablet Microgynon (an oral contraceptive pill) in the past for couple of years for contraception without any associated symptoms. She had an intradermal skin test and developed significant localised urticarial reactions to intradermal progesterone. She was then referred to a gynaecologist and treated with Gonadotropin Releasing Hormone Analogue (GnRH) analogue for 6 months with add back therapy which significantly improved her dermatological symptoms with no flare up.

Introduction

Autoimmune progesterone dermatitis (AIPD) is a rare premenstrual dermatological manifestation due to an allergic reaction to increased progesterone during the luteal phase of menstrual cycle [1]. It is characterised by the cyclical dermatosis with cutaneous manifestations such as urticaria, erythema multiforme and papulovesicular eruptions and even anaphylaxis [2-5]. The dermatological lesions usually appear 3 to 10 days prior to the onset of menses coinciding with the luteal phase of the cycle and remits shortly after menstruation [3-5]. AIPD has also been described in a man taking exogenous progesterone and postmenopausal woman receiving hormone replacement therapy and in the postpartum period [1,6]. It was first reported in 1921 by Geber [2].

Case Presentation

A 22-years old, nulliparous Caucasian female was referred to Gynaecology outpatient clinic by her dermatologist with a history of recurrent cyclical rash. She gave a history of pustular rash all over the body, more on the arms with different stages of healing indicating fresh and new rashes. Rashes usually flared up at the time of her periods and settled in between periods for last 2 years. She also felt generally unwell with nausea and hot flushes just before her periods. On examination, she had non-follicular papular and pustular rash all over her arms, legs and back (Figure 1). Patient felt this had affected her confidence as she cannot wear any dress without sleeves due to scarring from the rashes.

She was initially diagnosed with pityriasis lichenoids chronica by her dermatologist based on the clinical appearance and biopsy. However, treatment with oral Tetracycline and topical steroids lacked efficacy in complete clearance of the rash and subsequent biopsy did not show features of pityriasis lichenoides and immunofluorescence was negative. The diagnosis of autoimmune progesterone dermatitis was confirmed when she had very significant localised urticarial reactions to intradermal progesterone Injection.

She attained menarche at the age of 13 and had normal regular periods with cycle of 30 days. She had used tablet Microgynon in the past for couple of years and stopped 2 years ago as her partner has vasectomised. She had long term history of eczema since age of 3 years and had taken regular antihistamines.

After long discussion with the patient about conservative treatment options such as oral contraceptives (Microgynon was well tolerated in the past) and GnRH analogues (Injection Zoladex,

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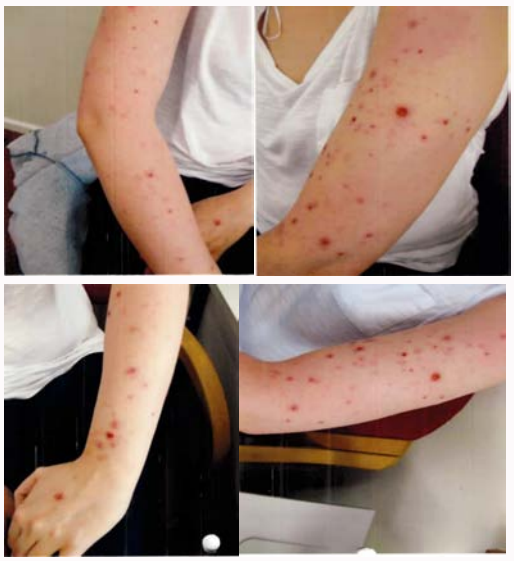

Figure 1: Rashes on the arm with different stages of healing indicating fresh and new rashes.

3.6mg monthly) to allow suppression of ovulation. Patient agreed for Zoladex injection with Tibolone (2.5mg daily) as add back therapy for 6 months and then start Tab Microgynon, an oral contraceptive pill. She was reviewed after 3 months and 5 months following Zoladex injection which showed significant improvement in her skin lesions with no new flare ups.

Discussion

Autoimmune progesterone dermatitis (AIPD) is an auto-allergic (autoimmune) reaction to endogenous progesterone during luteal phase of menstrual cycle, with less than 100 cases reported in literature [1]. The first reported case of urticarial rashes related to periods was described by Geber in 1921[2] and the challenges in the diagnosis and management of the condition were discussed in early literature [2]. Shelley et el in 1964 described a cyclical dermatitis flare with a pruritic vesicular eruption in a 27-year old woman related to premenstrual progesterone exposure. She was confirmed with ADP after positive oral challenge test with progesterone and eventually cured by oophorectomy [3]. The age of onset is variable, with the youngest reported case occurring at menarche [4] but the initial manifestation of the disease may be as late as 48 years of age. The exact pathogenesis of autoimmune progesterone dermatitis is unknown [1,5]. It is hypothesized that some women could have developed sensitization to previous use of exogenous progesterone resulting to an immune reaction with subsequent exposure [5]. Others have explained that it may be possible that some woman can only tolerate low level of progesterone and hence develop an inflammatory reaction in response to increased progesterone that peaks at the luteal phase of the period. Another theory for progesterone sensitization is due to cross- reaction of various hormones especially in patients who never had exogenous progesterone [3,5].

AIPD is a diagnosis of exclusion. So, we must first exclude other chronic dermatological conditions that can also have a peri-menstrual flare such as acne vulgaris, dermatitis herpetiformis, erythema multiforme, lichen planus, lupus erythematosus and psoriasis [3,6]. Detailed clinical history is key which should represent a cyclical pattern between the onset of dermatological manifestation and menses. Diagnosis is confirmed by manifestation of progesterone sensitization with intradermal testing or intramuscular or oral progesterone challenge test [1-9]. The hallmarks for diagnosis of AIPD are premenstrual flare, appearance of rash with intramuscular progesterone, and prevention of rash with inhibition of ovulation (Warin, 2001) [6]. Our patient was confirmed with diagnosis when she had very significant localised urticarial reactions to intradermal progesterone.

Definite treatment of AIPD is suppression of ovulation by inhibition of the secretion of endogenous progesterone during luteal phase [1,3-9]. Combined oral contraceptive pills with low dose progesterone is first line of treatment for AIPD [4,7]. Other effective agents includes GnRH analogues [2-4,7], which suppresses ovulation by suppressing the hypothalamic-pituitary axis. The use of GnRH causes symptoms of oestrogen depletion such as vaginal dryness, osteoporosis and hot flushes [1,3,5]. Tamoxifen a selective estorgen receptor antagonist has been used as treatment for AIPD but not a first line because of its association with bone reabsorption [3,5,9,10]. Surgical therapy with bilateral salpingo-oophorectomy is considered as a definitive treatment for AIPD in patients with completed family [2-5,8]. Our patient had significant improvement of skin rashes with no flare up which illustrates successful response to GnRH analogue with add back therapy for 6 months supporting the diagnosis of autoimmune progesterone dermatitis. The long term plan for her treatment is to have Injection Zoladex (GnRH analogue) for another 6 months and switch to Tab Microgynon as she had tolerated it well in the past.

Conclusion

Autoimmune progesterone dermatitis (AIPD) is a rare cyclical dermatos is due to hypersensitivity reaction to endogenous progesterone. Diagnosis is confirmed by skin allergy test with Progesterone. We have demonstrated treatment of AIPD with GnRH analogues to encourage dermal lesions to heal and then use oral contraceptive pill for long-term with exogenous progesterone.

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