International Journal of Medical and Pharmaceutical Case Reports
2(1): 14-17, 2015; Article no.IJMPCR.2015.004

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Autoimmune Progesterone Dermatitis with Post-Inflammatory Hyperpigmentation

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Authors' contributions

This article was written in collaboration between both authors. Author JEA interfaced with the index patient and wrote the first draft. Author EBH made the diagnosis, conceptualized the case report and revised the final manuscript. Both authors read and approved the final draft.

Article Information

DOI: 10.9734/IJMPCR/2015/13159
Editor(s):
(1) Rahul S. Khupse, Pharmaceutical Sciences, University of Findlay, USA.
Reviewers:
(1) Shawky Badawy, Department of Obstetrics and Gynecology, SUNY Upstate Medical University, Syracuse, New York 13210, USA.
(2) Ibrahim Yakasai, Bayero University Teaching Hospital Kano, Nigeria.
Peer review History: http://www.sciencedomain.org/review-history.php?iid=643&id=38&aid=6226

Case Study

Received 5th August 2014
Accepted 25th August 2014
Published 25th September 2014

ABSTRACT

Autoimmune Progesterone dermatitis is a rare disorder characterized by recurrent cyclical cutaneous eruptions during the menstrual period, and is due to hypersensitivity to progesterone. It is a dermatosis with myriad modes of presentation including urticaria, eczema, papulovesicles, angioedema, anaphylaxis, pruritus and erythema multiforme. We hereby present the first documented report from Nigeria - the case of a 35 year old woman with recurrent premenstrual eruption of erythematous patches, papulovesicular and urticated lesions with attendant distressing post-inflammatory hyperpigmented spots. Diagnosis was confirmed by the typical premenstrual cyclical presentation and a positive progesterone challenge test.

Keywords: Autoimmune; progesterone; dermatitis; cyclical; premenstrual; Nigeria.

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1. INTRODUCTION

Autoimmune Progesterone Dermatitis (APD) is a rare disorder resulting from hypersensitivity to endogenous or exogenous progesterone. Onset is usually anytime between menarche and menopause. Lesions develop 3 – 10 days before the menstrual cycle and continue until few days after menstruation. It is distinguished from other clinical perimenstrual entities by its positivity to intradermal progesterone challenge and resolution on suppression of ovulation.

2. CASE REPORT

A 35 year old evidently distressed woman visited our dermatology clinic with a 2 year history of recurrent skin rashes. They were first noticed during pregnancy but resolved without treatment. However, the rashes reoccurred on postpartum resumption of menstruation, subsequently appearing about 3 -5 days before menses and often lasting till approximately 3 days after the menstrual period. The eruptions were described as multiple mildly pruritic, reddish rashes mostly on the abdomen, thighs and buttocks which resolve leaving darkly pigmented spots. There were no associated mood changes or breast tenderness, she was however curious about the regular cyclical rash and worried about the spots which had affected her mode of dressing. She has a regular 28 day menstrual cycle and had an intrauterine contraceptive device inserted a year prior to consultation. She had no previous history of chronic skin disorder, no personal or family history of atopy and is not on any medications. Examination revealed multiple discrete polymorphic lesions comprising erythematous patches with central papules or vesicles, urticated wheals and numerous hyperpigmented healed scars with atypical target-like morphology, distributed mainly on the abdomen, thighs, buttocks,with a few on the distal part of the upper limbs (Figs. 1 and 2). The skin showed signs of chronic steroid abuse including striae. Complete blood count showed eosinophilia and histology of a skin biopsy sample revealed orthokeratosis with flattening of rete pegs, widened dermal papillae and mild spongiosis. There was moderate interstitial and superficial perivascular infiltrates composed of lymphocytes, neutrophils and eosinophils. An intradermal progesterone challenge test with a concentration of 50mg/ml of progesterone in oil showed exaggeration of skin lesions after 48 hours. Treatment with topical steroids combined with 2% hydroquinone led to lightening of the post inflammatory hyperpigmented spots, however the cyclical eruptions persisted. She declined the use of danazol or tamoxifen due to their documented side effects.

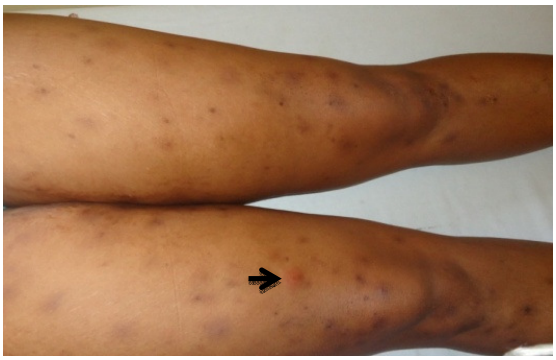

Fig. 1. Post inflammatory hyperpigmented spots on the thighs. Arrow shows new urticated lesion on the lower right thigh

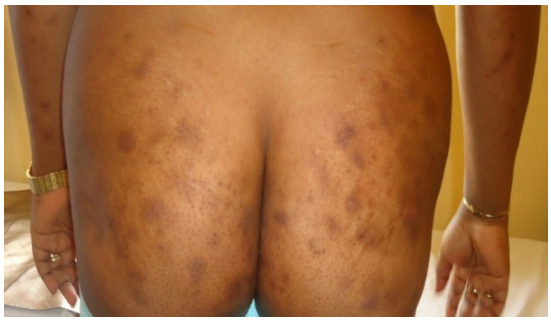

Fig. 2. Multiple Post Inflammatory hyperpigmented lesions on the buttocks

3. DISCUSSION

Premenstrual Syndrome is a common condition described as a constellation of physical and mental symptoms tied to a woman's menstrual cycle. Although dermatoses may also occur, they are infrequently mentioned, probably due to their rarity or afailure of association with the predominant mental and behavioural symptoms. However, peri-menstrual dermatoses have been recognized, and categorized into a group called cyclic catamenial dermatoses of which APD is one. These are different from the often observed exacerbation of some skin diseases such as acne and atopic dermatitis during menses.

Autoimmune Progesterone Dermatitis was first described by Geber in 1921 [1], many years after in 1995, Herzberg et al. [2] reviewed the existing English and German literature and discovered 42

documented cases. Nine years later in 2004, Baptist and Baldwin [3] stated that since Gerber's description, there have been approximately 50 cases of APD in the medical literature. At present, ten years after Baptist and Baldwin's publication, a PubMed search has revealed over 30 additional documented cases in the English literature. It is however still classified as a rare disorder by the National Institutes of Health [4]. (Disorders are considered rare if there are less than 200,000 reported cases). The marked increase in the number of reported cases within the last 10 years compared to the 83 years following its initial description presupposes an increase in awareness among clinicians.

Although the exact pathogenesis has not been fully elucidated, it is considered an auto-allergic (autoimmune) reaction to both endogenous and exogenous progesterone, because the skin eruptions are observed during the luteal phase of the menstrual cycle and resolve a few days after menses. This appearance and resolution has been found to correspond to the rise and fall of progesterone, [5] in addition, there have been reports that most patients with APD have prior exposure to exogenous progestin found in oral contraceptive pills. [6] The age of onset is variable, occurring between menarche and menopause. Risk factors include fertile women, previous history of exogenous progesterone intake and sometimes pregnancy as in our index patient; however, cases have been found to regress during pregnancy. The morphology of the skin lesions are wide ranging, including erythema-multiforme, annular erythema, urticaria, angioedema, eczematous and fixed drug eruption-like lesions, in addition, ulcerative stomatitis and pruritus have also been described in association with APD [2,7] Typically, these lesions develop 3 – 10 days before menses, and continue to 1-2 days after the menstrual period. Diagnosis of APD requires a positive history of a premenstrual flare and reproducible cutaneous lesions with intradermal progesterone challenge. To exclude other forms of cyclic catamenial dermatoses and premenstrual flares of existing chronic dermatoses, Warin [8] proffered a diagnostic criteria for APD, which includes (1) Association with menstrual cycle (2) positive response to intradermal testing with progesterone [which may be immediate within 30 minutes or delayed after 24-48 hours] (3) symptomatic improvement after inhibition of progesterone secretion by suppressing ovulation. Eosinophilia was observed in our patient, in some cases, eosinophilia has been correlated with the cutaneous symptoms, with a decrease in the total eosinophil count following therapy [9]. Eosinophils have even been suggested as having a role in the pathogenesis of the disorder [3]. A number of treatment modalities have been tried with varying degrees of success. This includes topical steroid for mild cases, high dose oral steroid, even progesterone desensitization with injection of extracts from corpus luteum; however, the most successful agents have been those that suppress ovulation such as oral contraceptive pills, Gonadotropin Releasing Hormone agonists, Tamoxifen, Danazol and when all else fails, oophorectomy which is the definitive treatment [2]. Antihistamines are mostly ineffective.

4. CONCLUSION

Autoimmune Progesterone Dermatitis is still a rare disease, and many cases remain undiagnosed due to a lack of awareness of the condition. The last decade has seen a surgein reports in the medical literature, but the pathogenesis remains largely unknown, and many women still suffer from the distressing condition. It is important that many more reports such as ours be disseminated into the public domain, which will in turn drive research, resulting in a better understanding of the condition, discovery of newer therapeutic agents with less adverse effects and a better quality of life for the majority of persons affected.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid= 643&id= 38&aid=6226