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Autoimmune Progesterone Dermatitis: A Curse for Female Anesthesiologists?

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Abstract

Autoimmune progesterone dermatitis is a rare cyclic premenstrual allergic reaction to progesterone produced during the luteal phase of a woman's menstrual cycle. Patients present with a variety of conditions including erythema multiforme, eczema, urticaria, angioedema, and progesterone-induced anaphylaxis. A thirty-seven-year-old female anesthesiologist reported erythema multiforme and urticarial rash prior to her menses for last five cycles. She was treated effectively with oral antihistaminic and life style modifications.

Keywords: Dermatitis; Eczema; Skin lesions; Polycystic ovarian disease; Progesterone.

Introduction

Autoimmune progesterone dermatitis is caused by an autoimmune response to endogenous progesterone in women of child-bearing age. Distressing skin lesions occur periodically during the luteal phase of the menstrual cycle due to increases in progesterone [1-3]. We discuss the symptomatology, diagnosis and treatment modalities available.

Case Report

A thirty-seven old married medical professional working as an anesthesiologist visited our outpatient gynaecological department with complaints of urticaria. She complained of having five episodes of erythema multiforme, urticaria and dermatographism all over the body. The itching started over the scalp and progressed rapidly all over the body. She had to be admitted twice in intensive care for aggravated symptoms. The patient was administered high dose of steroids, antihistaminic, calcium gluconate and was advised to avoid dairy products for relief without much improvement. The patient also informed that following these allergic reactions she had her menstrual period within 24 hours after four episodes while in one episode she had her periods after ten days. There was no significant medical and family history of allergic diseases. Episodes were not related to food, exercise, alcohol, or to use of any medications. The patient denied any changes in her diet, cosmetics, medications, or soaps that could account for the dermatitis. The patient's obstetrical history consisted of two pregnancy resulting cesarean section. Her first pregnancy was uneventful. Though after that she was diagnosed as a case of polycystic ovarian disease and was started on tablet sustained relief metformin 1gram once daily. After treatment for infertility she conceived. During her second pregnancy she developed gestational diabetes and was started on insulin, diet control. During pregnancy she was given intramuscular injections of progesterone. She delivered a premature baby at 31 weeks. Nine months after delivery the subject experienced the first episode.

Her complete blood count was normal; Immunoglobulin E levels were normal even during an acute phase. Allergy testing was done which was reported negative.

Our patient was diagnosed with autoimmune progesterone dermatitis based on history, physical and

laboratory examination. The allergy skin testing was performed with progesterone 5 mg/ml in normal saline. A full-strength intradermal test revealed a 25 × 40 mm wheal with erythema. Within 48 hours the arm in which injection was given became swollen and rash appeared, Patient was advised tablet levo-cetirizine 5 mg, an antihistamine, daily and was advised life style modifications, change in working environment which were successful in controlling her outbreaks.

Table 1: Investigations done for the patient.

Skin test to common foods	Negative
Skin test to inhalants	Negative
Skin test to medroxyprogesterone	Positive
Total serum IgE:	Within normal range
24-hour urine for 5-HIAA	Negative
24-hour urine for VMA	Negative
24-hour urine for Catecholamine	Negative

Discussion

Ever since Géber first described autoimmune progesterone dermatitis (APD) in 1921 very few cases have been reported in the literature [4]. APD is an allergic reaction to progesterone produced during luteal phase of a women's menstrual cycle. The etiopathogenesis is unknown and is postulated to be related to hypersensitivity reaction to endogenous progesterone production or exogenous intake of a synthetic progestin [5].

Our patient would develop symptoms in aggravated cyclical manner in premenstrual phase, which is typical of APD. In APD skin lesions usually develop 3-10 days before menstruation and persist up to 1-2 days after the end of the menstrual cycle, with recurrent cyclic aggravation. For confirming the diagnosis progesterone in oil is not preferred as it is more likely to cause an irritant reaction as compared to an aqueous suspension or aqueous alcohol solution of progesterone [6]. The skin reaction may be seen immediate within half an hour or delayed upto 48 hours. The criteria for the diagnoses of APD as proposed by Warin includes [7,8]:

- Cyclic skin flares related to the menstrual cycle.
- A positive skin test or oral/intramuscular challenge to progesterone.
- Demonstration of a circulating antibody or basophil degranulation tests to the progesterone.

Our patient tested positive for the above two criteria but was as our institute does not have facility for demonstrating circulating antibody to the progesterone or basophil degranulation tests; we were not able to confirm it. It is important to differentiate it from another rare entity catamenial anaphylaxis. In APD, sign and symptoms begin earlier in the pre-menstrual phase whereas in catamenial anaphylaxis symptoms appear in direct association with the start of the menstrual flow [9,10].

It is a well-known fact that stress has a strong co-relation with menstrual irregularities. Several health conditions and poor lifestyle can lead to menstruation problems. Non-pharmacological methods have been proven beneficial in menstrual irregularities [11].

The treatment modalities for APD range from danazol, gonadotropin releasing hormone analogs, tamoxifen, and oophorectomy with varying successes.

1) **Oral Contraceptives (OCPs):** OCPs has limited success due to the progesterone component of OCPs.
2) **Antihistamines:** Well tolerated, few side effects, does not address underlying mechanism [12].
3) **Conjugated Estrogens:** Avoids progesterone component of OCP, Increased risk of endometrial cancer [12,13].
4) **Glucocorticoids:** Able to suppress multiple components of the immune system, Usually not effective alone. Can be combined with other therapies
5) **GnRH Agonists:** If other medical treatment not effective. Can cause symptoms of estrogen deficiency (hot flashes, decreased bone mineral density).
6) **Alkaylated Steroids:** Can be combined with low dose steroids. Can cause symptoms of excess androgens (facial hair, hepatic dysfunction, mood disorders). Interferes with gonadal hormone receptors.
7) **Tamoxifen:** Has been used successfully in patients [14].
8) **Bilateral oophorectomy**: Definitive treatment, used if medical options [1,3,14,15].

Review literature suggests that the chronic exposure to anesthetic agents has a positive correlation with various harmful effects on female anesthesiologists [16]. All the options were discussed with the subject. The patient opted for oral antihistaminic beginning soon after ovulation and continued for three days after her periods with life style modification. For six months she worked

as anesthesiologist outside operating room and pre anesthetic clinic. The patient is asymptomatic at present.

Conclusion

Modern lifestyle along with the working environment in female anesthesiologists correlates with an increased rate of menstrual cycle disturbance leading to emergence of rare disorders like autoimmune progesterone dermatitis. Lifestyle modifications, including dietary changes and exercise, can go a long way toward restoring normal menstrual cycles.

Conflict of Interest

None declared.

Funding

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