An unravelling journey from diagnosis of furunculosis to autoimmune progesterone dermatosis

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Autoimmune progesterone dermatitis represents cyclical, pruritic eruptions of variable morphology of lesions corresponding to upsurge of the levels of progesterone in second half of the menstrual cycle. Eczematous, urticarial, target lesions are the most common manifestations, though unrelatable presentations like fixed drug eruption, anaphylactic shock, purpuric lesions, and acute generalized pustules are also reported in the literature. The authors report a case of a 38-year-old woman who first presented to our OPD with gravida 2, para 2, 32 weeks of gestation, being treated for recurrent furunculosis caused by methicillin-resistant *Staphylococcus aureus* with antibiotics. Biopsy of the lesions for histopathology and direct immunofluorescence was suggestive of furunculosis. The patient was reviewed 1.5-year after delivery and emphasized on history of premenstrual flare-ups and flare-up during third trimester of first pregnancy as well. Based on consolidating history by the patient, intradermal progesterone test conducted with progesterone 50 mg/ml showed a wheal and flare response of 18 mm as opposed to 3 mm of negative control. The patient was advised oral contraceptives containing desogestrel-ethinyl estradiol, after which the patient reported significant long-lasting improvement, preventing relapses premenstrually every month. This case highlights the versatile clinical presentation of autoimmune progesterone dermatitis, but consistent history of premenstrual flare-up with positive intradermal progesterone test helps in confirming the diagnosis and providing targeted treatment by temporary or permanent cessation of ovulation, resulting in cessation of apprehended flare-ups.

Keywords:
atypical autoimmune progesterone dermatosis, autoimmune progesterone dermatitis, autoimmune progesterone dermatosis, furuncles, progesterone hypersensitivity

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Introduction

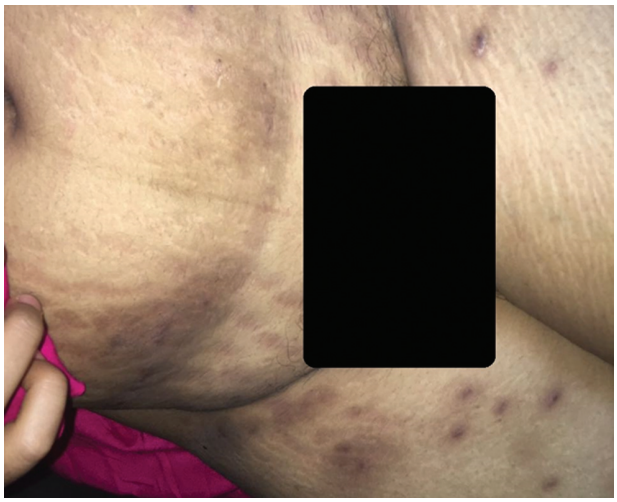
Autoimmune progesterone dermatitis is a rare, pruritic, cyclical disorder with characteristic premenstrual flare-up of cutaneous disease of various morphologies [1]. Varied manifestations ranging from wheal-like lesions to fixed drug eruption have been documented in the literature unified by the presence of aggravation during luteal phase of menstrual cycle and/or positivity of intradermal test for progesterone [2]. Owing to varied clinical presentations, patients of autoimmune progesterone dermatoses (APD) often go unrecognized or mislabeled. We present the first case of a patient with autoimmune progesterone dermatitis presenting with furunculosis.

Case report

A 38-year-old gravida 2, para 2 (G2P2), with 32 weeks of gestation, presented to the dermatology outpatient department with complaints of multiple pustules and nodules on an erythematous base over gluteal area, thighs, and abdomen since 3 years on and off, aggravated since 3 months. The patient experienced similar lesions in previous pregnancy as well, with the onset coinciding with the beginning of third trimester. Initially, the patient developed itching, which led to the formation of wheals, associated with tender erythematous nodules with discharge of fluid and pus over abdomen, thighs, and arms (Figs 1 and 2). The lesions in previous pregnancy subsided within 3 months after delivery spontaneously without any treatment. The patient was diagnosed as having gestational diabetes mellitus in view of high blood sugar levels and was started on oral hypoglycemics.

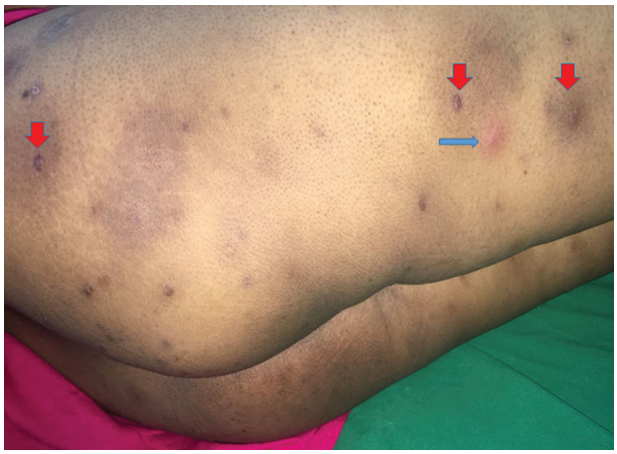
With an underlying history of pus-discharging nodules with the predisposing factor of gestational diabetes mellitus, a provisional diagnosis of furunculosis was

Figure 1



Anterior abdomen and thighs showing multiple erythematous to hyperpigmented nodules with postinflammatory hyperpigmentation.

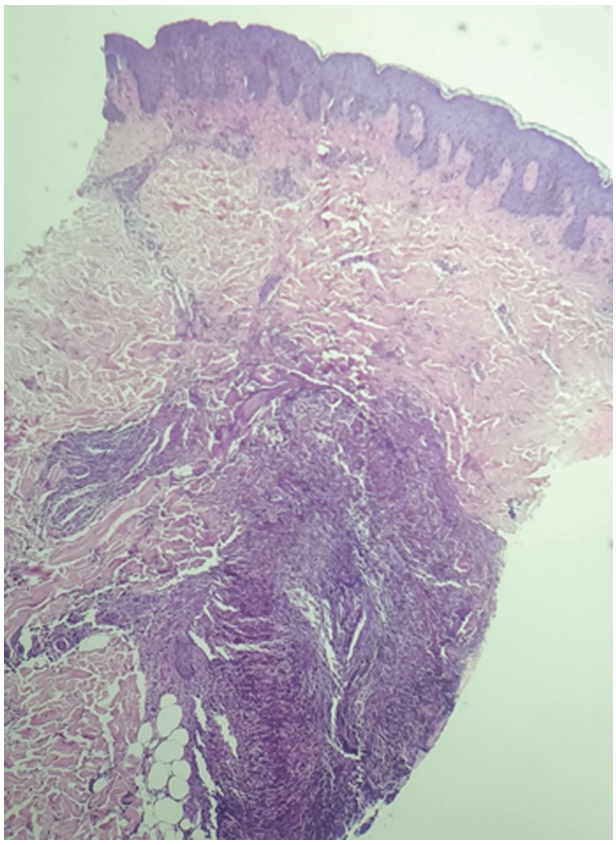
Figure 2



Posterior aspect of thighs and buttocks showing multiple hyperpigmented to erythematous nodules (red arrow) and erythematous wheal-like lesion (blue arrow) early lesion.

established. Owing to definite history of aggravation during pregnancies and presence of pustules, erythematous nodules, and wheal-like lesions, differential diagnoses of polymorphic eruption of pregnancy, pemphigoid gestationis, and Sweet syndrome were considered. A 3.5-mm punch biopsy from lesional skin over abdomen was taken for histopathology and peri-lesional skin for direct immunofluorescence. Biopsy and photographs were taken after obtaining respective consent from the patient. Histopatholgical examination revealed lymphohistiocytic infiltration surrounding the hair follicles, predominantly consisting of neutrophils suggestive of furunculosis (Fig. 3), and direct immunofluorescence did not show any features suggestive of immunobullous disorder. Pus culture

Figure 3

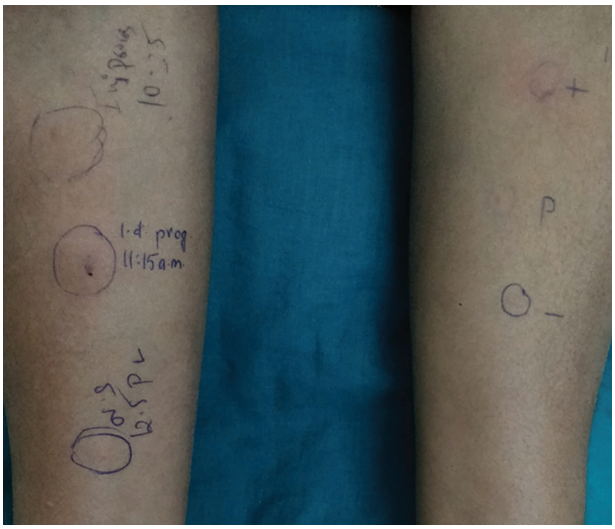


Infiltration around hair follicles in dermis with normal epidermis (hematoxylin and eosin, 20×).

demonstrated growth of *Staphylococcus aureus*. The patient reported complete clearance with oral amoxicillin and clavulanic acid and topical mupirocin after 1 week. The patient was reassured and advised to use chlorhexidine-based soap and topical mupirocin prophylaxis.

The patient revisited the OPD after 7 months with complaints of multiple recurrences of similar lesions as in the past, with blood sugar levels within normal limits. The patient dated the flare-up of lesions 7–8 days before menstrual bleeding. The patient was followed 1 week after her last menstrual period, that is, during follicular phase of menstrual cycle, and intradermal progesterone test and prick test using progesterone 50 mg/ml were performed with three negative controls. Prick test result was completely negative, whereas intradermal test result showed a definite positive reaction with a wheal and flare response of 18 mm (Fig. 4). Intradermal test result was negative in all three controls. The patient was started on oral contraceptives desogestrel-ethinyl estradiol from day 1 to 21 of her menstrual cycle, with which the patient reported significant remission.

Figure 4



Intradermal test using progesterone in the right forearm with negative control showing positive reaction with progesterone with erythema and edema measuring 18 mm in diameter, and left forearm showing negative prick test result.

Discussion

APD is an autoimmune-mediated rare pruritic disorder with hypersensitivity to endogenous or exogenous progesterone [3,4]. There are more than 200 cases reported in the literature, with most common presentations being dermatitis, urticaria, and erythema multiforme-like lesions. Other rare presentations reported are acute exanthematous generalized pustulosis, fixed drug eruption, Steven's-Johnsons syndrome, anaphylaxis, and folliculitis [5–9]. It has been rightly proposed to review the name of the entity from APD to progesterone hypersensitivity owing to a common underlying mechanism, resulting in varied clinical presentations. Pathogenesis of APD is not clearly known. Endogenous progesterone secreted from corpus luteum or exogenous progesterone in the form of oral contraceptive pills, progesterone depot preparations for in vitro fertilization, or maintenance of pregnancy can trigger it. Level of endogenous progesterone reaches its peak in luteal phase 3–10 days before onset of menstrual bleeding and subsides a few days after menstruation as levels of progesterone decline. Multiple pathways have been proposed for APD, including type I, type III, and type IV hypersensitivity. It is proposed that immunoglobulin E antibodies are formed against progesterone which cross-links with each other leading to degranulation of mast cells, with release of immediate and delayed mediators. Involvement of type I pathway of hypersensitivity can be justified owing to presentations of APD like urticaria, anaphylaxis, and positive prick test result to progesterone [10]. Delayed hypersensitivity is due to T-cell-mediated immune response, which can be demonstrated by delayed reaction with prick test or positive reaction to intradermal test performed using progesterone preparations [11]. Though, involvement of type III hypersensitivity has also been proposed, positive circulating antibodies to 17-hydroxyprogessterone were demonstrated only in few patients with perineal rash and erythema multiforme-like lesions [12]. However, the fact remains that increase in the serum level of progesterone leads to the manifestations, the underlying mechanism of which remains blur.

Warin proposed diagnostic criteria for APD, which included first, clinical features which fluctuate with menstrual cycle; second, positive progesterone intradermal progesterone test or reproducibility of rash with intramuscular progesterone; and third, improvement of disease after suppression of ovulation. Our patient fulfilled all three criteria's for APD with characteristic waxing and waning of clinical features with menstrual cycle as well pregnancy, strongly positive intradermal test, and improvement of symptoms with oral contraceptives [3,4].

Treatment for APD should be individualized as per patient's clinical features, requirements, pregnancy, and family status. Patients with this kind of hypersensitivity usually do not respond very well to steroids and antihistaminic. Suppression of ovulation is considered to be definite treatment; oral contraceptives, gonadotropin-releasing hormone analogs, and tamoxifen has been used for the same. Bilateral oophorectomy has been recommended as definitive treatment if feasible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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