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Pruritic urticarial papules and plaques in pregnancy following the second in vitro fertilization cycle: A case report

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Abstract

This report discusses a case of pruritic urticarial papules and plaques in pregnancy, which primarily affects primigravidas in the 3rd trimester of pregnancy or the postpartum period. Although factors such as assisted reproductive technology and multiple pregnancies contribute to its development, the exact mechanisms are unclear. In our case, the patient developed a widespread eruption of pruritic, erythematous papules and plaques that started on the abdomen and spread to the extremities. The plaques regressed spontaneously within 10 days after the surgery. We aim to demonstrate that when a thorough differential diagnosis is conducted, and it is confirmed that there is no underlying organic cause for pregnancy-related plaques, spontaneous regression of the plaques can be anticipated without the need for treatment.

Keywords: Pruritic urticarial plaques, plaques of pregnancy, assisted reproductive technology

Introduction

Pregnancy induces significant physiological changes, including endocrinologic, immunologic, metabolic, and vascular adaptations, which collectively impact various organ systems, including the skin [1]. Skin conditions during pregnancy can generally be classified into benign hormone-related changes, preexisting dermatoses, and pregnancy-specific dermatoses [2]. The latter group encompasses a diverse range of pruritic conditions, such as pruritic urticarial papules and plaques of pregnancy (PUPPP), pemphigoid gestationis (PG), intrahepatic cholestasis of pregnancy (ICP), and atopic eruption of pregnancy (AEP) [3].

Among these, PUPPP -also termed polymorphic eruption of pregnancy (PEP)- represents the most prevalent gestational dermatosis. This inflammatory condition predominantly manifests in primigravid women during the third trimester (89% of cases), with rare postpartum presentation and low recurrence rates in subsequent pregnancies [2, 4]. The incidence rate of PUPPP strongly correlates with fetal number, rising from 0.5% in singleton pregnancies to 2.9%–16% in multifetal gestations [5-7]. This trend also correlates with the elevated PUPPP prevalence observed in assisted reproductive technology (ART) pregnancies [8, 9], which carry a higher likelihood of multiple gestations.

Several factors have been proposed as contributing to PUPPP, including multiple gestation, excessive maternal weight gain, male fetal sex, Rh factor variations, increased progesterone receptor immunoreactivity, and elevated progesterone levels [10]. However, the precise etiology of the condition remains unclear.

Case(s)

A 35-year-old primigravida (G1A0P0) conceived via frozen embryo transfer (FET) after undergoing her second cycle of ART. Three months prior to the transfer, she had undergone a hysteroscopic polypectomy for abnormal uterine bleeding. In the second cycle, antagonist protocol treatment was preferred. Frozen embryo transfer was performed after ensuring endometrium compatibility with estradiol treatment before the procedure. After the FET procedure, micronized progesterone was

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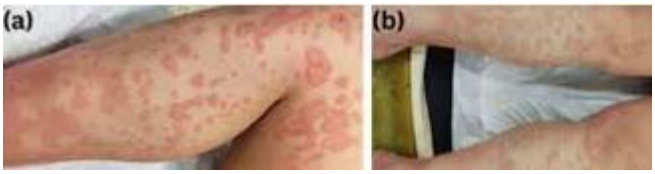
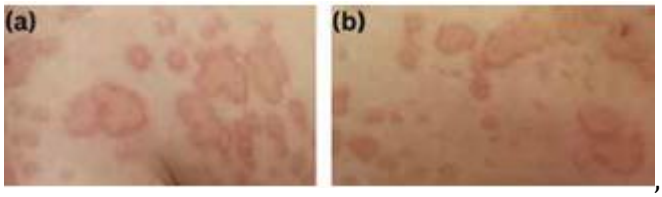
administered in an intramuscular form at a dosage of 100 milligrams (mg) until a heartbeat was detected on ultrasound. Following the confirmation of the heartbeat, the treatment was switched to intravaginal administration of 200 mg three times daily. There was no need for additional treatment beyond daily multivitamins, iron, and vitamin D replacement. Her prenatal workup was unremarkable, with normal findings on cell-free DNA (cfDNA) screening, oral glucose tolerance test (OGTT), and level II ultrasound anomaly scan. She began her pregnancy with a height of 158 centimeters (cm), a weight of 58 kilograms (kg), and a body mass index (BMI) of 23.4 kg/m^2 during the first trimester. By the end of her pregnancy, her weight had increased to 75 kg, resulting in a BMI of over 30 kg/m^2.

At 36 weeks of gestation, the patient developed a widespread eruption of pruritic, erythematous papules and plaques consistent with PUPPP. The rash initially affected her lower extremities, hips, back, and chest (Figure 1).



The lesions exhibited a polymorphic appearance, presenting as isolated papules as well as confluent plaques bordered by a lighter halo (Figure 2). Physical examination revealed no vesicles, bullae, purpura, or target lesions. Moreover, there were no mucosal lesions, lymphadenopathy , joint swelling, or systemic signs of vasculitis. Vital signs were within



normal limits and no other systemic abnormalities were detected. Notably, she had not experienced similar skin manifestations during ovulation induction or in earlier trimesters. After the appearance of the lesions at 36 weeks of gestation, the patient was promptly referred for dermatology consultation. An experienced dermatologist performed a full skin examination at the initial presentation, which confirmed the diagnosis of PUPPP based on clinical findings and distribution of lesions. No biopsy was deemed necessary due to the absence of atypical features. The patient was subsequently followed with scheduled dermatology visits throughout the remainder of the pregnancy and into the early post- partum period to monitor lesion progression and symptom resolution.

Differential diagnoses should include various pregnancy-related skin conditions, such as systemic vasculitis like urticarial vasculitis and erythema multiforme, pemphigoid gestationis, contact dermatitis, drug reactions, viral eruptions, intrahepatic cholestasis of pregnancy, and atopic eruption of pregnancy. Initially, systemic vasculitic disorders such as urticarial vasculitis and erythema multiforme were considered in the differential diagnosis. However, in the absence of systemic symptoms (e.g., fever, arthralgia, malaise) and with lesions confined solely to the skin, the likelihood of systemic vasculitis was deemed low, and further evaluation focused on dermatologic pregnancy-specific dermatoses [8]. The differential diagnosis was conducted by evaluating clinical findings based on the macroscopic appearance of the lesions and their specific location. A biopsy was not performed since both direct and indirect immunofluorescence tests were generally negative, and histopathological examination was nonspecific. The patient's history of ART, normal biochemical parameters, absence of additional medications, no viral diseases, and lesions appearing as papules and plaques on the lower extremities and back were considered indicative of pre-diagnosis PUPPP.

At 34 weeks of gestation, the pregnancy was complicated by oligohydramnios and fetal growth restriction (FGR). At 37 weeks, a 2,400-gram female infant (9th percentile) was delivered via cesarean section, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. Preoperative laboratory findings were unremarkable, as summarized in Table 1. Symptomatic treatment was provided, with no further interventions. Warm baths, skin compresses, and moisturizing creams like emollients were preferred to reduce itching. Oral antihistamines were not prescribed because they were generally not beneficial. Medium potency topical steroid cream treatments were planned on the second step, but were not needed since symptomatic treatment was sufficient for the patient. The rash resolved

spontaneously within 10 days postpartum.

Discussion

The pruritic dermatoses of pregnancy must be carefully.

Table 1. Preoperative laboratory results

Laboratory Parameter	Value
Hemoglobin (HGB)	12.1 g/dL
Platelet count (PLT)	136 × 10^9/L
White blood cell count (WBC)	7.2 × 10^9/L
Liver enzymes, ALT	16 U/L
Liver enzymes, AST	31 U/L
Blood type	O Rh-positive

Differentiated due to overlapping clinical features [11]. Papular dermatosis of pregnancy was also considered but excluded due to the polymorphic, rather than monomorphic, nature of the papules [12].

A differential diagnosis was made considering the range of pruritic disorders. The conditions evaluated included pruritic urticarial papules and plaques of pregnancy (PUPPP), pemphigoid gestationis (PG), intrahepatic cholestasis of pregnancy (ICP), and polymorphic atopic eruption of pregnancy (AEP) due to the presence of itchy and sudden-onset skin lesions. PG begins with abdominal urticarial lesions that may exhibit edematous dermal papillae, characterized by an inverted teardrop shape. A generalized bullous reaction follows, sparing the face, mucous membranes, and palms. The most common histopathologic features include a subepidermal vesicle and infiltrate with eosinophils ICP is typically characterized by itching (pruritus gravidarum) and skin lesions that are caused by scratching. The most sensitive marker for ICP is the elevation of serum bile acids, particularly after meals. Mild abnormalities in liver function tests are commonly observed, while a skin biopsy generally yields nonspecific results [13]. Additionally, atopic eruption of pregnancy (AEP) is a broad category that includes specific dermatoses, such as prurigo (PP) and pruritic folliculitis of pregnancy (PFP), which are possibly associated with atopy. AEP is an early-onset disease that occurs during the first or second trimester of pregnancy and is characterized by follicular papules and pustules. Both the immunofluorescence test and serologic results are negative, and a biopsy may reveal sterile folliculitis [8].

In this case, PG, a bullous autoimmune disorder, was excluded due to the absence of vesicles or bullae. AEP, which typically presents earlier in gestation with eczematous lesions in individuals with a history of atopy, was unlikely given the late onset. ICP was ruled out based on the presence of primary inflammatory lesions and normal liver function tests (ALT: 16 U/L, AST: 31 U/L). Also, the skin lesions observed in ICP are mostly secondary lesions that result from scratching. This systematic exclusion, combined with the patient's clinical presentatio -late third-trimester onset of polymorphic, pruritic lesions with centrifugal spread (Figures 1, 2), spontaneous post-partum resolution, and absence of systemic abnormalities (Table 1) strongly supports a diagnosis of PUPPP.

One hypothesized mechanism for the development of PUPPP involves mechanical stress from rapid abdominal distension, which may damage connective tissue in striae distensae and expose dermal antigens, triggering localized inflammation [10, 13]. Although our patient did not have striae, the complications of oligohydramnios and FGR, with a female infant weighing 2,400 grams (9th percentile), likely led to compensatory uterine adaptations, which may have exacerbated mechanical tension. The patient's BMI level increased to 30 kg/m^2 long with weight gain during pregnancy, supporting the idea that maternal weight gain can trigger plaque formation in the third trimester.

Exogenous progesterone, commonly used in ART protocols, may also play a role. Gungor et al. (2021) demonstrated that prolonged progesterone support in IVF pregnancies significantly increased the incidence of PUPPP (odds ratio 2.1, $p < 0.001$) [10]. Furthermore, the timing of the rash's onset, coinciding with peak progesterone exposure during late gestation, is consistent with findings of elevated progesterone receptor immunoreactivity in PUPPP lesions [14]. We believe that elevated progesterone levels after ART, specifically with high-dose micronized progesterone treatment, contribute to the pathogenesis of PUPPP and are consistent with the pathogenesis reported in the literature.

Male fetal sex is more commonly found in PUPPP co-horts than female sex, contrary to what is presented in this case, with a male-to-female ratio of 2:1 [15]. Fetal microchimerism, where male fetal DNA is

detected in maternal skin lesions [13], may provoke a graft-versus-host-like immune response via maternal $CD8^+$ T-cell activation. This immune reaction to paternal antigens could explain the male fetal predominance and the association with cesarean delivery in PUPPP cases [5, 16]. However, in this case, cesarean delivery was likely due to obstetric necessity rather than a direct association with PUPPP.

Although Rh-positive blood type has not been strongly linked to PUPPP, one study of 18 patients notably found that all were Rh-positive despite varied ABO blood types. Whether this association is coincidental or meaningful remains uncertain, and further research is needed [4]. Nevertheless, the typical postpartum resolution of symptoms in our Rh-positive patient, along with favorable fetal outcomes (Apgar 8/9), aligns with the self-limited nature of PUPPP. Pregnancy was successfully achieved after ART treatment in a primiparous patient. Follow-up with a diagnosis of PUP was considered appropriate due to the appearance of itchy papules and plaque-like lesions that began on the lower extremities during the 36th week of pregnancy and later spread to the trunk and back. Management focuses on symptomatic relief using topical corticosteroids and antihistamines, ensuring fetal safety [17]. While ICP and PG may lead to adverse neonatal outcomes like fetal distress, preterm labor, and stillbirth, PUPPP cases are thought to present no neonatal risk. Additionally, although there is a known risk of recurrence in subsequent pregnancies for ICP and PG, the potential for recurrence with PUPPP has not been established [13].

Conclusion

In conclusion, this case suggests that ART induced hormonal dysregulation and subtle mechanical stressors may play a role in the pathogenesis of PUPPP. Although the condition is typically self-limited, as evidenced by the spontaneous postpartum resolution observed in our patient, the atypical presentation in a singleton IVF pregnancy highlights a potential association between ART and PUPPP. This observation adds to the limited existing literature and underscores the importance of clinical awareness of dermatologic complications in ART pregnancies. Future studies should aim to clarify the individual impact of hormonal and mechanical influences on the development of this dermatosis.

References

1. Kurniawan RH, Dimas UU, Arista A. The pruritic urticarial papules and plaques of pregnancy (PUPPP). Indones J Obstet Gynecol. 2022;10:54–7.
2. Erlandson M, Wertz MC, Rosenfeld E. Common skin conditions during pregnancy. Am Fam Physician. 2023;107(2):152–8.
3. Kothamasu LS, Shetty V, Najmuddin F, Bhandary PR, Shetty NJ. A clinical study of pregnancy-induced dermatoses. J Pak Assoc Dermatol. 2016;26(4):205–9.
4. Ghazeeri G, Kibbi AG, Abbas O. PUPPP: epidemiological, clinical, and histopathological study of 18 cases from Lebanon. Int J Dermatol. 2012;51(9):1047–53.
5. Regnier S, Fermand V, Levy P, Uzan S, Aractingi S. A case-control study of polymorphic eruption of pregnancy. J Am Acad Dermatol. 2007;58(1):63–7.
6. Elling SV, McKenna P, Powell FC. PUPPP in twin and triplet pregnancies. J Eur Acad Dermatol Venereol. 2000;14(5):378–81.
7. 7. Vadakkumpadam MH, Abualiat AS, Sabrah TA. A review of literature of polymorphic eruption of pregnancy. Int J Res Dermatol. 2021;7(3):490.
8. Rudolph C, Al-Fares S, Vaughan-Jones S, Müllegger R, Kerl H, Black M. Polymorphic eruption of pregnancy: clinicopathology and potential trigger factors in 181 patients. Br J Dermatol. 2005;154(1):54–60.
9. Elling S, McKenna P, Powell F. Pruritic urticarial papules and plaques of pregnancy in twin and triplet pregnancies. J Eur Acad Dermatol Venereol. 2000;14(5):378–81.
10. Gungor ND, Gurbuz T, Ture T. Prolonged luteal phase support with progesterone may increase papules and plaques of pregnancy frequency in pregnancies through in vitro fertilization. An Bras Dermatol. 2021;96(2):171–5.
11. Ambros-Rudolph CM. Dermatoses of pregnancy. J Dtsch Dermatol Ges. 2006;4(9):748–61.
12. Pali-Schöll I, Namazy J, Jensen-Jarolim E.

Allergic diseases and asthma in pregnancy, a secondary publication. World Allergy Organ J. 2017;10:10. doi:10.1186/s40413-017- 0141-8

13. Himeles JR, Pomeranz MK. Recognizing, diagnosing, and managing pregnancy dermatoses. Obstet Gynecol. 2022;139(4):653–61.
14. Ahmadi S, Powell FC. Pruritic urticarial papules and plaques of pregnancy: current status. Australas J Dermatol. 2005;46(2):53–60.
15. Kroumpouzos G, Cohen LM. Specific dermatoses of pregnancy: an evidence-based systematic review. Am J Obstet Gynecol. 2003;188(4):1083–92.
16. Cohen LM, Capeless EL, Krusinski PA, Maloney ME. Pruritic urticarial papules and plaques of pregnancy and its relationship to maternal-fetal weight gain and twin pregnancy. Arch Dermatol. 1989;125(11):1534–6.
17. Chouk C, Litaiem N. Pruritic urticarial papules and plaques of pregnancy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; last update July 31, 2023. https://www. ncbi.nlm.nih.gov/books/NBK539700/ [PubMed][CrossRef]