SHORT REPORT

Three cases of pruritic urticarial papules and plaques of pregnancy (PUPPP) treated with intramuscular injection of autologous whole blood

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Abstract

Background Pruritic urticarial papules and plaques of pregnancy (PUPPP), also known as polymorphic eruption of pregnancy, is a common and benign but exceedingly uncomfortable dermatosis of pregnancy. Investigation of new treatment options has been limited by patient concerns about the negative fetal effects of medication.

Objective To assess the efficacy of intramuscular injection of autologous whole blood (AWB) for treatment of PUPPP.

Methods This is a retrospective descriptive case series of three patients with PUPPP, all of whom were treated with intramuscular injection of AWB.

Results All patients showed good responses to intramuscular injection of AWB, tolerated the treatment, and there were no adverse effects to the patients or their babies.

Conclusion AWB may be an alternative treatment option for patients with PUPPP who are worried about the risk of medication use during pregnancy or breastfeeding. Whole blood collected from the patient's own body may be preferable to foreign medications. Future investigation into the exact mechanism with controlled clinical studies using a large number of patients will be necessary to provide supporting evidence for this potential treatment.

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Conflicts of interest

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Introduction

Pruritic urticarial papules and plaques of pregnancy (PUPPP), also known as polymorphic eruption of pregnancy, is a common, benign, exceedingly pruritic dermatosis of pregnancy that predominantly occurs during the last trimester of primigravidas.[1] Histopathology findings are non-specific, and the pathogenesis of PUPPP remains unknown. Skin lesions usually begin as erythematous papules on the abdomen within the striae gravidarum, sparing periumbilical areas, then rapidly spread to the buttocks, breasts and extremities.[2] The average duration of symptoms is 4–6 weeks and usually improves after delivery.[3] Foetal and maternal morbidity or mortality is unaffected. Conservative management with topical corticosteroids and oral antihistamines is commonly used to relieve pruritus.[4] In severe cases, skin lesions and symptoms are efficiently controlled with a brief course of systemic corticosteroids.[5] Severe and intolerable itching can cause trouble with sleeping, and rarely, early induction of labour can be considered for treatment.[6]

The United States Food and Drug Administration (FDA) pregnancy risk categories classify drugs based on risk/benefit ratio. After risks and benefits are discussed with pregnant patients, medication use during pregnancy can be considered.[7] However, low compliance to medication is very common in pregnant women due to their concerns about potential adverse effects on the foetus, even when the symptoms are severe and benefits of the medications outweigh its risks.[8]

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Autologous whole blood (AWB) injection was often used for the treatment of chronic urticaria before the introduction of antihistamines and was also thought to have beneficial effects in treatment of viral diseases, circulatory disorders and atopic dermatitis.[9–12] The exact mechanism of AWB injection remains to be established; however, it is still popular in central Europe, mostly in private clinics.[13] However, AWB injection has not previously been used for treatment of PUPPP. In this study, we report three cases with PUPPP who demonstrated remarkable improvement after intramuscular injections of AWB.

Case reports

Case 1

A 30-year-old primigravida at 24 weeks gestation presented with multiple, variably sized, coalescent, intensely pruritic erythematous urticarial papules on the abdomen and both extremities. The skin lesions began on the abdomen, sparing the periumbilical area and spread to the back and buttocks (Fig. 1a). Based on the characteristic clinical presentation and disease course, she was diagnosed with PUPPP. She was informed of the safety profile and potential benefits of medications but remained reluctant to use medications during pregnancy, despite her severe symptoms. AWB injection was then considered for her treatment. Venous blood of 10 mL was drawn from the patient, followed by intramuscular injection of 5 mL of the blood on each side of her buttock. Two days later, her symptoms improved. She received two more weekly intramuscular AWB injections, and all symptoms improved, leaving only postinflammatory hyperpigmentation (Fig. 1b). No complications such as infection, abscess formation, or haematoma were observed at the injection site. She tolerated the treatment and delivered a healthy baby.

Case 2

A 28-year-old primigravida at 14 weeks gestation presented with multiple extremely pruritic, erythematous urticarial papules on the abdomen and both extremities for 2 weeks. She was diagnosed with PUPPP based on her clinical features. She declined medication despite her severe skin rash and pruritus. Therefore, intramuscular injection of 5 cc of AWB was performed. On the following day, pruritus and sleep disturbance improved. Despite receiving two more shots of 5 mL of AWB at 1-week intervals, she had no further improvement. Therefore, 5 mL of AWB was injected in each buttock, resulting in a total treatment of 10 cc of AWB. After the increased dose, the skin lesions and symptoms began to improve. After three more weekly injections of 10 mL AWB, all skin lesions and symptoms resolved. There was no recurrence for the 2 months until delivery. She tolerated the treatment, complained of no adverse effects after injection and delivered a healthy baby.

Case 3

A 29-year-old woman at 28 weeks gestation presented with multiple, variably sized, coalescent, severely pruritic erythematous urticarial papules and patches on the trunk and both extremities.

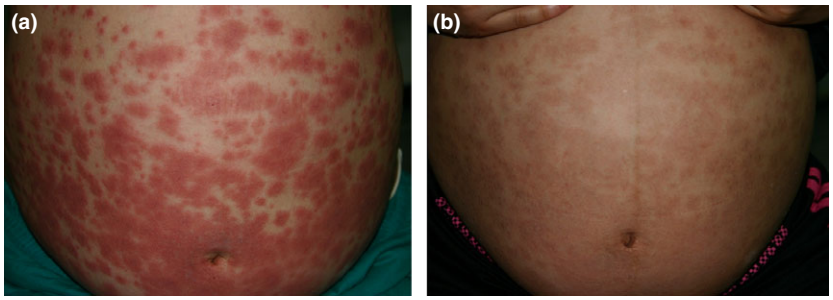

Figure 1 Clinical manifestations and treatment response of patient 1. (a) Before treatment. Multiple, variably sized, coalescent, pruritic erythematous urticarial papules on the abdomen. (b) After three injections of autologous whole blood. All symptoms disappeared, although postinflammatory hyperpigmentation remained.

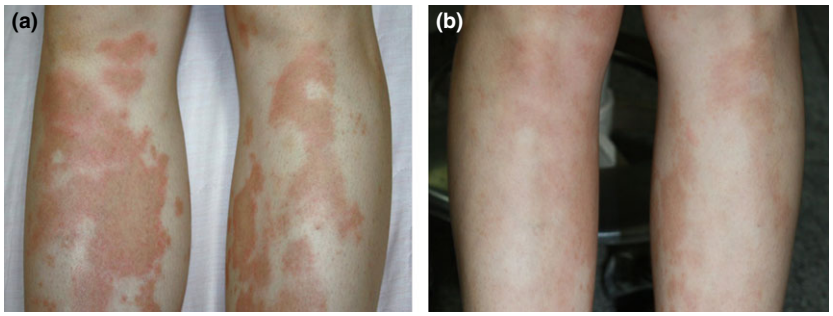

Figure 2 Clinical manifestations and treatment response of patient 3. (a) Before treatment. Multiple, variably sized, coalescent, pruritic erythematous urticarial papules on the lower legs. (b) Skin lesions improved after four injections of autologous whole blood.

She did not want to take medication despite her severe itching. Instead, she planned to deliver her baby with labour induction at 38-week gestation, earlier than the expected delivery time. She gave birth to a healthy baby; however, her skin lesions and pruritus persisted after delivery. She visited our clinic, presenting with persistent skin rash and pruritus 4 days after delivery (Fig. 2a). Due to her concern about the safety of medication during breastfeeding, intramuscular injection of AWB was considered. On the day after injection of 5 mL of AWB in both buttocks, pruritus and skin lesions began to resolve. She received three more weekly AWB injections and had complete clinical resolution without relapse (Fig. 2b). She tolerated the treatment and complained of no adverse effects.

Discussion

We report three patients with PUPPP, all of whom were treated with AWB injections (Table 1). These cases demonstrate the usefulness and safety of AWB injections for treatment of patients with PUPPP during pregnancy and breastfeeding.

The three patients were primigravidas, and AWB injection led to complete resolution of their symptoms, beginning within 2 days of the first injection. Injection volume was 5 mL in either or both buttocks, with total injection volume of 5–10 mL per session. The total number of injections varied from three to seven depending on treatment response. In case 2, the patient was treated with 5 mL of AWB and responded well immediately. But she had no further improvement with 5 mL of AWB, and 10 mL of AWB was required for rapid response. In addition, AWB injection was effective in the patient whose symptoms persisted even after delivery. It may be especially useful for breastfeeding mothers. All patients tolerated the treatment, and there were no adverse effects to the patients or their babies.

Table 1 Summary of patient characteristics

	Case 1	Case 2	Case 3
Age	30 years	28 years	29 years
Parity	Primigravida	Primigravida	Primigravida
Disease onset	24 weeks gestation	14 weeks gestation	28 weeks gestation
Distribution of skin lesions	Abdomen, both extremities	Abdomen, both extremities	Abdomen, both extremities
Disease duration	4 days	2 weeks	11 weeks
Number of AWB injections for complete remission	3	7	4
Recurrence after treatment	None	None	None
Maternal complications	None	None	None
Foetal complications	None	None	Planned early birth

AWB, autologous whole blood.

Patient compliance with medication influences treatment outcomes in the general population. In pregnant women, low compliance to medicine stems from feared side-effects, mistrust about the use of medication during pregnancy and disappearance of symptoms.[14] Some patients do not use medications even though they are not able to fall asleep because of severe pruritus. The United States FDA introduced pharmaceutical pregnancy categories to assess medication risks to the foetus. However, pregnant women tend to overestimate possible adverse foetal effects associated with medications and may not take them due to this concern. In many cases, however, the medications have not been proven to be harmful.[8]

In a randomized, placebo-controlled trial to investigate intramuscular injection of AWB for treatment of atopic dermatitis, AWB was helpful for reducing disease activity and improving quality of life.[12] Staubach *et al.* reported a randomized, single-blind study in which intramuscular injection of AWB improved chronic urticaria in patients with positive skin test reactions to autologous serum (ASST) but not in ASST-negative patients.[13] In another randomized, single-blind study concerning chronic urticaria, AWB decreased disease activity and improved patient quality of life, although neither intramuscular AWB nor autologous serum demonstrated better efficacy than the placebo.[15]

AWB treatment is based on the concept that a stimulus to the body facilitates a counter-regulation, which promotes 'self-healing processes'.[16] The exact mechanism of action of AWB remains unclear, although it seems to affect immune function in experimental and clinical models. In animal models, AWB increased resistance to infection, enhanced antibody production to antigens and activated cell-mediated immune defence. Induced desensitization also seems to play an important role in the mechanism of AWB injection.[17] We postulate that injection of AWB may have a positive effect on PUPPP by modulating maternal immune reactivity involved in disease development.

Our cases suggest that AWB injection may be an alternative treatment option for PUPPP, considering its effect and onset of response. AWB injection is inexpensive and easy to perform with few side-effects. In particular, its use avoids problems with non-adherence due to fear of medication side-effects because autologous treatment is perceived as less harmful to patients.

Our experience suggests that AWB injection could be an alternative treatment option for PUPPP, especially for women who worry about the use of medications during pregnancy or breastfeeding. In the future, further investigation of the exact mechanism and controlled clinical studies using a large number of patients should be performed to provide supporting evidence.

References

1 Matz H, Orion E, Wolf R. Pruritic urticarial papules and plaques of pregnancy: polymorphic eruption of pregnancy (PUPPP). *Clin Dermatol* 2006; **24**: 105–108.

2 Yancey KB, Hall RP, Lawley TJ. Pruritic urticarial papules and plaques of pregnancy. Clinical experience in twenty-five patients. *J Am Acad Dermatol* 1984; **10**: 473–480.

3 Rudolph CM, Al-Fares S, Vaughan-Jones SA, Mullegger RR, Kerl H, Black MM. Polymorphic eruption of pregnancy: clinicopathology and potential trigger factors in 181 patients. *Br J Dermatol* 2006; **154**: 54–60.

4 Ambros-Rudolph CM. Dermatoses of pregnancy - clues to diagnosis, fetal risk and therapy. *Ann Dermatol* 2011; **23**: 265–275.

5 Kroumpouzos G, Cohen LM. Dermatoses of pregnancy. *J Am Acad Dermatol* 2001; **45**: 1–19; quiz 19-22.

6 Beltrani VP, Beltrani VS. Pruritic urticarial papules and plaques of pregnancy: a severe case requiring early delivery for relief of symptoms. *J Am Acad Dermatol* 1992; **26**: 266–267.

7 Tyler KH, Zirwas MJ. Pregnancy and dermatologic therapy. *J Am Acad Dermatol* 2013; **68**: 663–671.

8 Matsui D. Adherence with drug therapy in pregnancy. *Obstet Gynecol Int* 2012; **2012**: 796590.

9 Chopra A, Chopra D. Autohaemotherapy in chronic urticaria. *Indian J Dermatol Venereol Leprol* 1995; **61**: 323–324.

10 Olwin JH, Ratajczak HV, House RV. Successful treatment of herpetic infections by autohemotherapy. *J Altern Complement Med* 1997; **3**: 155–158.

11 Bocci V. Autohaemotherapy after treatment of blood with ozone. A reappraisal. *J Int Med Res* 1994; **22**: 131–144.

12 Pittler MH, Armstrong NC, Cox A, Collier PM, Hart A, Ernst E. Randomized, double-blind, placebo-controlled trial of autologous blood therapy for atopic dermatitis. *Br J Dermatol* 2003; **148**: 307–313.

13 Staubach P, Onnen K, Vonend A *et al.* Autologous whole blood injections to patients with chronic urticaria and a positive autologous serum skin test: a placebo-controlled trial. *Dermatology* 2006; **212**: 150–159.

14 van Trigt AM, Waardenburg CM, Haaijer-Ruskamp FM. Questions about drugs: how do pregnant women solve them? *Pharm World Sci* 1994; **16**: 354–359.

15 Kocaturk E, Aktas S, Turkoglu Z *et al.* Autologous whole blood and autologous serum injections are equally effective as placebo injections in reducing disease activity in patients with chronic spontaneous urticaria: a placebo controlled, randomized, single-blind study. *J Dermatolog Treat* 2012; **23**: 465–471.

16 Asefi M, Augustin M. Regulative therapy: treatment with nonspecific stimulants in dermatology in traditional and modern perspectives. *Forsch Komplementarmed* 1999; **6**(Suppl 2): 9–13.

17 Klemparskaya N, Shalnova G, Ulanova A, Kuzmina T, Chuhrov A. Immunomodulating effect of autohaemotherapy (a literature review). *J Hyg Epidemiol Microbiol Immunol* 1986; **30**: 331–336.