Volume 19 Number 12
December 2013

Case Presentation

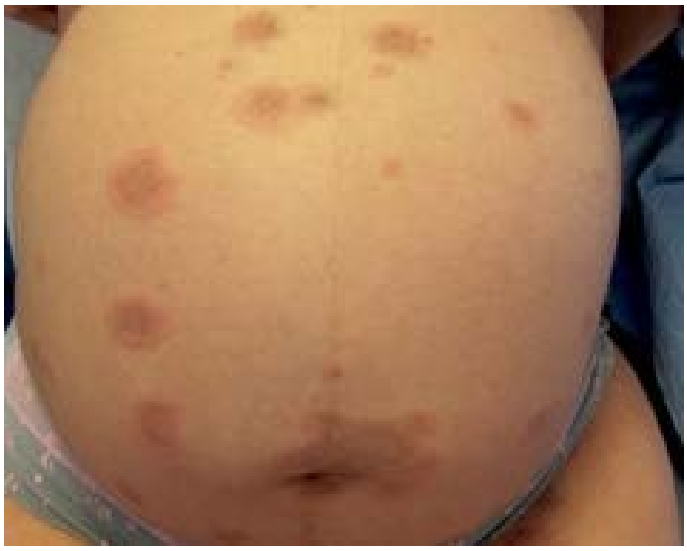
Mary L. Stevenson, MD, Shoshana Marmon, MD, PhD, Hui Tsou , MD, Kevin P. Boyd MD, Maria R. Robinson, MD, Shane A. Meehan, MD, and Rhonda Pomerantz, MD

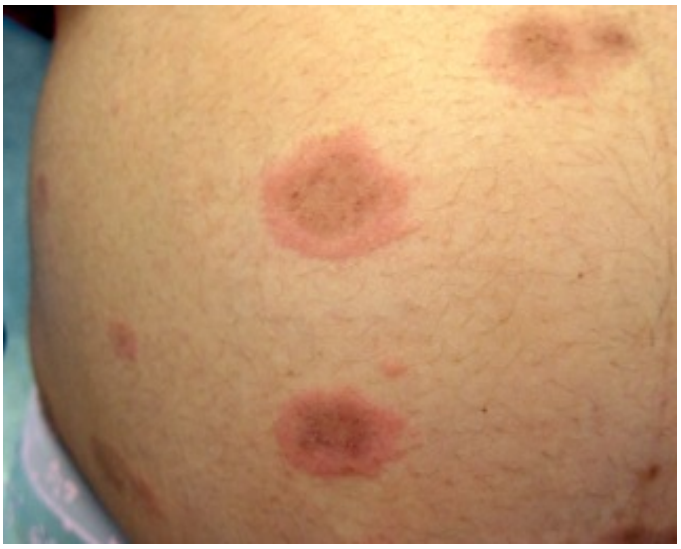
Dermatology Online Journal 19 (12): 11

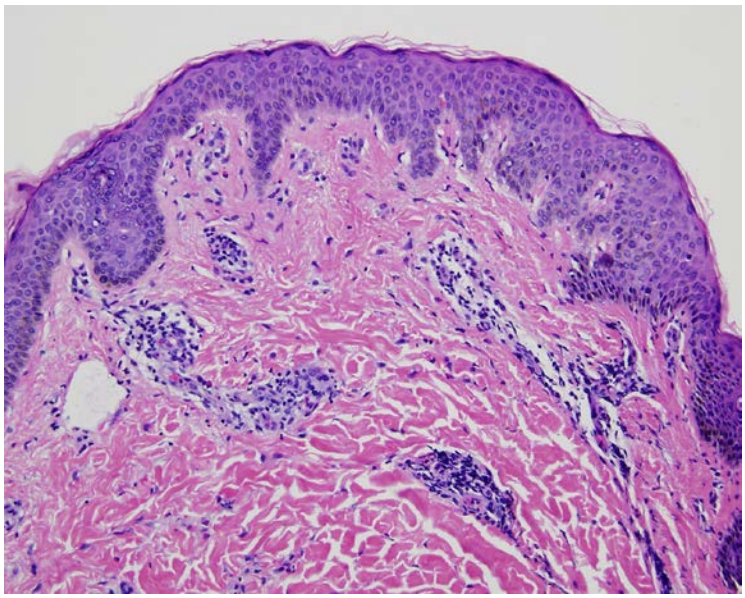
New York University School of Medicine

Abstract

We present a 21-year-old primigravida woman with a several-week history of pruritic, edematous, targetoid plaques that appeared initially on the abdomen, flanks, and legs and that progressed to involve the inner aspects of the upper arms and lateral aspects of the chest. The histopathologic findings showed perivascular and interstitial dermatitis with eosinophils and vacuolar changes with linear C3 deposition at the basement-membrane zone on direct immunofluorescence study. A diagnosis of pemphigoid gestationis was made. Pemphigoid gestationis is a rare, bullous dermatosis of pregnancy that may be associated with prematurity and small-for-gestational age birth weights. The diagnosis is often made with direct immunofluorescence studies of perilesional skin. Oral glucocorticoids remain the gold standard of therapy in moderate-to-severe cases. The edematous papules and plaques of pemphigoid gestationis may be particularly difficult to distinguish from polymorphic eruption of pregnancy; therefore, immunofluorescence studies are prudent. Prompt recognition and appropriate management may reduce morbidity of this disease, which often recurs with subsequent pregnancies.







Case synopsis

A 21-year-old primigravida woman in her third trimester of pregnancy presented to the dermatology clinic at Bellevue Hospital Center for evaluation of a pruritic eruption that had been present for three to four weeks. The eruption began in the umbilical region as a single lesion. That lesion had since resolved, but her eruption had evolved to become raised, red, papules and plaques that were associated with appreciable pruritus on the abdomen, flanks, arms, and anterior aspects of the upper thighs. She had been evaluated in the obstetrical urgent care one week prior to presentation and had been treated with oral diphenhydramine. This had improved her pruritus, but she declined a biopsy at that time. Upon presentation to the the dermatology clinic, she noted progression of her lesions to involve the inner aspects of the upper arms and lateral aspect of the chest; new lesions had formed on her abdomen and legs.

Past medical history was non-contributory. Surgical history consisted of a left hip repair after dislocation many years prior. She denied a history of oral or vaginal herpes simplex virus infection as well as any recent illness. She denied fevers, chills, night sweats, nausea, and vomiting.

Physical Examination: Edematous, blanching, targetoid plaques with dusky-to-hyperpigmented centers were scattered on the abdomen, chest, flanks, inner aspects of the upper arms, and legs. A hyperpigmented patch was present over the umbilicus. The oral mucosa was not involved.

Laboratory: The hemoglobin was 9.4 g/dL and hematocrit 29.2%. Hepatitis B surface antigen was negative, hepatitis B surface antibody was reactive, rubella immunoglobulin G antibody was reactive, and varicella-zoster immunoglobulin G antibody was positive. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* amplified DNA assays were negative. A vaginal swab culture was negative for beta-hemolytic *Streptococcus*.

Histopathology: Two punch biopsy specimens were obtained from the chest from lesional and perilesional skin for hematoxylin and eosin stain and direct immunofluorescence study, respectively. There is a sparse, superficial and mid perivascular infiltrate of lymphocytes with scattered eosinophils. There are focal vacuolar changes at the dermoepidermal junction. Direct immunofluorescence demonstrates a linear deposition of C3 at the basement- membrane zone.

Diagnosis: Pemphigoid gestationis

Discussion: Pemphigoid gestationis is a rare, bullous dermatosis of pregnancy that occurs with an incidence of 1:50,000, although some studies have reported an incidence as high as 1:1,700 [1,2]. First coined herpes gestationis by John Laws Milton in 1872, pemphigoid gestationis is characterized by a vesicobullous eruption that usually develops in the second or third trimester of pregnancy, although it may appear clinically during any trimester and may even appear postpartum. Lesions begin as edematous, pruritic papules and plaques in the umbilical region, which spread to involve the abdomen and often progress to vesicles and bullae on an erythematous base. In severe cases, lesions may spread to involve the entire body in a generalized, pemphigoid-like eruption. However, the mucus membranes and face typically are spared. Although many patients improve just prior to delivery, about 75% of patients flare at the time of delivery [1]. Spontaneous improvement of the eruption occurs postpartum, with recurrence of pemphigoid gestationis during subsequent pregnancies. Skip or uninvolved pregnancies are reported in about 8% of patients [1,3]. Flares with menses or oral contraceptive agents may also occur. Secondary autoimmune diseases, the most frequent of which is Grave disease, also have been reported. Rarely, it has been associated with hydatidiform mole and chorion epithelioma [4-6].

The pathogenesis of pemphigoid gestationis, similarly to bullous pemphigoid, involves autoantibodies that are directed against the non-collagenous (NC16A) domain of bullous pemphigoid antigen 2. The pathophysiology underlying the development of pemphigoid gestationis remains yet to be elucidated. However, it is hypothesized that major histocompatibility (MHC) II antigens found within the placenta may initiate an immune response that cross-reacts with maternal skin [7, 8]. An increased incidence of pemphigoid gestationis also has been reported in carriers of human leukocyte antigen (HLA)-DR3 and HLA-DR4 [7].

The diagnosis of pemphigoid gestationis often involves biopsy and direct immunofluorescence studies, which may aid in distinguishing pemphigoid gestationis from other dermatoses of pregnancy [9]. Linear deposition of C3 along the basement-membrane zone in perilesional skin is diagnostic. Enzyme-linked immunoabsorbent assay for bullous pemphigoid antigen 2 antibodies also are positive [8,10]. In contrast to pemphigoid gestationis, polymorphic eruption of pregnancy, which also is known as pruritic urticarial papules and plaques of pregnancy, usually presents in primigravida women in the first trimester as erythematous, edematous papules and plaques within striae. Sparing of the umbilical region is typical, and direct immunofluorescence studies are negative.

The treatment of pemphigoid gestationis is aimed at symptomatic relief and suppression of new blister formation. Oral glucocorticoids remain the treatment of choice for moderate-to-severe disease, but milder cases may be treated with antihistamines and topical glucocorticoid regimens. Plasma exchange, immunoadsorption, and intravenous immunoglobulin have been used in refractory cases and may possibly result in antibody removal from the serum or protection from antibody-induced apoptosis [11-15]. Known complications of pemphigoid gestationis include premature labor and small-for-gestational age birth-weights [10]. Additionally, a small percentage of infants may develop skin lesions.

References

1. Amrbos-Rudolph CM, Shornick JK. In: Pregnancy Dermatoses. Bolognia J, *et al*. eds. Dermatology, ed 3. St Louis, Elsevier Saunders, 2012: 439
2. Roger D, *et al*. Specific pruritic diseases of pregnancy: a prospective study of 3192 pregnant women. Arch Dermatol 1994; 130: 734
3. Jenkins RE, *et al*. Clinical features and management of 87 patients with pemphigoid gestationis. Clin Exp Dermatol 1999; 24: 255
4. Tindall JG, *et al*. Herpes gestationis in association with a hydatidiform mole: immunopathologic studies. Arch Dermatol 1981; 117: 510
5. Dupont C. Herpes gestationis with hydatidiform mole. Trans St Johns Hosp Dermatol Soc 1974; 60: 103
6. Tillman WG. Herpes gestationis with hydatidiform mole and chorion epithelioma. Br Med J 1950; 1: 1471
7. Shornick JK, *et al*. Anti-HLA antibodies in pemphigoid gestationis (herpes gestationis). Br J Dermatol 1993; 129: 257
8. Lardenoije CMJG, *et al*. Pemphigoid gestationis. BMJ Case Rep 2011; DOI: 10.1136/bcr.01.2010.2623
9. Lu PD, *et al*. Pemphigoid gestationis. Dermatol Online J 2010; 16: 10
10. Lipozenčić J, *et al*. Pemphigoid gestationis. Clin Dermatol 2012; 30: 51
11. Van de Wiel A, *et al*. Plasma exchange in herpes gestationis. Br Med J 1980; 281: 1041
12. Carruthers JA, Ewins AR. Herpes gestationis: studies on the binding characteristics, activity and pathogenetic significance of the complement-fixing factor. Clin Exp Immunol 1978; 31: 38
13. Westermann L, *et al*. Glucocorticosteroid-resistant pemphigoid gestationis: successful treatment with adjuvant immunoadsorption. J Dermatol 2012; 39: 168
14. Kreuter A, *et al*. Intravenous immune globulin in the treatment of persistent pemphigoid gestationis. J Am Acad Dermatol 2004; 51: 1027
15. Michael D, Grando SA. Novel mechanism for therapeutic action of IVIg in autoimmune blistering dermatoses. Curr Dir Autoimmun 2008; 10: 333