Published in final edited form as:

Int J Dermatol. 2020 February ; 59(2): 175–177. doi:10.1111/ijd.14513.

New onset bullae in a pregnant woman

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Clinical Findings

A 34-year-old Haitian woman, gravida 4 para 3, at an estimated gestational age of 19 weeks, presented to the emergency room complaining of a diffuse, blistering, pruritic rash that had started on her upper body two weeks prior and spread to involve the trunk, extremities, and oral mucosa. She denied any significant medical history and took no medications. She denied similar eruptions in prior pregnancies. She had no known recent exposures to Varicella. She reported otherwise feeling well, with no fever or chills, no ocular irritation, and no genital involvement. A 12-point review of systems was otherwise negative. On examination, the patient was well-appearing with stable vital signs. There were diffuse erosions with yellow crusting on an erythematous base and scattered tense and flaccid vesicles and bullae involving the chest, abdomen, umbilicus, back, buttocks, thighs, and arms (Fig. 1). Oral examination revealed erosions on the buccal and labial mucosa and tongue. The face, palms, and soles were spared.

Histopathological and other findings

Punch biopsy demonstrated prominent suprabasal acantholysis (Fig. 2a), tombstoning, and marked eosinophilia within the superficial dermis and epidermis (Fig. 2b). Direct immunofluorescence (DIF) revealed intercellular C3a (Fig. 3a) and IgG (Fig. 3b) depositions within the epidermis, without involvement of the basement membrane. Routine laboratory testing was within normal limits, with the exception of eosinophilia. Serum antibodies to Desmoglein 1 and 3, and Varicella IgG were detected.

What is your diagnosis?

Figure 1

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Conflicts of interest: none to disclose

Figure 2

Figure 3

Diagnosis

Pemphigus vulgaris

Clinical course

The patient was treated with topical corticosteroids as well as empirical acyclovir until Varicella could be excluded. Following the biopsy results, she received 3 doses of IV methylprednisolone 20mg. When no further developing vesicles were noted, she was transitioned to oral prednisone 60mg daily. One week later she had no new bullae and the previously seen bullae had been replaced by superficial crusted erosions. She continued to do well on oral prednisone taper.

Discussion

Pemphigus is a rare (0.75 to 5 cases per million) IgG-mediated autoimmune blistering disorder of the skin and oral mucosa. There are two classic forms of pemphigus: pemphigus vulgaris and pemphigus foliaceus. Pemphigus vulgaris is characterized by acantholysis deep within the epidermis and involvement of the oral mucosa, whereas pemphigus foliaceus is restricted to the superficial epidermis. Autoantibodies are directed against Desmoglein 1 and 3 epitopes on the keratinocyte cell surface. Immune-mediated attack results in structural separation of keratinocytes and blister formation. Without intervention, pemphigus is associated with significant mortality as a result of epidermal barrier dysfunction¹.

The differential diagnosis for a pregnant patient with vesicular lesions includes gestational pemphigoid, polymorphic eruption of pregnancy, drug eruptions, and Varicella. As in this case, it is important to consider non-pregnancy associated dermatoses. The diagnosis of pemphigus vulgaris requires a thorough clinical and histological evaluation. The histologic pattern of suprabasal acantholysis and intercellular IgG and C3 depositions within the epidermis by DIF test support the diagnosis of pemphigus vulgaris in this case. Alternatively, gestational pemphigoid is characterized by subepidermal vesicles, with a linear IgG and C3 deposition along the basement membrane by DIF.

Pemphigus in pregnancy presents unique challenges in the management of disease. The onset of pemphigus during pregnancy is exceptionally rare. A retrospective study showed that of 779 women diagnosed with pemphigus prior to 50 years of age, only 18 were diagnosed while pregnant². This study also reported that of women with pre-existing pemphigus who became pregnant, 54% had exacerbation of disease, 31% did not change, and 17% improved². Pemphigus in pregnancy is associated with pre-term labor, increased rate of fetal demise (10–11%), and neonatal pemphigus^{2,3}. Of note, neonatal pemphigus resolves within 4 weeks regardless of therapeutic intervention³.

The severity of disease is correlated with patient morbidity and mortality, and poor neonatal outcomes; therefore, treatment is often required. Prednisone (5–300mg/day) is the most common reported treatment of pemphigus during pregnancy³. Patients with flares of disease can often be controlled with small increases in the dose of prednisone or with topical corticosteroids². The use of immunomodulators have been strongly discouraged or are contraindicated in pregnancy due to the high potential for birth-defects. Azathioprine use has been reported in 7 cases of pemphigus during pregnancy⁴. A recent prospective study reported that azathioprine use during the first trimester is not associated with an increased risk of poor fetal outcomes⁵. Treatments should be tailored to the patient in a way that reduces disease severity while minimizing potential side-effects to the patient and fetus.

Funding:

This work was supported by a grant from the National Institutes of Health F30EY025527 (E.R.B).

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Figure 1.
Diffuse eroded plaques with scale on an erythematous base and scattered vesicles/bullae seen on the (a) gravid abdomen and (b) left anterior thigh.

Figure 2.

(a) Acantholysis of the suprabasal epithelium with blister formation (a: H&E, x40). (b) The blister floor is lined with intact keratinocytes, “tombstoning”. Frequent eosinophils are seen in epidermis and superficial dermis (b: H&E, x200).

Figure 3.
Direct immunofluorescence result: Intercellular C3a (a) and IgG (b) depositions within the epidermis. (x200).