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Case Report

Pemphigoid Gestationis: A Case Presentation and Review of the Literature

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Abstract

Pemphigoid Gestationis (PG) is a rare autoimmune skin disorder that occurs during pregnancy. It usually flares up at the time of delivery, and resolves spontaneously shortly after. However, relapses in subsequent pregnancies are common. It is characterized by pruritic urticarial plaques with the development of tense vesicles and bullae within the lesions. Oral glucocorticoids are the mainstay of therapy. Differentiation of pemphigoid gestationis from Polymorphic Eruption of Pregnancy (PEP) is essential because management and outcomes differ. Due to its rare occurrence, we are presenting this case to make clinicians aware of PG; hence, we review the pathogenesis, clinical characteristics, and management of PG.

Keywords: Blistering disease; Corticosteroids; Pregnancy; Pemphigoid gestationis

Abbreviations: PUPPP: Pruritic Urticarial Papules and Plaques of Pregnancy; PEP: Polymorphic Eruption of Pregnancy; PG: Pemphigoid Gestationis; IgG: Immunoglobulin G; BP180: Bullous Pemphigoid Antigen 180; HLA: Human Leucocyte Antigen; NC: Non-Collagenous

Introduction

Pemphigoid gestationis is a rare pregnancy-associated autoimmune blistering disease, affecting between 1 in 10,000 to 1 in 50,000 pregnancies [1,2]. Originally named herpes gestationis for the herpetiform morphology of the blisters, it has no association with the herpes virus whatsoever [1]. It usually begins abruptly during the 2nd or 3rd trimester of pregnancy; and, in 15%-25% of cases, during the immediate post-partum period [3,4]. The pathogenesis is not yet fully established, but it belongs to the group of autoimmune skin disorders characterized by an immune response directed against different hemidesmosomal proteins affecting the adherence between the dermis and epidermis causing blistering of the skin [1,2]. The clinical presentation is characterized by intense pruritus and polymorphic skin lesions including blisters [4]. The essential component for diagnosis is obtained from a biopsy of perilesional skin submitted for direct immunofluorescence [5]. Goals of treatment are to relieve symptoms, decrease further bullae formation and promote healing of the lesions. Most patients will respond to a course of corticosteroids [6]. Given its rarity and ability to mimic other dermatoses of pregnancy, high clinical suspicion is necessary to properly diagnose PG. We hereby present a case of PG initially misdiagnosed as Polymorphic Eruption of Pregnancy (PEP), a more common and milder dermatosis of pregnancy.

Case Report

A 36-year-old woman, primigravida, at 26-weeks' gestation, presented to our department with a widespread, pruritic and erythematous popular rash localized to the umbilicus. Despite oral antihistamines, the rash worsened, coalescing into large, urticarial patches and plaques that spread to the extremities, chest, neck and back. At 28 weeks, blister formation prompted dermatology referral. The patient reported no allergies or current medications, and her personal and family history was unremarkable. Physical examination showed widespread erythematous plaques with vesicles on the trunk, umbilicus, back and proximal aspects of the arms, thighs, hands, and feet (Figure 1 and 2). Plaques on

the extensor extremities vesiculated into tense, fragile bullae. No facial or mucous membrane involvement was present. Laboratory values were within reference range.

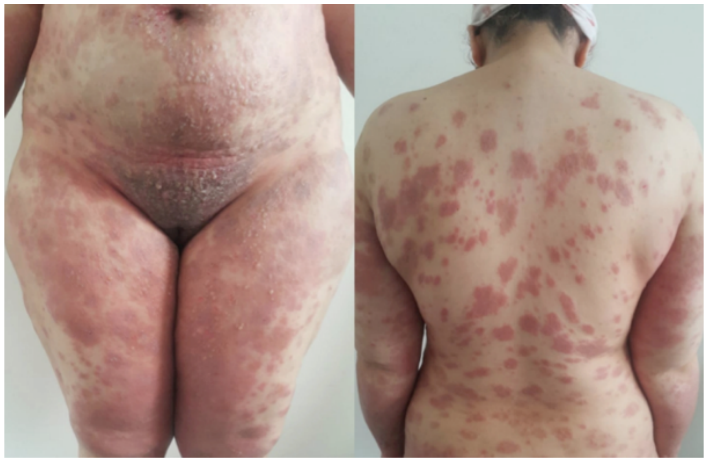

Figure 1: Pemphigoid gestationis in a periumbilical pattern on the abdomen.

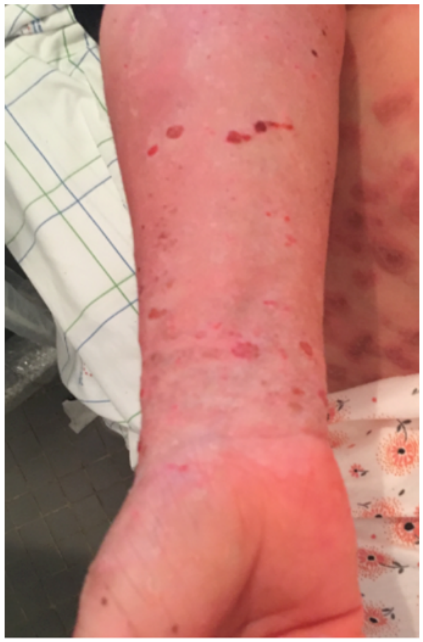

Figure 2: Urticarial plaques with multiple bullae and vesicle formation on the right posterior forearm. Palms were not included.

Although the patient was initially diagnosed with Polymorphic Eruption of Pregnancy (PEP), new bullae suggested a vesiculo-bullous disorder. Therefore, skin biopsy specimens were obtained from the edge of erythema with vesicles on the arm of the patient. Histopathology exam found a perivascular infiltrate of lymphocytes and eosinophils. Eosinophils were present at the dermo-epidermal junction with associated early subepidermal vesiculation; which strongly suggested PG. Direct immunofluorescence shows deposition of C3 in a linear pattern along the basement membrane; whereas IgG was weakly positive and IgA and IgM were not detected. We recommended topical steroids; and given the spread of the lesions, we also recommended general corticosteroids at 1 mg/kg/day.

After 1 week of oral prednisone at 60 mg per day, the rash stopped spreading and pruritus improved, so the dose was decreased to 40 mg. At next follow up, there were no new vesicles or bullae. The dose was decreased to 20 mg/day over the next 2 weeks, after which her pruritus subsided completely (Figure 3). At 37 weeks of gestation, she had a spontaneous vaginal delivery of a healthy female infant of 3600g who had no evidence of skin lesions or adrenal suppression at birth. However, at 1 week postpartum the patient experienced a resurgence of her PG. Again, the patient was started on the same prednisone taper used during her pregnancy and her lesions completely resolved. She was later warned of the high likelihood of recurrence of the PG and was therefore invited to see us again as soon as the first signs appeared.

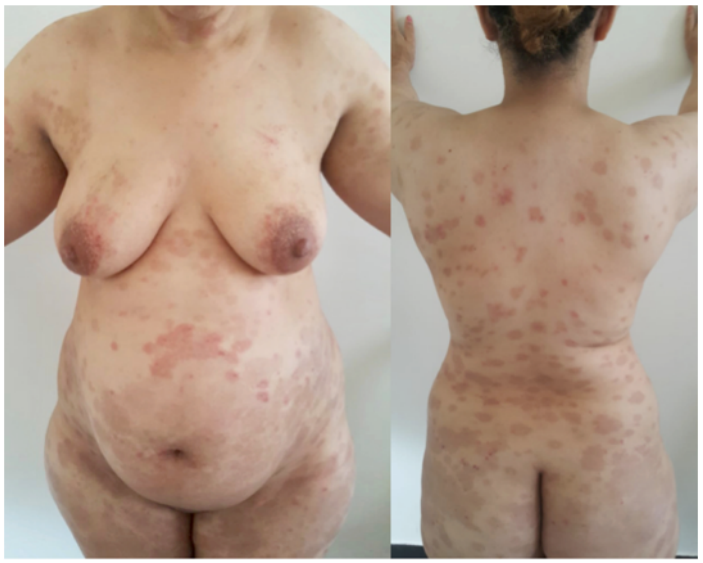

Figure 3: Post systemic corticotherapy decrease of the PG.

Discussion

PG is a rare, pregnancy-associated, blistering disorder that usually develops during the second or third trimester of a pregnancy but can also occur after delivery [5]. The antibody responsible for the eruption begins expression in the second trimester and binds to a target on the basement membrane of the skin [5-7]. Pemphigoid gestationis is hypothesized to arise from pathologic maternal IgG induced by paternal HLA antigens found in the placenta [7]. Pruritic urticarial papules and plaques are the primary lesions that evolve into vesicles and blisters. Lesions often start from the periumbilical area and extend to the flexural areas. As the

disease progresses within days to weeks, a generalized eruption of tense blisters occurs, sparing the face and mucous membranes [5-9]. Histopathologic analysis shows papillary dermal edema that may result in subepidermal vesicle formation and a dermal inflammatory infiltrate with abundant eosinophils [8,9]. Definitive diagnosis of PG is made by immunofluorescence staining of skin biopsies.

These lesions demonstrate linear deposits of C3 along the basement membrane zone. And in approximately 25% to 30% of cases, IgG deposition can also be found along the basement membrane [8-10]. It is important to rule out infectious or allergic causes of the skin eruptions. Distinguishing PG from other dermatoses of pregnancy can be difficult, especially polymorphic eruption of pregnancy, previously known as pruritic urticarial papules and plaques of pregnancy, which can resemble non-bullous PG clinically and histopathologically. Thus, the differentiation between the PG and PEP may be confirmed by the presence of anti-basement-membrane zone antibodies by immunofluorescence study, immunoblots, or ELISA study [10]. A commercially available ELISA to the NC16A domain of BP180 has been shown to have a sensitivity of 96 % and a specificity of 96 % in differentiating PG from PEP [11]. Powell et al. demonstrated that the serologic test measuring the major immunoreactive portion of the NC16A domain of BP180 antigen can be used to verify the diagnosis of PG and differentiate it from PEP [11].

Sitaru et al. also supported the use of NC16A levels to measure the presence of autoantibodies and assist in the diagnosis of PG [12]. Furthermore, because NC16A levels correlate with disease activity, they can be used to follow disease progression and consequently may impact the course of treatment [12,13]. Likewise, Aoyama et al. described an association between BP180 ELISA titers and disease severity as well as the important role that anti-BP180 titers may play in therapeutic planning [14]. Regarding treatment, the primary aim is to relieve itching, prevent blister formation and treat any secondary infection. The majority of patients with PG require systemic corticosteroids for disease control; and, in some cases, with the addition of corticosteroid-sparing immunosuppressant agents for increased disease control [15]. Most cases of PG respond well to low dosages (20- 60 mg daily), but the need for higher dosages up to 180 mg daily have been reported [15]. However, mild cases respond well to topical corticosteroid treatment only [16].

Our patient initially was started on a 1mg/kg/day dose of oral prednisone and topical steroid; she showed a good response at 1-week follow-up. She was well controlled with a lower maintenance dose through the rest of the pregnancy. Our case demonstrates that early treatment with systemic steroids can ease PG symptoms and that positive outcomes result from gradual tapering followed by an increase immediately after delivery. The course of PG is variable. Most cases remit in the first several weeks after delivery. However, exacerbations have been documented during subsequent pregnancies, during menstruation, and with oral contraceptive use [17,9]. There have been case reports of pemphigoid gestationis that persisted for years after delivery, in which the diagnoses of chronic pemphigoid gestationis or conversion to bullous pemphigoid must be considered [18].

Correct diagnosis is important to allow for early control of the disease and appropriate counselling of the mother regarding her course of treatment and risk of developing PG during future pregnancies. One of the most important considerations in approaching the patient with PG is the effect the disease may have on the fetus. Most studies show that the risk of preterm birth and fetal growth restriction is greater in PG pregnancies compared to normal population [15]. Some infants of PG mothers, approximately 5% to 10%, have a transient subepidermal blistering eruption that resolves on its own with no known sequelae. This finding is most likely due to transplacental passage of antibodies from the mother to the baby [19]. In our case, the infant was born 3 weeks early but had no complications [20].

Conclusion

Pemphigoid gestationis is a rare pregnancy-associated autoimmune skin disease. It is most common during the second and third trimesters of pregnancy. Clinically, PG is characterized by intense pruritus and polymorphic skin eruptions. The diagnosis is based upon clinical presentation and typical histopathological findings. The greatest differential diagnostic challenge of PG is PEP. Despite rather similar clinical features, negative immunofluorescence analysis of perilesional skin biopsy in PEP differentiates it explicitly from PG. Symptoms can be reduced with the use of topical and systemic corticosteroids, oral antihistamines, and systemic immunosuppressants. As PG is associated with a considerable morbidity for pregnant women and carries fetal risks, it is important for the clinician to quickly recognize this disease and refer it for dermatological evaluation and treatment.

Declarations

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Availability of Data and Materials

Supporting material is available if further analysis is needed.

Competing Interests

The authors declare that they have no competing interests.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Ethics Approval and Consent to Participate

Ethics approval has been obtained to proceed with the current study. Written informed consent was obtained from the patient for participation in this publication.

References

1. Sävervall C, Sand FL, Thomsen SF (2015) Dermatological diseases associated with pregnancy: Pemphigoid gestationis, polymorphic eruption of pregnancy, intrahepatic cholestasis of pregnancy, and atopic eruption of pregnancy. Dermatol Res Pract 2015: 979635.
2. Kroumpouzos G (2010) Specific dermatoses of pregnancy: Advances and controversies. Expert Rev Dermatol 5: 633-648.
3. Sadik CD, Lima AL, Zillikens D (2016) Pemphigoid gestationis: Toward a better understanding of the etiopathogenesis. Clin Dermatol 34: 378-382.
4. Cianchini G, Masini C, Lupi F, Corona R, De Pità O, et al. (2007) Severe persistent pemphigoid gestationis: Long-term remission with rituximab. Br J Dermatol 157: 388-389.
5. Cobo MF, Santi CG, Maruta CW, Aoki V (2009) Pemphigoid gestationis: Clinical and laboratory evaluation Clinics (Sao Paulo) 64: 1043-1047.
6. Engineer L, Bhol K, Ahmed AR (2000) Pemphigoid gestationis: A review. Am J Obstet Gynecol 183: 483-491.
7. Kroumpouzos G (2012) Skin disease in pregnancy and the puerperium. Gabbe SG, Niebyl JR, Simpson JL, Landon MB, Galan HL, Jauniaux ERM, Driscoll, DA, (Eds). Obstetrics: Normal and Problem Pregnancies (6thedn); Philadelphia (PA): Elsevier/Saunders 1091-1093.
8. Shornick JK (1998) Dermatoses of pregnancy. Semin Cutan Med. Surg 17: 172-181.
9. Jenkins RE, Hern S, Black MM (1999) Clinical features and management of 87 patients with pemphigoid gestationis Clin Exp Dermatol 24: 255-259.
10. Lin MS, Arteaga LA, Diaz LA (2001) Herpes gestationis. Clin Dermatol 19: 697-702.
11. Semkova K and M Black (2009) Pemphigoid gestationis: current insights into pathogenesis and treatment. Eur J Obstet Gynecol Reprod Biol 145: 138.
12. Powell AM, Sakuma-Oyama Y, Oyama N, Albert S, Bhogal B, et al. (2005) Usefulness of BP180 NC16a enzyme-linked immunosorbent assay in the serodiagnosis of pemphigoid gestationis and in differentiating between pemphigoid gestationis and pruritic urticarial papules and plaques of pregnancy. Arch Dermatol 141: 705-710.
13. Barnadas MA, Rubiales MV, González MJ, Puig L, García P, et al. (2008) Enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence testing in a bullous pemphigoid and pemphigoid gestationis. Int J Dermatol 47: 1245-1249.
14. Sitaru C, Powell J, Messer G, Bröcker EB, Wojnarowska F, et al. (2004) Immunoblotting and enzyme-linked immunosorbent assay for the diagnosis of pemphigoid gestationis. Obstet Gynecol 103: 757-763.
15. Aoyama Y, Asai K, Hioki K, Funato M, Kondo N, et al. (2007) Herpes gestationis in a mother and newborn: immunoclinical perspectives based on a weekly follow-up of the enzyme-linked immunosorbent assay index of a bullous pemphigoid antigen noncollagenous domain. Arch Dermatol 143: 1168-1172.
16. Lawley TJ, Stingl G, Katz SI (1978) Fetal and maternal risk factors in herpes gestationis. Arch Dermatol 114: 552-555.
17. Yancey KB (1990) Herpes gestationis. Dermatol Clin 8: 727-735.
18. Al-Fouzan AS, Galadari I, Oumeish I, Oumeish OY (2006) Herpes Gestationis (Pemphigoid Gestationis). Clin Dermatol 24: 109-112.
19. Amato L, Mei S, Gallerani I, Moretti S, Fabbri P (2003) A case of chronic herpes gestationis: persistent disease or conversion to bullous pemphigoid? J Am Acad Dermatol 49: 302-307.
20. Chorzelski TP, Jablonska S, Beutner EH, Maciejowska E, Jarząbek-Chorzelska M (1976) Herpes gestationis with identical lesions in the newborns: passive transfer of the disease? Arch Dermatol 112: 1129-1131.