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Pemphigoide of Pregnancy: Case Report and Review of the Literature

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Abstract

Pemphigoid of pregnancy (PG) is a rare autoimmune bullous dermatosis, affecting 1 in 20000 to 50000 pregnant women. PG is linked to anti-BP180 autoantibodies whose synthesis follows a breakdown in mother-fetal immunological tolerance. Bullae formation results from a complex mechanism involving TH2 lymphocytes, cytokines and polynuclear cells. PG manifests itself as a pruritic erythematopapular rash of varying extent, progressing to the inconstant but suggestive appearance of vesicles and bullae. The disease progresses to gradual recovery after delivery, sometimes after a post-partum flare-up. Recurrence during subsequent pregnancies is frequent. Relapses can also be triggered by estrogen-progestogen contraception. Diagnosis is confirmed by direct immunofluorescence, which shows C3 +/- IgG deposits along the basement membrane. The BP180-NC16A ELISA technique is highly sensitive for the detection of circulating antibodies. Fetal prognosis is good, but early onset in the 1st or 2nd trimester of pregnancy of pregnancy and the presence of bullae are risk factors for prematurity or hypotrophy. Very rarely, the newborn may present transient bullae. Several publications show that very strong dermocorticoids are effective and can be used as first-line treatment for moderate PG. We report the case of a patient admitted to a maternity hospital emergency department, with a pregnancy of 37 weeks' gestation and a non-reassuring fetal condition presenting as pemphigoid of pregnancy (PG).

Keywords: Pemphigoid, Pregnancy, Rash, Prurit

Introduction

Pemphigoid gestationis is a rare autoimmune bullous dermatosis specific to pregnancy. Its frequency varies from 1/4000 to 1/50,000 pregnancies **[1]**. The condition is characterized by a pruritic, maculopapular, bullous eruption occurring in the 2nd or 3rd trimester of pregnancy. The dermal-epidermal junction is affected, and the diagnosis can only be made by skin biopsy **[2]**. Congenital cutaneous aplasia, on the other hand, is defined as a localized absence of epidermis, dermis and sometimes subcutaneous tissue. The authors report the case of a patient with pemphigoid gestationis whose newborn had congenital cutaneous aplasia, suggesting a possible relationship between the two pathologies.

Case report

Mrs N.M, 35 years old, multiparous, followed for 2 years for PG on dermocorticoids during her first pregnancy. At present, the patient carried a singleton pregnancy to term, during which she presented with a pruritic, vesiculopapular rash. These skin lesions predominated in the periumbilical region, arms, thighs and periareolar region, with no mucosal involvement **(Figure 1, Figure 2, Figure 3, Figure 4**).

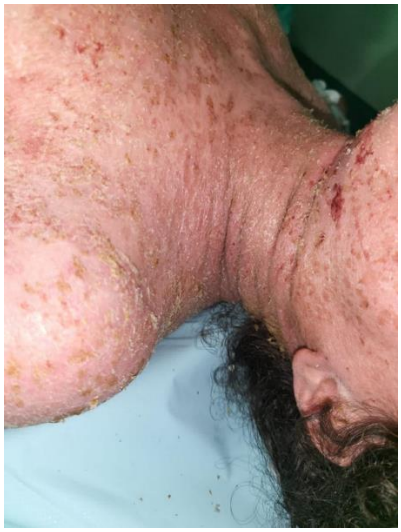

Figure 1: vesiculo-papular rash on the neck and shoulder area

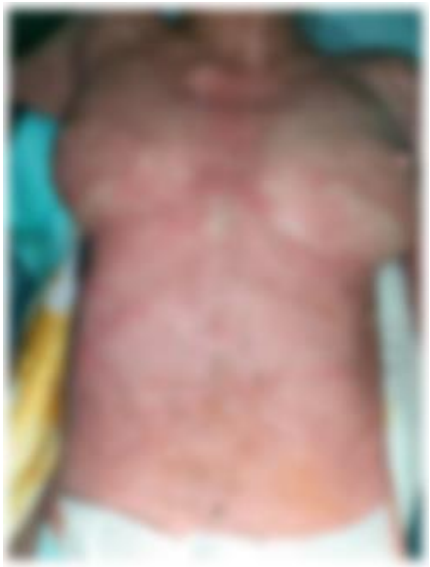

Figure 2: vesiculo-papular rash in the periumbilical region

The dermatological diagnosis of pemphigoid gestationis was made after skin biopsy with direct immunofluorescence examination, which showed an eosinophilic infiltrate, subepidermal edema and linear deposits of IgG and complement fraction C3 along the dermal-epidermal junction. The latter sign is pathognomonic of pemphigoid gestationis. Local corticosteroids rapidly regressed the skin lesions.

Delivery by caesarean section had taken place at 37 days' gestation of a male newborn, birth weight 2100 g, who presented with acute fetal distress, necessitating delivery by the high route. The rest of the examination was unremarkable. A work-up including the usual viral serologies (cytomegalovirus, rubella, herpes, varicella) and bacterial serologies (in particular listeria and chlamydia), an irregular agglutinin test, a vascular-renal work-up (uricemia, platelet count, hepatic-renal work-up, proteinuria) and a thyroid work-up had been carried out, showing no abnormalities.

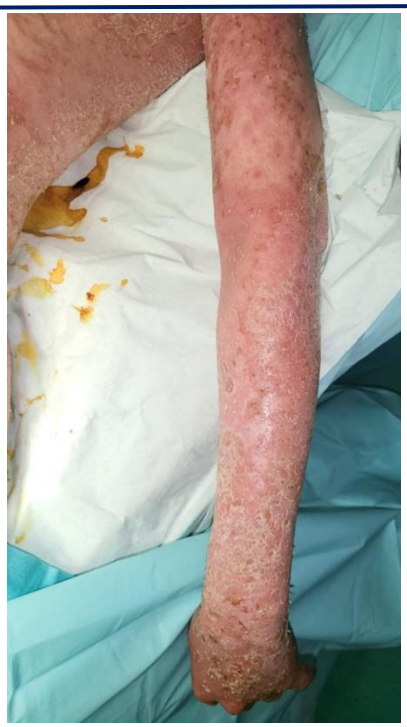

Figure 3: vesiculo-papular rash in the arm area

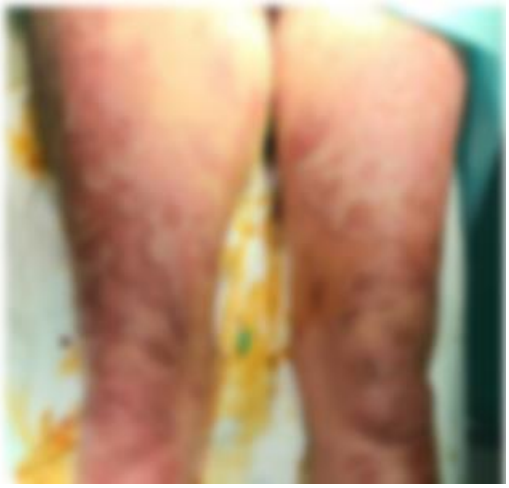

Figure 4: vesiculo-papular rash on thighs and knees

Discussion

Pemphigoid gestationis is an acquired autoimmune bullous dermatosis generally occurring during pregnancy (between 28 and 32 weeks' gestation), but also in the immediate post-partum period, or in cases of hydatidiform mole or even choriocarcinoma. It may be associated with other autoimmune pathologies, notably thyroid disease. Pruritus precedes the eruption by one to four weeks. Typically, the topography of this rash is periumbilical with centrifugal extension, but the face is often respected. Mucosal involvement is also possible.

The evolution of pemphigoid involves clinical improvement in the six to eight weeks preceding delivery, followed by a transient exacerbation in the immediate postpartum period in 75 to 85% of cases **[2]**. Sometimes scarring macular pigmentation persists.

One of the characteristics of pemphigoid is its tendency to recur with each pregnancy. The onset of the disease is then usually earlier and more severe. Some relapses have been described when taking oestroprogestins. These facts need to be clarified for a patient suffering from a first episode of pemphigoid gestationis. The rather complex pathophysiology

involves immune dysregulation between the fetoplacental unit and the mother, occurring in a predisposed genetic background (HLA haplotype DR3-DR4). Maternal tolerance of the fetus is reduced, creating a reaction against placental antigens, some of which are paternal in origin. These antigens are polymers with particles in common with dermo-epidermal junction antigens. The antibodies synthesized destroy the basement membrane, leading to the formation of sub-epidermal bullae.

Direct immunofluorescence is pathognomonic, revealing linear deposits of IgG and complement fraction C3 along the dermal-epidermal junction. Indirect immunofluorescence tests for a circulating serum autoantibody (Herpes gestationis factor) of the IgG type. Specificity is 100%, but sensitivity is only 75%. The differential diagnosis of pemphigoid gestationis is initially that of isolated pruritus, then that of any pruritus associated with dermatological lesions during pregnancy.

First and foremost, a thorough clinical examination should be carried out. This will enable the various etiologies to be considered in the presence of pruritus, whether naked or associated with a dermatosis. Skin biopsy and direct immunofluorescence analysis will help differentiate pemphigoid gestationis from other gravid dermatoses (dermatitis herpetiformis, toxic rash, etc.). In rare cases of bullous lupus, direct immunofluorescence takes on a different appearance: immunoglobulin deposits are discontinuous on the basement membrane.

The usual treatment for pemphigoid gestationis is local corticosteroid therapy. In severe forms, systemic corticosteroids are necessary. Other therapeutic alternatives are possible (intravenous immunoglobulins, plasmapheresis or sulfonamides), but their use remains exceptional **[3]**.

The maternal consequences of pemphigoid gestationis are dominated by the risk of recurrence in subsequent pregnancies (earlier and more severe) **[2]**, but also by the threat of premature delivery (variable rate depending on the author, from 0 to 23%) **[1]**. Contraception with oestroprogestins exposes the patient to the risk of recurrence **[4]**.

The fetal consequences are manifold: intrauterine growth retardation **[5]** or fetal death in utero (0 to 7.7% of cases) **[1,6]**. After birth, early neonatal lesions may occur before the 7th day of life. These occur in 5-10% of cases, and their frequency depends on the low transplacental passage of autoantibodies. These neonatal lesions are essentially cutaneous (bullous lesions identical to those of the mother **[1,7]**), but also neurological in rare cases (cerebral haemorrhage **[8,9]**. The predominance of cephalic lesions (73%).

While the association of associated malformations is 37.1%, underlying bone involvement is 9% and associated malformative syndromes is 13.7%. The key question for the clinician is whether congenital cutaneous aplasia is truly isolated, or whether it is one of the clinical signs of a malformative syndrome **[10,11]**. A review of the literature reveals no cases of pemphigoid gestationis associated with congenital cutaneous aplasia.

Clinically, PG manifests as a pruritic, erythematopapular, urticarial rash, sometimes cocardiform, more or less extensive, classically starting on the abdomen but not always, evolving towards the inconstant (60-80% of cases) but suggestive appearance of vesicles and bullae. The trunk (particularly the periumbilical region) and lower limbs are most commonly affected, although facial involvement is also possible, as is, rarely (0 to 15-20% depending on the study), involvement of the oral mucosa **[12-14]**.

The main differential diagnosis is polymorphic dermatitis of pregnancy, presenting as a pruritic eczematous or urticarial rash that is usually non-bullous **[12,15]**. Rarely, palmar-plantar vesicles may be present, or even exceptionally, true bullae **[16]**. Consistently negative direct immunofluorescence tests help to rectify the diagnosis.

A flare-up of the disease may be observed in the days following delivery, linked to a sudden increase in antibody levels, detectable by ELISA, just before and just after delivery **[17]**. Cure usually occurs within a few weeks to a few months after delivery (median cure 16 weeks after delivery **[18]**), but very prolonged courses are possible, up to 12 years.

These very chronic evolutions pose a nosological problem: very prolonged PG or conversion of PG to bullous pemphigoid **[19,20]**.

The relapse rate in subsequent pregnancies is significant

and independent of the eventual change of sire **[18]**, contrary to earlier beliefs that showed a higher rate of PG in the event of a change of sire (18). In Jenkins' study, only 8% of women had a normal or minimally relapsed subsequent pregnancy, and 10% had flare-ups triggered by estrogen-progestogen oral contraception **[21]**.

Skin biopsy of a recent bullous lesion reveals a subepidermal bulla with a superficial dermal infiltrate rich in neutrophils and eosinophils. If the biopsy is performed on an area that has not detached, the histological image is non-specific, but still shows a dermal neutrophilic and eosinophilic infiltrate. Direct immunofluorescence confirms the diagnosis, demonstrating a fine, linear deposit of C3 and sometimes IgG at the dermal-epidermal junction **[14]**.

The evolution of autoantibody levels by ELISA technique follows the course of the disease **[22]**. Direct immunofluorescence and circulating antibody tests are consistently negative in other dermatoses of pregnancy **[18]**. Jenkins et al. report on a series of 80 PGs in which the vast majority of patients (80%) were treated with general corticosteroids, while the remainder were controlled with local corticosteroids **[12]**.

In 2004, Mokni et al. highlighted the value of dermocorticoids in moderate forms of the disease. Only half of patients received general corticosteroid therapy **[13]**. Castro et al. treated 3 of their 10 patients with 8 dermocorticoids, the others with general corticosteroids **[23]**. In 2008, Saidi et al. reported on their experience where, out of 7 GPs, only 3 required general corticosteroid therapy, 2 of them after failure of dermocorticoids. The other 4 patients were successfully treated with dermocorticoids, and the average duration of treatment in all cases (dermocorticoids and general corticosteroid therapy) was 12 weeks **[24]**.

The experience of other teams, however, tends to favor general corticosteroid therapy, such as Cobo et al. who reported in 2009 that out of 7 patients, 6 used high-dose oral corticosteroids (0.5 to 1 mg/kg/d), a priori as first-line treatment **[16]**. No specific maternal or fetal adverse effects of local or general corticosteroid therapy were reported in these studies.

Conclusion

Pemphigoid gestationis is rare, and its association with congenital cutaneous aplasia seems fortuitous. A relationship between the two pathologies seems difficult to establish, due to the exceptional occurrence of such associations.

References

1. Engineer L., Bhol K., Razzaque Ahmed A. Pemphigoid gestationis:a review. Am J Obstet Gynecol. 2000;183(2):483–91. [PubMed] [Google Scholar]
2. Shornick J. Herpes gestationis. J AmAcad Dermatol. 1987;17(4):539–56. [PubMed] [Google Scholar]
3. Wojnarowska F., Kirtschig G., Khumalo N. Treatment of subepidermal immunobullous diseases. Clin Dermatol. 2001;19(6):768–77. [PubMed] [Google Scholar]
4. Sasseville D., Wilkinson R., Schnader J. Dermatoses of pregnancy. Int J Dermatol. 1981;20(4):223–41. [PubMed] [Google Scholar]
5. Holmes R., Black M. The fetal prognosis in pemphigoid gestationis. Br J Dermatol. 1984;110(1):67–72. [PubMed] [Google Scholar]
6. Lawley T., Stingl G., Katz S. Fetal and maternal risk factors in herpes gestationis. Arch Dermatol. 1978;114(4):552–5. [PubMed] [Google Scholar]
7. Chen SH., Chopra K., Evans TY., Raimer SS., Levy ML., Tyring SK. Herpes gestationis in a mother and child. J Am Acad Dermatol. 1999;40 (5 Pt 2):847–9. [PubMed] [Google Scholar]
8. Powell J., Wojnarowska F., James M., Allott H. Pemphigoid gestationis with intra–uterine death associated with fetal cerebral haemorrhage in the mid–trimester. Clin Exp Dermatol. 2000;25(5):451–3. [PubMed] [Google Scholar]
9. Berthier M., Nasimi A., Boussemart T., Cardona J., Oriot D. Neurologic manifestations in a child of a mother with gestational herpes. Arch Pediatr. 1996;3(5):460–2. [PubMed] [Google Scholar]
10. Lowe PM., Fryer J., Shumack S. Pemphigoid gestationis occurring in a patient with HELLP syndrome. Austr J Dermatol. 1996;37(2):89–92. [PubMed] [Google Scholar]
11. Mesrati H., Amouri M., Chaabane H., Meziou TJ.,

Mseddi M., Turki H. Journées dermatologiques de Paris 2012. Annales de Dermatologie et de Vénéréologie. December. 2012; 139(12):160.

12. L Ambros–Rudolph CM., Müllegger RR., Vaughan–Jones SA., Kerl H., Black MM. The specific dermatoses of pregnancy revisited and reclassified:results of a retrospective two–center study on 505 pregnant patients. J Am Acad Dermatol. 2006; 54:395–404. [PubMed]
13. Mokni M., Fourati M., Karoui I et al. Pemphigoid gestationis:a study of 20 cases. Ann Dermatol Venereol. 2004**;**131:953–6. [PubMed]
14. Cobo MF., Santi CG., Maruta CW et al. Pemphigoid gestationis :clinical and laboratory evaluation. Clinics. 2009; 64:1043–7. [PubMed]
15. Petropoulou H., Georgala S., Katsambas AD. Polymorphic eruption of pregnancy. Int J Dermatol. 2006; 45:642–8. [PubMed]
16. Sherley–Dale AC., Carr RA., Charles–Holmes R. Polymorphic eruption of pregnancy with bullous lesions:a previously unreported association. Br J Dermatol. 2010; 162:220–2. [PubMed]
17. Aoyama Y., Asai K., Hioki K et al. 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. 2007; 143:1168–72. [PubMed]
18. Jenkins RE., Hern S., Black MM. Clinical features and management of 87 patients with pemphigoid gestationis. Clin Exp Dermatol. 1999; 24:255–9. [PubMed]
19. Amato L., Mei S., Gallerani I et al. A case of chronic herpes gestationis:persistent disease or conversion to bullous pemphigoid? J Am Acad Dermatol. 2003; 49:302–7. [PubMed]
20. Chi CC., Wang SH., Charles–Holmes R et al. Pemphigoid gestationis :early onset and blister formation are associated with adverse pregnancy outcomes. Br J Dermatol. 2009; 160:1222–8. [PubMed]
21. Jenkins RE., Vaughan Jones SA., Black MM. Conversion of pemphigoïde gestationis to bullous pemphigoïde:two refractory cases highlighting this association. Br J Dermatol. 1996; 135:595–8. [PubMed]
22. Sitaru C., Powell J., Messer G et al. Immunoblotting and enzyme–linked immunosorbent assay for the diagnosis of pemphigoid gestationis. Obstet Gynecol. 2004; 103:757–63. [PubMed]
23. Castro LA., Lundell RB., Krause PK et al. Clinical experience in pemphigoid gestationis:report of 10 cases. J Am Acad Dermatol. 2006; 55:823–8. [PubMed]
24. Saidi W., Joly P. Topical or systemic corticosteroids in patients with pemphigoid gestationis and polymorphic eruption of pregnancy. Ann Dermatol Venereol. 2008; 135:865–6. [PubMed]