

Pemphigoid gestationis: A Moroccan study

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ABSTRACT

Introduction: Pemphigoid gestationis (PG) is a rare autoimmune skin disorder that occurs during pregnancy. **Materials and Methods:** Prospective study including all cases of PG diagnosed between 2010 and 2015. **Results:** We reported 16 patients: 12 multiparous and 4 primiparous, the average age was 30.43 years. The onset of the disease was done in 43.75% of cases at 3 trimester, and 25% of the 2 trimester with three cases of early post partum and post abortum cases. All patients had urticarial papules, vesicle were found in 85.7%. The beginning was done in periumbilical 62.5%. Histology objectified in all cases a sub epidermal detachment, and the IFD performed in 8 cases, objectified in 6 patients a linear deposit of C3 along the dermoepidermal junction. All patients were treated with Bethametasone at 30 g/d with a progressive degression over several months. Concerning the fetal prognosis we found two cases of prematurity, and one case of fetal death. One patient had a choriocarcinoma complicated molar pregnancy. **Conclusion:** All our patients evolved well under topical corticosteroids of very strong class, even with extensive lesions, so suggesting their first-line use, avoiding the recourse to the oral corticotherapy.

Key words: Autoimmune bullous dermatosis; Pregnancy; Topical steroids

INTRODUCTION

Pemphigoid gestationis (herpes gestationis) is a rare devastating autoimmune bullous dermatoses occurring in approximately one in 50,000 pregnancies [1-3]. It usually presents during the second or third trimester, but it may be present at any stage of pregnancy or the puerperium [3]. Classically, pemphigoid gestationis (PG) is characterized by pruritic, urticarial plaques and tense vesicles and blisters within the lesions [4]. The periumbilical site is usually the first area involved. Pruritus is a prominent symptom associated with the onset of disease [3]. Blister formation is due to a complex mechanism involving Th2 lymphocytes, cytokines and polymorphonuclear cells [5]. In routine histological examination a subepidermal vesicle detected [6].

The purpose of this study was to demonstrate the demographic data, clinicopathologic features and therapeutic outcome of the patients with PG in Moroccan population.

MATERIALS AND METHODS

We present a monocentric prospective study conducted in the dermatology department of Hassan II University Hospital in Fez over a period of five years, from January 2010 to December 2015. Demographic data, clinical manifestation including the time of disease onset, site of lesions, and frequency in multigravida and primigravida and treatment modalities were analyzed.

Ethics Statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent was obtained from all patients for being included in the study.

How to cite this article: Radia C, Salim G, Kawtar I, Zahra MF, Taoufiq H. Pemphigoid gestationis: A Moroccan study. Our Dermatol Online. 2017;8(2):128-132.

Submission: 27.07.2016; **Acceptance:** 16.01.2017

DOI: 10.7241/ourd.20172.36

RESULTS

On this 5-year period from 2010 to 2015, we collected 16 cases of PG. These are summarized in the Table 1.

Sixteen patients with PG were diagnosed in our department between January 2010 and December 2015. The patients age ranged from 17 to 49 years (mean 30,43 years).

Twelve out of the 16 cases were multigravida and 4 cases were primigravida.

The onset of the disease was reported in the third trimester of pregnancy in 43,75% and in the second trimester of pregnancy in 25% but three patients had a flare up of disease during the postpartum and one out of cases in postabortion period.

The main complaint of the patients was itching. The lesions started from abdomen especially periumbilical area in eleven cases, lower extremities in two patients and upper extremities in three cases.

Mucosal involvement was not seen but facial lesions detected in two patients.

The clinical appearance of the lesions was urticarial plaques and vesicles in 85.7% and target lesions and pustules in 37.5% (Fig. 1).

Histological examination revealed subepidermal blistering with inflammatory lymphohistiocytic and eosinophilic infiltrations in all cases (Fig. 2).

Direct immunofluorescence released in 8 cases and showed a linear deposition of the third component of the complement along the basement membrane zone in six cases. (Fig. 3).

One patient was discovered as having hypercalcemia secondary to primary hyperparathyroidism.

All patients were treated with bethametasone at 30 g/day with a progressive degression over several months. No exacerbation postpartum was observed, with only one case of recurrence during subsequent pregnancy.

Table 1: Summary table of 16 observations

case	Age	Obstetric history	The onset of the disease	site of the onset	Histopathology	DIF	Treatment	Newborn
1	17	MG	3T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	Healthy
2	27	MG	After delivery	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	Healthy
3	37	MG	1T	Limbs	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	Negative	TS	Healthy
4	32	MG	2T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	fetal death in utero
5	28	MG	2	Limbs	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	UN
6	32	MG	Post-aborum	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	UN
7	24	PG	3T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Choriocarcinoma
8	30	MG	2T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	Negative	TS	fetal death in utero
9	33	MG	3T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	C3	TS	Healthy
10	42	MG	3	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	Negative	TS	UN
11	49	MG	After delivery	Limbs	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Healthy
12	36	MG	2T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Premature twins
13	26	MG	After delivery	Limbs	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Healthy
14	26	PG	3T	Limbs	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Premature
15	25	PG	3T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	Healthy
16	30	MG	2T	Periumbilical	Subepidermal bulla, lymphohistiocytic and eosinophilic infiltrations	ND	TS	UN

DIF: Direct immunofluorescence, MG: Multigravidae, PG: Primigravidae, 2T: Second trimester, 3T: Third trimester, ND: Not done, TS: Topical steroid, UN: Unknown



Figure 1: Pemphigoid gestationis (Plaques and blisters) involving the abdomen in 2nd trimester.

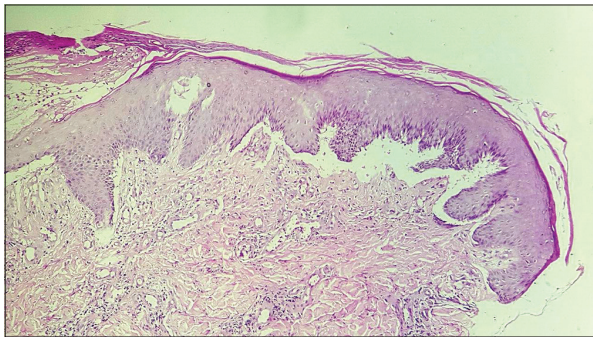


Figure 2: Case of pemphigoid gestationis shows subepidermal blister.

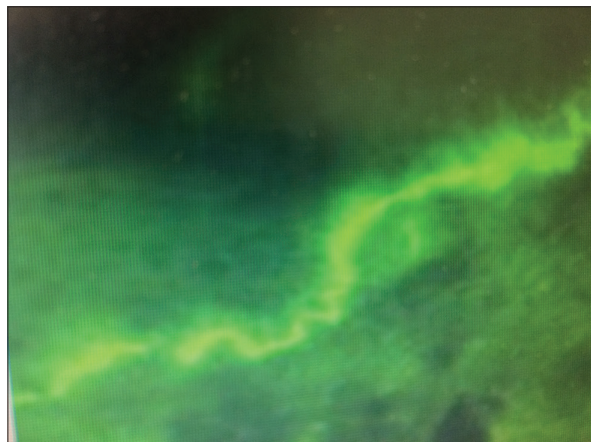


Figure 3: Linear positivity of C3 in basement membrane.

Concerning the fetal prognosis we found two cases of prematurity, and one case of fetal death. One patient had a choriocarcinoma complicated molar pregnancy.

DISCUSSION

Pemphigoid gestationis (PG) is intensely pruritic and a rare autoimmune vesiculobullous dermatosis of

pregnancy closely related to the pemphigoid group of blistering disorders, with an incidence of 1:50,000 to 60,000 pregnancies [7-9]. Synonyms for PG include herpes gestationis, dermatitis multiformis gestationis, and gestational pemphigoid. The dermatosis was originally named “herpes gestationis” by Milton in 1872 [8]. On the basis of the morphologic herpetiform feature of the blisters; however, the name was revised to PG, because PG is not related to or associated with any active or prior herpes virus infection [7].

The onset of symptoms is usually during the second trimester of pregnancy. However, an earlier or later start may be observed. The cases of PG in postpartum were also observed [10]. In our study, the disease most commonly started in the third trimester of pregnancy. PG usually begins with intense itchy erythematous urticarial papules and plaques surrounding the umbilicus. The lesions quickly spread to the abdomen, back, chest and extremities, mucosal surfaces, palms, and soles of the feet with habitual respect of the face [11,12]. In our series we noticed the involvement of the face in two cases.

Results of routine laboratory test are usually within normal reference ranges. Only the blood eosinophilia is suggestive [7]. In our series one patient was discovered as having hypercalcemia secondary to primary hyperparathyroidism.

Microscopically, the presence of a subepidermal bulla with a prominent eosinophilic infiltrate may be highly suggestive of PG. Other histologic findings included dermal edema, mild perivascular inflammation with eosinophils, focal spongiosis, and epidermal ulceration. The histopathologic features of PG may vary greatly depending on the timing of the biopsy and the nature of the primary lesion [13-15]. Therefore, in many PG patients, nondiagnostic histologic findings are expected. Confirmation of the diagnosis depends on additional laboratory studies [16,17].

The diagnosis must be confirmed by direct immunofluorescence examination of a snap-frozen perilesional skin biopsy reveals the linear accumulation of complement C3 in the basement membrane zone at the interface of the epidermis and dermis. Linear IgG positivity is also detected in about 25-50% of the samples, but it is not a criterion for the diagnosis [18-20].

Evolution is cyclical with lesions disappear within weeks or months after delivery and recurrence in

subsequent pregnancies, or sometimes minima during menstruation, during ovulation or during the combined hormonal outlet [21]. Exacerbation in immediate postpartum period is noted in 50 to 75 percent. 100 cases in the literature [22,23] and occurs in 12 to 48 first hours after birth. It was not found in our series. Recurrence is the rule in subsequent pregnancies with more severe and early lesions. However, cases of subsequent pregnancies free of PG outbreaks have been reported [10].

The risk of preterm birth and fetal growth restriction is greater in PG pregnancies compared to normal population [24,25]. The pregnancy risks of PG are thought to be associated with mild placental failure caused by BP180 antibodies [25,26]. In addition to accumulation of C3 complement and IgG, mild villitis and collections of immature fibrotic villi have been observed in histologic examinations of PG placentas [27]. Antibody concentrations do not as such correlate with the occurrence of pregnancy complications, and no association has been demonstrated between cortisone treatment and PG pregnancy complications [25]. No follow-up guidelines for pregnancies complicated by PG have been published, most likely due to the rarity of the condition.

Treatment with corticosteroids is effective in most cases and seems not to have side effects on the fetus. Severe forms most often require systemic corticosteroid therapy at a dose of 0.5 to 1 mg/kg/day [10].

Pauci bullous forms and/or little extended usually respond to topical steroids based on very strong activity dermocorticoids class I [28].

The dapsone may have beneficial effects in combination with corticosteroid treatment and can be prescribed during pregnancy at a dose of 100 to 200 mg/d. [10]

From our study, we particularly emphasize the efficiency of class I corticosteroids in the treatment of PG. We believe that, as in bullous pemphigoid [29] class I topical corticosteroids could be used as first-line to reduce the side effects of corticosteroids while maintaining excellent efficiency.

Finally, we emphasize the fact that the pregnancy of a woman reached with PG should be considered an at-risk pregnancy: obstetric ultrasounds must be of good quality to detect intrauterine growth retardation,

the patient should be followed in center capable of managing premature labor and the newborn should be cared for in a neonatal department.

CONCLUSION

PG is a rare skin disorder in pregnancy. The severe itching and blistering caused by the disease can be quite debilitating. The diagnosis of PG is made in a specialized care setting at a dermatology department. Since PG is associated with a risk of prematurity and fetal growth restriction, pregnancy monitoring by an obstetrician is recommended. Mothers with PG should be informed of the natural course of the disease, good fetal prognosis, the possibility of relapses after delivery, and the risk of relapses in subsequent pregnancies and with hormonal contraception.

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Source of Support: Nil, **Conflict of Interest:** None declared.