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DERMATOSES EM GRÁVIDAS E PUÉRPERAS OBSERVADAS NUM SERVIÇO DE URGÊNCIA – AVALIAÇÃO DE 86 CASOS

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RESUMO – **Introdução**: Além da morbilidade relacionada às lesões cutâneas e prurido, as dermatoses da gravidez causam preocupação psicológica e algumas formas implicam riscos fetais. **Objectivo**: Avaliação do tipo, frequência e características clínicas das dermatoses nas grávidas e puérperas que recorreram ao Serviço de Urgência. **Métodos**: Estudo retrospectivo das dermatoses nas grávidas e puérperas observadas por Dermatologia no Serviço de Urgência entre Setembro de 2006 e Setembro de 2010. **Resultados**: O estudo incluiu 79 grávidas e 7 puérperas, com idade mediana de 33 anos. Foram diagnosticadas dermatoses específicas de gravidez em 42 doentes (48,8%). A forma mais comum foi a erupção polimorfa da gravidez (n=16), seguida por eczema da gravidez (n=12), prurigo da gravidez (n=8), penfigóide gestacional (n=5) e foliculite pruriginosa da gravidez (n=1). Observamos outras dermatoses em 44 doentes (51,2%), incluindo: pitiríase rósea (n=11), infecções e infestações, eczema desidrótico, dermatite de contacto, lúpus eritematoso e pustulose exantemática aguda. Nas dermatoses com apresentação atípica a biópsia ajudou na caracterização da doença. Em 43 casos analisou-se o estado dos recém-nascidos, com registo de parto pré-termo em 3 casos. **Discussão**: As dermatoses específicas de gravidez têm maior tendência de ocorrer na segunda parte da gravidez, especialmente durante o terceiro trimestre. Nas grávidas com lesões cutâneas exuberantes ou atípicas, o estudo laboratorial e histológico é imprescindível para o diagnóstico específico, permitindo abordagem terapêutica adequada e avaliação dos riscos fetais.

PALAVRAS-CHAVE – Doenças da Pele; Prurido; Complicações da Gravidez.

DERMATOSES IN PREGNANT AND POSTPARTUM WOMEN ATTENDING AN EMERGENCY DEPARTMENT – A STUDY OF 86 PATIENTS

ABSTRACT – ***Introduction:*** *Besides morbidity related to skin lesions and pruritus, dermatologic disorders during pregnancy cause psychological concern and some of them carry a fetal risk.* ***Objective:*** *Assessment of the type, frequency and clinical characteristics of the dermatoses seen in pregnant and postpartum women seeking support from the Emergency Department.* ***Methods:*** *Retrospective study of pregnant and postpartum women observed by dermatologists at the Emergency Department between September 2006 and September 2010.* ***Results:*** *The study included 79 pregnant and 7 postpartum women, with a median age of 33 years. Specific dermatoses of pregnancy were diagnosed in 42 patients (48.8%). Polymorphic eruption of pregnancy was the most frequent specific dermatosis (n=16), followed by eczema in pregnancy (n=12), prurigo of pregnancy (n=8), pemphigoid gestationis (n=5), and pruritic foliculitis of pregnancy (n=1). Other dermatoses were diagnosed in 44 patients (51.2%), including: pityriasis rosea (n=11),*

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infections and infestations, dyshidrotic eczema, contact dermatitis, lupus erythematosus and acute generalized exanthematous pustulosis. In the cases with an atypical presentation, the biopsy helped in the characterization of the disease. The fetal outcome was assessed in 43 cases, only 3 cases of preterm delivery being registered. ***Discussion:*** *The onset of the specific dermatoses of pregnancy was more likely to occur in the late pregnancy, especially the third trimester. In pregnant women with exuberant or atypical skin lesions, laboratory and histological study are indispensable for the specific diagnosis, allowing appropriate therapeutic approach and fetal risk assessment.*

KEY-WORDS *– Skin Diseases; Pregnancy Complications; Pruritus.*

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BACKGROUND

The pregnancy state can bring physiological skin changes, specific dermatoses or can influence the course of non-specific skin disorders. The specific dermatoses of pregnancy are a heterogeneous group of pruritic skin diseases that develop during gestation or shortly after delivery. They include the following entities: polymorphic eruption of pregnancy (also called pruritic urticarial papules and plaques of pregnancy), pemphigoid gestationis, eczema of pregnancy, prurigo of pregnancy, pruritic foliculitis of pregnancy and intrahepatic cholestasis of pregnancy[1]. Besides the psychological concern and the morbidity related to skin lesions and pruritus, some of them carry a fetal risk, ranging from small-for-date babies, prematurity and skin lesions in pemphigoid gestationis[2] to stillbirth in the case of intrahepatic cholestasis of pregnancy.

OBJECTIVE

This study aims to evaluate the type and clinical characteristics of the dermatoses seen in pregnant and postpartum women seeking support from the Emergency Department (ED) of a tertiary hospital.

METHODS

The medical records of pregnant and postpartum women observed by dermatologists in the ED of our hospital in a period of four years (September 2006 - September 2010) were retrospectively analyzed. The following data were included: age, parity, history of atopy, onset of lesions (during the pregnancy/postpartum or out of pregnancy), morphology, topography and symptomatology of the lesions, laboratory and histological exams, response to the therapy and neonatal outcome. The patients were divided in two groups: specific dermatoses of pregnancy diagnosed according to the criteria presented in Table 1, and other dermatoses.

Statistical analysis of the data was performed using the *SPSS Statistics 19*. The χ^2-test was used to determine the two-tailed statistical significance of differences between proportions in 2x2 tables (categorical variables). A *p* value of less than 0.05 was considered significant.

Table 1 - Criteria used for the diagnosis of specific dermatoses of pregnancy (adapted from Ambros-Rudolph *et al*[1]). DIF - Direct Immunofluorescence

Pregnancy dermatosis	Diagnostic criteria
Polymorphic eruption of pregnancy	Papulourticarial eruption on trunk and limbs; *striae distensae* involvement; negative DIF
Eczema of pregnancy	Pruritic, mainly flexural eruption; previous or family history of atopy ± high serum IgE
Prurigo of pregnancy	Excoriated papules and nodules on trunk and limbs
Pemphigoid gestationis	Urticarial and bullous eruption; positive DIF (linear deposits of C3± IgG at the dermoepidermal junction)
Pruritic foliculitis of pregnancy	Follicular papulopustular eruption
Intrahepatic cholestasis of pregnancy	Pruritus; elevated liver function tests and serum bile acids

RESULTS

The study included 79 pregnant and seven postpartum women with a median age of 33 years (range 18-41). Most of them were primigravidae (61.6%) and had single gestation pregnancies (97.6%).

In most cases, the specific diagnosis of the dermatosis was based on clinical features and laboratory workup, when needed. Skin biopsy was performed in 11 patients in order to substantiate the clinical diagnosis.

Specific dermatoses of pregnancy were diagnosed in 42 (48.8%) patients with median age of 30 years and other dermatoses were seen in 44 (51.2%) patients with median age of 28 years. In the first group, 59.5% of the women were primigravidae, similar with the proportion in the second group (63.6%). The onset of skin lesions was in the third trimester in the majority (61.9%) of the specific dermatoses cases compared with only 22.7% of the other dermatoses group. This difference was statistically significant (p=0.001). Half of the other dermatoses had the first manifestation in the second trimester.

The specific pregnancy dermatoses observed were: polymorphic eruption of pregnancy (n=16), eczema of pregnancy (n=12), prurigo of pregnancy (n=8), pemphigoid gestationis (n=5), and pruritic foliculitis of pregnancy (n=1). Seven of these patients (three with polymorphic eruption of pregnancy, two with eczema of pregnancy and two with pemphigoid gestationis) presented to the ED between the 4th and the 14th day of postpartum due to exacerbation of the dermatoses which had started in the third trimester.

Among the 16 patients with polymorphic eruption of pregnancy, 12 were primigravidae. The four multiparous did not report similar skin changes during the previous pregnancies. The majority had the onset of the lesions in the third trimester (12 patients), three of them experiencing a worsening in the postpartum period. The eruption was characterized by urticarial papules and plaques (mostly), with the presence of vesicular and polycyclic lesions and caused moderately to intense pruritus. It began on the distended skin of the abdomen, thighs and breasts, particularly affecting the *striae distensae*, and then spread to the other parts of the body, spearing the periumbilical region (Fig. 1). The complete blood count and serum chemistries were normal in all of the seven patients tested. A skin biopsy was performed in three cases showing alterations of the dermis with moderate perivascular lymphocytic infiltrate and participation of neutrophils and eosinophils (Fig. 2) and negative DIF.

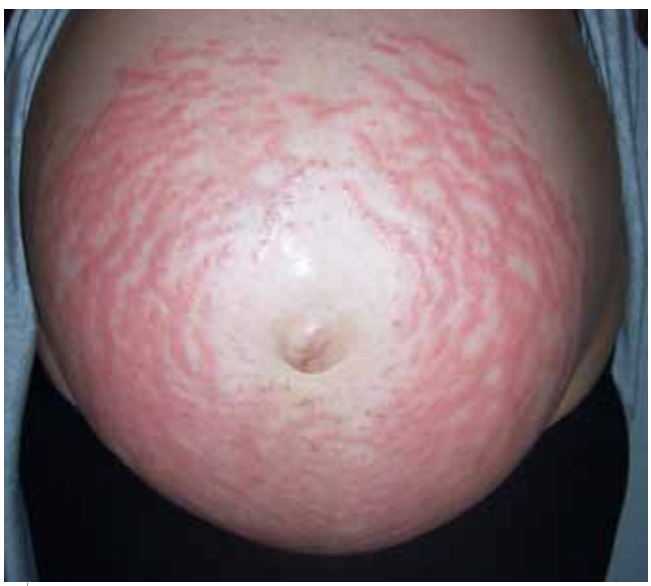

Fig. 1 - Polymorphic eruption of pregnancy. Urticarial plaques affecting the striae distensae and spearing the periumbilical region.

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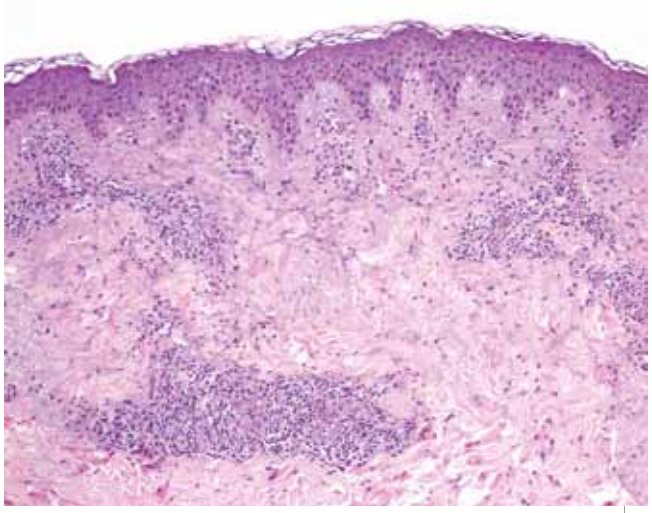

Fig. 2 - Polymorphic eruption of pregnancy. Skin biopsy showing moderate perivascular lymphocytic infiltrate with participation of neutrophils and eosinophils.

Eczema of pregnancy was found in 12 patients, nine of them being primigravidae. The three multiparous did not refer similar skin changes during the previous pregnancies. The gestational age at the onset varied, with one patient in the first trimester, 6 in the second and 5 in the third. Nine patients had the first manifestation of the atopic dermatitis during the pregnancy, while 3 had prior atopic eczema with an exacerbation during the pregnancy. In 8 patients there was either a personal or family (first-degree relative) history of atopy (eczema, asthma, allergic rhinitis). Four patients had no prior history or family history of an atopic disease but were included due to the typical lesions. The clinical presentation consisted of a pruritic, predominantly flexural eruption. Laboratory work-up including CBC and serum chemistries was performed in 4 patients, with no alteration except eosinophilia (1920/mm^3) in one pregnant woman with generalized eczema. On the histopathology of the skin fragment irregular achantosis and parakeratosis, spongiosis and dermal lymphocytic infiltrate were evident.

There were 8 women with prurigo of pregnancy, five of them multiparous, not reporting similar lesions previously. The skin changes started generally lately in pregnancy, with second trimester onset in 4 patients, and third trimester in 4 patients, one of which had an exacerbation in postpartum. The clinical picture was characterized by excoriated papules and nodules distributed on trunk, arms and legs, with a predilection for the extensor surfaces. Laboratory work-up was performed in 5 cases, with no alterations of the complete blood count and serum chemistries. Skin biopsy was made in one case, showing unspecific changes. Four of the patients had an associated condition: diabetes *mellitus*, asthma, nephrolithiasis, and anxiety disorder.

Pemphigoid gestationis was diagnosed in five patients and four of them were multiparous. A history of bullous dermatosis in previous pregnancies was present in two cases. The lesions had the onset in the second trimester in one case and in the third trimester in the other four, two of them manifesting a flare in postpartum. The clinical picture started with pruritic urticarial plaques on limbs or trunk, commonly involving the periumbilical area (three cases) (Fig. 3). Rapidly after, tense bullae (Fig. 4) appeared in four of the patients with palmo-plantar involvement in two women, but no mucosal lesions. Of note, in the two cases with a history of bullous lesions during a prior pregnancy, the current clinical expression was more severe than previously and occurred earlier in the gestation comparing with the two multiparous without prior lesions (mean gestational age 22.5 weeks and 32 weeks respectively). All the patients had peripheral eosinophilia (710-1040/mm^3) and four patients had circulating anti--basement membrane antibodies. The biopsy performed in all cases showed a subepidermal separation with eosinophilic infiltrate (Fig. 5) and positive DIF (linear deposits of C3± IgG at the dermoepidermal junction).

Pruritic foliculitis of pregnancy was diagnosed in a multiparous woman with follicular pruritic papulo--pustules of the scalp, starting on the second trimester.

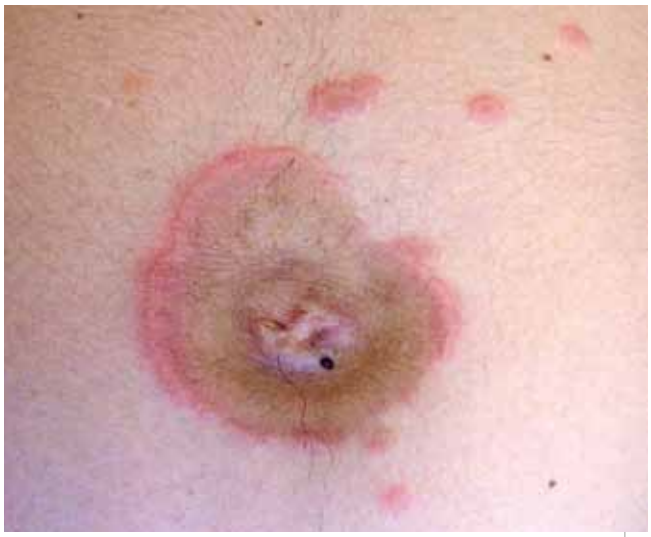

Fig. 3 - Pemphigoid gestationis. Urticarial plaques involving the periumbilical area.

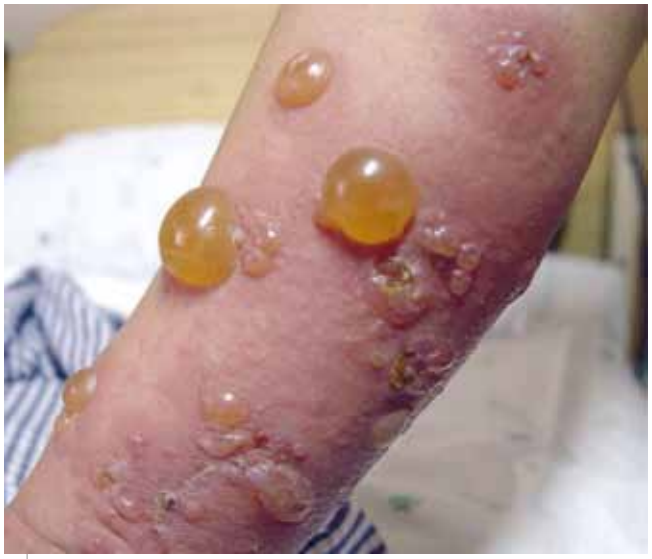

Fig. 4 - Pemphigoid gestationis. Tense bullae on the arm of a pregnant woman.

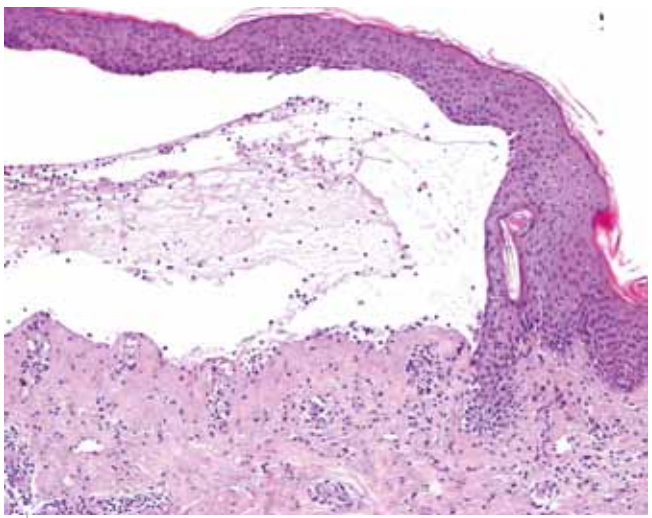

Fig. 5 - Pemphigoid gestationis. Skin biopsy showing subepidermal separation with eosinophilic infiltrate.

Concerning the treatment, in most of the cases of specific dermatoses of pregnancy the skin lesions and symptoms were controlled with topical medium-high potency corticosteroids, oral anti-histaminic drugs (loratadine, hydroxyzine, cetirizine) and emollients. Four of the five patients with pemphigoid gestationis received oral prednisolone (0.6-1mg/kg) with slow tapering and then topical steroid application until two to four weeks postpartum. One patient was treated successfully with potent topical corticosteroid alone (betamethasone dipropionate 0.05% cream). Oral steroid was necessary in a case of generalized eczema and UVB phototherapy was used for the disease control in a case of prurigo of pregnancy with doses of 0.4-1 j/cm^2 in 10 sessions (three before and seven after delivery).

Other dermatoses were seen in 44 patients and are presented in Table 2.

Table 2 - Other dermatoses diagnosed in pregnant women in our study

Other dermatoses	Number of patients
Inflammatory disorders	**29**
Pityriasis rosea	11
Contact dermatitis	3
Dyshidrotic eczema	3
Polymorphic light eruption	3
Psoriasis	2
Rosacea	2
Seborrheic dermatitis	2
Urticaria	2
Systemic lupus erythematosus	1
Infections and infestations	**7**
Herpes simplex	2
Herpes zoster	1
Molluscum contagiosum	1
Impetigo	1
Scabies	2
Drug reactions	**1**
Acute generalized exanthematic pustulosis	1
Others	**7**
Arthropod bite	2
Pyogenic granuloma	2
Epidermoid cyst	1
Acrochordon	1
Miliaria	1

Pityriasis rosea was the most frequent disorder in this group, with 11 patients. The onset was in the second trimester in four cases and in the third trimester in seven. An atypical form of pityriasis rosea was registered in a 32 years old pregnant woman who had two episodes of fever and erythematous scaly plaques on the trunk, neck and upper limbs at seven and nine weeks of gestation. The biopsy was consistent with pityriasis rosea and the search of Human Herpesvirus 7 by PCR was positive in the skin fragment. The lesions resolved completely after seven weeks. Polyhydramnios was found in the third trimester. The histology of the placenta showed lymphohistiocytic villitis. The newborn was normal.

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Systemic lupus erythematosus was diagnosed in a previously healthy 27-year-old primigravida with red-violaceous plaques on the face (Fig. 6) and brain hemorrhage occurring in the second trimester, together with laboratory findings of anemia, leucopenia and elevated antinuclear antibodies (ANA) titer (1/1000). After the delivery the skin lesions subsided but the elevation of the ANA persisted, with no other clinical manifestation during the two years of follow-up. No clinical or laboratory signs of neonatal lupus was registered.

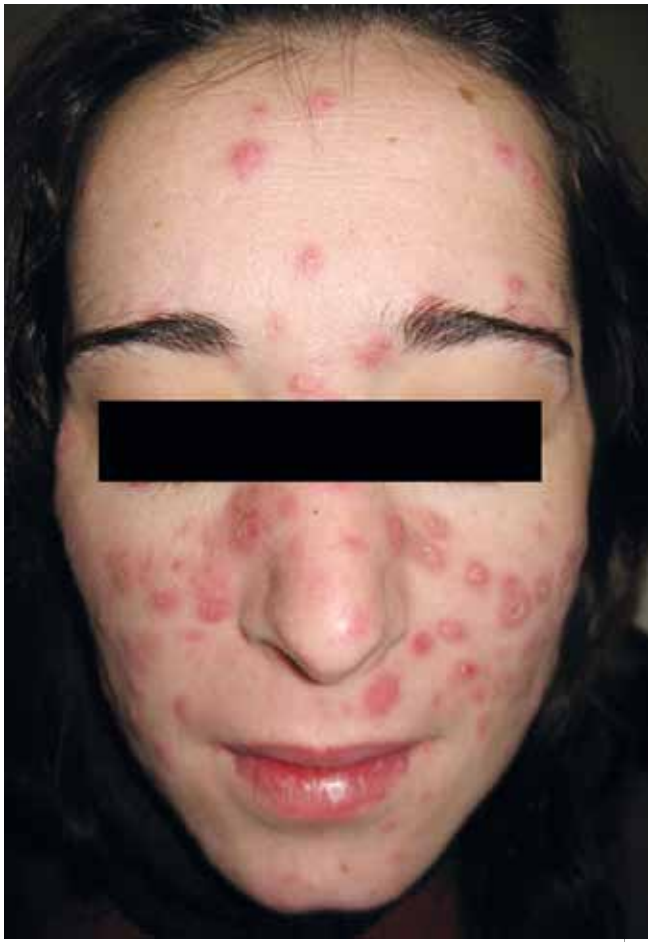

Fig. 6 - Lupus erythematosus. Red-violaceous desquamative plaques on the face.

Data about newborn were available in 42 cases. Three cases of preterm delivery were recorded; two of them in twin pregnancies (one patient with polymorphic eruption of pregnancy and another with eczema) and another one in the patient with systemic lupus erythematosus.

DISCUSSION

The terminology and classification of the specific dermatoses of pregnancy was a matter of debate along the years. A newly proposed classification by Ambros-Rudolph *et al*[1] refers to the entities presented in Table 1.

The estimated incidence ranges from of 1 per 130 to 1 per 300 pregnancies in polymorphic eruption of pregnancy, from 1 per 300 to 1 per 450 in prurigo of pregnancy, from 1 per 10000 to 1 per 50000 in pemphigoid gestationis and is about 70 per 10000 pregnancies in intrahepatic cholestasis of pregnancy[3].

The present study includes patients observed by dermatologists at an ED, which is the main form of pregnant women referral, and does not embrace the patients sent by general practitioners or obstetricians under general ambulatory regimen.

In our study, specific dermatoses of pregnancy were found in almost half (48.8%) of the pregnant women seeking support from the ED for dermatologic complaints. Comparing with the group of other dermatoses, their onset was more likely to occur in the late pregnancy, especially third trimester, consistent with previously published data[3]. No significant difference was found concerning the median age or parity of the women in the two groups.

Polymorphic eruption of pregnancy was the most frequent specific dermatosis in our study (16 patients), followed by eczema in pregnancy (12 patients). Polimorphic eruption of pregnancy is classically considered the most common specific dermatosis of pregnancy[4] and occurs predominantly in primigravidae during the third trimester as we also verified in this study. Some authors suggested that rapid abdominal wall distension in primigravidae may cause damage of the connective tissue in the *striae distensae* triggering an inflammatory process[5].

Two new studies recognized eczema of pregnancy as the most frequent dermatosis of pregnancy[1,6]. As atopic dermatitis overall is considered to be a T-helper-2 (Th2) dominant disease,[7] it was postulated that the Th2 shift associated with pregnancy may favor its exacerbation.[1] Most of our patients had a history of atopy and 75% of them had the first manifestation of the eczema during pregnancy, similarly to other published data[6].

The proportion of pemphigoid gestationis cases (5.8%) was relatively high for this patient' series, being possible related to ED referral of the bullous dermatoses.

No case of intrahepatic cholestasis of pregnancy was registered in our study, probably due to the low incidence of this disorder and to the relatively small sample of patients. Moreover, the lack of primary cutaneous lesions may lead to a reduced referral to Dermatology.

Onset of the skin lesions in postpartum is rare in polymorphic eruption of pregnancy but is reported in 20% of the cases in pemphioid gestationis[3]. Flare at the time of delivery is considered a typical feature in pemphioid gestationis, as it may be seen in up to 75% of the patients[8,9]. Seven patients with specific dermatoses of pregnancy had a postpartum worsening of the skin lesions in our study. This underlines the importance of considering the diagnosis of pregnancy dermatoses if the patients present with a compatible clinical picture in the first month after delivery, in order to make the appropriate treatment and counseling.

Pemphigoid gestationis often occurs in subsequent pregnancies, appearing earlier in gestation and in a more severe form[10], as we verified in two of the four multiparous patients. This is probably related to the re--exposure to the placental (paternal) antigens, with the subsequent production of anti-placental antibodies that cross-react with the same proteins in skin[11].

The management of the pregnancy dermatoses consists of controlling the skin lesions and pruritus and counseling regarding the prognosis.

Mild (face, intetriginous areas) or moderate (rest of the body) topical corticosteroids may be used, while uncontrolled long-term use of potent corticosteroids should be avoided[12]. When systemic corticosteroids treatment is needed (pemphigoid gestationis, severe cases of polymorphic eruption of pregnancy, eczema or prurigo), prednisolone is the choice, usually in a short-course therapy (<4 weeks), with an initial dose of 0.5-2mg/kg/day and then tapering[13]. Oral antihistamines may be used for the control of pruritus. Older substances (dimethindene, clemastine) are preferable in the first trimester due to the greater experience[13]. Loratadine and cetirizine can be administrated in the second and third trimesters[14].

In our study, oral prednisolone was necessary in four of the five cases of pemphigoid gestationis and in one case of eczema, while topical corticosteroids with or without oral antihistamines were sufficient for the symptoms control in the other patients.

The prognosis of pregnancy dermatoses is generally good. The lesions usually improve significantly with treatment and resolve after delivery. They may recur in subsequent pregnancies. Pemphigoid gestationis and intrahepatic cholestasis of pregnancy may be associated with fetal risk, but the other pregnancy dermatoses do not seem to impair the fetal prognosis. Pemphigoid gestationis is associated with an increase in prematurity and small-for-gestational-age infants[2]. Due to the passive transfer of the antibodies from the mother to the fetus, 10% of the newborn develop mild skin lesions that resolve spontaneously within days to weeks[15]. Intrahepatic cholestasis of pregnancy is associated with an increased risk of prematurity (19-60%), peripartum fetal distress (22-33%) and stillbirth (1-2%)[16]. The overall fetal mortality was <5% in a study of 200 women with dermatoses of pregnancy[2]. The fetal outcome in our study was favorable with no mortality and only 3 cases of preterm delivery in two twin pregnancies, probably not related to the dermatoses, and in the patient with systemic lupus erythematosus.

Regarding the group of other dermatoses, besides coincident disorders, the study also included a case of lupus erythemathosus flare and two cases of pyogenic granuloma, known to have an increased incidence during pregnancy, probably related to hormonal changes. Pitiryasis rosea was found in a representative number (n=11) of patients, with an atypical presentation in one case. Besides having a higher incidence during pregnancy, pitiryasis rosea may be related to prematurity and abortion[17], but its management is a matter to be defined.

The history and physical assessment are important in recognizing specific dermatoses of pregnancy and disorders whose course may influence the gestation. In pregnant women with exuberant or atypical skin lesions, laboratory and histological studies are essential for the specific diagnosis, allowing appropriate therapeutic approach and fetal risk assessment.

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