Herpes gestationis, also known as pemphigoid gestationis (PG) is an extremely rare autoimmune bullous dermatosis of the gestation and postpartum period. The disease was originally named herpes gestationis on the basis of the morphological herpetiform feature of the blisters. We report a 21-year-old woman, pregnant in the third trimester, who presented with a pruritic bullous cutaneous eruption of two weeks duration. The disease started with a red plaque in the abdominal area accompanied by mild itching. Soon after, blisters appeared and affected almost the entire body. Physical examination revealed a primiparous woman in good general state, pregnant in 36 weeks of gestation. The skin changes affected the abdomen, back of the trunk, upper and lower extremities, hands and feet. They were manifested by a polymorphous eruption, consisting of erythematous urticaria-like plaques, small tense vesicles and multiple excoriations. Mucous membranes were not affected. Routine laboratory examinations were within normal limits. Direct immunofluorescence (DIF) on perilesional skin showed linear deposition of IgG (++) and C3 (++) at the cutaneous basement membrane zone (BMZ). Indirect immunofluorescence (IIF) on human esophagus substrate revealed circulating IgG anti-BMZ antibodies at a titer of 1:80. ELISABP180 NC16A was strongly positive. The diagnosis of PG was confirmed and a treatment with systemic methylprednisolone 60 mg/day was initiated, later gradually tapered to 20 mg/day, together with topical corticosteroids. As a result on the 10th day of the treatment with reduction of erythema and itching, absence of new skin lesions. Significant improvement was achieved about the 10th day of the treatment with reduction of erythema and itching and absence of new skin lesions (Fig. 5a, b). The pregnancy ended in term with successful childbirth. A healthy female newborn with anthropometric parameters within the normal ranges was born. No flare of the skin disease was observed in the puerperal period.

Key word: Pemphigoid gestationis, herpes gestationis, pregnancy, direct and indirect immunofluorescence, methylprednisolone.

INTRODUCTION:

Herpes gestationis (HG), currently known as pemphigoid gestationis (PG), is a rare autoimmune blistering dermatosis of pregnancy with an incidence ranging up to 1:50 000 pregnancies.[1] The term PG was introduced by Holmes and Black in 1982 and is largely used in Europe but in the USA the former name HGIs still preferred.[2, 3] PG typically affects pregnant women in the second or third trimester but may appear at any time during pregnancy or even during the immediate postpartum period.

CASE REPORT:

We present a 21-year-old woman pregnant in the third trimester. The disease started two weeks before her admission in the Department of dermatology with red plaques on the abdominal skin, around the umbilicus, accompanied by itching. Soon after, blisters appeared on this background and quickly spread to affect almost the entire body. The physical examination revealed a woman in good general condition, afebrile, pregnant at 36 weeks of gestation. Cardiovascular and respiratory systems were without pathological changes - blood pressure 120/70 mmHg, heart rate 80 beats/min. The neurological status was normal. The dermatological examination found pathological skin changes affecting the skin of the abdomen, the back, upper and lower extremities, hands and feet. The eruption consisted of erythematous, urticaria-like plaques with small tense vesicles upon them and multiple excoriation. (Fig. 1a, b) The mucous membranes and skin appendages were not affected. Routine laboratory investigations were within normal limits. Histological examination of a biopsy specimen from a fresh vesicular lesion showed edema in the dermis, mixed perivascular inflammatory infiltrate with a predominance of eosinophils (Fig. 2). Direct immunofluorescence (DIF) on perilesional skin showed linear deposition of IgG (+++) and C3 (+++) at the cutaneous basement membrane zone (BMZ) (Fig. 3). Indirect immunofluorescence (IIF) on human esophagus substrate revealed circulating IgG anti-BMZ antibodies at a titer of 1:80 (Fig. 4). ELISABP180NC16A (ELISA kit, MBL, Nagoya, Japan) was strongly positive - 88.2 U/ml (cut off <9 negative; ≥ 9 positive). Based on the data from the medical history, the clinical features and the results from the laboratory studies, the diagnosis PG was confirmed. Treatment with systemic methylprednisolone 60 mg/day was initiated, later gradually tapered to 20 mg/day, together with topical corticosteroids. Significant improvement was achieved about the 10th day of the treatment with reduction of erythema and itching and absence of new skin lesions (Fig. 5a, b). The pregnancy ended in term with successful childbirth. A healthy female newborn with anthropometric parameters within the normal ranges was born. No flare of the skin disease was observed in the puerperal period.
Fig. 2. Histopathology: A marked edema, with a dense inflammatory infiltrate (predominantly with eosinophils) in the dermis.

Fig. 1a, b. Confluent urticaria-like plaques covered with tense vesicules and excoriations on the abdomen and back of the trunk.

Fig. 3. Direct immunofluorescence (DIF) on perilesional skin: linear deposition of IgG (+++) and C3 (++) at the cutaneous basement membrane zone (BMZ).

Fig. 4. Indirect immunofluorescence (IIF) on human esophagus substrate: circulating IgG anti-BMZ antibodies at a titer of 1:80.
DISCUSSION:

PG is a self-limiting, autoimmune subepidermal bullous dermatosis of pregnancy. Its pathogenic mechanism remains unclear but is considered to result from lack of recognition of the fetoplacental unit by the maternal immune system. This leads to subsequent production of anti-placental antibodies. Similarly to bullous pemphigoid, the main target antigen in PG is BP antigen II (also known as BP180), in particular its non-collagenous 16A (NC16A) domain, which is constituent of both the placenta and the skin. The skin pathology in PG results from the ability of the anti-placental antibodies to cross-react with the same proteins of the skin. Blister formation results from a complex mechanism involving TH2 lymphocytes, cytokines and polymorphonuclear cells.[4, 5, 6] PG has also been reported in association with MHC class II HLA antigens DR3 and DR4.[1] The disease usually starts in the second or third trimester of pregnancy and is characterized with an acute onset of erythematous, urticarial papules and plaques that progress to tense vesicles and blisters, followed by severe pruritus. The lesions usually arise on the abdomen, often involving the umbilicus, and spread centrifugally. Recovery occurs generally in a few weeks after delivery but relapses are frequent in subsequent pregnancies.[7, 8] The diagnosis of PG relies on the appropriate clinical presentation, the histologic findings of a subepidermal blistering and linear C3 deposition along the BMZ, with or without deposition of IgG on DIF. ELISA BP180NC16A may be very useful in such cases due to its high sensitivity to detect circulating auto-antibodies against NC16A domain of BP180, which is the major antigenic epitope in PG.[9]

The treatment of PG depends on the severity of the disease. Mild cases may be treated with topical corticosteroids and oral antihistamines. Potent topical glucocorticoids and oral corticosteroids (prednisone 0.5-1 mg/kg/day) are reserved for more serious cases.[1] Several cases resistant to corticosteroid therapy have been described, but successfully treated with intravenous immunoglobulin and azathioprine or with adjuvant immunoadsorption.[10, 11, 12] Fetal prognosis is good, but early onset in 2nd trimester and blister formation are risk factors for prematurity and low birth weight. Rarely the newborn may be affected by very transitory blisters.[7]

In our case, clinical suspicion of PG was confirmed by DIF and IIF findings, as well as by ELISA BP180NC16A, the latter being strongly positive. Systemic treatment with methylprednisolone (0.5mg/kg/day) was initiated during the pregnancy with gradual clinical improvement until delivery. A healthy asymptomatic infant was born in term without cutaneous lesions. To date the patient has not reported a flare.

CONCLUSION

The presented case highlights the importance of a timely clinical and immunohistological diagnosis of PG. Differentiation of PG from other conditions like pruritic urticarial papules and plaques of pregnancy (PUPPP) is essential because management and outcomes differ. In cases in which the clinical diagnosis is difficult, immunofluores-
cience tests and ELISA studies for anti-BMZ antibodies are useful in establishing the diagnosis. An interdisciplinary approach is also of crucial importance for the benefit of the mother and child during pregnancy, as well as during the postpartum period.

REFERENCES:


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