Pemphigoid gestationis – a rare dermatosis of the prenatal period. Case report

Pemfigoid ciężarnych – rzadka dermatoza okresu prenatalnego. Opis przypadku

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SŁOWA KLUCZOWE: pemfigoid ciężarnych, opryszczka ciążowa, dermatozy ciążowe.

ABSTRACT

Introduction. Most skin lesions during pregnancy are associated with hormonal changes. Pemphigoid (herpes) gestationis (PG) is a significant dermatosis of the prenatal period reflecting pathology affecting the mother and fetus.

Objective. The aim of the study was to present a PG case, a rare pregnancy dermatosis with a severe clinical outcome during the postpartum period.

Case report. We present a case of a patient in whom skin lesions with tense blisters occurred at the 40th week of pregnancy. Herpes gestationis – a rare skin disease – was diagnosed based on the clinical picture. During the first days of puerperium, because of an aggressive disease course, the patient was transferred to a reference centre for skin disease treatment. She was given corticosteroid therapy, which brought the expected results.

Conclusions. Pemphigoid gestationis is a rare and serious dermatosis of the prenatal period. Although the treatment of such diseases is the dermatologists’ task, obstetricians are responsible for diagnosis and for fetal monitoring considering placental pathology.

STRESZCZENIE

Wprowadzenie. Większość zmian skórnych w okresie ciąży wiąże się ze zmianami gospodarki hormonalnej. Pemfigoid (opryszczka) ciężarnych jest ważną dermatozą okresu prenatalnego odzwierciedlającą patologię toczącą się w jednostce matczyno-plodowej.

Cel pracy. Przedstawienie przypadku pemfigoidu ciężarnych, rzadkiej dermatozy ciążowej, o ciężkim przebiegu klinicznym w okresie połogu.

Opis przypadku. Przedstawiamy przypadek pacjentki, u której w 40. tygodniu ciąży zaobserwowano zmiany skórne w postaci napiętych pęcherzy, co pozwoliło na podstawie obrazu klinicznego rozpoznać rzadką chorobę skóry, jaką jest opryszczka ciężarnych. W pierwszych dniach połogu ze względu na agresywny przebieg choroby pacjentka została przekazana do ośrodka referencyjnego leczenia chorób skóry. Zastosowana tam terapia glikokortykosteroidami przyniosła zamierzony efekt.

Wnioski. Pemfigoid ciężarnych jest rzadką dermatozą okresu prenatalnego, której terapię prowadzą dermatolodzy, a zadaniem położników jest rozpoznawanie choroby i monitorowanie stanu płodu z uwzględnieniem faktu patologii łożyska.
INTRODUCTION

The generally accepted classification suggested by Ambros-Rudolph et al. [1] is used to describe skin diseases typical for pregnancy. It includes the characteristics of all types of dermatoses occurring only during pregnancy, i.e. prurigo of pregnancy, polymorphic eruption of pregnancy, pemphigoid gestationis (PG), and intrahepatic cholestasis of pregnancy [1].

Most pregnancy-specific skin conditions have no clinical significance and are associated with physiological insulinemia, as well as an increase in estrogen, progesterone and melanotropin concentrations [2].

Physiological changes in the prenatal period include the following:
- skin pigmentation in the area of the nipples and areola (at about 20 weeks of gestation), underarms, and external genital organs,
- linea nigra,
- melasma (on the forehead, cheeks and the lower jaw),
- connective tissue changes such as striae distensae and skin polyps [3, 4].

The majority of these changes may be reversible, to a certain extent, after delivery. Vascular changes, which are partially caused by increased estrogen levels, are the effect of widening of the blood vessels, their instability, and capillary proliferation occurring on the skin surface. Telangiectasias are more noticeable in women with a fair complexion and occur preferentially around the eyes, on the neck, on the chest, and on the upper limbs.

Exacerbation of these changes occurs in the second trimester of pregnancy and disappears about 2 months after postpartum [5]. Some skin lesions which occur in pregnant women may reflect complications of the prenatal period such as intrauterine growth restriction (IUGR), the risk of premature delivery, or even intrauterine fetal death. Therefore, it is crucial to diagnose dermatoses such as intrahepatic cholestasis of pregnancy or bullous pemphigoid in pregnancy, which is also known as herpes gestationis, to assure proper care of pregnant women. Pemphigoid gestationis occurs relatively rarely, with the estimated incidence of 1/700 to 1/50 000 pregnancies, according to different sources. The changes develop dominantly in the pre-delivery period. However, blistering is present in about 75% of the patients during delivery. Skin changes disappear after about 2–6 weeks postpartum in the majority of affected patients. Dermatosis is a recurrent disease; it can occur in subsequent pregnancies and run a more severe course. Menstruation and hormonal contraception are among other provoking factors [12]. A correlation has been found between the presence of PG and IUGR. Data on such correlation are of low diagnostic value, but they indicate the need for careful fetal monitoring in that group of patients [13].

Moreover, inflammatory processes in the skin also affect the placental tissue. They are probably the reason for IUGR and can lead to all the consequences associated with this disorder [14].

A similar rash occurring immediately after the delivery can be observed in about 10% of infants born to mothers with PG, as a result of passive transfer of the antibodies from the mother [15]. Pemphigoid gestationis occurs with other autoimmune diseases such as Graves’ disease. Therefore, thyroid function tests are recommended in this group of patients [16].

Pemphigoid gestationis is etiologically an autoimmune disease, and its association with HLA-DR3 and HLA-DR4 haplotypes has been proven. Due to the fact that early clinical diagnosis presents a certain challenge, skin biopsy is helpful but direct immunofluorescence test (DIF) is necessary to make the final diagnosis. The material undergoes pathomorphological examination and the DIF test is performed. In a typical course of the disease, cell degeneration of the stratum basale (the cause of blistering) and epidermal spongiosis are found in microscopic analysis. Deposits of the C3 component of complement along the basement membrane are observed in the DIF test. Complement binding IgG antibodies occur in half of the affected patients [7].

The indirect immunofluorescence test (IIF) of blood or the fluid obtained from the changes shows the presence of IgG antibodies directed against bullous pemphigoid antigen 2, which is located on hemidesmosomes along the basement membrane [8].

Treatment during pregnancy relies on reduction of change intensification and is most often individualized. If the locally acting drugs are ineffective, intravenous pharmacotherapy should be initiated, the base of which, apart from histamine antagonists, are corticosteroids. Ciclosporin, which seems safe for the fetus, has also been approved for PG treatment, but it cannot be used during lactation [9, 10]. Prednisolone, the safest of the corticosteroids, is subject to almost complete placental metabolism [11].

The disease has periods of remission and exacerbation. Regression of the changes is observed predominantly in the pre-delivery period. However, blistering is present in about 75% of the patients during delivery. Skin changes disappear after about 2–6 weeks postpartum in the majority of affected patients. Dermatosis is a recurrent disease; it can occur in subsequent pregnancies and run a more severe course. Menstruation and hormonal contraception are among other provoking factors [12]. A correlation has been found between the presence of PG and IUGR. Data on such correlation are of low diagnostic value, but they indicate the need for careful fetal monitoring in that group of patients [13].

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CASE REPORT

The patient, at 37 weeks of gestation, was admitted to the Department of Pathology of Pregnancy due to intense skin pruritus and rash around the navel. Based on the data gathered during the interview, the course of pregnancy was assessed as physiological. In the differential diagnosis of the above ailments, intrahepatic cholestasis of pregnancy and polymorphic eruption of pregnancy were distinguished. In the performed laboratory tests, significant aberrations were not observed. In the IF test an elevated titer (1:160) of antinuclear antibody with a coarse speckled pattern was detected.

Second-generation antihistamines were administered due to persistent pruritus, improving the general condition of the patient. Fetal ultrasound (biophysical profile, Doppler ultrasound test) was normal. The patient was discharged from the hospital.

The patient was readmitted at 40 weeks of gestation due to intensified pruritus and the presence of an erythematous papular rash on the abdomen and small blisters on the upper limbs (Figures 1 A, B). Pemphigoid gestationis was suspected after consultation with a dermatologist. As the disease is associated with placental pathology, labor was induced. Cesarean section was performed due to abnormal cardiotocography. A male infant (weight 3380 g, Apgar scores of 9) was delivered.

A few hours after the operation, progression of skin lesions, with intense pain and pruritus, was observed (Figure 2). Systemic corticosteroid therapy (prednisone 30 mg/day; dexamethasone 12 mg/day), calcium carbonate and antibiotic therapy resulted in slight alleviation of the symptoms. Lactation was inhibited. During postoperative day 1, blisters (1 cm in diameter) occurred and were located mainly on the medial thighs and the forearms (Figures 3 and 4 A, B). The therapy proved ineffective, and therefore, on postoperative day 5, the patient was transferred to the reference center for treating skin diseases. Herpes gestationis was clinically diagnosed at the Department of Dermatology. Skin biopsy was performed and treatment including methylprednisolone (48 mg/day for 4 days), cefuroxime (3 g/day for 10 days), antianemic drugs and anticoagulants was initiated. The IIF test was negative.

Skin lesions were treated topically with hydrocortisone, oxytetracycline hydrochloride, and clobetasol propionate, resulting in gradual regression of lesions and general improvement of the patient’s condition. The puerperium during the dermatosis treatment was otherwise uneventful. On day 13 of hospitalization, the general condition of the patient was good and she was discharged from hospital. The patient was advised to continue treatment with...
methylprednisolone for 5 days, with gradual dose reduction under ambulatory control of the clinical state. Antianemic drugs and topical application of chloramphenicol ointment were also recommended. Histopathological results of the biopsy confirmed the initial clinical diagnosis, i.e. herpes gestationis. IgG and IgA deposits at the basement membrane zone (+BMZ) and in the same location abundant deposits of complement component C3 (+++BMZ) were found in tissue examination by DIF test in the biopsy of healthy skin near the skin lesion.

DISCUSSION

Skin lesions, which occur in a normal pregnancy, are usually associated with physiological insulin resistance and hyperestrogenism [2]. Also, they are sometimes symptoms of pregnancy-specific diseases.

Pemphigoid gestationis, which frequently occurs with IUGR, is an inflammatory process occurring not only in the skin but also in the trophoblastic tissue. The IUGR is defined as fetal growth below the expected genetic potential. It results in a significant increase in perinatal mortality and vascular complications such as stroke and myocardial infarction in adulthood. Insufficient fetal development in the dermatosis is associated with placental vascular pathology. The inflammation in the trophoblastic tissue can lead to infarcts and calcification, which can inhibit nutrient exchange between the mother and the fetus [17]. In the present case, early stages of the dermatosis were not typical and were suggestive of intrahepatic cholestasis of pregnancy. They resolved after treatment with ursodeoxycholic acid, which not only alleviates clinical symptoms but also reduces the risk of fetal complications [18]. Exacerbation of the disease occurred just after delivery and took an aggressive course. The symptomatic treatment proved ineffective. Therapy with high doses of steroids was initiated in the reference center for treatment of dermatosis and brought the expected, satisfactory effects. Corticosteroids must be used carefully because they can increase the risk of osteoporosis in pregnant patients. Therefore, it is recommended to conduct the symptomatic treatment using topical therapy. In order to alleviate the symptoms, first-generation or second-generation antihistamines such as cetirizine or loratadine (which are classified in category B according to the FDA) should be administered. The only side effect of loratadine may be rarely occurring hypospadias [19–23].

In case of an aggressive course of disease, individually adjusted prednisolone dosing should be administered (it is most often 0.5 mg/kg/body weight reducing the dose by 5 mg every 3 days), because it is safe for the fetus and entirely metabolized by the human placenta [15]. If escalating the dose above 7.5 mg is necessary, it is recommended to monitor kidney functions and blood pressure. Since more severe disease symptoms can occur before delivery, it is recommended to increase the dose 7 days before the due date. Broad-spectrum antibiotic therapy should be implemented. Ciclosporin is a safe medication in the therapy for pregnant women [9] but it is contraindicated during lactation due to possible immunosuppressive activity and possible induction of neutropenia [10]. During puerperium immunosuppressive medications can be used and plasmapheresis can be performed [24].

The patient remains under dermatological and gynecological ambulatory care in a hospital outpatient clinic. Pruritus occurs in the area of the navel and on the medial compartment of both thighs before and during menstruation. Neurotic excoriations on the skin have been noted.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

References


