Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/14491
DOI URL: http://dx.doi.org/10.21474/IJAR01/14491

RESEARCH ARTICLE

PEMPHIGOID GESTATIONIS : CASE REPORT AND REVIEW OF LITTERATURE

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Manuscript Info

Manuscript History
Received: 25 January 2022
Final Accepted: 28 February 2022
Published: March 2022

Abstract

Pemphigoid gestationis (PG) is a rare autoimmune bullous dermatosis associated with pregnancy. Its previous designation, herpes gestationis, is obsolete. PG is characterized by a subepidermic separation induced by the presence of peripheral blood autoantibodies against two hemidesmosomal antigens: BPAG1 and BPAG2. Clinical diagnosis is confirmed by histology and positive cutaneous immunofluorescence tests. The most discriminant examination for other pruritic dermatoses of pregnancy is the enzyme-linked immunosorbent assay (Elisa) NC16A BP 180. First-line treatment is local corticosteroid therapy; if local treatment fails, general corticosteroid therapy should be administered. The prognosis is good for mother and child, except that there is a risk of preterm delivery and of moderate fetal growth restriction. Management in a specialized setting is therefore necessary. Recurrence is possible during subsequent pregnancies. We report a case of PG identified in our department, with a review of literature about physiopathology, diagnosis and treatment of this rare pathology.

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Introduction:-

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. (1-2)

The dermatosis was originally named “herpes gestationis” by Milton in 18721 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.(3)

It is believed to result from a breakdown of the immunological tolerance of the mother to the fetoplacental unit resulting in autoantibodies to the main target antigen collagen XVII (BP180), which is presented to the maternal immune system by aberrantly expressed human leucocyte antigen (HLA) class II molecules in the placenta.(4)

If the maternal and fetal prognosis is usually good, diagnosis and therapy are a specialized management.

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Observation:-

A 32-year-old woman with no significant pathological history, gravida 3 para 3 with 2 live children. G1: caesarean section performed for transverse fetal lie, birth weight 3200g, good psychomotor development. G2: vaginal delivery, birth weight 2800g, good psychomotor development. G3: third pregnancypresented seven months into pregnancy with a 2 month history of pruritus and fluid-filled bullae on extremities, chest, back and abdomen. (Figure 1)The rash had spread and the itch was interfering with her sleep. She was otherwise healthy and had no complications during pregnancy. Medical and family histories were negative for any dermatologic or autoimmune disease. Examination revealed multiple, annular, erythematous papules and plaques on abdomen, back, arms and legs and a few large bullae, particularly on the right forearm. No mucosal lesions noted. A biopsy was obtained from one of the bullae with routine hematoxylineosin staining showing mixed dermatitis rich in eosinophils consistent with pemphigoid gestationis. Direct immunofluorescence was positive for IgG and C3 in a linear pattern along the basal membrane of the epidermis. The treatment she received is oral and topical corticosteroids during all the pregnancy. The patient gave birth at 36 SA. Lesions and pruritus disappeared a few months after delivery. The newborn has been examined at birth and has no skin dermatosis.

Discussion:-

Définition

Pemphigoid gestationis is a rare, autoimmune blistering dermatosis of pregnancy, with an incidence ranging up to 50.000-60.000 pregnancies depending on the prevalence of the HLA-haplotypes DR3 and DR4 (5,6). PG typically develops in the second or third trimester of pregnancy, with an abrupt onset, but may appear any time during pregnancy or even in the immediate postpartum period. Severe pruritus is followed by the appearance of erythematous, urticarial papules and plaques that progress to tense vesicles and blisters.

Physiopathology:

Current immunopathological data show that pathogenic autoantibodies are essentially IgG1 and IgG3 which fix and activate the complement.(7) These autoantibodies target BP180 which is present in the placenta at the amnio/trophoblast junction. This antigen is only expressed after the first trimester of pregnancy, which explains the chronology of the beginning of PG. Self-immunization occurs through a 180 kDa placental antigen tolerance break. This process would be facilitated by abnormal expression of class II HLA antigens during gestation. (7)

PG is exclusively a disease of pregnancy, so possible causes are focused on immunogenetics and potential cross-reactivity between maternal transfer to infant and placental tissue and skin.(8, 9) Most patients exhibit complement C3 or C3 and immunoglobulin G (IgG) deposition along the basement membrane zone on immunofluorescence. (10)

Oestrogen and progesterone are also proposed to play a role in disease pathogenesis, as demonstrated by the flare of PG in the immediate postpartum period, during menstruation and following oral contraceptive use. A relative remission is seen in the last trimester of pregnancy. While progesterone seems to be protective against PG, it is possible that oestrogen has immune-enhancing properties through the stimulation of B cells. (11)

Clinical features :
The lesions usually arise on the abdomen, often involving the umbilicus, and spread centrifugally, sparing face, palms, soles and mucous membranes (< 20% cases). Flares have been observed at or immediately after delivery, pre-menses and with the use of oral contraceptives (25% of patients).(12-13)

The eruption may show an alternating pattern of appearance during the course of gestation.The mean duration of the disease upon the completion of pregnancy is 4 weeks for bullous eruptions and 14 weeks for the urticarial component. Patients with onset in early pregnancy have a better prognosis and PG terminates soon after delivery.(14-15-16)

Diagnosis :
The skin biopsy of a recent bullous lesion shows a subepidermal bubble with a superficial dermal infiltrate rich in neutrophils and eosinophils. If the biopsy is done on an undiluted area, the histological image is not specific but still shows a neutrophil infiltrate and eosinophil dermal infiltrate. Direct immunofluorescence confirms the diagnosis by showing a fine linear deposition of C3 and sometimes IgG at the dermo-epidermal junction (10). The detection of circulating antibodies can be done by indirect immunofluorescence technique in the presence of complement (HG-factor), currently discontinued, by Elisa BP180-NC16A technique, or by immunoblot, positive in 90% of cases (17-18-19). The level of autoantibodies in the Elisa technique follows the progression of the disease [23].Direct immunofluorescence and the search for circulating antibodies are constantly negative in other dermatoses of pregnancy (5).

The criteria for the diagnosis for PG include an appropriate clinical presentation and specific histologic findings of a subepidermal blistering process and a linear C3 deposition along the basement membrane in direct immunofluorescence, with or without deposition of immunoglobulin G (20-25% of cases). (21)

Prognosis :
Patients who develop PG during pregnancy have a higher risk of complications for the mother and the fetus due to placental insufficiency. Most common complications are associated with preterm delivery and small for gestational age. Associated risks correlate with disease severity in the mother. (22)

No cases of fetal malformation or fetal death in utero have been described. In a recent study of 61 complicated pregnancies of PG, the authors put in evidence that the occurrence of PG in the 1st or 2nd trimester of pregnancy, as well as the presence of bubbles are, in multivariate analysis, risk factors for the occurrence of fetal complications of prematurity type (< 37 SA), hypotrophy (< 2500 g) or low weight for gestational age (< 10th percentile). The administration of general corticosteroid therapy does not appear to be a risk factor, but the authors insist that the study lacks the power to definitively confirm this (22).The occurrence of a bullous rash in children is rare (<3%) and transient, linked to the transplacental passage of maternal antibodies with a elimination half-life of 15 days (23,24)

Traitement:
Treatment is challenging in PG and is based on clinical experience.(6) Oral corticosteroids are the therapeutic mainstay in pregnancy and postpartum.(3,6) When planning the treatment, it should be borne in mind that this dermatosis always disappears after delivery; however, treatment is needed to alleviate pruritus and to prevent eruption of vesicles and bullae. In mild forms of the disease, oral antihistamines and topical (potent or very potent) corticosteroids are applied.(3-10) General consideration is that treatment with topical corticosteroids is less effective.(8) Severe cases require use of systemic corticosteroids (prednisone, 0.5-1.0 mg/kg/d) gradually tapered to a maintenance dose, which can be increased in the peripartum period when exacerbation of the disease usually occurs.(3-10) Alternatives to corticosteroids are azathioprine, dapsone, intravenous immunoglobulin, pyridoxine, cyclosporine, plasmapheresis, minocycline/nicotinamide, (3, 26) methotrexate, and cyclophosphamide.(8,25) Although plasmapheresis, cyclophosphamide, azathioprine, cyclosporine, and dapsone are beneficial, they have potential side effects and can be considered in the most severe cases. (25) Immunoapheresis represents a helpful therapeutic option in patients unresponsive to conventional treatment.(26)

Post Partum

PG tends to improve postpartum without scarring; however, it may be weeks, months, or years before resolution is complete. The clinical course of PG may be modified by changes in estrogen and progesterone levels. (28) Although the disease tends to recur in subsequent pregnancies, about 8% of subsequent pregnancies are spared.(28) Relapses with the use of oral contraceptives or during menstruation can be expected in 25% of patients.(27-28) A change of partner does not increase the risk of developing PG, but it is unclear whether it alters the risk of recurrence.(28)

Conclusion:-

PG is an autoimmune bullous dermatosis of pregnancy whose maternal and fetal prognosis is generally good, at the condition of a support in a specialized environment, including dermatologists and obstetricians. The treatment of first intention of skin lesions is based on Class I dermocorticotherapy which must be managed by practitioners accustomed to the treatment of autoimmune bullous dermatoses.

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