ISSN: 2576-2842

Case Report

Journal of Gynecology & Reproductive Medicine

Management of Pemphigus Vulgaris in Pregnancy - Case Report

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Submitted: 21 June 2019; **Accepted**: 26 June 2019; **Published**: 15 July 2019

Abstract

Pemphigus vulgaris is a rare autoimmune bullous disease caused by producing autoantibodies directed against transmembrane glycoproteins of desmosomes that can lead to steric hindrance to homophilic adhesion of desmogleins. The development of pemphigus during the pregnancy is rare. The disruption of the Th1:Th2 balance in the autoimmune disease during the pregnancy plays a crucial role and explains why some studies have reported the exacerbation of disease, while others observe improvements during the pregnancy. We present aclinical case of a 31-year-oldprimigravida, with dichorionic - diamniotic twin pregnancyassociatedwith pemphigus vulgaris, being discovered 2 years ago, who went under treatment with Medrol 64mg/day and Imuran 50mg/day. She was admitted to the hospital at 31 weeks of gestation with non-systemic contractions of moderate intensity. The clinical findings are multiple erosions and blisters which have been accentuated during the second semester and have been remitted after delivery. Nowadays, the therapeutic management of the pemphigus during the pregnancy is not yet established and all of these cases are individual evaluated with the primary target to control the disease with the safety of the fetus.

Introduction

The development of pemphigus, including pemphigus vulgaris (PV) and pemphigus foliaceus, in association with pregnancy is rare, with fewer than 50 published reports and the infants of these mothers may probably have various outcomes from stillbirth to transient lesions [1,2]. The fetal negative effects are more common in PV compared with pemphigus foliaceus.

T helper (Th) cells play a crucial role in the development of autoimmune diseases and inflammatory disorders. During the pregnancy a disruption of the Th1:Th2 balanceoccurs, due to maternal cytokines process,situation which can lead to more differentiation of native CD4+ cells into Th2 cells, raising the number of Th2 and decreasing the number of Th1. Indeed, we can explain the different outcomes in: Th1-dominant autoimmune diseases (Rheumatoid Arthritis, Multiple Sclerosis and Psoriasis) with favorable outcomes, differing from Th2-dominant autoimmune diseases or inflammatory disorders (Pemphigus, Systemic Lupus Erythematosus, Atopic Dermatitis and Asthma) that can aggravate autoimmune response during the pregnancy and cannot be controlled at this time [3].

PV is an autoimmune disease with autoantibodies directed against desmoglein (anti-desmoglein-1 and anti-desmoglein-3), a cell-to-cell adhesion molecule, that can cause mucosal and/or cutaneous erosions with flaccid bullae, histologically characterized by suprabasilar acantholysis [4].

This pathology can endanger the lives of patients, and its treatment is a challenge for the practitioner. When it occurs, during the pregnancy, the therapy and monitoring of the mother and fetus will become more difficult due to the change in the mother's hormone level and the effect of drug therapy on both the mother and her fetus [5].

For the therapeutic management of PV, the first line agents are represented by systemic corticosteroids, even though, the long-term use is associated with fetal and pregnancy risks. A recent review demonstrates the reliability of association between azathioprine and steroids.The use of immunosuppressive treatment should be carefully evaluated, because of the risk of having low weight babies, infections, adrenal insufficiency, and preterm delivery. Also, the literature presents some reports which recommend rituximab, cyclosporine intravenous immunoglobulin, dapsone and plasmapheresis as safety as well [6,7].

Case Report

The 30-year-old patient, known with Pemphigus Vulgaris from April 2016 (confirmed by histopathology exam: thin epidermis with an intra dermal bubble with suprabasilar and intraepidermal acantholysis with dermal infiltrate composed of lymphocytes, neutrophils, and eosinophils and direct immunofluorescence showed:showed intercellular deposition of complexes IgG and C3) and with dichorionic - diamniotic twin pregnancy at 10 weeks of gestation is hospitalized in the dermatology clinic for the exacerbation and extension of lesions from this disease which were disseminated

to the healthy skin: trunk and limbs and mucous membranes without a spontaneous healing tendency, with the Nicolsky sign +. The gravida is under treatment with corticosteroids (April - June 2016 Prednisone 60 mg / day) associated with Azathioprine 100 mg / day with favorable response. In the context of bilateral pain on the knee joint, the patient stopped the prescribed medication. In August 2016, for the recurrence of Pemphigus lesions, the patient was hospitalized at the Dermatology clinic where Medrol 12 mg x 4 / day and Methotrexate 15 mg / week were developed at that time with favorable progression.

During the hospitalization, the Tzanckcytodiagnosis was performed: a rich cellular smear containing an abundant inflammatory infiltrate with relatively frequent polymorph nuclear, which associates relatively acantholytic cells.From the paraclinic point of view, the patient presented at the time of admission an inflammatory syndrome, hepatocytolysis, hypertriglyceridemia, hypoproteinemia, and the urine culture reveals the presence of Escherichia coli. The bacteriological examination of vaginal secretions does not isolate pathogenic microbial flora. Nasal and pharyngeal exudates, Ag Hbs, Anti-HCV Antibody, IgM antibodyto hepatitis A and E virus, RPR, TPHA, HIV, IgM antibody to Epstein-Barr virus, IgM antibody to cytomegalovirus were negative.

After the gynecological exam, corticotherapy is admitted during pregnancy and the following treatment is established: Medrol 56mg/day associated with corticosteroids, KCl 1g/day, Pepsane and Augmentin (1g/12h for 10 days to eradicate urinary tract infection).

At 19 weeks of pregnancy, the patient returns to the Dermatology Clinic for exacerbation of rash and the paraclinic exam showed: anti-desmoglein 1 and 3 antibodies, an inflammatory syndrome, hepatocytolysis, a mixed dyslipidemia. The medical attitude was to modify the sketch treatment: Medrol 64 mg/day, Imuran 50 mg/day and corticosteroids. The patient performed also, at the 19 weeks of pregnancy, the gynecology ultrasound exam, morphology, and double test within normal limits.At 27 weeks of pregnancy, the bacteriological examination from the post-erosion level reveals infection with Staphylococcus aureus for which was established treatment with Fucidin for 7 days.

Throughout the pregnancy, because the treatment with corticosteroids the patient followed the hypolipidemic and low sodium diet, and at lesions level she applied Safetac patch. Due to the Pemphigus back skin lesions during the pregnancy the patient, for a healthy sleep, bought a special mattress – alternating pressure system anti bedsores and anti-decubitus.

This gravida with dichorionic - diamniotic twin pregnancy with pemphigus vulgaris, was admitted to the Department of Obstetrics and Gynecology at the "Cuza Voda" Maternity in Iasi, Romania, during 31 weeks of pregnancy for non-systemic contractions of moderate intensity. The patient has a pruritic erythematous-squamous rash, multiple erosions, residual hyperpigmentations and blisters which have been accentuated during the second semester, on the back, anterior chest wall, abdomen and the lower limbs (Fig. 1). The eruption started from the abdomen and extended shortly to the upper and lower back and the lower limbs and the Nikolsky sign tested positive.

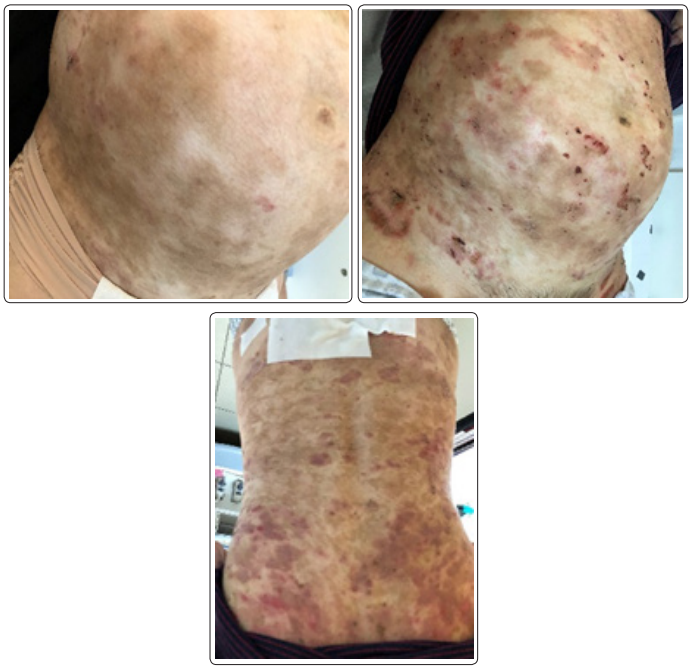

Figure 1: Confluent crusted lesions from early pregnancy to 31 weeks of gestations

Because the patient was admitted in the hospital for imminent of preterm birth, it has been prescribed tocolytic therapy with Atosiban administered intravenously in 3 successive phases: a first bolus dose of 6.75mg/0.9ml solution for injection given in 1 minute, instantly followed by a sustained high dose infusion of Tractocile 24 ml/hour (3 hours intravenous loading infusion), followed by a lower dose of Tractocile 8ml/hour (7 hours intravenous loading infusion). Also, during her hospitalization, progesterone (Arefam 200mg 3 tb/day) and selective beta 2-adrenoreceptor agonist treatment (intravenous Hexoprenaline sulfate infusion) was enforced without any favorable result.

Six hours later, after the treatment was initiated, the first fetus presented premature preterm rupture of membranes with green amniotic liquid, and the gravida underwent to systematic painful contractions, hypogastrium and lumbar pain of high intensity. After 10 hours of Atosiban treatment the patient was transferred to Intensive Care Unit and emergency caesarian section was made without complications.The patient gave birth to twin, weighed 1450g, respectively 1500g, both of them having 5-min Apgar score 7. After delivery, the patient agreed to continue the treatment with Medrol 16mg 4tb/day and Imuran 50mg 2tb/day, being important to underline that Pemphigus vulgaris was not transmitted to the newborns.

Due todisruption of Th1:Th2 balance during the pregnancy, with raising the number of Th2 and decreasing the valueof Th1, like in the most cases from the literature, in this case the symptoms remitted spontaneously in postpartum period under treatment with Medrol 64mg/day and Imuran 100mg/day.

Discussions

Pemphigus developed during pregnancy is rare, few cases being published in the literature [2]. The disease may occur firstly during pregnancy or as an episode of pathology aggravation.In second situation, the symptoms develop, during the first trimester of

pregnancy, which is concordant with the literature data.Early onset of PV in the second trimester with cutaneous erosions is a risk factor for prematurity and low birth weight, but rarely the newborn are affected by transitory blisters [8].

The target of the treatment is to remit the symptoms and to prevent the new blisters in balance with side effects on the fetus and should be associated with close obstetric monitoring. In the mild form of PV disease, the topical steroid administration can be very a useful and safe therapeutic option. Even though the treatment of severe form of PV disease is reduced, it is very difficult because of immunosuppressive side effects medication on fetus and newborn [9].

Ozhan et al., treated 4 unresponsive cases of PV during pregnancy with topical and systemic glucocorticoids drugs, using cyclosporine (300mg/day) combined with prednisolone, had a good response on the treatment. In one of these cases, with persistent postnatal PV cyclosporine was used after intravenous immunoglobulin administration [7].

Moreover, regarding the unknown primary stimulus for autoimmune disease during pregnancy, JiwonGye et al. reported a case with Pemphigus vulgaris associated with herpes simplex type 1 (HSV-1), on a 32-year-old gravida at 37 weeks of gestations who presented for multiple vesicular and erosive lesions, initiated from the per umbilical region and spreaded to the oral mucosa and the skin of the back which persisted more than one month, cured with steroids and antiviral agents [10]. The possible role of viruses, especially HSV-1 and Epstein-Barr, have been proposed in the pathogenesis of PV, due to its ability of inducing and/or exacerbating pemphigus vulgaris in genetically susceptible host [11].

Sophia Elmuradi et al. described an extremely rare case with Oral Pemphigus Vulgaris during pregnancy and opted for an individual therapeutic management with immunosuppressive medication which was coordinated between appropriate health care providers [12-15].

Conclusions

From the gynecological point of view, the patient was carefully monitored throughout the pregnancy by specialized clinical and paraclinic examinations, ultrasound examinations (S9; S16; S20; S28), fetal morphology and double test within normal limits. Following the patient`s dynamic, we remarked a significant reduction in skin Pemphigus` lesions after delivery, and on the gynecologist ultrasound control on one month after caesarian intervention the uterus and annexes were normal with the absence of fluid in Douglas.

Pemphigus vulgaris can endanger the lives of patients, and its treatment is a challenging for the doctors. When it occurs during a pregnancy, the therapy and monitoring of mother and fetus will become more difficult. Adverse outcomes on PV infants are associated with poor maternal disease control and with higher titers of antibodies against desmoglein.

Management of pregnant women with pemphigus vulgaris diagnosis should be performed in specialized centers. The prognosis of PV complicated pregnancies is generally favorable, but obtaining auspicious results probably depend on collaborative efforts between dermatologist and obstetrician to ensure a personalized treatment and to avoid the emergence of ethical conflicts.

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