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Pemphigusvulgaris in pregnancy. A rare case report

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Abstract

Pemphigus vulgaris (PV) is an autoimmune, bullous, mucocutaneous and potentially life-threatening disease. During pregnancy the occurrence of PV is exceedingly rare and its condition will become more complicated due to different mother's hormone level and the effect of treatment on both mother and her fetus. PV may be associated with an adverse outcome, such as fetal growth restriction and preterm births. We report a case of a 33-year-old woman who was firstly diagnosed with PV during pregnancy. Treatment of high-doses systemic corticosteroids was instituted to control the disease. She delivered a healthy live preterm baby, appropriate for gestational age with no skin or mucosal lesions or other apparent complications.

Key words: Pemphigus vulgaris; corticosteroids; autoimmune; pregnancy

Introduction

Pemphigus vulgaris is an extremely rare autoimmune, mucocutaneous blistering disease. There are mainly three types of pemphigus: Pemphigus vulgaris (PV), Pemphigus foliaceus (PF), and other variants of pemphigus. PV produces blisters in skin and mucous membranes, while pemphigus foliaceus involves skin only, paraneoplastic pemphigus produces blisters in patients with underlying malignancy¹. The pathogenesis of pemphigus vulgaris is associated with autoantibodies directed against transmembrane glycoproteins of desmosomes, which causes the formation of Dsg3-depleted desmosomes in PV and loss of cell-cell adhesion in the basal and suprabasal layers of the deeper epidermis, with keratinocytes in the

superficial layers of the epidermis maintaining their cell adhesion. This leads to intercellular edema with loss of intercellular attachments in basal layer and suprabasal epidermal cells separate from basal cells to form clefts and blisters².

It usually affects the elderly, between 5th and 6th decade of life and genetics seem to play an important role. Although all races are affected, Jews are more susceptible. It is common in eastern countries like India, Malaysia and China and rare in west³. The occurrence of PV in pregnancy is very rare. PV in females may be associated with other autoimmune diseases and infertility⁴. Impact on the fetus may be due to the disease by itself or because of the effect of

treatment given to the mother⁵. Literature review on pemphigus in pregnancy is limited to 47 cases, reported between 1966 and 2014, with diagnosis before or during pregnancy⁶. The neonatal pemphigus is a very rare complication and there are only 29 reported cases on literature review⁷. Mortality rates associated with PV have decreased to 10% -15% with systemic corticosteroids from a mortality rate as high as 70% in the precorticosteroid era⁸.

Case reports

A 33-year-old albanian national, tertigravida (G:3,P:2) with no known chronic illness or medication use, presented at her 23rd week of pregnancy with widespread blistering dermatitis in the abdomen with associated burning and pruritus and erosions over the buccal mucosa. On examination, there were multiple ruptured blisters in the abdomen, a singleton fetus with cephalic presentation and appropriate weight for the week of gestation and rest of the examination was normal.

Differential diagnoses considered of: 1) Herpes simplex infection 2) Herpes zoster 3) Porphyria 4) Impetigo 5) Toxic epidermal necrolysis 6) Systemic lupus erythematosus 7) Pemphigoid gestationis 8) Steven Johnson's syndrome 9) Pemphigus vulgaris. Lab tests were done including Tzanck smear for herpes, herpes simplex virus (HSV) antibodies, ANA& ANCA tests, PCR for HSV 1 and 2 and a skin biopsy was performed and sent for histopathology and immunofluorescence. Skin biopsy histologically revealed sub-prabasal acantholysis, and direct immunofluorescence showed diffuse intercellular IgG in the epidermis and basal intercellular C3, which confirmed the diagnosis of PV (Figure 1-2). In addition, anti-desmoglein I, III antibodies were positive. All lab tests were normal except from the previous mentioned confirmatory tests for PV that were positive.

After discussions with the patient about possible adverse effects to the fetus, treatment of high-doses

systemic corticosteroids was instituted to control the disease, in collaboration with dermatologists. Possible alteration of the course of pemphigus due to the hormonal and immunologic changes seen in pregnancy was considered before starting the treatment. Due to the severity of the disease she was hospitalized. Prednisolone 0,7 mgr/kg iv daily was initiated from 23 weeks to 28 weeks of gestation with satisfactory clinical response during the first month. Oral ulcers improved, lesions on the abdomen started healing and began to dry up.

The patient developed gestational diabetes and was treated with long acting insulin. Mother and fetal well-being were monitored closely. Following improvement of symptoms and with no new-onset clinical-skin manifestations, prednisolone was tapered off to 0.6 mgr/kg iv daily from 28 weeks to 29 weeks of gestation, 0.5 mgr/kg iv daily from 29 weeks to 31 weeks of gestation and 0,4 mgr/kg per os daily from 31 weeks to 34 weeks of gestation, when the mother gave birth. She underwent emergency caesarean delivery (history of 2 cesarian sections) due to premature uterine contractions. She delivered a premature, otherwise healthy newborn boy 2.180 gr and it was noted that the neonate showed no skin or oral-mucosa lesions or anomalies while in the neonatal intensive care unit.

The postpartum status of pemphigus vulgaris in the mother was slightly exacerbated after delivery, with new onset lesions under the breast and abdomen. She also developed endometritis three weeks after delivery and was hospitalised and administered intravenously antibiotics. She is still under follow-up for pemphigus vulgaris, 3 months after delivery.

Discussion

Pemphigus is expressed by extensively distributed bullae and erosions on the skin and mucosa membranes. Pemphigus vulgaris during pregnancy is ex-

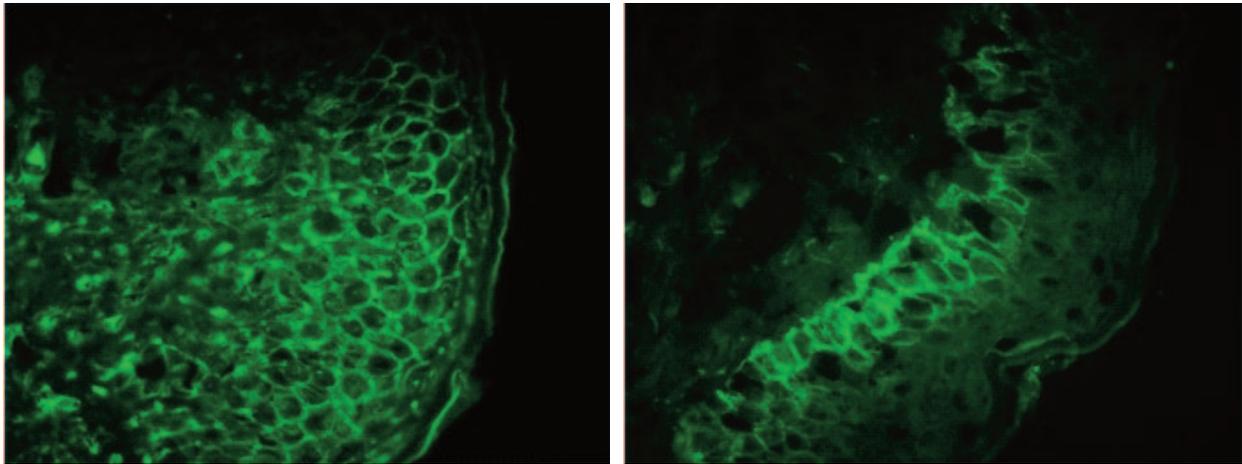


Figure 1,2. Immunofluorescence showed diffuse intercellular IgG in the epidermidis and basal intercellular C3, which confirmed the diagnosis of PV.

tremely rare because it is associated with infertility when it is active⁴.

Pemphigus and pregnancy interact with each other making treatment more complicated for the clinician. The appropriate treatment in pemphigus vulgaris patients during pregnancy is glucocorticoids and it is similar to the treatment without pregnancy⁹. In our case, prednisolone (FDA pregnancy category C) was administered, which can be relatively safely used as immunosuppressive drug during pregnancy as it does not readily cross the placenta and is partially inactivated as it cross the placenta¹⁰. Prednisolone is safer drug compared with other less used glucocorticoids such as dexamethasone and betamethasone. It should be avoided, if possible, during the first trimester, when risk for defects of the hard palate are highest^{11,12}. In our case 6 weeks after treatment, there was remission of the disease with no presence of new clinical-skin manifestations and the disease was slightly aggravated postpartum. The disease is exacerbated most commonly during the first, second trimester, and postpartum, and is stable during the third trimester. This could be due to the increased level of endogenous corticosteroid hormone chorion of the placenta and consequent immunosuppression¹³. In our patient, there was

postpartum aggravation of the disease, which is consistent with some studies that report the postpartum flare up of pemphigus vulgaris due to the rapid decrease of corticosteroid hormones levels⁴.

Treatment is often required to control both maternal disease and fetal outcomes. PV may be associated with an adverse outcome, such as fetal growth restriction, intrauterine death, premature delivery, and in approximately 30% neonatal PV of the newborns¹⁴. Neonatal pemphigus is caused by the transplacental transmission of antibodies, and only a small amount of immunoglobulin G (IgG) is synthesized by the neonate itself¹⁵. Poor outcomes have been related with inadequate maternal disease control and higher Dsg antibody titers from maternal serum or umbilical cord blood¹⁶. In our case, PV was well controlled and the mother gave birth to a premature, otherwise healthy neonate that showed no skin or oral-mucosa lesions or anomalies.

Typical complications observed in these PV patients are skin infections, sepsis, hypokalemia, hypoalbuminaemia and Cushing's syndrome due to prolonged steroids usage. She developed postpartum endometritis and skin infections many times and was treated with antibiotics. Our patient is totally treated for 5 months and is still under follow-up.

Conclusion

Pemphigus vulgaris in pregnancy is very rare and treatment guidelines have not yet been clarified, thus, management of these cases is individually determined, presenting challenges for the clinician. The good outcome of pregnancies complicated by pemphigus vulgaris is more likely to be obtained from the close collaboration of obstetricians and dermatologists. Current data suggest increased rate of perinatal morbidity and mortality. In summary, pregnancy may have an adverse course, therefore, careful monitoring of the high risk mother and fetus is mandatory.

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