

## Pemphigus Vulgaris during Pregnancy: A Rare Case Report.

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**Abstract:** *Pemphigus vulgaris (PV) is an uncommon immune-mediated bullous dermatosis which is very rare during pregnancy. Its management during pregnancy is a challenge and sometimes very difficult. Only few cases have been reported in literature so far. The disease may be associated with adverse fetal outcomes such as prematurity and fetal death. The neonate can develop transient skin lesions. We report a case of pemphigus vulgaris who conceived during courses of treatment with corticosteroids and delivered pre term intrauterine death (IUD).*

**Keywords:** *Pemphigus vulgaris, Immunosuppression, Pregnancy, IUD*

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### I. Introduction

Pemphigus vulgaris is a severe, potentially life-threatening autoimmune bullous disease of the skin and mucous membranes [1]. Predisposition to pemphigus is linked to genetic factors: first-degree relatives of patients are more susceptible to the development of autoimmune diseases [2]. Certain major histocompatibility complex (MHC) class II molecules are common with it [3]. The pathogenesis is linked to the presence of auto antibodies directed against desmoglein 3, a desmosome trans-membrane glycoprotein belonging to the cadherin family [4]. These auto antibodies cause blisters which result from loss of cell to cell adhesion in the basal and suprabasal layers of the deeper epidermis, with the keratinocytes in the superficial layers of the epidermis [5]

The disease affects all races and more frequently affects middle aged women including those with childbearing years. Compared to western countries it occurs at younger age in our part of the world. The disease may occur for the first time during pregnancy or it may precede the pregnancy with or without exacerbation of the disease, more during the first and second trimester, and also in the post partum period [1]. The effect of pemphigus varies during pregnancy like intrauterine growth retardation, preterm birth and even stillbirth. Clinical manifestation varies with only mucosal lesions in some patients and both cutaneous and mucosal lesions together in some others.

Impairment of fertility is associated with various autoimmune disorders, such as autoimmune premature ovarian failure, pernicious anaemia, Crohn's disease, systemic sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus and chronic active hepatitis. Recently an association of PV with infertility was described [6].

The reported perinatal mortality rate is 12% [1]. In 30% to 45% of cases there is some transfer of antibodies through the placenta from the mother to foetus causing transient neonatal pemphigus which resolve completely within a few months. However, in most cases, the neonates are born completely free of the disease [5].

The management of PV during pregnancy is similar to that in the non pregnant women; however it is more challenging and difficult during pregnancy. Steroids such as prednisolone are the first choice. Corticosteroids are safe during pregnancy; however, high dose or aggressive therapy may increase the risk for having low weight babies, infection, adrenal insufficiency, preterm delivery etc. Azathioprine and cyclosporine A which are used in non pregnant women are not safe during pregnancy.

### II. Case Report

A forty year old normotensive non-diabetic female Gravida 2, Para 1, with 2 living issues with 20 wks of gestation developed blisters over the abdomen which gradually extended all over the body. She was diagnosed as pemphigus vulgaris eight months back when she had develop some crusted lesions over the scalp, which was confirmed by skin biopsy and direct immunofluorescence test showing suprabasal clefts with acantholysis and Immunoglobulin deposits in fish net pattern respectively. She conceived during the course of treatment with oral prednisolone; however, she stopped the medication after which the lesions became more extensive. The

eruptions started with severe pruritus over trunk, limbs and whole body followed by flaccid vesicles and superficial erosions bilaterally on the trunk and both upper and lower limbs.

On general physical examination, there was edema of the hands and feet with mild dehydration but no fever, pallor, jaundice or cyanosis. Systemic examination was normal. Cutaneous examination revealed bilaterally symmetrical, erythematous erosions, flaccid bullae, erythematous and yellowish crusted plaques over the extremities and trunk including the scalp with involvement of the mucous membranes. Nikolsky's sign was positive. Palms and soles were spared. On investigation, complete haemogram, liver function tests, kidney function tests, thyroid profile and abdominal ultrasonography were normal. She was treated with injectable antibiotic, oral prednisolone 20mg 2 times daily, which was further increased to 60mg per day in two divided doses after two weeks due to poor response, and other conservative management. The skin lesions showed significant improvement after which the steroid dose was reduced to 40 mg per day. However, after five weeks of undergoing treatment, there was sudden loss of foetal movement followed by IUD. And the baby was delivered by spontaneous vaginal delivery.

### **III. Discussion**

*Pemphigus vulgaris* is associated with infertility in its active phase; therefore, PV during pregnancy is rare. Pregnancy may exacerbate PV, which has been a similar finding in other well-documented autoimmune diseases.

In a retrospective study eight of nine patients suffering from PV failed to conceive. Four patients had luteal phase defects, four had follicle stimulating hormone defects and anti-sperm antibodies were detected in two patients. Only one became pregnant, but only during full remission. Notably, none of the eight patients conceived even after discontinuation of medications (corticosteroids, azathioprine or cyclophosphamide). In contrast, our patient conceived during the courses of treatment, implying that disease does not necessarily cause infertility [6].

Pregnancy may precipitate or aggravate PV, as reported in better-known autoimmune diseases, such as systemic lupus erythematosus, myasthenia gravis [7]. Our patient clearly demonstrated disease flare-up during the period of conception and early pregnancy, with difficulty in controlling the disease at that time.

Transplacental transmission of PV Ig-G antibodies from mother to fetus may result in clinical manifestations in the neonate [8]. Neonatal PV has not been reported to progress to adulthood, and if the lesions do appear on the neonate they tend to improve spontaneously within 3 weeks [9]. Of the 26 previously reported cases of PV in pregnancy, four ended in intrauterine fetal death. All of these cases were associated with severe, active and difficult to control maternal disease [9, 10, 11]. As in our case, there is early neonatal death probably due to severity of the disease.

The aetiology of pre-term premature rupture of membranes (PPROM) which led to preterm delivery in the reported case may be related to the vigorous steroid therapy administered to the patient during her pregnancy. This connection has been previously described, where a significant increase was shown in preterm delivery, premature labour and PPRM in pregnant women treated with prednisone (0.5–0.8 mg/kg) and aspirin (100 mg/day) in comparison with those given placebo. As low-dose aspirin is not associated with prematurity, the authors related the adverse outcome of the reported pregnancies to corticosteroid treatment [12].

If a woman with known PV is planning to become pregnant, it is recommended to first control and suppress the disease so that therapy can be minimal during the pregnancy. It also is recommended to use aggressive topical therapy if possible to control PV in a pregnant woman [13]. This option would not have been efficacious in our patient because of her severe widespread disease. Prednisone is considered one of the first-line treatments of PV and has been historically successful as a treatment for pregnant patients with PV if maintained at a low dosage. Prednisone, similar to other corticosteroids, can cross the placental barrier and can increase the chance of premature birth, infection, and mortality in high doses [14]. Immunosuppressive drugs should be withheld although azathioprine may be added. Inadequate treatment and control of PV can be life threatening to the patient because of the severe infection that may ensue; thus it is necessary for the health of the patient and fetus to suppress the PV. One alternative to treatment with steroids and immunosuppressants is plasma exchange, which has been successful in the clinical context of pregnancy. The cons of plasma exchange are repeat procedures, the need to give the patient more immunosuppressants to prevent a rejection, and the return of the autoantibody [15]. Multiple case reports state that both one and two courses of intravenous rituximab therapy at a dosage of 375 mg per square meter of body surface area given once weekly for 4 weeks proved to be useful in clinical improvement for patients with refractory disease. Studies are currently underway to look at the effects of rituximab on pregnancy and the fetus. Preliminary findings show neonates may have B-cell abnormalities initially yet recover fully without infectious complications or sequelae. Rituximab currently is a pregnancy

category C drug, and women are counseled to avoid pregnancy for at least 12 months after rituximab exposure and use contraception while actively taking the drug [16]



**Figs – Showing extensive crusted haemorrhagic plugs, erosion and flaccid bullae.**

### **Conclusion**

In a case of PV it is essential to take preventive measures before conception to avoid complications. For example, efforts should be made to taper or stop any immunosuppressive agent. The dose of prednisolone should be reduced to the lowest effective dose. On the other hand, an adequate control of the disease is required before conception as it is expected that pregnancy can aggravate pre-existing PV as it does in other autoimmune diseases. However Lehman et al believe that adverse pregnancy outcome is more closely related to poor control of maternal disease and high titres of pemphigus antibodies. Corticosteroids are the first choice of treatment for PV. If disease is not controlled then steroid-sparing immunosuppressive agents may be added to therapy such as azathioprine but its use during pregnancy should be avoided. Plasmapheresis could be used as treatment during pregnancy but its use is still experimental.

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