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Case Report

A rare case of pemphigus vulgaris in pregnancy: Challenge in management

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Abstract Pemphigus vulgaris (PV) is an immune-mediated disease manifested as flaccid bullae and extensive erosions of the skin and mucosa. The incidence of PV before or during pregnancy is uncommon, with only 36 cases were published in current English articles between 1966 and 2014. Management of PV includes immunosuppressive, intravenous immunoglobulins, or biologic agents. Currently, there is no established guideline for the management of PV in pregnancy. A 22-year-old pregnant woman at 13 weeks of gestation complained of skin erosions and blisters that worsen for 2 months before hospital admission. Dermatological examination revealed painful erosions and blisters with positive Nikolsky signs on the entire body and numerous oral ulcers accompanied by dysphagia and difficulties in eating. Histopathological examination showed suprabasal clefts filled with acantholytic cells extending to hair follicle units consistent with pemphigus vulgaris. She had been managed with systemic corticosteroid under obstetrician supervision, antibiotic, and supportive care. Her condition was significantly improved over the first month of medical treatment. Pemphigus vulgaris in pregnancy is a challenging case due to the course of the disease itself and the complications of long-term use of the therapeutic agents to both maternal and fetal. Without proper treatment, PV may be fatal due to dehydration and secondary bacterial infections. Patients with PV in pregnancy should be monitored intensively with a multidisciplinary approach to obtain a good outcome for the maternal and the baby.

Key words
Pemphigus vulgaris, pregnancy, bullous disease, corticosteroid, histopathology.

Introduction

Pemphigus vulgaris (PV) is an immune-mediated bullous disorder manifested as painful erosions and flaccid blisters on the skin and mucosa with predilection on the trunk, extremities, face, and scalp.[1] The global incidence per million/ year varies from 0.76 to 16.1. The prevalence of PV is higher in females than males with a ratio range from 1:1.5 to 1:4.[2]

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Immunoglobin G (IgG) is the main autoantibodies against desmoglein (Dsg) 1 and 3. Desmoglein is one of the cadherin proteins which can be found in desmosomes.[3] Diagnosis of PV is based upon disease history, clinical manifestation, histopathology, and immunochemical study. Microscopically, PV demonstrates suprabasal blister, "row of tombstones appearance" of basal keratinocytes, and acantholytic cells. Direct immunofluorescence may exhibit IgG depositions against Dsg 1 and 3 on the cell surface of keratinocytes in perilesional skin.[4] Systemic corticosteroid is still the mainstay therapeutic agent for PV. The occurrence of PV during pregnancy is rare. Between 1966 and 2014, there were only 36 published cases

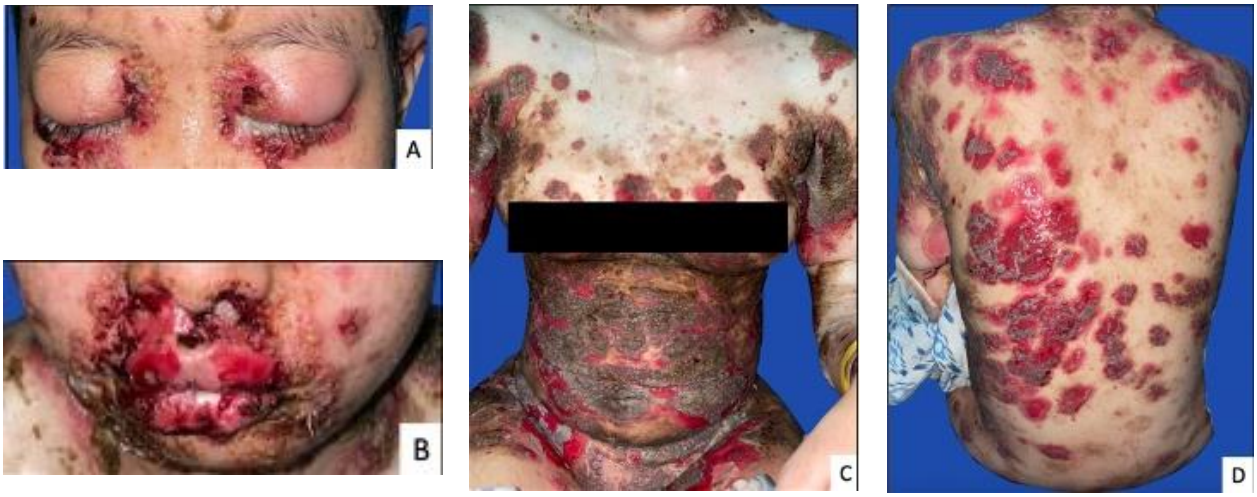

Figure 1 A-D. Multiple erythematous plaques with erosions, blisters, and long-standing crust all over the scalp, face, trunk, upper and lower extremities along with multiple erosions and dark-red crusts on the oral and erosions on the genital.

reported in English literature related to pemphigus before or during pregnancy with the various newborn outcome.[5]

Case report

A 22-year-old pregnant female at 13 weeks of gestation was admitted to the emergency unit with a chief complaint of painful erosions and blisters on the trunk, extremities, face, and scalp. Skin erosions have erupted 9 months ago that worsened for the last 2 months. Two months before skin eruption, there were multiple painful oral ulcers, leading to difficulties in eating. The blisters were rapidly ruptured, leaving multiple extremely painful erosions covered with crusts. Previously, she was diagnosed with bullous pemphigoid in August 2020 and treated with methylprednisolone 32 mg which gradually tapered to 2 mg. She was pregnant since February 2021, routinely visited an obstetrician with a normal pregnancy condition. There was no history of fever, cough, joint pain, urinating, or defecating dysfunction. She had no history of allergy, diabetes, hypertension, malignancy, and renal or liver disease. There were no similar symptoms in the family.

She was moderately ill with hypertension (147/108 mmHg) and tachycardia. Dermatological examination revealed multiple redness plaques, erosions, blisters, and long-standing crust covering the scalp, periorbita, perioral, axillae, abdomen, back, and upper arms. There were multiple erosions with dark-red crusts on the oral and the genital (**Figure 1A-1D**). The body surface area affected was 46% with a positive Nikolsky sign. Left cervical lymph nodes showed slight enlargement as large as 1 cm. Laboratory investigations showed normal renal and liver function, leukocytosis, hypoalbuminemia, and high C-reactive protein and procalcitonin. Gram stain from skin erosions showed abundant leukocytes moderate and gram-positive cocci. Microbial culture of skin erosion showed staphylococcus aureus isolate sensitive to these following antimicrobials: cefoxitin and erythromycin (first line); ampicillin/ sulbactam, cephalothin, clindamycin, amoxicillin/ clavulanate and cefoperazone/ sulbactam (second line); cefepime, vancomycin, teicoplanin, linezolid, levofloxacin, and moxifloxacin (third line). A histologic examination from a fresh blister on the right elbow revealed the tell-tale row of tombstones pattern of basal keratinocytes, acantholysis

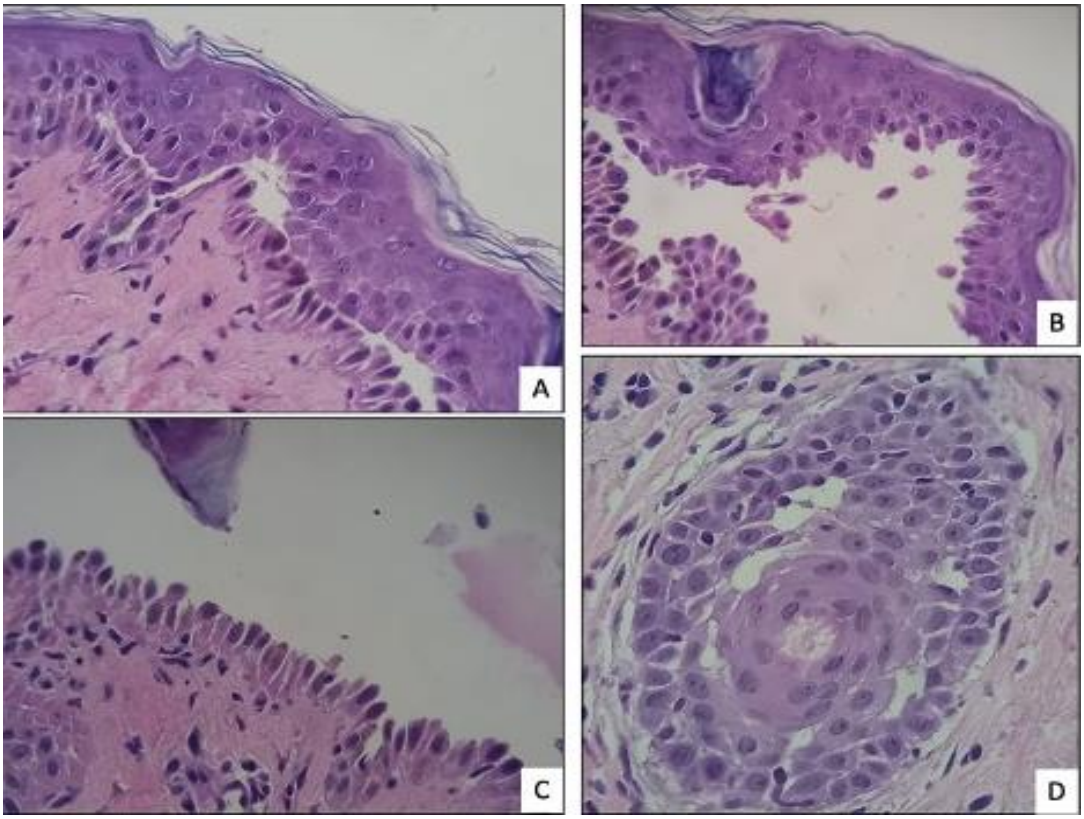

Figure 2 Skin biopsy from a vesicle demonstrated characteristic pathology of pemphigus: A-C. Suprabasal clefting, acantholysis, and lining of basal keratinocytes resembling "row of tombstones", D. Involvement of skin appendages with acantholytic process (HE, 100-400X).

(**Figure 2A-2C**), and suprabasal separation down to follicular units (**Figure 2D**). Despite negative immunofluorescence findings, clinicopathologic features were otherwise consistent with PV. The patient was consulted for obstetric examination; an intrauterine live fetus without congenital abnormalities was confirmed.

She was hospitalized and treated with intravenous methylprednisolone 1,25 mg/kg, oral amoxicillin-clavulanate 3x625 mg, pain killer, and daily wound care. Skin erosion was treated with wet dressing followed by chloramphenicol tulle, coconut oil on the scalp, and urea 20% cream on the nails and surrounding skin lesions. She received methyldopa 2x500 mg and nifedipine 10 mg from internal medicine, celecoxib 200 mg and metformin 2x500mg from the obstetrician, high protein diet of 1500 kcal, vitamin D 5000 IU, and albumin capsule from the clinical nutritionist, topical preparations of chloramphenicol, steroid, and artificial tears from the ophthalmologist, and topical steroids for erosions around the lips and dexamethasone gargle from oral medicine. After 12 days of hospitalization, she was discharged from the hospital with clinical improvement and continued routine follow-up in the Dermatology outpatient clinic. She still received oral methylprednisolone 40 mg for one month and daily wound care. Her condition was significantly improved without new skin blisters or oral erosions (**Figure 2A-2D**), thus the methylprednisolone was gradually tapered off. She also visited a high-risk obstetric clinic on

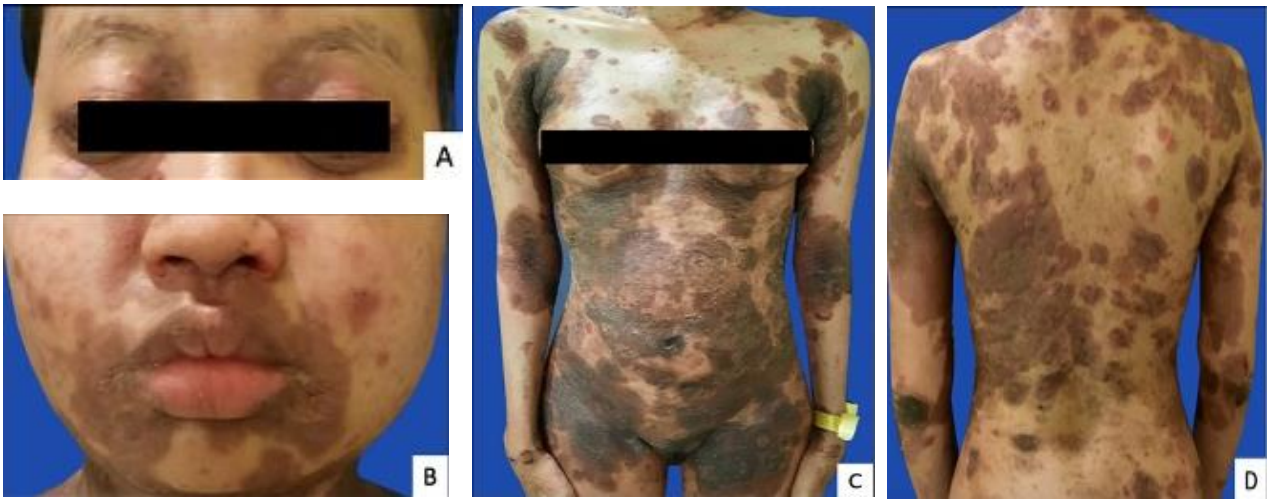

Figure 3 A-D. One month following treatment, the patient's condition was significantly improved without new skin blisters or oral erosions.

monthly basis. The obstetric examination revealed her pregnancy was in normal condition.

Discussion

Pregnancy may precipitate or aggravate PV. One review reported that 22% of women with PV experienced an exacerbation of disease during their pregnancy.[6] Frequently, PV is worsening during the first six months of pregnancy and the postpartum period, while it is relieved during the third trimester. It is believed because of the escalation of the endogenous steroid concentration and suppression of immune function.[5] PV in pregnancy should be recognized as "high-risk". The disease needs to be managed with safe medications to prevent neonatal pemphigus and pregnancy complications, for example, preterm delivery, low birth weight, pre-eclampsia, fetal death, and abortion.[7] Neonatal pemphigus occurs in 30-45% of carriers' newborns as a result of the passive transmission of maternal antibodies via the placenta, manifested as short-term flaccid blisters and erosions predominantly on the trunk. However, it infrequently appears on the mucosa. Neonatal pemphigus is a self-limiting disease at 2 to 3 weeks without long-term clinical significance and it has never been occurred to continue after the neonatal period or develop to PV in adults.[6]

PV in pregnancy has to be managed with multidisciplinary teams to reduce the complications and to ensure a good outcome for both the maternal and the baby. Systemic corticosteroids are still considered the first line and safe treatment. A high dose of corticosteroid (30-360 mg/day) for several weeks then gradually reduced to maintenance dose is usually successful in achieving skin clearance.[5,6] Prednisone and cortisone are recommended formulations for the treatment of PV during pregnancy because 11-beta hydroxysteroid dehydrogenase in the placenta rapidly deactivates those drugs, reducing the risk to the fetus. Intravenous methylprednisolone is recommended for treating advanced PV. Long-term treatment with corticosteroids may cause preeclampsia/eclampsia, increase blood pressure, diabetes, osteoporosis, impaired wound healing, development of striae, glaucoma, and risk of puerperal and post-operative infections. Therefore, those side effects should be carefully monitored.[9]

Immunosuppressive drugs such as methotrexate, mycophenolate mofetil, and cyclophosphamide are contraindicated during pregnancy because of the teratogenicity effects.[9] Cyclosporine is rarely used in PV, although its use in pemphigoid gestationis was found to be successful.[10] Azathioprine was reported beneficial in preconception management of PV, thus the use of corticosteroids can be reserved for disease flares during pregnancy.[11] Currently, rituximab, an anti-CD20 monoclonal antibody targeting B cells, is particularly successful in the treatment of moderate to severe PV. Rituximab also demonstrates a steroid-sparing effect.[12] However, it is contraindicated in pregnancy, especially in the third trimester because of the risk of fetal lymphocyte B depletion.[7]

The method of delivery recommended should be vaginal birth if there are no obstetric contraindications and skin lesions in the genital area. This is considered as pregnant PV patients receiving a high dose of steroids might develop the risk of skin infection after caesarian section and impair wound healing.[6] However, vaginal delivery should be performed prudently because any trauma and injury at the vagina during baby delivery provoke extension and deterioration of PV lesion.[13,14]

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