

Pemphigus, Pregnancy, and Plasmapheresis

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Pemphigus vulgaris (PV) is an autoimmune blistering disorder that usually occurs in the fifth and sixth decades of life but may occur at younger ages and during pregnancy. Circulating intercellular antibodies directed at desmosomal proteins may cross the placenta and place children at risk for neonatal pemphigus (NP). We describe the case of a pregnant woman with PV treated successfully with a combination of systemic corticosteroids and plasmapheresis. The possibility of PV should be considered in any pregnant woman with a worsening, widespread, mucocutaneous, blistering disease. Plasmapheresis offers a useful alternative to immunosuppressive therapy in the setting of pregnancy. Cutis. 2004;73:327-329.



Figure 1. Flaccid bullae on an erythematous base.

Pemphigus vulgaris (PV) affects men and women equally and usually occurs in the fifth and sixth decades of life. PV is rare in young individuals but occurs with greater frequency in individuals of Jewish or Mediterranean descent. Medications may be associated with the development of PV, and some forms of pemphigus have been associated with infectious triggers. Circulating autoantibodies in PV are pathogenic.¹ Immunoglobulin G (IgG) antibodies bind desmoglein 3, a 130-kd transmembrane glycoprotein of the cadherin family. These antibodies result in a loss of cellular adhesion.² Passive transplacental transfer of maternal antibodies may result in the development of neonatal pemphigus (NP). The skin lesions of NP are usually mild and resolve spontaneously over several weeks as maternal antibodies dissipate.³ We report the case of a woman

with PV whose son developed NP and discuss the diagnosis and management of PV in pregnancy.

Case Report

A 29-year-old white woman, gravida 2, para 1, presented at 16 weeks' gestation to her primary care physician with painful oral blisters. She was in good health and denied a history of oral or genital herpes simplex virus infection. A pregnancy 3 years previously was preterm at 28 weeks but otherwise uncomplicated. She was treated empirically for impetigo and thrush with oral erythromycin, trimethoprim-sulfamethoxazole, and nystatin, without improvement. The clinical diagnosis of erythema multiforme was later made at 20 weeks' gestation by a consulting dermatologist. The patient improved after treatment with oral prednisone 40 mg daily, tapered over 3 weeks. After completing the last dose of prednisone, however, she became febrile and developed cutaneous blisters. Results of a culture of an oral lesion revealed herpes simplex virus 1, and the patient was hospitalized and treated with intravenous acyclovir, without improvement.

The patient was referred to our dermatology clinic at 28 weeks' gestation with worsening, painful oral erosions and widespread, flaccid bullae and crusted erosions involving the face, neck,

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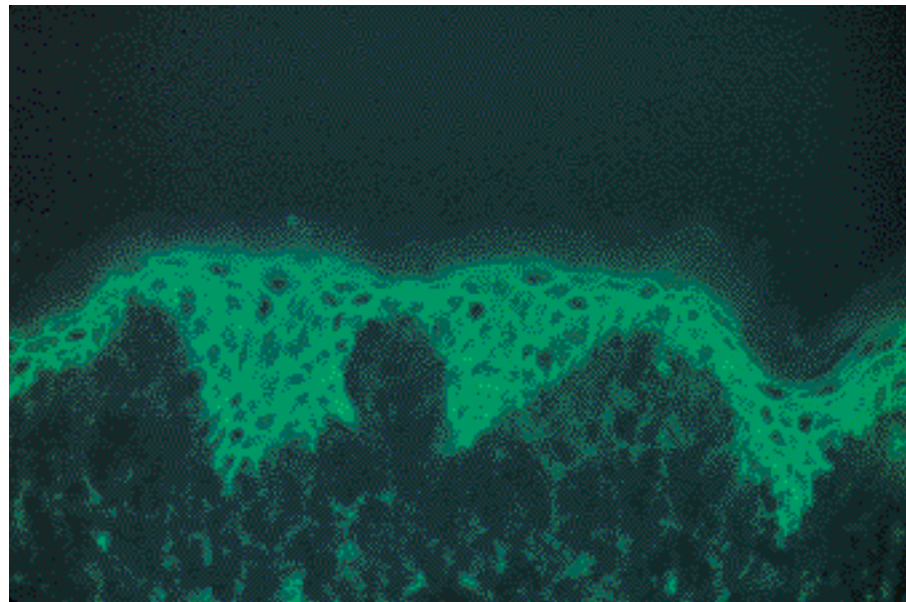


Figure 2. Direct immunofluorescence of lesional skin showing intercellular IgG deposition (original magnification $\times 100$).

trunk, axillae, and inguinal folds (Figure 1). She had lost 30 pounds over the course of the pregnancy. Results of a biopsy of a blister on the abdomen revealed suprabasilar acantholysis consistent with PV. Direct immunofluorescence of lesional skin showed characteristic epidermal deposits of intercellular IgG (Figure 2). Indirect immunofluorescence testing on monkey esophagus yielded an antibody titer of 1:320. The patient's previous viral culture was considered to represent viral shedding. Treatment with systemic prednisone 60 mg per day was started, and the dosage was increased to a maximum of 100 mg per day. This regimen resulted in a rapid reduction in antibody levels to 1:80 after 1 week, but the patient remained symptomatic.

At 35 weeks' gestation, outpatient plasmapheresis was performed via peripheral venous access on 3 of 4 successive days, according to previously published guidelines.⁴ Each outpatient treatment exchanged 3500 mL of plasma with 5% human albumin. The patient tolerated the treatments well. Her antibody titers remained constant at 1:80 after each of the 3 sessions, and her symptoms improved. At 36 weeks, 3 days after the last plasmapheresis, the patient gave birth vaginally to a healthy male infant weighing 2.95 kg. The birth was uncomplicated, and no mucocutaneous lesions were observed on the infant at delivery. The infant was discharged, but on postpartum day 4, oral lesions, gingival bleeding, decreased oral intake, and irritability were noted. The baby was admitted to the hospital with 2 small erosions on the midline of the hard palate and gingivae (Figure 3). Results



Figure 3. Erosion on the hard palate.

of complete blood cell count and differential, erythrocyte sedimentation rate, routine chemical analyses, and urinalysis were within reference range. NP and herpes infection were considered in the differential diagnosis. Because of the high morbidity rate associated with neonatal herpes infection, treatment with intravenous acyclovir 30 mg every 8 hours was started until the diagnosis of neonatal herpes was excluded by negative cultures in the nasopharynx, rectum, and cerebrospinal fluid. Cultures of blood, urine, and ocular and cerebrospinal fluid were also negative for bacteria and fungi. NP was diagnosed based on biopsy results of the palatal erosion showing intraepidermal acantholysis (Figure 4). Indirect immunofluorescence studies were not performed. Triamcinolone in

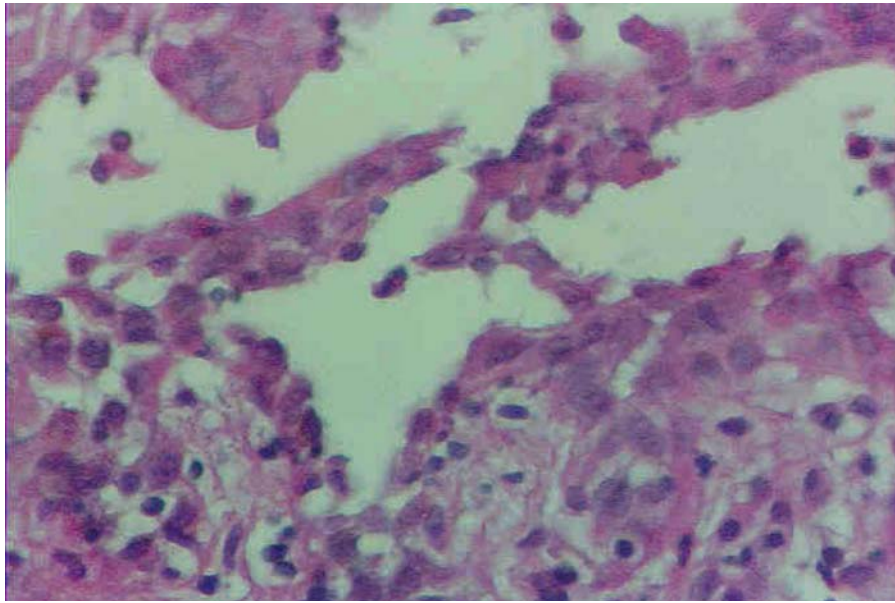


Figure 4. Neonatal pemphigus. Intraepidermal acantholysis (H&E, original magnification $\times 200$).

Orabase[®] gel was administered, and the infant's oral intake improved. Two weeks later, the baby's oral lesions had completely resolved. He was noted to be thriving and developing appropriately for his age. The mother's lesions also had resolved, and 3 weeks postpartum, her indirect immunofluorescence antibody titers had further decreased to 1:40. She is currently in remission on mycophenolate mofetil 2 g daily and prednisone 20 mg daily.

Comment

Standard therapy for PV consists of systemic glucocorticoids, alone or in combination with other immunosuppressive agents such as azathioprine, cyclophosphamide, methotrexate, or mycophenolate mofetil. For recalcitrant disease, plasmapheresis and intravenous IgG have been utilized.⁵ Plasmapheresis removes pathogenic antibodies from plasma in exchange for an isotonic solution of albumin. Depletion of circulating antibodies is often followed by a rebound synthesis of autoantibodies, necessitating concomitant administration of immunosuppressive agents to achieve clinical remission.⁶

In pregnant patients, cytotoxic agents are best avoided because of potential teratogenicity and immunosuppression. The use of systemic steroids is considered safe in pregnancy,⁷ yet some study findings have suggested an increased incidence of placental insufficiency, preterm labor, maternal and fetal infection, and low birth weight.⁸⁻¹⁰ Plasmapheresis is a safe treatment option and may minimize the need for glucocorticoid treatment. Side effects of plasmapheresis are mild but may include

fluid-electrolyte imbalances, hypotension, citrate toxicity, and depletion of clotting factors.⁴

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