CASE REPORT

Pemphigus vulgaris in pregnancy: a case report and review of literature

Ofer Fainaru, Roy Mashiach, Michael Kupferminc, Michael Shenhav, David Pauzner and Joseph B. Lessing

Department of Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, and Sackler Faculty of Medicine, Tel Aviv University, Israel

1To whom correspondence should be addressed at: Department of Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel

Pemphigus vulgaris (PV) is an uncommon, immune-mediated bullous dermatosis, which, during its active phase, has been associated with infertility. Pemphigus vulgaris during pregnancy is exceedingly rare—only 26 cases with immunopathological confirmation have been reported. The disease may be associated with adverse neonatal outcome, including prematurity and fetal death. Transient skin lesions may occasionally appear in the neonate. We report a patient who conceived during the active phase of PV, required high doses of corticosteroids to control the disease, and was delivered of a pre-term, appropriate-for-gestational age newborn.

Key words: pemphigus vulgaris/pregnancy

Introduction

Pemphigus vulgaris (PV) is a rare, autoimmune, bullous dermatosis. The disease affects all races and both sexes, appears in middle age and rarely affects children. Jewish people, especially Ashkenazi (central or eastern European) Jews, have an increased susceptibility to PV (Korman, 1990). Predisposition to pemphigus is linked to genetic factors: first-degree relatives of patients are more susceptible to the development of autoimmune diseases (Firooz et al., 1994), certain major histocompatibility complex (MHC) class II molecules are more common in patients with PV (specifically, an HLA-DR4 allele) (Bhol et al., 1996) and finally, pemphigus occurs in patients with other disorders characterized by immunological disturbances such as myasthenia gravis and lupus erythematosus (Cruz et al., 1987). The pathogenesis is linked to the presence of autoantibodies directed against desmoglein 3, a desmosome transmembrane glycoprotein belonging to the cadherin family (Joly et al., 1997). These autoantibodies cause blisters which result from loss of cell–cell adhesion in the basal and suprabasal layers of the deeper epidermis, with keratinocytes in the superficial layers of the epidermis that maintain their cell adhesion (Amagi et al., 1996). Clinical manifestations include numerous skin vesicles, most of which result in widespread erosions and ulcerations that heal without scarring, as the erosions are entirely epidermal. Involvement may be localized or generalized but the disease has a predilection for the scalp, face, axillae, groins and pressure points. The oral and nasal mucosae are often involved (50–70% of patients). They may precede cutaneous lesions by months or may be the only manifestation of the disease. Other mucosal surfaces may be involved including the vulva (Marren et al., 1993). Diagnosis is based on lesion biopsy showing the presence of acantholysis, suprabasal cleft formation and deposition of immunoglobulin (Ig)-G and complement in the intercellular spaces of the epidermis. Immunoglobulin-G antibodies against the pemphigus antigen may be detected by indirect immunofluorescence in the serum (Daniel et al., 1995). Before the availability of corticosteroid therapy the disease was usually fatal, due to secondary infection and sepsis, or electrolyte imbalance (Ruach et al., 1995). Treatment with systemic steroids has reduced mortality to between 5–15%, but some of the patients succumb to complications of chronic steroid therapy and presence of comorbidity (Rosenberg et al., 1976; Carson et al., 1996).

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 (Ouahes et al., 1997).

PV is extremely rare in pregnancy, and with the addition of our case, only 27 reported cases can be found in the English literature. We report the case of a patient with PV who conceived during the active phase of the disease, required high doses of corticosteroids for control, and gave birth to a pre-term, but otherwise healthy, appropriate-for-gestational-age (AGA) newborn.

Case report

A 32-year-old Ashkenazi Jewish woman, with a history of removal of basal cell carcinoma from scalp and right breast, was admitted to the Dermatology Department because of multiple skin lesions and throat pain that persisted for over a month. The lesions included pustules and erosions over the oral mucosa, including the epiglottis, and over the skin of the arms, thorax, abdomen and thighs. The diagnosis of PV was confirmed by histological examination, direct immunofluores-
cence-detected, intercellular deposition of Ig-G and C3, and pemphigus antibody titres that were positive by indirect immunofluorescence. Prednisone, 100 mg/day was initiated; after 8 days the dose was increased to 120 mg/day for 15 days, and the patient was discharged on 80 mg/day with improvement in both vesicles and wellbeing.

Two weeks after diagnosis and beginning of treatment, the patient had her last menstrual period. An intrauterine pregnancy was diagnosed by ultrasound with a crown–rump length of 4 cm, dating the pregnancy 5 days earlier than that estimated by the last menstrual period. Therefore, the patient must have conceived 8–9 weeks after the first symptoms of PV.

The woman continued prednisone therapy during pregnancy, which was tapered to 15 mg/day. During the 13th week of gestation, she was hospitalized due to a severe flare-up of her disease. This included vesicles and erosions over the skin of the neck, abdomen, back, breasts, and thighs, this time with no mucosal involvement. The patient was discharged with a prednisone dosage of 50 mg/day. The disease was controlled with no appearance of new lesions and slow improvement in existing lesions throughout the remainder of her pregnancy.

Pregnancy follow-up was normal regarding blood pressure examinations, maternal weight gain, and glucose tolerance test. Amniocentesis was performed and demonstrated a male fetus with normal karyotype. Repeated ultrasonographic follow-up showed normal fetal growth (abdominal circumference – 50th percentile; head circumference – 40th percentile and femur length – 50th percentile). Intrauterine echocardiography, performed because of a ‘golf ball’ finding, showed mild thickening of one chorda tendinae in the right ventricle, with no haemodynamic significance.

The patient was admitted to our labour unit because of premature rupture of the membranes in her 33rd week of gestation. Fetal heart monitoring showed a single variable deceleration, after which it was reactive. Oxytocin induction of labour resulted in vaginal delivery. A male infant weighing 2270 g (AGA) was born, with Apgar scores of 9 at 1 minute and 10 at 5 min. Cord blood gases were normal.

The premature newborn was admitted to the neonatal intensive care unit because of his age and weight. Apart from a transient event of hypoglycaemia, which was effectively treated with i.v. glucose, and phototherapy due to indirect hyperbilirubinaemia, the newborn was otherwise healthy, without manifestations of PV.

**Discussion**

In a retrospective study (Ouahes et al., 1997), 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 disease flare-up, implying that active disease does not necessarily cause infertility.

Pregnancy may precipitate or aggravate PV, as reported in better-known autoimmune diseases, such as systemic lupus erythematosus (Kaufman et al., 1988). Our patient clearly demonstrated disease flare-up during the period of conception and early pregnancy, with difficulty in controlling the disease at that time. As shown in our patient, improvement in disease control during the third trimester may well be explained by rising endogenous corticosteroid production by the chorion and consequent immunosuppression (Weinberg, 1984).

Transplacental transmission of PV Ig-G antibodies from mother to fetus may result in clinical manifestations in the neonate (Wasserstrum and Laros, 1983). Previous reports suggested a high incidence of skin lesions in the neonate (up to 61%). This high incidence of skin lesions, not reflected in our case, may represent over-publication of reports on neonates with PV lesions (Ruach et al., 1995). 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 (Chowdhury and Natarajan, 1998). Furthermore, there is a lack of association between the clinical manifestations of the disease in mother and newborn. Another case was reported (Hern et al., 1998) in which the mother had oral disease without cutaneous involvement, whereas the child presented with cutaneous blisters.

PV may also be associated with a more adverse neonatal outcome, such as fetal growth restriction and preterm births. 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 (Terpstra et al., 1979; Green et al., 1982; Wasserstrum and Laros, 1983; Ross et al., 1986). As in our case, there is no obvious relationship between maternal disease severity and neonatal outcome (Merlob et al., 1986). The only adverse neonatal outcome in our case was premature rupture of membranes and delivery of a 33-week AGA, pre-term fetus.

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 (Laskin et al., 1997), where a significant increase was shown in preterm delivery, premature labour and PPROM 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.

Management of PV in pregnancy is similar to that in non-pregnant women. High dose prednisone (60–360 mg/day) for several weeks and gradual tapering to a maintenance dose is usually successful, as previously described (Hern et al., 1998) and as shown in this case. Although no increase in congenital malformations has been reported (as discussed by Hern et al., 1998), corticosteroid treatment in pregnancy has been associated, as in our case, with PPROM and preterm births (Laskin et al., 1997). Therefore, the management in pregnancy should involve individual balancing of the risks of the disease and its complications against the potential adverse effects of therapy on both mother and child. Immunosuppressive drugs should be withheld although azathioprine may be added (Hayashi,
Pemphigus vulgaris in pregnancy


Received on August 9, 1999; accepted on February 2, 2000

References


