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Pemphigoid gestationis and intravenous immunoglobulin therapy☆

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ABSTRACT

Pemphigoid gestationis, which is also known as herpes gestationis, is a rare, pregnancy-associated, autoimmune bullous disease. Treatment depends on the severity of the disease for each patient and the safety and use of these drugs during pregnancy and breastfeeding must be taken into consideration to guide their use. We describe the therapeutic response of two cases of pemphigoid gestationis that did not respond to conventional immunosuppressive therapy or adverse effects limited their use. Both patients eventually received treatment with intravenous immunoglobulin therapy, which resulted in clinical remission. This clinical improvement with disappearance of lesions and a reduction in pruritus was paralleled in a decline in Bullous Pemphigoid Disease Activity Index activity scores, which is a validated scoring system to measure the related condition, bullous pemphigoid.

Introduction

Pemphigoid gestationis (PG), which is also known as herpes gestationis, is a rare, pregnancy-associated, autoimmune bullous disease. Patients develop intensely pruritic vesiculobullous lesions that involve any part of the body but often the periumbilical area. The intense pruritus causes significant morbidity and interferes with patients' quality of life. Symptoms usually resolve after pregnancy but in some women, the condition and symptoms can persist for months to years (Intong and Murrell, 2011a).

Treatment depends on the severity of the disease for each patient and the safety and use of these drugs during pregnancy and breastfeeding must be taken into consideration to guide their use (Intong and Murrell, 2011a, 2011b). We describe the therapeutic response of two cases of PG that did not respond to conventional immunosuppressive therapy or adverse effects limited their use. Both patients eventually received treatment with intravenous immunoglobulin (IVIG) therapy, which resulted in clinical remission. This clinical improvement with the disappearance of the lesions and a reduction in pruritus was paralleled with a decline in Bullous Pemphigoid Disease Activity Index (BPDAI) activity scores, which is a validated scoring system to measure the related condition, bullous pemphigoid (Wijayanti et al., 2017).

Case 1

A 28-year-old, pregnant, Caucasian patient developed a pruritic rash at 28 to 40 weeks of gestation. This was her first pregnancy and her medical history included type 1 diabetes mellitus, hyperthyroidism, and asthma. Her medications included a continuous insulin pump, metformin 500 mg three times per day, and ranitidine 150 mg daily. During the examination, pruritic erythematous papules and tense bullae were observed arising on erythematous annular patches and plaques in a periumbilical distribution on her abdomen and thighs (Fig. 1).

Punch biopsies of representative lesions on her thigh were performed for histopathological examination and direct immunofluorescence (DIF) studies. The histopathology demonstrated mild acanthosis and spongiosis with overlying parakeratosis. A subepidermal vesicle was seen with eosinophils and lymphocytes. The upper

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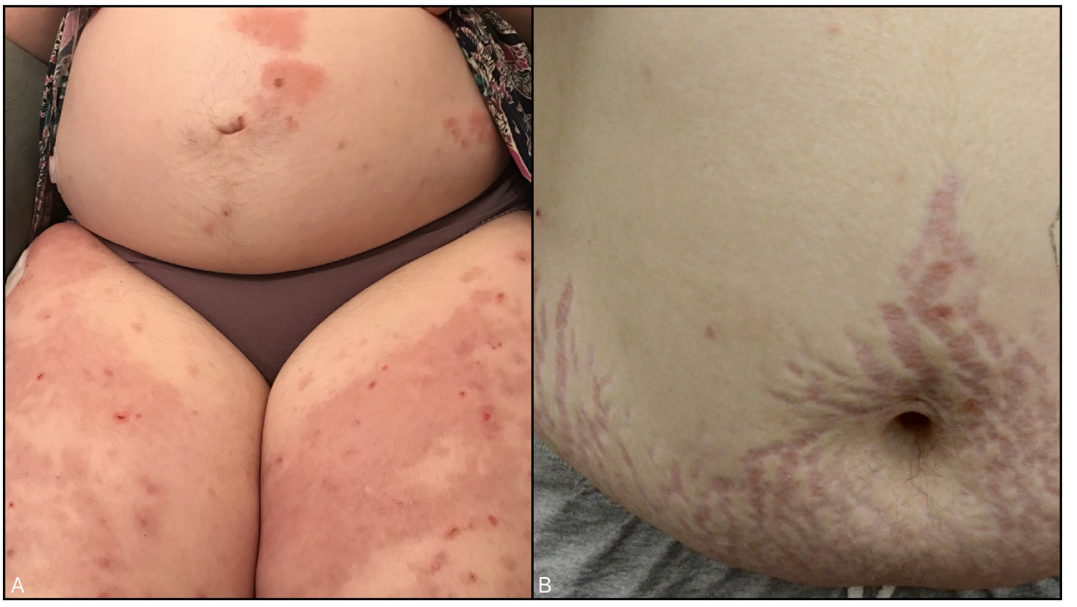

Fig. 1. A) Case 1 after the initiation of treatment, urticarial plaques with bullae on the abdomen and thighs. B) Case 1 with steroid-induced striae as an additional adverse effect of prolonged prednisone use.

dermis demonstrated prominent edema that consisted of moderate-to-heavy dermal inflammatory infiltrate with perivascular lymphocytes and interstitial eosinophils. DIF demonstrated a linear deposition of C3 and scant immunoglobulin (Ig) G along the basement membrane zone at the dermo-epidermal junction, which is also in keeping with a diagnosis of PG. Indirect serum investigations were performed and demonstrated C3 and scanty IgG on salt split skin at the basement membrane zone.

The patient was initially managed by another dermatologist and initiated 25 mg of prednisone, which was increased to 35 mg/day to control the ongoing blister formation. She also initiated an antihistamine with no additional relief from her pruritus.

She delivered a healthy newborn in February 2017. The patient continued to have flare-ups 10 weeks postpartum and any attempt to reduce the prednisone dose resulted in new lesions. She did not wish to stop breastfeeding to trial treatment with azathioprine or mycophenolate. However, systemic steroid medications alone were ineffective to keep the disease under control and the prednisone resulted in a significant lability to her blood glucose levels as she began to develop severe prednisone-related striae (Fig. 1).

The patient was referred to our clinic for further management of PG that was not responding to systemic steroid medications in the setting of type 1 diabetes. Further investigations of her sera at that time with the Biochip (EuroImmun, Lubeck, Germany) demonstrated indeterminate results on the salt split skin and positive reactivity for BP180 but negative to BP230. The enzyme-linked immunosorbent assay was positive for BP180 but negative for BP230 and well as desmogleins 1 and 3.

At the time of her initial review on prednisone, her BPDAI activity and damage scores were 13 and 4, respectively. Her quality of life score with respect to her blistering disease was measured with the Autoimmune Bullous Quality of Life (ABQOL) and was 29/51. Her treatment ABQOL score, which reflects the toll of treatment, was 29/51. In light of her type 1 diabetes, persistent disease, and desire to continue breastfeeding, IVIG therapy was discussed as a safer alternative. While awaiting approval for IVIG treatment, the patient was commenced on oral cromolyn sodium 100 mg daily to reduce mast cell-derived itch and inflammation as well as erythromycin 400 mg three times a day in view of not being able to receive tetracycline while breastfeeding.

The patient was initiated on IVIG therapy at 2 g/kg divided over 3 days every 4 weeks while her prednisone was at 25 mg/day. She developed a headache after her second dose, which resolved and was managed with prehydration preceding her subsequent doses. A month after the cycles of IVIG, she had had no new lesions and her BPDAI score was improving so her prednisone was weaned in

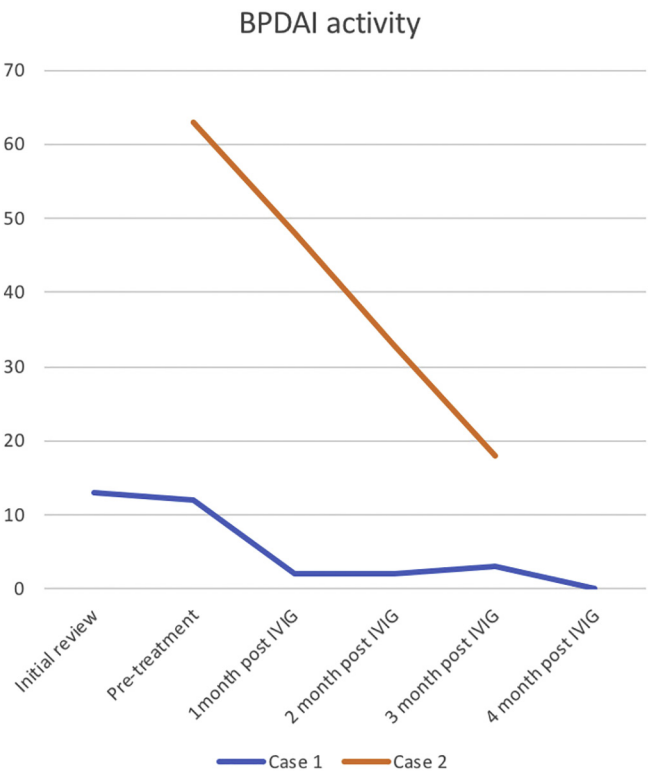

Fig. 2. Bullous Pemphigoid Disease Activity Index (BPDAI) activity score. Case 1: Pre-IVIG treatment BPDAI activity score 13, which demonstrates a downward trend to 0 at 4 months post-IVIG. Case 2: Pre-IVIG treatment BPDAI activity score 63, which demonstrates a downward trend to 13 at 3 months post-IVIG.

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