Recalcitrant, delayed pressure urticaria treated with long-term intravenous immunoglobulin

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INTRODUCTION

Delayed pressure urticaria (DPU) may compose up to 37% of all physical urticarias, which also includes cholinergic urticaria, solar urticaria, and cold urticaria, but rarely as a primary inducible urticaria.[1] The diagnosis of DPU can be made with a pressure challenge test, which may pose diagnostic difficulties and lead to a lower reported incidence rate. The testing comprises applying sustained pressure to the skin. Often, test responses occur between 30 minutes and 12 hours after exposure, lasting up to 72 hours. However, test response should be assessed within the first 6 hours. Few studies have found the efficacy and safety of treatment options for DPU. Current treatments include antihistamines, montelukast, oral steroids, nonsteroidal anti-inflammatory drugs, cyclosporine, omalizumab, and intravenous immunoglobulin (IVIG).[2,3] Here we describe the case of a female patient with recalcitrant DPU maintained on long-term IVIG therapy.

Abbreviations used:

DPU: delayed pressure urticaria
IVIG: intravenous immunoglobulin

CASE PRESENTATION

A 42-year old white woman presented with a 22-year history of DPU, which was treated with IVIG for 12 years. Her symptoms were generalized and, prior to IVIG therapy, included erythematous, edematous plaques, consistent with DPU, and dermatographism on the face, lips, abdomen, hands, and feet. Furthermore, she often experienced postprandial gastrointestinal upset and feelings of malaise during episodes of DPU. When uncontrolled, symptoms of her condition have made it difficult to complete daily activities such as standing for extended periods or cooking meals. She reported remission of urticarial symptoms with pregnancy and breastfeeding. Pathology found a mild degree of perivascular lymphocytic infiltrate throughout the dermis, an unremarkable epidermis, and many eosinophils. This finding was consistent with urticaria. Complete blood counts with differential, antinuclear antibody, thyroid-stimulating hormone, thyroid antibodies, cryoglobulins, complement levels, and serum tryptase results were within normal limits.

Currently, at 12-week intervals, the patient receives 1 g/kg actual body weight IVIG every day for 3 consecutive days through an Infusaport (C.R. Bard, Cranston, RI) because of difficult vascular access. The patient receives a 3-day course of oral prednisone before receiving IVIG and is premedicated with meperidine, promethazine, and hydrocodone-paracetamol as needed for infusion headaches. The patient's adverse events have been limited to intermittent, mild headaches surrounding IVIG infusions.

During the patient's 3 pregnancies, she was treated with IVIG. During the initial pregnancy, she received 2 courses of IVIG at 18 weeks and 37 weeks, and she delivered via normal vaginal delivery without complications. Each course was a cumulative dose of 2 g/kg IVIG over 5 days. During her later pregnancies, she delivered via cesarean section because of failure to progress. All newborns were healthy at birth. It is important to note that a multidisciplinary team, including dermatology and

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maternal fetal medicine, followed the patient very closely during each pregnancy.

Prior treatments include topical corticosteroids for symptomatic relief, high-dose antihistamines, ketotifen, montelukast sodium, cromolyn, sodium, psoralen and ultraviolet-A, methotrexate, oral prednisone, and an experimental trial of omalizumab. None were successful.

DISCUSSION

DPU is an uncommon condition characterized by a delayed, swelling reaction on areas affected by pressure. Often, the symptoms start after 4 to 8 hours and may last up to 72 hours.[4] Episodes of DPU may be accompanied by delayed dermatographism and generalized flulike symptoms. One study found that the quality-of-life impairment associated with DPU is significantly higher than that in people with chronic spontaneous urticaria, mostly affecting areas of work/study, leisure, and symptoms.[5] There is little known about the natural course of DPU. However, a study found that although 47.4% of patients with chronic spontaneous urticaria remit after 1 year, only16.4% of those with physical urticaria, including DPU, are free of symptoms after 1 year.[6] Reports state that some patients may be affected with DPU for up to 40 years.[4] Furthermore, treating DPU is difficult because of the variable courses, spontaneous remissions, and inconsistent results in the literature regarding medical management.[7]

IVIG is a pooled plasma product, composed mostly of IgG, and has been used in numerous autoimmune, oncologic, and idiopathic conditions including pemphigus vulgaris, chronic lymphocytic leukemia, and Kawasaki disease. In the case of chronic urticarias, it has been suggested that IVIG contains anti-idiotypic antibodies, which may suppress the IgE molecules, implicated in these conditions.[8] Common side effects of IVIG include tension headaches, nausea, malaise and a low-grade fever.[9] More severe symptoms are uncommon but may include aseptic meningitis, acute renal failure, and myocardial infarction. Thus, it is important to perform a comprehensive history and physical examination before prescribing IVIG for any condition.

One retrospective study found that 3 of 8 patients with recalcitrant pressure urticaria achieved full remission after 1 to 3 infusions of IVIG.[10] Two patients showed improvement without remission. Adverse events were limited to headache, malaise, nausea, low-grade fever, and flulike illness. Although most symptoms resolved within 24 hours after infusion, 2 patients had persistent headaches lasting 3 days.

To our knowledge, there are no reports of patients with recalcitrant DPU maintained on long-term IVIG therapy nor reports of management during pregnancy. This treatment has greatly improved the quality of life of our patient with minimal adverse events. This case report highlights the need for randomized, clinical trials investigating the benefits of IVIG and other therapies for patients affected by DPU.

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