Correspondence

MULTIPLE TREATMENT CYCLES OF HIGH-DOSE INTRAVENOUS IMMUNOGLOBULIN FOR CHRONIC SPONTANEOUS URTICARIA

To the Editor: We commend Mitzel-Kaoukhov et al[1] for their study of high-dose intravenous immunoglobulin (IVIG) therapy for chronic spontaneous urticaria (CSU), in which patients received 2 g/kg across 2 days at monthly intervals (for 5 of 6 patients). Four of 6 patients had complete remission after 2 to 4 cycles, maintaining remission for 10 to 24 months without IVIG therapy. However, their favorable results contrast with our experience using IVIG in 3 patients with corticosteroid-dependent CSU. Our patients achieved only partial remission with subsequent relapse, similar to the results of Asero.[2]

The 3 patients (2 men and 1 woman) had a mean age of 29 years (range, 23-35 years) and a mean CSU duration of 30 months (range, 6–72 months). All 3 patients took daily prednisone and had failed high-dose H1 antihistamine (4 times normal dosing), H2 antihistamine, and montelukast therapy. One patient failed cyclosporine, sulfasalazine, and dapsone therapy. Herein we summarize their response to IVIG, 2 g/kg, infused across 5 days.

Patient 1 experienced temporary improvement and was controlled with once-daily fexofenadine. Urticaria increased in severity 5 months after IVIG infusion, at which time he required twice-daily fexofenadine. Patient 2 experienced temporary improvement and required only cetirizine, 10 mg daily. However, urticaria returned to baseline 6 weeks after IVIG therapy. A second IVIG cycle resulted in 18 days of improvement followed by relapse of urticaria to baseline. These 2 cases illustrate that a single IVIG cycle is unlikely to produce complete remission, and multiple IVIG infusions are likely necessary for sustained benefit.

Patient 3 presented to the clinic on day 3 of the 5-day IVIG cycle with severe frontal and occipital headache, photophobia, phonophobia, and stiff neck. A lumbar puncture revealed a cerebrospinal fluid white blood cell count of 861/cm^3 with negative cultures, confirming a diagnosis of aseptic meningitis likely secondary to IVIG infusion. This case demonstrates the risk of high-dose IVIG therapy; when administration was discontinued, urticaria returned to baseline in 2 weeks.

With current evidence based on uncontrolled case series, IVIG is off-label (no Food and Drug Administration indication) for CSU, was recommended as third-line therapy in a recent review,[3] and was given a category C strength of recommendation in a recent consensus document.[4] Our experience and that of Asero[2] suggest that a single cycle (2 g/kg) is unlikely to induce sustained remission. In the series by O'Donnell et al,[5] only 2 of 10 patients achieved complete remission with a single infusion. In the series by Mitzel-Kaoukhov et al,[1] 5 of 6 patients received 4 or more infusions, possibly explaining their favorable results. The high expense, likely need for multiple infusions, and adverse effect profile of IVIG (including aseptic meningitis) balance the possible benefit of sustained remission. Future controlled studies examining the optimum dosing (400 mg vs 1 g vs 2 g/kg) and cycle length (1 vs 2 vs 5 days) would be invaluable toward defining the role of IVIG in severe CSU.

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INTRAVENOUS IMMUNOGLOBULIN AS A THIRD-LINE THERAPY IN CHRONIC SPONTANEOUS URTICARIA

Author Response: We thank you for your annotation to our series about intravenous immunoglobulin (IVIG) therapy. Of course, observations such as case report series are not comparable with big controlled studies. For different reasons (eg, costs), there is no chance of obtaining results across large randomized studies in the near future.

From our point of view, it is necessary to discuss some possible causes of the different outcomes. It is known that patients with severe autoreactive urticaria respond positively to IVIG. Do you start an autologous serum skin test before treatment? The literature shows that IVIG seems to work more effectively in patients with autoimmune mechanisms.[1] As recommended by German guidelines for the treatment regimen of autoimmune diseases with IVIG and as shown in recent studies, a single IVIG cycle is usually not enough to achieve long-term remission. It is recommended monthly for a longer period to reach a stable status of remission.[1,2] In our series, we continued

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