Case Report
Allergy Asthma Immunol Res. 2012 July;4(4):245-247.
http://dx.doi.org/10.4168/aair.2012.4.4.245
pISSN 2092-7355 • eISSN 2092-7363

AAIR
Allergy, Asthma & Immunology Research

Plasmapheresis in a Patient With "Refractory" Urticarial Vasculitis

Ozgur Kartal,[1]* Mustafa Gulec,[1] Zafer Caliskaner,[1] Oral Nevruz,[2] Turker Cetin,[2] Osman Sener[1]

Divisions of Immunology and Allergic Diseases,[1] Haematology,[2] Gülhane Military Medical Academy and Medical School, Ankara, Turkey

Immune complexes are found in the circulation of 30%-75% of patients with urticarial vasculitis and much evidence supports the role of these immune complexes in the pathogenesis of urticarial vasculitis. Plasmapheresis is effective for removing these immune complexes; however, there are few reports on the use of plasmapheresis in the treatment of urticarial vasculitis. We describe a case of "refractory" urticarial vasculitis in which the symptoms improved after plasmapheresis treatment. We suggest that plasmapheresis be considered as an option in patients with severe or treatment-resistant urticarial vasculitis.

Key Words: Plasmapheresis; treatment; urticarial vasculitis

INTRODUCTION

Approximately 40% of patients with chronic urticaria (CU) have functional autoantibodies against FcεRIa or IgE on mast cells and basophils.[1] The same antibodies play a role in the pathogenesis of urticarial vasculitis (UV),[2] a subtype of CU (2%-20% of cases) that is more common in women (60%-80%).[3]

Antihistamines and systemic steroids are the most common drugs used in the treatment of CU, but the response to therapy is often incomplete.[4] In patients with UV or antihistamine-resistant or steroid-dependent CU, immunomodulators such as cyclosporin A, sulfasalazine, and hydroxychloroquine have been shown to be effective in randomized controlled trials.[3] However, there are concerns regarding the safety of these alternative treatment regimens.

In a few studies, plasmapheresis has been performed as an alternative therapy to remove excessive circulating autoantibodies in patients with CU or UV who do not respond to the above-mentioned treatments.[5-7]

This report describes a 35-year-old woman with UV who was treated successfully with plasmapheresis.

CASE REPORT

A 35-year-old woman presented with a 9-year history of recurrent episodes of generalized painful urticarial plaques associated with swelling of parts of her body. The urticarial plaques were accompanied by a burning sensation, rather than itching, and resolved gradually over 2-3 days without residual hyperpigmentation. There was no history of food or drug allergies. The patient had no complaints of arthralgias, abdominal pain, or fever.

The physical examination revealed multiple urticarial plaques distributed over her entire body, particularly the extremities, palms, and soles. The patient's quality of life had declined because of the unpleasant appearance and frequency of the lesions.

The initial laboratory studies were within the normal range, including a complete blood count, thyroid function tests, thyroid autoantibodies, erythrocyte sedimentation rate, hepatitis markers, liver and renal function tests, urinalysis, stool analysis for parasite ova, total IgE, C3, C4, C1q, CH50, and C1 inhibitor levels, and antinuclear antibodies.

Skin prick testing was negative for foods commonly consumed in Turkey, including egg whites, egg yolks, cow's milk, walnuts, peanuts, hazelnuts, almonds, sesame, lemons, tuna fish, mixed fish, beef, chicken meat, celery, beans, spinach, tomatoes, potatoes, green peas, soybeans, mushrooms, oranges, apples, peaches, apricots, and seven mixed cereals (Stallergènes; Antony, France).

Correspondence to: Ozgur Kartal, MD, Division of Immunology and Allergic Diseases, Gülhane Military Medical Academy and Medical School, Ankara 06018, Turkey.
Tel: +90-312-304-4133; Fax: +90-312-304-4139;
E-mail: drozkartal@hotmail.com
Received: August 5, 2011; Revised: November 21, 2011;
Accepted: December 15, 2011
• There are no financial or other issues that might lead to conflict of interest.

To obtain further information on the nature of her CU, we performed an autologous serum skin test (ASST), which was positive. This result suggested an autoimmune basis for the condition. A biopsy from an affected area of skin showed perivascular lymphocyte and neutrophil infiltration and extravasation of erythrocytes in the superficial dermis typical of UV. Direct immunofluorescence revealed IgM, IgG, IgA, C3, and fibrinogen deposits on the superficial dermal blood vessels. Based on the biopsy results, the patient was diagnosed with UV.

Treatment with different elimination diets, H1/H2-antihistamines in standard and increased dosages, and oral corticosteroids (1 mg/kg/day) was unsuccessful; therefore, hydroxychloroquine 400 mg/day was added to the treatment regimen. The hydroxychloroquine had to be stopped after 2 months due to the development of keratopathy. At this point, the patient was regarded as having "refractory" UV and plasmapheresis was considered.

The patient underwent two plasma exchanges 6 months apart, using 5% albumin as replacement fluid. One plasma volume was processed in each session. The procedure was performed with a Fresenius Cell Separator (ASTEC 204; Fresenius Kabi). The plasmapheresis procedures were completed without any adverse events.

Thirteen months after the plasmapheresis, the urticarial plaques reappeared, but the severity and duration of symptoms were lower than before the plasmapheresis. The new lesions were treated with oral desloratadine 5 mg/day for 5 days.

DISCUSSION

The cutaneous lesions of UV resemble urticaria; these lesions are composed of painful or nonpruritic urticarial plaques that typically persist for more than 24 hours.[3] UV can be associated with normal or low complement levels and usually resolves with hyperpigmentation.[3] UV may be local or systemic, and angioedema and arthritis are other clinical manifestations. The typical histological findings are essential for the diagnosis of UV. Immunofluorescent studies show granular deposits of immunoglobulins, fibrin, and complement.[3]

Approximately 40%-50% of patients with CU have functional IgG autoantibodies against either the high-affinity IgE receptor (FcεRIa) or IgE, as revealed by positive ASST responses. These autoantibodies and immune complexes have also been found in the circulation of patients with UV.[2] Jones et al.[8] demonstrated the role of immune complexes in UV.

The treatment of these patients is often difficult. Antihistamines are used for symptomatic treatment, but are ineffective for controlling inflammation. Therefore, antihistamines cannot alter the disease prognosis.[2] Additional treatments with immunomodulators such as cyclosporin A, sulfasalazine, and hydroxychloroquine are most commonly used to alter the course of the disease and to reduce the dosage of corticosteroids required.[2] However, there are concerns regarding the safety of these treatment options. Our patient refused treatment with a second immunosuppressive drug after developing keratopathy.

Alternative treatment modalities for the therapy of patients with UV include plasmapheresis or therapeutic plasma exchange. Plasmapheresis removes a variety of proteins from plasma, including antibodies, immune complexes, paraproteins, inflammatory mediators, drugs, toxins, and other plasma constituents. Plasmapheresis may have immunomodulatory effects via several mechanisms. The patient's plasma is replaced with other colloids, such as albumin or allogeneic plasma. In addition, plasma is separated by filtration or centrifugation and the remaining blood cells are returned to the patient in the replacement fluid. However, plasmapheresis should not be considered innocuous. The many complications of plasmapheresis include hypotension, respiratory distress, fluid-electrolyte abnormalities, allergic reactions, coagulation abnormalities, infection, and even death.[9,10]

In addition to removing the pathogenic plasma components directly, plasma exchange may also affect the immune system by enhancing the function of the reticuloendothelial system, removing blocking antibodies, and making lymphocytes more vulnerable to immunosuppressive drugs. Furthermore, plasma exchange has been shown to improve T-cell-suppressor function.[11]

There are reports on the beneficial effects of plasmapheresis in the treatment of CU and UV.[5-7] Plasmapheresis allows for the temporary resolution of the urticarial lesions by transiently removing the circulating immune complexes. It has no effect on the production of new autoantibodies. Therefore, as Jiang et al.[6] emphasized, plasmapheresis treatment is an "auxiliary" treatment option in a patient with UV.

In conclusion, this case report supports the usability of plasmapheresis in patients with "refractory" UV. Further clinical studies are needed to confirm our experience.

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