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Autohemotherapy in Chronic Urticaria: What Could Be the Autoreactive Factors and Curative Mechanisms?

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Dear Editor:

Chronic urticaria (CU) is characterized by recurrent wheals and pruritus with surrounding erythema presenting on all or most days of the week for >6 weeks.

At least 80%~90% of patients with CU are found to have no external cause for their condition. These patients are traditionally known to have chronic idiopathic urticaria (CIU). CIU affects up to 3% of the population at some point in their lives, and up to 20% of these patients can have symptoms for 10 years. CIU is more common in adults than in children; it has a female-to-male ratio of 4 : 1, and middle-aged women are reported to be the most affected group.

Recent evidence suggests that a subset of patients with CU may have an autoimmune basis for their condition, as shown by a positive skin test reaction to autologous serum skin test$^+$ (ASST$^+$)[1].

As circulating histamine-releasing factors including autoantibodies are responsible for the induction of urticarial symptoms in ASST$^+$ patients with CU[2], autohemotherapy, a historic form of CU treatment, may be considered a promising specific and potentially curative therapeutic option for this subgroup of patients with CU. Autohemotherapy, i.e. repeated intramuscular injections of autologous whole blood (AWB) sometimes treated with ozone or ultraviolet light, was commonly used to treat patients with CU before the development and introduction of antihistamines. Several evidence shows that autohemotherapy, which is also claimed to have therapeutic value in allergic diseases, circulatory disorders, viral diseases, and cancer, is curative in patients with CU[3-5]. Although its curative mechanism is not known, it is postulated that autohemotherapy modulates the immune response to autologous antigens that are supposed to be involved in histamine release from mast cells and basophils. It is supposed that with this method, i.e. injection of AWB or serum into the muscle, the access or route of circulating histamine-releasing factors (or their stimulators) into the immune system is changed, thereby causing some immunomodulations to occur, which finally results in tolerance induction to histamine- releasing factors (or their stimulators).

In searching for the nature of the above factors, although some ASST$^+$ patients with CU have been shown to express autoantibodies directed against the high-affinity receptor for IgE (anti-FcεRI) or immunoglobulin E (IgE) itself (anti-IgE), we found that many ASST$^+$ patients do not have anti-IgE or anti-FcεRI autoantibodies but still respond to autohemotherapy[6]. Therefore, factors other than the above-mentioned autoantibodies in these patients should be investigated.

One of the potential autoantibodies could be autoreactive IgE directed against any soluble antigen in serum that could bind to FcεRI. Thereafter, its specific antigen (any soluble antigen in serum) would induce cross-links between the FcεRI receptors in mast cells or basophils. Detection of these autoantibodies should be performed[7]; however, it should be kept in mind that these antibodies could be attached to the FcεRI and might not be detectable in serum. The above-mentioned soluble antigens in autologous serum could be autoantigens or even foreign allergens.

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The other potential autoantibody could be autoreactive IgE directed against autologous epitopes in cellular components of blood or other body tissues. If the cellular antigens do not exist or if they could not be traced in the serum, the patient could show a negative ASST. This could be a reason why some ASST$^-$ patients respond to whole-blood autohemotherapy[5,8], like some of our patients at Ganjavian Hospital (unpublished).

Thus, if the above-mentioned potentially autoreactive factors could be detected, some potentially curative mechanisms of autohemotherapy could be suggested. One possible mechanism is the stimulation of anti-idiotype production against the above-mentioned autoantibodies, which could block their binding to the FcεRI of mast cells or basophils. The second possibility could be tolerance induction to IgE or FcεRI. The third possible mechanism of autohemotherapy could be tolerance induction to other blood autoantigens or even foreign allergens. With autohemotherapy, the above-mentioned antigens, like a vaccine, are processed and presented to the immune system by muscular dendritic cells, with a different immune response priming potential that may convert a previously disease-causing antigen into a regulatory antigen that activates regulatory T cells, which could suppress effector T cells[9,10].

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