

Foreword

Urticaria: An Evolving Story



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Chronic spontaneous urticaria affects nearly 20% of the population. Although it is commonly considered a mast cell-mediated disease, the mechanism of mast cell activation remains a medical mystery. A number of new developments in this field got us quite excited. The demonstration of the presence of an anti-IgE receptor autoantibody and sometimes an anti-IgE autoantibody in serum from urticaria patients suggested an autoimmune mechanism. Although some studies have shown that these autoantibodies are more prevalent in patients with severe urticaria, the clinical correlation is not very strong. This is similar to autoantibodies found in rheumatologic disorders. It is possible that the anti-IgE autoantibody primes the mast cells, which require a second trigger for full activation and manifestation of the disease. We need to further understand the specific role of these autoantibodies in pathogenesis. There are a number of tests that detect this autoantibody. We need a standardized approach for optimal detection of the autoantibodies.

Another important development in the field is the impressive efficacy of omalizumab in antihistamine-resistant urticaria. The clinical implication of this finding is huge. However, the result raises questions about how omalizumab exerts its beneficial effect in urticaria. Omalizumab reduces the level of unbound IgE in the serum. This is associated with reduced FcεRI on mast cells and basophils. If reduced FcεRI is key to clinical improvement, it would imply a fundamental role for this receptor in the pathogenesis of urticaria.

Finally, there is a subgroup of urticaria patients whose basophils are unresponsive to activating stimulation, such as an anti-IgE antibody. This subgroup is called the nonresponder. Some preliminary observations suggest an increased expression of certain cytosolic phosphatases (SHIP1 and 2) in this subgroup. These phosphatases downregulate FcεRI signaling by inhibiting the activating kinases. It would be important to

Supported by NIH Grants RO1 AI091614 and N01 HHSN272200700048C.

demonstrate that the tissue mast cells also manifest a similar increase. If this is confirmed in larger populations, it would suggest that this subgroup utilizes a mechanism of mast cell activation that is different from FcεRI. These are exciting findings, indeed. To update us on these evolving stories, I have invited Dr Malcolm Greaves as guest editor. Dr Greaves is an internationally recognized leader in the field. He has brought together an outstanding group of authors and topics for this issue.

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