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Short Communication

Autoimmune Thyroid Disease and Chronic Urticaria: Is there a Causative Relationship or are they Separate Presentations of an Autoimmune Process?

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Autoimmune thyroid disorders are the most prevalent organ specific idiopathic autoimmune disorders affecting up to 5% of the population and it is characterized by the presence of thyroid autoantibodies and lymphocytic cell infiltration of thyroid tissue [1].

Urticaria is a common condition characterized by sudden and recurrent development of itchy skin wheals, with or without angioedema. The wheals are caused by vasodilation, increased blood flow and vascular permeability due to the activation and degranulation of mast cells, releasing inflammatory mediators such as histamine [2]. Chronic spontaneous urticaria (CSU) is defined as recurrence of urticarial heaves for more than 6 weeks in the absence of a triggering factor [3]. Although acute urticaria is mostly related to some definable triggers such as foods, drugs, insect bites or infections, 80 - 90% of CSU cases are idiopathic [4]. Several mechanisms have been suggested to explain the etiopathogenesis of CSU, one of which is autoimmunity and it is thought to play role in 30-40% of all subjects with CSU [1,5]. In this hypothesis, mast cell activation, degranulation and resultant urticaria are thought to occur secondary to an autoimmune process. This theory is supported by the fact that some autoimmune disorders, including thyroid autoimmune diseases, are more prevalent in patients with CSU when compared to healthy subjects. In these group of patients, anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) positivity have been found to be significantly more common, even in euthyroid subjects [1]. However, it is unclear whether antithyroid antibodies play a causative role in the development of chronic urticaria or whether they are two separate conditions of an autoimmune process. In the former situation, circulating antithyroid IgG antibodies are thought to induce mast cell degranulation causing urticaria, while in the latter situation, patients with urticaria and autoimmune thyroid disease are thought to have a tendecy to react to self; in which case, urticaria and thyroid disease develop simultaneously related to self-stimulation of mast cells and thyroid gland, respectively. Some investigators have also reported that some patients with CSU may have IgE antibodies against TPO, which bind and activate mast cells and cause autoimmune histamine release [6]. It has also been suggested that thyroid pathology may worsen urticaria through the activation of complement system [7]. Thyroid hormones are also known to regulate skin functions and epidermal homeostasis through thyroid hormone receptors found on many cell types of skin tissue. Therefore, in case of co-existing urticaria and autoimmune thyroid disease, treatment of thyroid pathology may cause improvement of urticaria [8]. In addition, some infectious agents are thought to be involved in the pathogenesis of both CSU and autoimmune thyroid disease, while the presence of a direct cause and effect relationship between infectious agents and pathogenesis of autoimmunity is unclear. Some studies suggested *Staphylococcus aureus* [9-11], *Helicobacter pylori* [12] and Hepatitis C virus [13,14] as etiologic factors for autoimmune processes, especially for thyroid autoimmune diseases. Similarly, a possible relationship between CSU and *Helicobacter pylori* infection has been suggested, which may indicate that a common infectious etiology may play role in the development of both condition.

Despite this clear correlation between autoimmune thyroid disease and chronic urticaria, recent urticaria guidelines do not recommend the measurement of thyroid hormones and autoantibodies in every case with chronic urticaria for identification of underlying thyroid pathology. Instead, further evaluation for thyroid disease is indicated as extended diagnostic programme only when clinical history and physical examination is suggestive of thyroid disease [15]. We think that thyroid pathologies are quite common in the subjects with CSU, therefore, thyroid hormone status might be considered as a routine part of evaluation for CSU. However, although thyroid autoantibodies are sensitive markers for autoimmune thyroid pathologies, their positivity does not indicate that the patient has actually

thyroid disease, structural damage or dysfunction in thyroid gland [1]. Although some studies suggest that urticaria may resolve following thyroid hormone therapy in patients with thyroid autoantibodies, irrespective of the initial thyroid function status, this information requires further definitive studies before a strong recommendation for thyroid hormone replacement as a treatment for CSU can be made. Therefore, thyroid autoantibody investigations may be conserved for patients with CSU in whom thyroid hormone levels are abnormal. In case of CSU without thyroid dysfunction, these patients should be accepted as under-risk population and followed for the development of autoimmune thyroid disease [2].

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