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Editorial

Real-World Disease Burden of Chronic Urticaria and Vaccine Hesitancy

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▸ See the article "Chronic Spontaneous Urticaria in Hong Kong: Clinical Characteristics, Real-World Practice and Implications for COVID-19 Vaccination" in volume 15 on page 32.

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Chronic urticaria (CU) is characterized by the occurrence of wheals, angioedema, or both for longer than 6 weeks.[1] It may occur spontaneously (chronic spontaneous urticaria) or in response to certain factors, such as cold, heat, solar radiation, or pressure (chronic inducible urticaria). It affects a substantial proportion of the global population, with overall lifetime and point prevalence rates of 1.4% and 0.7%, respectively. A recent meta-analysis found a higher point prevalence of CU (1.4%) in Asian countries than in Europe (0.5%) and Northern America (0.1%).[2] CU affects 0.16%–2.3% of the Korean population, and its prevalence increases annually.[3] Patients with CU have considerably impaired quality of life and increased healthcare resource utilization. Unpredictable and severe pruritus in CU negatively influences activities of daily living and sleep quality. Comorbidities, such as anxiety and depression, affect >30% of patients with CU, worsening their quality of life. In a multicenter, cross-sectional real-world study from Korean tertiary hospitals, more severe symptoms of CU were associated with a more significant impairment of quality of life and higher healthcare resource utilization.[4]

In CU, treatment aims to minimize the signs and symptoms and achieve disease remission. Current guidelines for CU recommend stepwise treatment based on symptom severity and treatment response.[1] Pharmacotherapy for CU is initiated with standard doses of second-generation H1-antihistamines, which can be increased up to 4-fold. Antihistamine-refractory CU is treated with omalizumab. Patients with insufficient response to omalizumab are treated with cyclosporine.[1] Despite the recommended pharmacotherapy, almost 50%–70% of CU patients have the moderate-to-severe disease.[4] In addition to pharmacotherapy, identifying and avoiding provocative factors, such as drugs (*e.g.*, non-steroidal anti-inflammatory drugs), food, and stress, are essential.[1]

During the coronavirus disease 2019 (COVID-19) pandemic, concerns about adverse drug reactions, including allergic reactions and the development of allergic diseases after COVID-19 vaccination, resulted in vaccine hesitancy. Vaccines, like other drugs, have the potential to cause allergic reactions. However, immediate severe reactions, including anaphylaxis or serious T cell-mediated systemic hypersensitivities, are extremely rare.[5]

Anaphylaxis occurs in 4.7–11.1 cases per million doses of the BNT162b2 vaccine, which is higher than that for other vaccines (1.31 cases per million doses).[6] Vaccine-associated anaphylaxis is more common in patients at high risk of allergy, including those with a history of anaphylaxis to drugs, multiple drug allergies, multiple allergies, or mast cell disorders, compared to those at low risk of allergy, including those with a history of non-anaphylactic reaction to a single drug or CU.[7] COVID-19 vaccine has been proposed to be involved in CU development and relapse.[8] Almost 8% of CU patients on regular treatment with antihistamines and omalizumab develop urticaria after COVID-19 vaccination.[9,10] CU patients who experience a relapse of urticaria have a higher baseline urticaria activity score-7 (UAS7) compared to those without relapse.[10] These reactions may be caused by immunoglobulin E (IgE)-mediated or non-IgE-mediated responses. Most CU relapses occur due to non-IgE-mediated responses; therefore, the diagnosis of vaccine allergy should be assigned after careful consideration.[11]

In the current issue of *Allergy, Asthma & Immunology Research*, Kan *et al.*[12] evaluated real-world CU management in Hong Kong and emphasized the role of immunologists/allergists in effectively treating CU and avoiding inappropriate COVID-19 vaccine hesitancy. A substantial proportion of CU patients in Hong Kong received inappropriate treatments, including regular first-generation H1-antihistamines and systemic corticosteroids, and had persistently uncontrolled disease. Urticaria severity assessed by the UAS7 was significantly reduced after consultation with immunologists/allergists, particularly in patients with uncontrolled CU. In line with this study, a previous real-world study that investigated the disease burden of CU in European countries reported a high proportion of uncontrolled CU and highlighted the need for physician education and adherence to CU guidelines to improve treatment outcomes.[13] Meanwhile, a recent real-world, multicenter study of CU burden in Korea found that, despite compliance with CU treatment guidelines, patients had poor quality of life and unmet needs, suggesting a need for better treatment.[4]

Although there is no evidence of the increased frequency of severe allergic reactions to the COVID-19 vaccine in CU patients, and CU is not a contraindication for COVID-19 vaccination,[14] there are concerns regarding COVID-19 vaccination in CU patients. Kan *et al.*[12] found that a significantly lower proportion of CU patients received 2 doses of the COVID-19 vaccine than the general adult population (65% vs. 73.2%, respectively). Notably, previous studies have not found increased allergic responses to vaccines in CU patients. Additionally, COVID-19 vaccine uptake was associated with regular pharmacological treatment of CU and inversely associated with suspected drug allergy. Because CU does not increase the risk of IgE-mediated allergic reactions to the COVID-19 vaccine, it is essential to distinguish between CU exacerbation after COVID-19 vaccination and vaccine allergy.[11] The Center for Disease Control states that previous anaphylaxis or allergy to the COVID-19 vaccine or its components is a contraindication for COVID-19 vaccination.[15] Conversely, routine vaccination with 15-min monitoring is recommended for patients with other drug allergies.[14] Immunologists/allergists play an important role in diagnosing drug allergies, to alleviate the inappropriate concerns of patients regarding vaccine allergy and to increase the rate of vaccine uptake.

CU is associated with a substantial healthcare burden worldwide, which may be attributable to non-adherence to CU treatment guidelines and lack of education. Further studies are required to understand the gap between clinical practice and CU treatment guidelines and to identify the hurdles in following the guidelines. In general, CU is not a contraindication for COVID-19 vaccination. However, accurate diagnosis of drug allergy by immunologists/allergists is essential to increase the rate of COVID-19 vaccination and immunity against COVID-19 infection.

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