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Editorial

Asthma-chronic obstructive pulmonary disease overlap (ACO): An emerging entity in allergic respiratory diseases

In *Allergology International* (AI) Vol. 67 Issue 2, we feature a set of review articles entitled “Asthma-chronic obstructive pulmonary disease overlap (ACO): An emerging entity in allergic respiratory diseases” as well as original articles and letters to the editor. We believe that this issue will be of great help in understanding how ACO is defined and what characteristics ACO has.

It has been long recognized that some patients with airflow limitation have symptoms both of asthma and of COPD. More than a half century ago, Orie and Sluiter proposed the “Dutch hypothesis,” in which asthma and COPD share a common origin with the divergence explained by an individual's unique genetic background and environmental exposure.¹ The terms “asthma-COPD overlap syndrome (ACOS)” or “asthma-COPD overlap (ACO)” were coined only a decade ago. However, definitions of ACO vary considerably among international respiratory societies, suggesting gaps in our knowledge of the pathophysiology, clinical features, treatment, and prognosis of patients with ACO.

In 2014, the Global Initiative for Asthma (GINA)/the Global Initiative for Chronic Obstructive Lung Disease (GOLD) released a document providing a pragmatic approach to the diagnosis of ACO.² Then the Japanese Respiratory Society (JRS) very recently published ACO guidelines.³ Although ACO is not a new concept and patients who display features of both asthma and COPD are frequently encountered in clinical practice, our understanding of ACO is limited, especially with regard to treatment.

In this issue, Uchida *et al.* describe the epidemiology of ACO.⁴ Reports of the prevalence of ACO vary considerably in the literature (from 0.9% to 11.1% in the general population), which can be attributed to differences in how ACO is defined. Yanagisawa and Ichinose discuss ACO mainly based on the definition in the GINA/GOLD document and the new JRS guidelines.⁵ Although the GINA/GOLD document is practical and easy for clinicians to use in diagnosing ACO, it is largely based on symptoms and does not include the use of biomarkers. In the JRS guidelines, treating ACO according to disease severity is recommended. Hikichi *et al.* describe the pathophysiology of ACO, particularly factors that tend to increase the probability of a patient developing ACO.⁶ Kondo and Tamaoki discuss how best to manage ACO, emphasizing selecting a therapeutic approach according to its severity.⁷ The strategy of triple combination therapy with ICS/LABA/LAMA is already commonly employed in clinical practice. Moreover, molecularly targeted drugs against IgE and IL-5 can be used along with the triple combination

therapy for severe patients. In addition, anti-neutrophil intervention may also be considered.

Benralizumab, an anti-IL-5 receptor antibody, was very recently approved in Japan as a new therapy for severe asthma (in January 2018). In contrast to mepolizumab, which neutralizes IL-5, benralizumab directly induces eosinophil cell death by antibody-dependent cellular cytotoxicity. In this issue, Ohta and colleagues report a subgroup analysis of 46 Japanese cases registered in the CALIMA study, a randomized, placebo-controlled phase 3 trial of benralizumab.^{8,9} The primary endpoint of the trial was the annual exacerbation rate (AER) during a 56 week-treatment period in severe asthmatics with peripheral blood eosinophil counts $\geq 300/\mu\text{L}$. In the original study population, the AER ratio versus placebo was decreased by 36% and 28% under treatment with benralizumab every 4 or 8 weeks, respectively.⁹ AER reduction was much greater in Japanese patients, ranging from 66% (Q4W) to 83% (Q8W).⁸ Pooled analysis of two phase 3 trials (the CALIMA and SI-ROCCO studies) also demonstrates better responses to benralizumab in all Asian patients (AER ratio versus placebo 53% [Q4W], 79% [Q8W]) than in Caucasians (41% [Q4W] and 39% [Q8W]).¹⁰ Post-marketing surveillance with more cases would further clarify the impact of ethnicity on the effectiveness of anti-IL-5 treatments.

Everybody knows that urticaria is a type I allergic reaction, but we had wondered about the contribution of IgE to this skin disorder. Then anti-IgE antibody gave us a clear answer to this question, and omalizumab was approved to treat antihistamine-refractory chronic spontaneous urticarial (CSU) in Japan, beginning in March 2017. In this issue, Hide *et al.* demonstrate that omalizumab is a safe and beneficial option for treatment of CSU in Japanese patients.¹¹ Readers will find this article to be especially interesting and valuable based on the analysis relating to individual patient responses to treatment, paired with the assessment of omalizumab serum concentrations and changes in IgE serum levels over time.

Minami *et al.* performed a unique study to explore whether transdermal exposure to food allergens, via damaged skin, is linked to development of food allergy in adults. They used a web-based questionnaire survey of occupational kitchen workers and non-occupational housewives.¹² Current hand eczema and current diagnosed food allergy were more common among the kitchen workers than among the housewives. In the workers, current hand eczema was associated with increased risk of current diagnosed food allergy, i.e., those with more severe hand eczema were more likely to develop food allergy. This article clearly demonstrates a close relationship between food contact with hands affected by eczema

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and transdermal sensitization to that same food in adults, as is known to be the case in children. Controlling occupational hand eczema may be more important for prevention of food allergy than we ever imagined.

Sublingual immunotherapy (SLIT) using standardized Japanese cedar pollen extract was approved by the Japanese government in 2014. Although SLIT is an effective treatment for allergic rhinitis, its efficacy varies among patients. Yonekura *et al.* analyzed the factors related to SLIT's effectiveness on allergic rhinitis induced by Japanese cedar pollen.¹³ When they compared the baseline characteristics of good (49.0%) and poor (17.4%) responders, a significant difference was observed in body mass index (BMI) such that the patients with BMI >25 presented with lower treatment efficacy. This article is the first to report the association between BMI and efficacy of SLIT, using standardized Japanese cedar pollen extract to show that BMI may modify the effect of SLIT.

We offer our appreciation to all the authors for their contributions to the present issue of Allergology International.

Conflict of interest

The authors have no conflict of interest to declare.

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