Establishing the Diagnosis: When is It Severe Asthma?

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Recognition of chronic airway inflammation with eosinophils and implementation of use of inhaled corticosteroids (ICS) have improved prognosis of asthma remarkably. However, some asthmatics could not be controlled with regular controller treatment, and severe or therapy-resistant asthma is increasingly recognized as a major unmet need. According to the ERS/ATS task force report on severe asthma, severe asthma is defined as asthma which requires treatment with guidelines suggested medications for GINA steps 4-5 asthma (high dose ICS and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for 50% or more of the previous year to prevent it from becoming "uncontrolled" or which remains "uncontrolled" despite this therapy. What we should keep it in our mind is the fact that the definition is applicable only when a diagnosis of asthma is confirmed and comorbidities addressed. This is a key point to distinguish severe or intractable asthma from difficult-to-treat asthma in which factors such as wrong diagnosis, comorbidities, risk factors (e.g. smoking and allergen exposure), poor adherence, or incorrect inhaler techniques. The strategies to confirm diagnosis of severe asthma is shown by guidelines including GINA as well as national or regional guidelines including ours, namely JGL.

When a patient is not controlled with GINA steps 4-5, we need to reconsider if the diagnosis of asthma is correct by differentiating from other cardio-pulmonary diseases such as COPD, vocal cord dysfunction, endotracheal tumor or tuberculosis, heart failure, pulmonary thromboembolism, spontaneous pneumothorax, and drug-induced cough (e.g. ACE inhibitors). The next step to be checked is if a patient keeps good adherence and appropriate inhalation technique. Repeated instruction for inhalation technique and checking adherence to treatment have found to be effective to maintain appropriate medication especially in aged patients. We also pay attention to risk factors each patient may have. Risk factors such as smoking and/or allergen exposure should be avoided but it may require a lot of efforts by a patient. Regarding allergen exposure, pet allergen is sometimes experienced by noticing

remarkable improvement of asthma after pet's death. Furthermore, comorbidities should be checked. When we studied prevalence of allergic rhinitis in 26,680 asthmatics in Japan, 67.3% showed having allergic rhinitis and higher VAS score of asthma control (higher is worse). GERD or mental health impairment are known to influence asthma control. We also need to pay attention to the existence of underlying diseases such as AERD (aspirin exacerbated respiratory disease), EGPA (eosinophilic granulomatosis with polyangiitis), other systemic vasculitis, and allergic bronchopulmonary aspergillosis (ABPA), since continuous administration of a systemic steroid or immunosuppressant or biologics may be needed in addition to the treatment for asthma.

Once diagnosis of severe asthma is confirmed, a new strategy for treatment with biologics could be applied after phenotypes and endotypes are analyzed to find out molecular targets for precision medicine. For the sake of over 300 million asthmatics in the world, global collaboration is essential to improve their burden of asthma by establishing better therapeutic strategy with guidelines based on EBM and by inventing new agents effective and beneficial for severe intractable asthma treatment.