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REVIEW ARTICLE

Advances in upper airway cough syndrome

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Abstract Upper airway cough syndrome (UACS), previously referred to as postnasal drip syndrome, is one of the most common causes of chronic cough. However, the pathogenesis of UACS/postnasal drip syndrome remains unclear, and physicians in countries throughout the world have different definitions and ways of treating this disease. The various proposed pathogeneses of UACS include the early postnasal drip theory, subsequent chronic airway inflammation theory, and a recent sensory neural hypersensitivity theory. Additionally, some researchers suggest that UACS is a clinical phenotype of cough hypersensitivity syndrome. While the general principles involved in treating UACS are similar throughout the world, the specific details of treatment differ. This review summarizes the various definitions, pathogenic mechanisms, treatments, and other aspects of UACS, to aid clinicians in expanding their knowledge of how to diagnose and treat this syndrome.

Introduction

In 2006, the American College of Chest Physicians (ACCP) defined upper airway cough syndrome (UACS), previously referred to as postnasal drip syndrome (PNDS), as one of several critical pathogeneses of chronic cough [1,2]. In UACS patients, cough can be caused by a variety of upper respiratory disorders, including nasal and sinus diseases [3]. It can also result from anatomic abnormalities and physically or chemically-induced rhinitis, as well as pharyngeal diseases [4–6]. UACS/PNDS is the most common cause of chronic cough in the USA, and accounts for 24–52% of chronic coughs secondary to cough-variant asthma in China [2,7].

Although chronic cough can be effectively controlled in some patients, problems such as cough recurrence after drug withdrawal continue to occur. Additionally, UACS/PNDS is difficult to diagnose and treat because it often coexists with other disorders that contribute to chronic cough [8]. Finally, chronic cough can seriously affect a patient's quality of life, and even cause depressive symptoms [9].

Although UACS/PNDS has been proposed as a specific syndrome for > 100 years and become a severe clinical

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problem, knowledge concerning its pathogenesis and management has remained inconsistent across different countries. This review summarizes the various aspects of UACS/PNDS.

Concepts

PNDS was first mentioned by Frank in 1794, and later proved to be a common cause of chronic cough by Irwin et al [10] in the 1980s. Until recently, UACS has been regarded as a clinical diagnosis not supported by using specific objective methods of examination. In most cases, UACS has been diagnosed based on its clinical symptoms and the patient's response to treatment with an H_1 receptor antagonist. Some researchers support the still controversial idea of "silent PNDS", which stipulates that PNDS/UACS can be diagnosed when a cough is relieved with an H_1 receptor antagonist, even without the presence of relevant clinical manifestations [11]. Medical societies in several countries, including the USA, support the concept of PNDS/UACS.

The European Respiratory Society (ERS) characterizes postnasal drip as a symptom rather than a disease, and supports the premise that most patients with postnasal drip do not cough. Based on this premise, the ERS believes that postnasal drip cannot fully explain the cause of a cough, and does not accept a diagnosis of PNDS/UACS. Instead, PNDS/UACS is described as "rhinitis/rhinosinusitis" or "upper airway diseases-caused cough". While such diseases account for 6—21% of chronic cough cases in Europe, this prevalence is lower in the USA [6,10—12].

The Japanese Respiratory Society guidelines for management of cough indicate that UACS/PNDS is not a common etiology of chronic cough [13], and instead suggest sinobronchial syndrome (SBS) and atopic cough (AC) as the most common causes of chronic cough in Japan. SBS is characterized by a chronic cough caused by chronic rhinosinusitis, and its symptoms are effectively treated with 14- or 15-member ring macrolides and expectorants. AC is a disorder induced by atopic diseases, and its diagnostic criteria include one or more of the following findings, which suggest an atopic predisposition: (1) current or past history of an allergic disorder such as rhinitis, and other than asthma; (2) elevated peripheral blood eosinophils, increased serum total immunoglobulin E (IgE), positive for a specific IgE, positive allergen intradermal test, or elevated eosinophils in induced sputum. In reality, 80% of AC cases can be diagnosed as nonasthmatic eosinophilic bronchitis, and many other cases can be diagnosed as UACS according to the diagnostic criteria. Therefore, there is some overlap among SBS, AC, and UACS/PNDS, and the exact definition of each disorder remains to be determined. The relationships among UACS, AC, and SBS are shown in Fig. 1. Additionally, the guidelines provided by ACCP and ERS do not offer specific diagnostic criteria for AC and SBS, and in China, SBS and rhinitis induced chronic cough are both described as UACS/PNDS [3].

Pathogenesis

Although the pathogenesis of UACS/PNDS is unclear, there are several theories, which are described below.

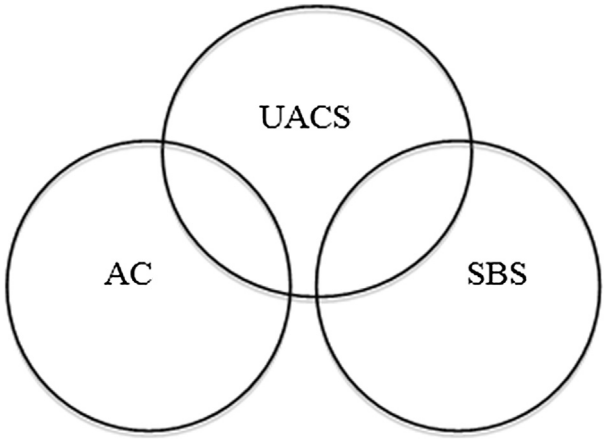

Figure 1. Relationships among upper airway cough syndrome (UACS), atopic cough (AC), and sinobronchial syndrome (SBS).

Postnasal drip theory

In the past, chronic cough from UACS/PNDS was considered to result from postnasal drip-inducing mechanico- or chemostimulation of the afferent nerves innervating the pharynx, larynx, or lower airways [2,3]. Cho et al [14] found that cough sensitivity in some chronic coughers was closely related with extrathoracic airway responsiveness during capsaicin provocation. Thus, extrathoracic airway hyperresponsiveness irritated by postnasal drip might be a mechanism of cough.

However, postnasal drip and transport of nose and paranasal sinus mucous secretions to the pharynx or larynx are normal physiological processes. Bardin et al [15] placed a radionuclide in the maxillary sinus of sinusitis patients, and 24 hours later detected its presence in the maxillary sinus, nasopharynx, esophagus, and lower gastrointestinal tract; however, its presence was not detected in the pulmonary aspirate of any patient. The entire experimental process included the patient's sleep time, which is theoretically the most likely period of time for aspiration to occur. This study showed that, after 24 hours, secretions of the nasal sinus had barely entered the lower airways. O'Hara and Jones [16] followed up 108 consecutive rhinitis/rhinosinusitis patients who displayed symptoms of postnasal drip, and found that only 21% complained of cough. Among the patients with a cough, only 8% had postnasal drip and a cough with no other discernible pathology such as bronchiectasis, asthma, or sarcoidosis. These data indicate that cough is uncommon in patients with postnasal drip, and may not be associated with postnasal drip. Thus, a growing number of scholars now doubt the postnasal drip theory. Due to this uncertain causal relationship, starting in 2006, the ACCP has used the term UACS to replace PNDS [2].

Airway inflammation

Lower airway inflammation theory

Recent studies have shown that lower airway inflammation is commonly associated with chronic cough. Multiple inflammatory mediators, including histamine and prostaglandins, can increase the sensibility of cough via