Laryngeal allergy

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Abstract

Many patients with allergic rhinitis have accompanying laryngeal symptoms such as persistent cough and/or globus. Chronic laryngeal allergy is suspected to be an important cause of these laryngeal symptoms. We have been working toward establishing the concept of a new pathological condition termed “laryngeal allergy” since 1988. In Japan, the first diagnostic criteria for laryngeal allergy were established in 1995. However, these early criteria were inadequate because there was inadequate distinction between laryngeal allergy and other causes of persistent cough and globus. Therefore, more advanced criteria were reconstructed from a completely different viewpoint in 2005 to correctly distinguish laryngeal allergy from other similar diseases. The criteria established in 2005 were modified slightly in 2011 to improve the diagnostic accuracy based on the results of fundamental and clinical investigations. The Japanese Respiratory Society (JRS) included chronic laryngeal allergy in the diagnostic flowchart of the JRS guidelines for the management of cough and sputum in 2019, and chronic laryngeal allergy has recently gained wider recognition in Japan. The accurate diagnosis of conditions resembling laryngeal allergy is important in controlling cough and/or globus and preventing the unnecessary use of medical resources. Therefore, further investigations are warranted to better understand laryngeal allergy and similar diseases.

Keywords: Laryngeal allergy, Chronic cough, Atopic cough, Cough variant asthma, Gastroesophageal reflux disease

Introduction

Since 1988, we have been working toward establishing the concept of a new pathological condition termed “laryngeal allergy”, as many patients with allergic rhinitis have accompanying laryngeal symptoms such as persistent cough and/or globus. Chronic laryngeal allergy is suspected to be an important cause of these laryngeal symptoms. We have been working toward establishing the concept of a new pathological condition termed “laryngeal allergy” since 1988. In Japan, the first diagnostic criteria for laryngeal allergy were established in 1995. However, these early criteria were inadequate because there was inadequate distinction between laryngeal allergy and other causes of persistent cough and globus. Therefore, more advanced criteria were reconstructed from a completely different viewpoint in 2005 to correctly distinguish laryngeal allergy from other similar diseases. The criteria established in 2005 were modified slightly in 2011 to improve the diagnostic accuracy based on the results of fundamental and clinical investigations. The Japanese Respiratory Society (JRS) included chronic laryngeal allergy in the diagnostic flowchart of the JRS guidelines for the management of cough and sputum in 2019, and chronic laryngeal allergy has recently gained wider recognition in Japan. The accurate diagnosis of conditions resembling laryngeal allergy is important in controlling cough and/or globus and preventing the unnecessary use of medical resources. Therefore, further investigations are warranted to better understand laryngeal allergy and similar diseases.

History

Williams (1972) and Pang (1974) published early summaries of the history of laryngeal allergy. At the early stage in the history of laryngeal allergy, laryngeal allergy was confused with hereditary angioneurotic edema caused by a congenital deficiency of C1 inhibitor, which is the primary inhibitor of the complement pathway. The first presentation of laryngeal allergy was reported in 1940, and was a case of angioneurotic edema of the larynx due to sensitivity to chicle, which is a raw material used to make chewing gum. Subsequently, there have been several case reports of laryngeal allergy due to antibiotics, bee sting, serum injection, and mosquito bite. A study published in 1966 reported that 42 of 48 patients with spasmodic croup and laryngotracheitis developed laryngeal allergy, and stressed the association between allergy and upper airway inflammation. In 1968, Alinov reported the causes of allergies in 69 of 245 patients with laryngitis, and administered antigen-specific immunotherapy to this patient group. Williams (1972) reported that the antigens in 22 patients with laryngeal allergy included dust, mold, wheat, corn, egg, milk, beef, chocolate, tomato, penicillin, and iodine; this study mentioned that laryngeal allergy had been ignored as a causative factor because its existence had been poorly recognized.

In 1974, Pang categorized laryngeal allergy into acute and chronic types. Acute or anaphylactic laryngeal allergy causes rapid and fatal laryngeal stenosis, and an ICD-10 code was assigned for this patient group who require occasional hospitalization to receive immediate treatment or a series of treatments. In contrast, it has proven difficult to accurately diagnose chronic laryngeal allergy, which resembles allergic rhinitis or bronchial asthma (BA). Chronic laryngeal allergy was initially assumed to involve simple chronic inflammation of the larynx, and efforts to define chronic laryngeal allergy subsequently declined in Western countries.
In Japan, volunteer researchers founded an inquiry group in 1988 to study chronic laryngeal allergy, as no large-scale studies had investigated laryngeal allergy. The group members published studies on chronic laryngeal allergy, and the first diagnostic criteria for chronic laryngeal allergy were established in 1995. Although these initial criteria were unable to distinguish chronic laryngeal allergy from other diseases that cause persistent cough and globus, more advanced criteria were reconstructed from a completely different viewpoint in 2005 to correctly distinguish laryngeal allergy from similar diseases, such as BA, cough variant asthma (CVA), eosinophilic bronchitis (EB), atopic cough (AC), gastroesophageal reflux disease (GERD), postnasal drip syndrome (PDNS), post-infectious cough (PIC), radiotransparent foreign body in the respiratory tract, and psychogenic cough. In 2011, the inquiry group was designated by the JLA as the formal committee for the standardization of criteria for the diagnosis of chronic laryngeal allergy. A secretariat of the committee was established in the Department of Otolaryngology, Fujita Health University, to support each investigation and the joint research projects performed by the committee members. The criteria established in 2005 were slightly modified in 2011 to improve the diagnostic accuracy. The JRS published guidelines for the management of cough and sputum in 2019, which included chronic laryngeal allergy in the diagnostic flowchart. In recent years, chronic laryngeal allergy has gained wider recognition in Japan.

**Fundamental and clinical investigations**

In Japan, the prevalence of cedar pollinosis has increased in recent decades because of the increase in the amount of pollen and changes in social environments. Several clinicians have reported treating patients with cedar pollinosis with accompanying laryngeal symptoms, and this condition was suspected to be caused by laryngeal allergy. The notion that laryngeal manifestations in patients with cedar pollinosis might be generated by an allergic reaction of the larynx is supported by fundamental studies involving animal sensitization experiments. Ishida et al. demonstrated that mucosal mast cells, which are major allergic inflammatory cells, primarily accumulate in the artenoid and subglottic epithelium. Furthermore, microfold cells (antigen-sampling cells overlying the lymphoid follicles in the gastrointestinal tract) and Langerhans cells and macrophages (antigen-presenting cells) have been observed in the human larynx. Yamashita et al. nebulized pyokutanin blue through the nose or mouth of guinea pigs and found that mouth breathing tremendously enhanced blue staining in the artenoid and subglottic regions, suggesting possible contact between the antigen and the laryngeal mucosa. Suzuki et al. used an environmental pollen challenge chamber to show that laryngeal symptoms in patients with cypress hay fever were markedly enhanced by pollen exposure only through the mouth, and that allergic reactions in the larynx are likely to be involved in this enhancement. These investigations indicate that the larynx is able to be locally exposed to antigens.

Chronic laryngeal allergy is distinguished into seasonal and perennial types in the 2005 diagnostic criteria. These criteria are further divided into broad and strict categories. The broad criteria are used in the daily clinical setting, whereas the strict criteria are applied in medical research. Patients with laryngeal allergy diagnosed using the strict criteria for perennial laryngeal allergy proposed in 2005 showed prominent improvements after the administration of oral histamine H1 receptor blocker (antihistamine). This suggested that the criteria were adequate for application in an actual clinical setting. Furthermore, Katada et al. investigated 159 patients with hay fever caused by birch pollen and found that the 2005 broad criteria for diagnosing seasonal laryngeal allergy could be used to distinguish laryngeal allergy from oral allergy syndrome.

In 2011, these criteria for laryngeal allergy were revised to improve the diagnostic accuracy, as shown in Tables 1, 2, 3, and 4. These are the most current criteria, and the 2019 JRS guidelines recommend the clinical use of the 2011 broad criteria for perennial laryngeal allergy by general physicians.

| Table 1 | Strict diagnostic criteria for perennial laryngeal allergy (2011) (translated into English from the Japanese text in reference 17) |
|----------|----------------------------------------------------------------------------------------------------------------------------------|
| 1. Dried cough without wheezing for more than 8 weeks |
| 2. Foreign body, itching, ticklishness, and/or tingling sensation in the larynx for more than 8 weeks |
| 3. Atopic factors*1 |
| 4. No definitive evidence of acute inflammation, infection (diphtheria, tuberculosis, or syphilis), mycosis, foreign body, or tumor in the larynx |
| 5. Normal pulmonary function and chest X-ray findings |
| 6. No findings of gastroesophageal reflux disease*2 or postnasal drip syndrome*3 |
| 7. Complete or marked effectiveness of treatment with H1 blockers |

*1. Atopic factors (at least one of the findings listed below) |
(1) History of allergic diseases, except for classic bronchial asthma |
(2) Peripheral blood eosinophilia |
(3) Elevated total IgE level in serum |
(4) Positive for allergen-specific IgE in serum |
(5) Positive skin reaction to allergen |

*2. Findings of gastroesophageal reflux disease (at least one of the findings listed below) |
(1) Abnormal range of 24 h pH level in the esophagus |
(2) Abnormal esophageal fiberoscopic findings |
(3) Abnormal findings on esophagography |
(4) Response to proton pump inhibitors |
(5) Heartburn and belching |

*3. Findings of postnasal drip syndrome (at least one of the findings listed below) |
(1) Postnasal drip |
(2) Positive findings on visual inspection |
(3) Positive findings on nasal fiberoscopic examination |

| Table 2 | Broad diagnostic criteria for perennial laryngeal allergy (2011) (translated into English from the Japanese text in reference 17) |
|----------|----------------------------------------------------------------------------------------------------------------------------------|
| 1. Dried cough without wheezing for more than 3 weeks |
| 2. Foreign body, itching, ticklish, and/or tingling sensation in the larynx for more than 3 weeks |
| 3. Atopic factors*1 |
| 4. No definitive evidence of acute inflammation, infection (diphtheria, tuberculosis, or syphilis), mycosis, foreign body, or tumor in the larynx |
| 5. Moderate effectiveness of treatment with H1 blockers |

*1. Atopic factors (at least one of the findings listed below) |
(1) History of allergic diseases, except for classic bronchial asthma |
(2) Peripheral blood eosinophilia |
(3) Elevated total IgE level in serum |
(4) Positive for allergen-specific IgE in serum |
(5) Positive skin reaction to allergen |

72
Table 3  Strict diagnostic criteria for seasonal laryngeal allergy (2011) (translated into English from the Japanese text in reference 17)

1. Dry cough without wheezing during the pollination season
2. Foreign body, itching, ticklish, and/or tingling sensation in the larynx during the pollination season
3. Proof of type I allergy to causal pollen
4. No definitive evidence of acute inflammation, infection (diphtheria, tuberculosis, or syphilis), mycosis, foreign body, or tumor in the larynx
5. Normal pulmonary function and chest X-ray findings
6. Absence of gastroesophageal reflux disease and postnasal drip syndrome
7. Complete or marked effectiveness of treatment with H1 blockers

*1. Proof of type I allergy to pollen (at least one of the findings listed below)
(1) Positive skin reaction to causal pollen
(2) Pollen-specific IgE detected in serum

*2. Findings of gastroesophageal reflux disease (at least one of the findings listed below)
(1) Abnormal range of 24 h pH level in the esophagus
(2) Abnormal esophageal fiberoscopic findings
(3) Abnormal findings on esophagography
(4) Response to proton pump inhibitors
(5) Heartburn and belching

*3. Findings of postnasal drip syndrome (at least one of the findings listed below)
(1) Postnasal drip
(2) Positive findings on visual inspection
(3) Positive findings on nasal fiberoscopic examination

Table 4  Broad diagnostic criteria for seasonal laryngeal allergy (2011) (translated into English from the Japanese text in reference 17)

1. Dry cough without wheezing during the pollination season
2. Foreign body, itching, ticklish, and tingling sensation in the larynx during the pollination season
3. Proof of type I allergy to causal pollen
4. No definitive evidence of acute inflammation, specific infection (diphtheria, tuberculosis, or syphilis), mycosis, foreign body, or tumor in the larynx
5. Moderate effectiveness of treatment with H1 blockers

*1. Proof of type I allergy to pollen (at least one of the findings listed below)
(1) Positive skin reaction to causal pollen
(2) Pollen-specific IgE in serum

patients with laryngeal allergy. Both groups showed marked sensitivity to house dust and mites, but there were significantly more patients with sensitivities to moths and cockroaches in other similar diseases, including CVA, AC, EB, PNDS, heartburn and belching.

Table 4: Broad diagnostic criteria for seasonal laryngeal allergy (2011) (translated into English from the Japanese text in reference 17)

| Criterion                                                                 | Description |
|---------------------------------------------------------------------------|-------------|
| 1. Dry cough without wheezing during the pollination season               |             |
| 2. Foreign body, itching, ticklish, and tingling sensation in the larynx  |             |
| 3. Proof of type I allergy to causal pollen                               |             |
| 4. No definitive evidence of acute inflammation, infection                |             |
| (diphtheria, tuberculosis, or syphilis), mycosis, foreign body, or tumor  |             |
| 5. Normal pulmonary function and chest X-ray findings                     |             |
| 6. Absence of gastroesophageal reflux disease and postnasal drip syndrome |             |
| 7. Complete or marked effectiveness of treatment with H1 blockers         |             |

*1. Proof of type I allergy to pollen (at least one of the findings listed below)
(1) Positive skin reaction to causal pollen
(2) Pollen-specific IgE detected in serum

*2. Findings of gastroesophageal reflux disease (at least one of the findings listed below)
(1) Abnormal range of 24 h pH level in the esophagus
(2) Abnormal esophageal fiberoscopic findings
(3) Abnormal findings on esophagography
(4) Response to proton pump inhibitors
(5) Heartburn and belching

*3. Findings of postnasal drip syndrome (at least one of the findings listed below)
(1) Postnasal drip
(2) Positive findings on visual inspection
(3) Positive findings on nasal fiberoscopic examination

Differential diagnoses

Laryngeal allergy has been distinguished from several diseases that cause persistent cough. The most common differential diagnoses for laryngeal allergy are CVA, AC, allergic bronchitis, and EB. Fundamentally, these diseases do not show apparent abnormal findings in the lungs, in contrast to tuberculosis, cancer, and fibrosis. Table 5 shows the clinical features of these differential diagnoses for laryngeal allergy. The incidences of allergic bronchitis and EB in Japan have decreased over time.

BA causes stridor, dyspnea, and persistent dry cough, whereas CVA only causes cough without stridor and dyspnea. The pathology of CVA is relatively similar to that of BA, and both conditions can only be treated by the administration of a bronchodilator and/or inhaled corticosteroid, not by the administration of oral antihistamines.

It is difficult to distinguish AC from laryngeal allergy, as both conditions cause persistent dry cough, globus, atopic factors, the absence of bronchial hyperresponsiveness, and are responsive to antihistamines. Thus, laryngeal allergy and AC are included in the same category in the diagnostic flowchart of the 2019 JRS guidelines.

PND is a common cause of chronic cough. PND presents as...
a productive cough, while other causes of cough usually trigger a dry cough. Chronic sinusitis is assumed to be the most feasible reason for PND. Chronic sinusitis is also sometimes accompanied by BA; hence, it is important to determine whether patients with chronic sinusitis have a cough caused by PND, BA, or both conditions.

PIC is a complex condition that is difficult to distinguish from other similar conditions. This prolonged cough following a common cold typically demonstrates the natural course of improvement without specific treatment.

GERD is an important condition that must be distinguished from laryngeal allergy. In Japan, the first case of persistent cough due to GERD was reported in 1992 by Fujimori et al. Cough and/or globus caused by GERD is primarily treated by the administration of a proton pump inhibitor. Surgical treatment might be recommended for some GERD patients who are resistant to proton pump inhibitors.

The presence of a foreign body in the airway can cause persistent coughing. Hence, the otolaryngologist should look for a transparent foreign body in the respiratory tree on X-ray. Furthermore, computed tomography is useful in identifying foreign bodies that are not apparent on chest X-ray.

Psychogenic cough is described as barking, foghorn, and brassy. Patients with this condition cough only in the daytime and sleep well at night, while patients with other types of persistent cough often experience insomnia. Psychogenic coughing usually occurs in school-aged and adolescent patients.

Shimizu et al. reported that the cause of chronic cough is unknown in 7% of patients. We reported a case of chronic cough with unknown causes that was initially suspected to be caused by laryngeal allergy. In recent decades, the number of individuals in Japan with specific IgE to mites and/or pollens has increased considerably. Therefore, more attention should be paid to chronic cough and/or globus due to atopic factors.

Finally, Shimizu et al. described several adult patients with persistent cough caused by overlapping reasons such as laryngeal allergy and GERD or CVA and GERD. Consequently, clinicians should consider several causes of cough, even in adults.

| Symptom          | CVA       | Atopic cough | Allergic bronchitis | EB         | Laryngeal allergy |
|------------------|-----------|-------------|---------------------|------------|-------------------|
| Duration         | Dry cough | Dry cough   | Dry cough           | Dry cough  | Dry cough         |
| Atopic factors   | More than 1 month | More than 8 weeks | Persistent | Chronic | More than 8 weeks |
| Methacholine sensitivity | + | - | - | + | + |
| Bronchodilator   | Effective | Ineffective | Ineffective        | Ineffective | Ineffective     |
| Cough suppressant| Ineffective | Ineffective | Ineffective        | Ineffective | Ineffective     |
| Steroid          | Effective | Effective   | Effective           | Effective  | Unknown           |
| Antihistamine    | Ineffective | Effective   | Ineffective        | Unknown   | Effective         |
| Outcome          | Progression to asthma | No progression to asthma | Unknown | Unknown | Unknown |

CVA: cough variant asthma, EB: eosinophilic bronchitis without asthma

References

1. Naito K, Iwata S, Yokoyama N. Laryngeal symptoms in patients exposed Japanese cedar pollen: allergic reactions and environmental pollution. Eur Arch Otorhinolaryngol 1999; 256: 209–11.
2. Naito K, Baba R, Ishii G, Yokoyama N, Iba K. Laryngeal allergy; a commentary. Eur Arch Otorhinolaryngol 1999; 256: 455–7.
3. Naito K. Laryngeal allergy. Arerugi 2003; 52: 985–8 (in Japanese).
4. Ishida H, Iwase S, Amatsu M. Basic research for laryngeal type I allergy. Jibi to rinsyo 1995; 41: 860–5 (in Japanese).
5. Yamashita T, Yamaguchi M, Takeda N, Shimada T, Hori Y, Tachibana F, Kimoto K, Takeuchi S, Kashima K, Kinoshita M, Abe K, Tamura K, Isitani Y, Koike Y, Nunomata S, Kondo A. Basic and clinical study of laryngeal allergy. Jibi to rinsyo 1995; 41: 871–977 (in Japanese).
6. The Japanese respiratory society. The JRS guideline for the
management of cough and sputum 2019. Tokyo: Medical Review Co.,
Ltd; 2019.
7. William RI. Allergic laryngitis. Ann Otol 1972; 81: 558–65.
8. Pang LG. Allergy of the larynx, trachea, and bronchial tree. 
Otolaryngol Clin North Am 1974; 7: 719–34.
9. Osler W. Hereditary angio-neurotic oedema. Am J Med Sci 1888; 95:
362–7.
10. Frank DI. Angioneurotic edema of the larynx due to sensitivity to 
chile. Arch Otolaryng 1940; 32: 1067–70.
11. Anderson OE. Laryngeal obstruction due to antibiotic therapy. AMA 
Arch Otolaryng 1951; 54: 34–7.
12. Paparella MM. Unusual foreign body of trachea and intrinsic bee sting 
of the larynx. J Laryngol Otol 1986; 78: 89–92.
13. Cohen S. Urticaria of the larynx. Laryngoscope 1970; 35: 309–10.
14. Brodnitz FS. Allergy of the larynx. Otolaryngol Clin North Am 1971;
4: 579–82.
15. Wolf JI. Allergic factors in the etiology of spasmodic cough and 
laryngo-trachitis. Ann Allergy 1966; 24: 79–82.
16. Alinov AI. Clinical symptomatology in the diagnosis of allergy in 
acute and chronic laryngitis. Vestn Otorhinolaryngol 1968; 30: 71–5.
17. Naito K. Laryngeal allergy. Otolaryngology-Head and Neck Surgery 
(Tokyo) 2015; 87: 673–7 (in Japanese).
18. Yamada T, Saito H, Fujieda S. Present state of Japanese cedar 
pollinosis: the national affliction. J Allergy Clin Immunol 2014; 133:
632–9.
19. Naito K, Ishii G, Ogawa T, Yokoyama N, Iwata S. Specific IgE and 
IgG4 antibodies to Japanese cedar pollen and total IgE antibody in 
chronic cough. Arch Otolaryngol 1940; 32: 1067–70.
20. Sakurai K, Naito K, Ishii G, Ogawa T, Takeuchi K, Miyata S, Baba 
R. Influence of local antigen exposure dose in the upper respiratory 
tract on sensitization with cedar pollen. Allergol Int 2002; 51: 9–12.
21. Ishida H, Iwase T, Amatsu M. Antigen-presenting cells in human 
laryngeal mucosa. J Jpn Broncho-esophageal Soc 1997; 48: 216–20 
(in Japanese).
22. Kihara T, Fujimura Y, Uchida J, Miyashima N, Nagasaki S. Structure 
and origin of microfold cell (M cell) in solitary lymphoid follicle of 
human larynx. J Clin Electron Microscopy 1986; 19: 5–6.
23. Naito K, Baba R, Saito S, Ito C, Mimura H, Shimizu H, Okazima M, 
Sakakibara H. Efficacy of cetirizine hydrochloride on laryngeal allergy 
diagnosed strictly. J Jpn Immunol Allergol Otolaryngol 2006; 24: 25–9 
(in Japanese).
24. Suzuki T, Okamoto Y, Yonekura S, Okuma Y, Sakurai T, Sakurai D. Characteristics of laryngeal symptoms induced in patients with 
allergic rhinitis in an environmental challenge chamber. Ann Allergy 
Asthma Immunol 2016; 116: 491–6.
25. Katada A, Kunibe I, Yoshizaki K, Hayashi T, Kumai M, Nonaka S, 
Harabuchi Y. Pharyngolaryngeal symptoms and laryngeal allergy in 
patients with birch pollen nasal allergy. The Larynx Japan 2011; 23:
12–8 (in Japanese).
26. Imon K, Hirakawa K, Watanabe H. Causative antigens and laryngeal 
findings of perennial laryngeal allergy—Study based on the criteria 
proposed by the society of study for laryngeal allergy in Japan (2011) —. 
The Larynx Japan 2017; 29: 1–7 (in Japanese).
27. Imoto Y, Takabayashi T, Sakashita M, Tokunaga T, Morikawa 
T, Ninomiya T, Okamoto M, Narita N, Fujieda S. Combination 
therapy with montelukast and loratadine alleviates pharyngolaryngeal 
symptoms related to seasonal allergic rhinitis. J Allergol Clin 
Immunol Pract 2019; 7: 1068–70.
28. Masuda S. Case of pediatric seasonal laryngeal allergy. The Larynx 
Japan 2015; 27: 10–3 (in Japanese).
29. Corrao WM, Braman SS, Irwin RS. Chronic cough as the sole 
presenting manifestation of bronchial asthma. N Engl J Med 1979;
300: 633–7.
30. Irwin RS, Curley FJ, French CL. Chronic cough. The spectrum and 
frequency of causes, key components of the diagnostic evaluation, 
and outcome of specific therapy. Am Rev Respir Dis 1990; 141:
640–7.
31. Niimi A, Amitrani R, Suzuki K, Tanaka E, Murayama T, Kuze F. 
Eosinophilic inflammation in cough variant asthma. Eur Respir J 1998;
11: 1064–9.
32. Fujimura M, Sakamoto S, Matsuda T. Bronchodiilator–resistive cough 
in atopic patients: bronchial reversibility and hyperresponsiveness. 
Intern Med 1992; 31: 447–52.
33. Nakajima S. Allergic diseases in airway. J Jpn Broncho-esopagol Soc 
1987; 38: 114–24 (in Japanese).
34. Gibson PG, Dolovich J, Denburg J, Ramsdale E, Hargreave F. 
Chronic cough: eosinophilic bronchitis without asthma. Lancet 1989;
17: 1346–8.
35. Macedo P, Saleh, Torregro A, Arbery J, MacKay I, Durham SR, Chung 
KF. Postnasal drip and chronic cough: An open interventional study. 
Respir Med 2009; 103: 1700–5.
36. Kaliner M. Medical management of sinusitis. Am J Med Sci 1998;
315: 21–8.
37. Kwon NH, Oh MJ, Min TH, Lee BJ, Choi DC. Causes and clinical 
features of subacute cough. Chest 2006; 129: 1142–7.
38. Fujimori K, Suzuki E, Arakawa M. Clinical features of Japanese patients with chronic cough induced by gastroesophageal reflux. 
Allergol Int 1997; 46: 51–6.
39. Niimi A. Gastroesophageal reflux disease: An important condition for 
respiratory disorder. Respir Invest 2017; 55: 291–2.
40. Fujimori K, Sato M, Sasagawa M, Suzuki E, Arakawa M. A case 
of chronic persistent cough (CPC) caused by gastroesophageal reflux 
(GER), Including a study of CPC caused by suspected GER. Arerugi 
1992; 41: 454–8 (in Japanese).
41. Specchler SJ, Hunter JG, Jones KM, et al. Randomized trial of medical 
versus surgical treatment for refractory heartburn. N Engl J Med 
2019; 381: 1513–23.
42. Catanese AJM, Reibscheid SM, Ruiz Jr RL, Ferrari GF. Foreign body 
in the tracheobronchial tree. Clin Pediatr 1997; 36: 701–6.
43. Grumet GW. Psychogenic coughing: A review and case report. 
Compr Psychiatry 1987; 28: 28–34.
44. Shimizu H, Hayashi M, Saito Y, Mieno Y, Takeuchi Y, Sasaki F, 
Sakakibara H, Naito K, Okazawa M. Classification of chronic cough 
by systemic treatment cascade trial starting with beta agonist. Cough 
2013; 9: 4.
45. Naito K, Murashina T, Okada T, Kato H, Sakurai K. A case report 
– Unknown cause of chronic cough suspected to be laryngeal allergy. 
The Larynx Japan 2013; 25: 15–9 (in Japanese).
46. Sakashita M, Hirota T, Harada M, Nakamichi R, Tsunoda T, Osawa 
Y, Kojima A, Okamoto M, Suzuki D, Kubo S, Imoto Y, Nakamura Y, 
Tamura M, Fujieda S. Prevalence of allergic rhinitis and sensitization 
to common aeroallergen in a Japanese population. Int Arch Allergy 
Immunol 2010; 151: 253-61.