

Cough variant asthma with coexisting gastroesophageal reflux disease: A case report

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Abstract. Chronic cough is a common clinical challenge and a leading cause of outpatient visits to respiratory clinics. In primary care settings, limited diagnostic resources and the absence of standardized evaluation protocols often result in misdiagnosis and suboptimal management. The present report presents the case of a 30-year-old woman with a >1-year history of persistent, non-productive cough unresponsive to initial anti-inflammatory and antitussive therapies. Comprehensive evaluations revealed coexisting cough-variant asthma and gastroesophageal reflux disease, supported by a positive bronchial provocation test, elevated fractional exhaled nitric oxide and laryngoscopic evidence of reflux laryngitis. Early treatment with a combination of inhaled corticosteroid, leukotriene receptor antagonist, acid suppressant and prokinetic agents produced only a limited response. However, a pathophysiology-guided dual therapy approach ultimately resulted in the full resolution of symptoms, as reported by the patient during structured telehealth follow-up over 6 months. The present case underscores the multifactorial nature of chronic cough and highlights the value of systematic evaluation, personalized treatment strategies and multidisciplinary collaboration. It also emphasizes the importance of improving diagnostic capacities in primary care to prevent the mismanagement of chronic cough.

Introduction

In clinical practice, patients who present with cough as the sole or primary symptom lasting >8 weeks and exhibit no marked abnormalities on chest radiographs are often diagnosed with chronic cough (1,2). Chronic cough affects ~10% of the general population and accounts for over one-third of visits to respiratory outpatient clinics in China (3). Epidemiological studies of the Chinese population report a prevalence of chronic cough ranging from 2.0 to 28.3% (3), with the majority of cases occurring in individuals aged 30-40 years and a nearly equal sex distribution (4).

Chronic cough has diverse etiologies, with common causes including cough variant asthma (CVA), upper airway cough syndrome (UACS), eosinophilic bronchitis (EB), gastroesophageal reflux cough (GERC) and atopic cough. These conditions account for 70-95% of cases, with multicenter data identifying CVA as the most prevalent, responsible for 32.6% of cases in China (5,6). The prevalence of GERC is rising, likely due to changes in diet and lifestyle. Despite thorough evaluation, 8.4% of chronic cough cases remain unexplained (7). Reported risk factors for chronic cough include air pollution, seasonal changes, dietary triggers, occupational exposure, allergens, smoking, female sex, advanced age, obesity and certain medications (8).

CVA typically responds well to anti-asthmatic therapy, including inhaled corticosteroids (ICSs) and leukotriene receptor antagonists. Early diagnosis and treatment are crucial, as untreated CVA may progress to classic asthma. Diagnosis relies on objective evidence of airway hyperresponsiveness (AHR), such as that obtained by bronchial provocation testing (9). Gastroesophageal reflux disease (GERD) and CVA frequently coexist and may exacerbate each other: Reflux can aggravate AHR, while persistent coughing may increase intra-abdominal pressure, promoting reflux (10,11). This bidirectional relationship is supported by studies showing that gastric contents can induce bronchoconstriction via vagally-mediated reflexes and microaspiration, thereby contributing to airway inflammation and hyperresponsiveness (12,13). Conversely, coughing in CVA may increase the frequency of transient lower esophageal sphincter relaxations, facilitating reflux episodes and establishing a cycle of mutual exacerbation (14). This interrelationship highlights the

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importance of a combined therapeutic approach. In clinical practice, the management of GERC typically involves lifestyle modifications, acid suppression and prokinetic therapy, with surgical intervention considered in refractory cases (10).

Given the multifactorial nature of chronic cough and its often prolonged course, effective management requires accurate diagnosis and individualized treatment plans (15,16). However, misdiagnosis and inadequate treatment remain common in primary care, largely due to limited diagnostic tools and clinical experience. The present report describes a case of CVA complicated by GERC, manifesting as persistent dry cough. The case underscores the importance of the flexible application of clinical guidelines in primary care and highlights that timely referral to specialized centers is necessary when patients have an unclear diagnosis or poor response to empirical therapy. Enhancing diagnostic and therapeutic capacity in primary care is essential for improving outcomes in patients with chronic cough.

Case report

Case presentation. A 30-year-old married woman with a college education, who worked as a manual laborer, presented to the Department of General Medicine, Shenzhen Longhua District Central Hospital (Shenzhen, China) in June 2021, with a history of chronic, non-productive cough lasting >1 year. The cough was predominantly nocturnal and irritating, without identifiable triggers. Associated symptoms included throat itchiness, a foreign body sensation, and mild postprandial acid reflux. The patient denied heartburn, recurrent sore throat, nasal congestion, rhinorrhea, postnasal drip, chest pain, hemoptysis, palpitations, shortness of breath, fever, night sweats, dizziness or headache. Prior treatments with anti-infectives and antitussives at a community clinic were ineffective, prompting referral for further evaluation. Despite sleep disturbances due to nocturnal coughing episodes, the general condition, appetite and weight of the patient remained stable.

Medical and personal history. The patient reported no history of chronic respiratory, cardiovascular, metabolic or gastrointestinal diseases, and had no prior history of major infections, surgeries or blood transfusions. Allergies included seafood and eggs, which caused cutaneous reactions, but no drug allergies were reported. The patient also had no history of angiotensin-converting enzyme inhibitor use, did not smoke, consume alcohol, or report exposure to occupational or environmental irritants. Her menstrual and obstetric history were unremarkable, and her psychosocial background was stable.

Physical examinations. On admission, vital signs were within normal limits: Temperature 36.6°C, pulse 78 bpm, respiratory rate 20 breaths/min, blood pressure 102/67 mmHg and BMI 19.53 kg/m². Throat examination revealed no congestion or tonsillar enlargement, and there was no tenderness over the sinus regions. Chest examination revealed slightly coarse breath sounds bilaterally, without rales or wheezes. Cardiovascular, abdominal and neurologic examinations detected no abnormalities. No peripheral edema was observed.

Laboratory and imaging analyses. Routine laboratory tests were largely unremarkable, with a mildly reduced hemoglobin level of 111 g/l, white blood cell count of 4.4×10^9 /l, platelet count of 170×10^9 /l, neutrophil level of 63.9% and eosinophil count of 0.1×10^9 /l. A positive *Mycoplasma pneumoniae* IgM titer of 1:80 suggested recent or past infection. Fractional exhaled nitric oxide (FeNO) testing revealed elevated levels, with FeNO measured at a flow rate of 50 ml/sec yielding a value of 50 parts per billion, suggestive of eosinophilic airway inflammation.

Chest computed tomography (Fig. 1) revealed no evidence of pulmonary infiltrates, nodules or structural abnormalities. Pulmonary function testing (Fig. 2) demonstrated normal baseline spirometry but a positive bronchial provocation response; the forced expiratory volume in 1 sec (FEV₁) declined by >20% after a cumulative acetylmethacholine dose of 2.504 mg, which is indicative of AHR.

Esophagogastroduodenoscopy revealed chronic non-atrophic gastritis. Fiberoptic bronchoscopy (Fig. 3) revealed hyperemia and edema of the mucosa in the right and left main bronchi and their branches, with no evidence of tuberculosis, neoplasia or fungal infection. Bronchoalveolar lavage cultures were negative. Fiberoptic laryngoscopy (Fig. 4) showed chronic mucosal edema and erythema in the interarytenoid region and vocal cords, consistent with reflux laryngitis.

Diagnosis. Based on clinical presentation and objective findings, the patient was diagnosed with CVA and GERC. The diagnosis of CVA was supported by characteristic features, including chronic nocturnal dry cough, the absence of wheezing or dyspnea, elevated FeNO levels, and a positive bronchial provocation test. Structural lung diseases and infections were excluded by imaging and bronchoscopy. GERC was diagnosed based on postprandial acid reflux and throat irritation, along with laryngoscopic evidence of reflux laryngitis. Although the patient denied typical GERD symptoms such as heartburn, the presence of extra-esophageal manifestations supported this diagnosis.

Differential diagnosis. UACS was considered due to the persistent dry, irritative cough. However, the absence of recurrent nasal congestion, rhinorrhea or postnasal drip made this diagnosis less likely. EB was also evaluated given the chronic dry cough and absence of abnormal lung CT findings. However, the presence of airway hyperresponsiveness on bronchial provocation testing rendered EB an unlikely diagnosis, since it is typically characterized by normal airway responsiveness.

Treatment and management. The treatment plan integrated both non-pharmacological and pharmacological approaches, aiming to alleviate symptoms, address underlying causes and promote long-term disease control. The patient was advised to avoid environmental irritants such as secondhand smoke, harmful gases and known allergens, and to modify her daily habits by not lying down immediately after meals to help manage reflux symptoms. In addition, regular physical activity was encouraged to improve overall health and strengthen immunity, with the aim of preventing respiratory infections. Psychological support was provided to ease anxiety associated with her chronic symptoms and disrupted sleep, contributing to

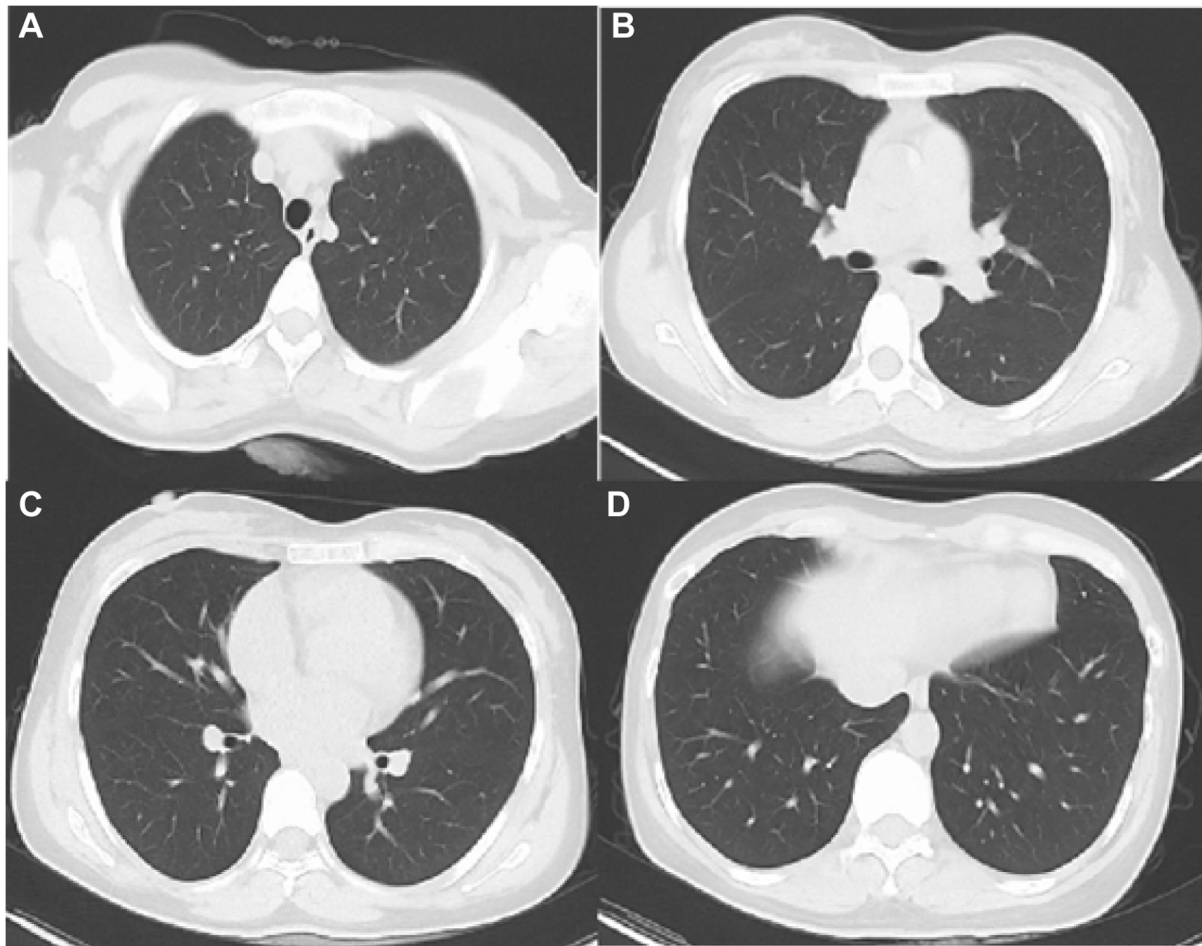


Figure 1. High-resolution chest CT scans of the patient. No evidence of pulmonary inflammation, infiltrates, nodular lesions, bronchial wall thickening or interstitial abnormalities was observed. The lung parenchyma appears clear and symmetrical, with no signs of infection, bronchiectasis or mass-like lesions. (A) Axial CT image at the upper lung level showing the apices and upper lobe structures. (B) Axial CT image at the mid-lung level demonstrating the hilar vessels and airway structures. (C) Axial CT image at the lower lung level showing the bilateral lower lobes. (D) Additional axial CT slice at a slightly different lower lung level illustrating the lower lobe structures. CT, computed tomography.

overall symptom relief and quality of life. To ensure continuity of care, the patient was advised to establish a family doctor contract with a community health center for regular follow-up and monitoring.

During hospitalization, pharmacological treatment primarily targeted CVA. On the second day of admission, after completion of the bronchial provocation test, the patient was started on terbutaline (5 mg) and budesonide (1 mg) via nebulization every 8 h, along with oral montelukast (10 mg) once nightly. For symptomatic relief, dextromethorphan hydrobromide and guaifenesin syrup (15 ml) was administered three times daily. On the fourth day of hospitalization, treatment for GERD was initiated, consisting of omeprazole (20 mg) twice daily and domperidone (10 mg) three times daily to suppress gastric acid and enhance gastrointestinal motility.

After a 13-day hospitalization, the patient was discharged. At discharge, the treatment regimen was adjusted to ensure long-term control of the two conditions. The patient was transitioned to budesonide-formoterol inhalation powder twice daily for asthma maintenance, and the montelukast therapy was continued. GERD management with omeprazole and domperidone was also maintained. Comprehensive instructions on inhaler use, medication adherence and potential side

effects were provided to optimize therapeutic effectiveness and safety.

Follow-up. By the time of discharge, the patient reported a marked improvement in cough severity. Follow-up through telephone and app-based messages confirmed high compliance with the treatment regimen. At the 6-month follow-up, the patient reported complete resolution of the chronic cough, defined as the absence of daytime and nighttime coughing episodes for at >4 consecutive weeks. In addition, the patient experienced improved sleep quality and no recurrence of gastrointestinal symptoms.

Discussion

The present case report describes a young female patient with a chronic, non-productive cough and an allergic predisposition, ultimately diagnosed with CVA complicated by subclinical GERD. The patient initially presented with features typical of CVA, including a persistent, dry, irritating cough, and no evident radiographic or ventilatory abnormalities. Elevated FeNO levels and a positive bronchial provocation test supported the CVA diagnosis, while fiberoptic bronchoscopy

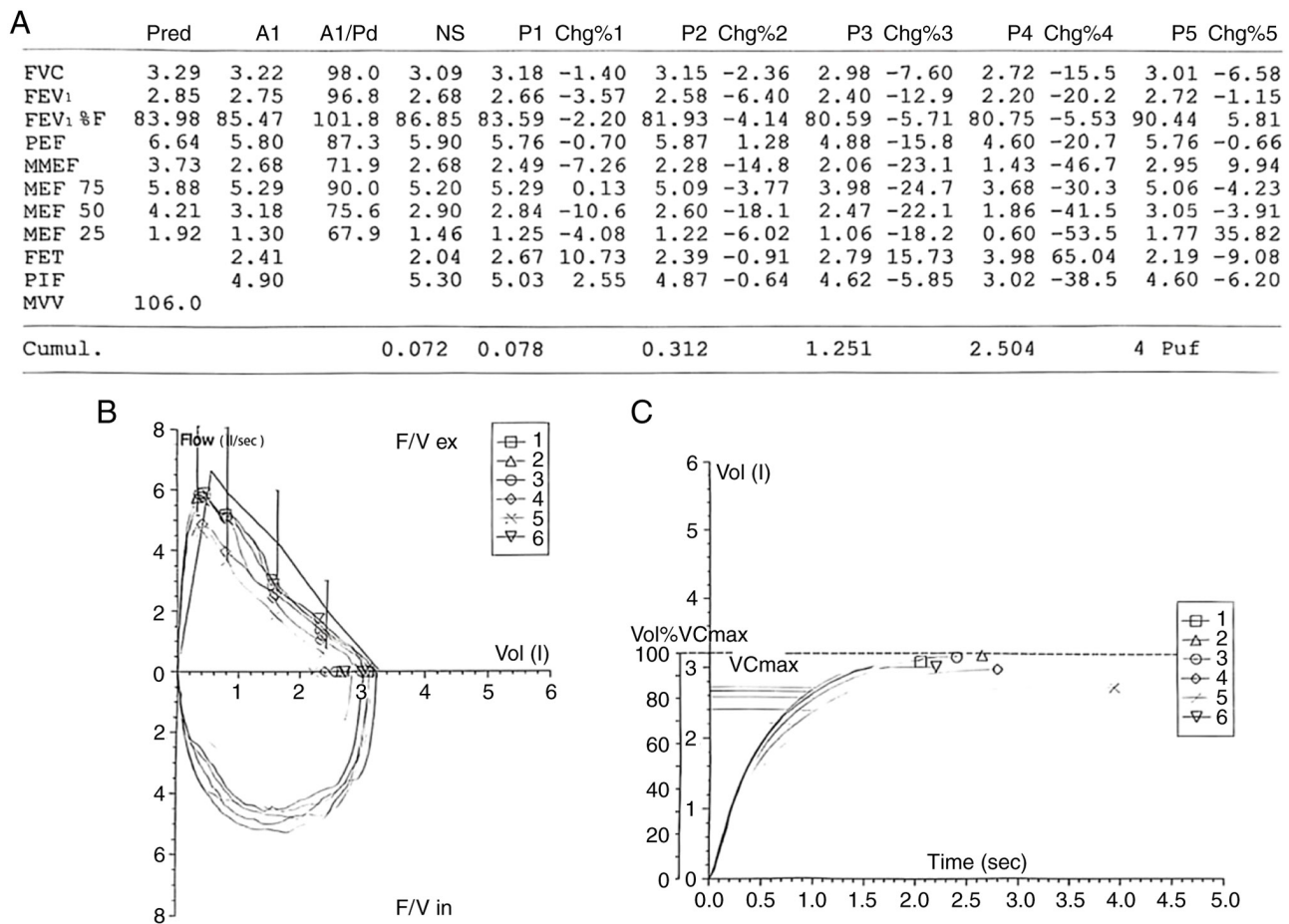


Figure 2. Pulmonary function test with acetylmethacholine bronchial provocation. Baseline spirometry demonstrated normal ventilatory function with a normal FEV₁. However, during the acetylmethacholine challenge, progressive airway hyperresponsiveness was observed. A $\geq 20\%$ decline in FEV₁ occurred at a cumulative acetylmethacholine dose of 2.504 mg, confirming a positive bronchial provocation result consistent with cough-variant asthma. The provocative dose causing a 20% reduction in FEV₁ is indicative of heightened bronchial sensitivity. (A) Table summarizing spirometric measurements across multiple test repetitions. (B) Flow-volume loop graph; curves labeled 1-6 correspond to repeated test attempts. (C) Volume-time curve; curves labeled 1-6 correspond to repeated test attempts. FEV₁, forced expiratory volume in 1 sec; FVC, forced vital capacity; FEV₁%F, FEV₁/FVC ratio, the percentage of the forced vital capacity that is exhaled in the first second; PEF, peak expiratory flow; MMEF, maximal mid-expiratory flow; MEF 75/50/25, maximum expiratory flow at 75/50/25% of FVC; FET, forced expiratory time; PIF, peak inspiratory flow; MVV, maximum voluntary ventilation; Cumul., cumulative; F/V ex, flow/volume during exhalation; F/V in, flow/volume during inhalation; Vol, volume; VCmax, maximum vital capacity; Vol%VCmax, volume as a percentage of VCmax. Pred, predicted value; A1, measured value at baseline; A1/Pred, measured value as a percentage of predicted; P1-P5, values obtained during different test phases, including post-bronchial provocation and post-bronchodilator administration; Chg%1-5, percentage change in measured values compared to baseline, reflecting response over successive test repetitions.

ruled out other possible etiologies such as bronchial tuberculosis, foreign bodies or airway tumors.

Despite the initiation of standard CVA treatment, including an ICS, a leukotriene receptor antagonist and a cough suppressant, the patient's response was limited. Notably, she also reported symptoms suggestive of gastroesophageal reflux, and the laryngoscopy findings were consistent with reflux laryngitis. These observations prompted a shift in diagnostic focus, highlighting GERD as a potential exacerbating factor. Following a 10-day course of anti-reflux therapy with omeprazole and domperidone, her symptoms significantly improved, suggesting an important role of GERD in the clinical presentation.

The delayed recognition of GERD was attributable to the absence of classic symptoms such as heartburn or regurgitation. The initial therapy was focused solely on CVA; however, GERD-induced airway hypersensitivity and inflammation likely compromised asthma control. Additionally, the

typically delayed onset of extra-esophageal symptom relief with the proton pump inhibitor (PPI) omeprazole may have masked the early benefits of anti-reflux therapy. Ultimately, a combined pathophysiology-based approach targeting both CVA and GERD was necessary to achieve symptom resolution.

The present case exemplifies the diagnostic complexity of overlapping CVA and GERD, particularly when reflux presents atypically. While the initial focus on CVA was reasonable given the patient's allergic history and positive bronchial challenge test, the limited response prompted a broader evaluation. Gastroenterology consultation was prompted by the laryngoscopic findings and clinical suspicion, and confirmed subclinical GERD. Interdisciplinary collaboration subsequently enabled a refined diagnostic approach and the initiation of tailored anti-reflux therapy which, in combination with asthma-directed treatment, led to progressive and ultimately sustained symptom relief.

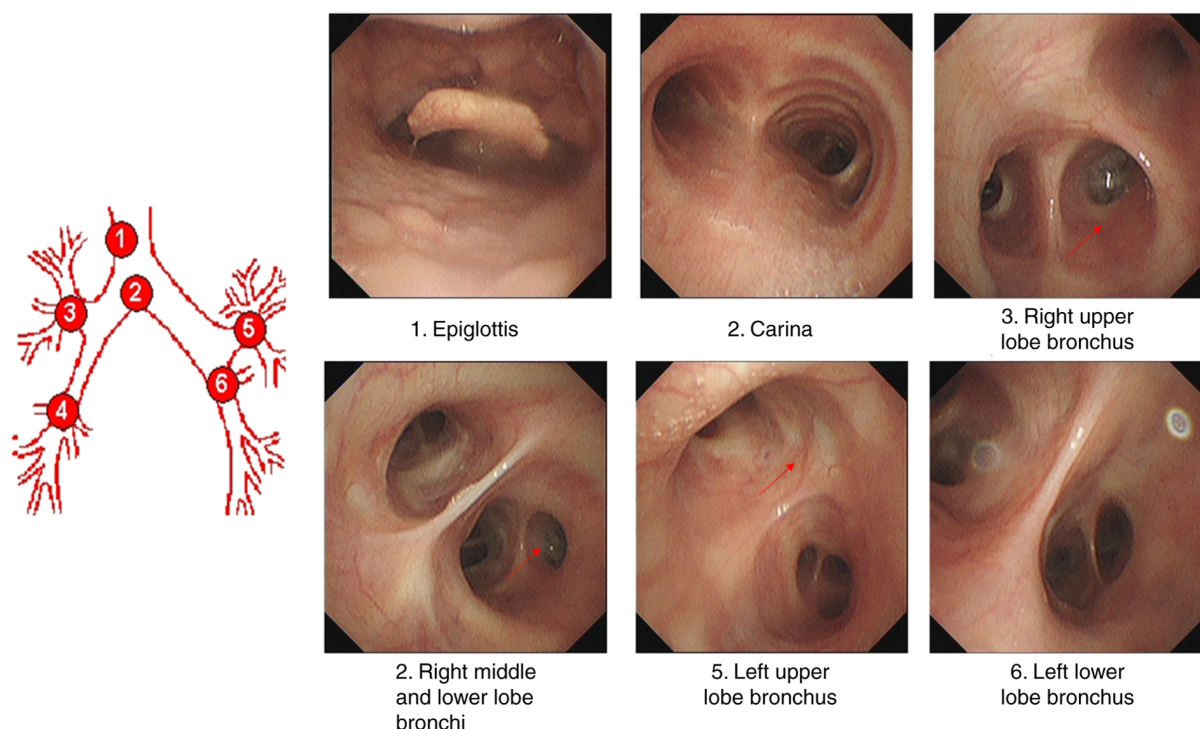


Figure 3. Fiberoptic bronchoscopy. Schematic diagram of airway anatomy and corresponding images. Fiberoptic bronchoscopy revealed normal upper airway anatomy, with a normal epiglottis and mild lymphoid follicular hyperplasia on the posterior pharyngeal wall. The vocal cords were mobile with good closure. The trachea was patent with a sharp carinal ridge and normal mobility. The mucosa of the right and left main bronchi and their branches appeared hyperemic and edematous as indicated by the red arrows, but the lumens were unobstructed. A small amount of secretion was observed, but no evidence of structural obstruction, foreign bodies, neoplasia or bronchial tuberculosis was observed.

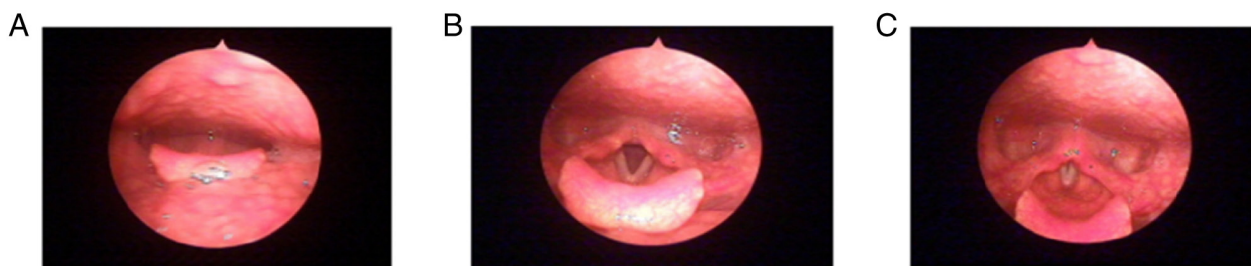


Figure 4. Fiberoptic laryngoscopy. Laryngoscopic images demonstrating chronic erythema and edema of the interarytenoid area and vocal folds, indicative of laryngopharyngeal reflux consistent with reflux laryngitis. (A) Posterior view of the vocal cords, showing the posterior glottis, posterior laryngeal wall and part of the epiglottis. (B) Mid-glottic level, visualizing the vocal folds, glottic cleft and the epiglottis. (C) Anterior view of the vocal cords, including the anterior glottis, anterior laryngeal wall, epiglottis and the anterior aspects of the arytenoid cartilages.

The roles of the respiratory and gastroenterology departments were clearly delineated throughout the care of the patient. The respiratory team conducted the initial assessment, pulmonary function testing, FeNO measurement and bronchial provocation testing. Following limited response to initial treatment, the gastroenterology team was consulted to assess potential reflux pathology, interpret laryngoscopy results, and initiate acid-suppressive and prokinetic therapy. Although no formal joint consultations were conducted, close communication between the two departments ensured coordinated management and appropriate follow-up planning.

Importantly, the present case highlights that GERD should be considered in patients with chronic cough who are unresponsive to conventional asthma therapies, even in the absence of typical gastrointestinal symptoms. While GERD and CVA

are each well-established causes of chronic cough, their coexistence is relatively common and clinically relevant. However, atypical presentations, such as chronic cough in young female patients without heartburn or regurgitation (17,18), may delay diagnosis and treatment, particularly in primary care settings. Extra-esophageal manifestations such as chronic cough occur in up to 30-40% of patients with GERD and are frequently underdiagnosed (18). Unlike most reports that address CVA and GERD separately, the present case demonstrates the diagnostic value of recognizing their overlap and the therapeutic efficacy of a sequential, physiology-guided dual treatment strategy.

Another important aspect is the role of multidisciplinary collaboration. Coordinated care between respiratory and gastrointestinal specialists enabled a tailored treatment strategy in the present case, with monitoring for potential long-term

effects, such as bone loss associated with ICS and PPI use. This underscores the value of integrated, patient-centered care in managing complex overlapping conditions.

The successful use of telemedicine played a crucial role in the follow-up of the patient. Remote monitoring through structured questionnaires and video consultations facilitated continuity of care, reinforced adherence and enabled timely interventions, which are particularly beneficial in settings with limited access to in-person services.

The present case also highlights the importance of clinical reasoning and flexible diagnostic strategies in resource-limited environments. While advanced diagnostic tools such as 24-h pH monitoring or induced sputum eosinophil counts were unavailable, clinical assessment, FeNO measurements and laryngoscopic findings effectively guided the diagnosis. The achievement of a favorable response further validated this pragmatic approach.

However, several limitations must be acknowledged. A major constraint was the lack of objective pre- and post-treatment comparison data, including follow-up FeNO levels, spirometry parameters (e.g., FEV₁) and standardized cough scores. This was primarily due to the patient's early discharge, which was prompted by significant symptom relief, as well as a need to return to work in another city. As a result, follow-up was conducted remotely via telephone, limiting the ability of the medical team to quantify the treatment response using physiological measures. Additionally, although initial laboratory tests, such as eosinophil counts and *Mycoplasma pneumoniae* antibody titers, supported the diagnostic process, serial monitoring of these indicators was not conducted, which restricts the ability to associate treatment effects with biomarker trends. These limitations reflect the challenges of conducting detailed longitudinal assessments in resource-limited or remote follow-up settings.

However, the present case highlights several important considerations for clinical practice. For primary care physicians, it emphasizes the importance of considering GERD as a potential contributor to chronic cough, even in the absence of classical gastrointestinal symptoms, particularly when patients do not respond to standard asthma treatments. For pulmonologists, the case supports the adoption of a pathophysiology-based diagnostic and therapeutic approach for the management of complex or refractory cases of chronic cough. For multidisciplinary teams, it illustrates the practical benefits of shared decision-making and role-specific expertise. Furthermore, at the healthcare system level, it underscores the value of integrating telemedicine into the follow-up and fostering multidisciplinary collaboration to improve the diagnosis, treatment and long-term management of overlapping chronic conditions.

In conclusion, while CVA and GERD are each common conditions individually, the novelty of the present case lies in their atypical concurrent presentation in a young female with no classic reflux symptoms. In addition, the case highlights the dynamic diagnostic shift and effective cross-specialty collaboration that led to symptom resolution without invasive testing. This reinforces the importance of a systematic, individualized approach when evaluating chronic cough, which is a frequently encountered but diagnostically challenging condition in clinical practice.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

FY and WG were responsible for clinical data collection, patient assessment and data analysis. XQ assisted with clinical evaluations and manuscript preparation. XC and LN supervised the clinical management of the patient, contributed to manuscript drafting and provided critical revisions. FY and WG confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This case report was reviewed and approved by Ethics Committee of Shenzhen Longhua District Central Hospital (Shenzhen, China; approval no. 2024-096-01).

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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