

Familial Tracheobronchopathia Osteochondroplastica in Two Mongolian Siblings: A Case Report

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Case Report

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Abstract

Background

Tracheobronchopathia osteochondroplastica (TO) is a rare disorder characterized by submucosal cartilaginous or ossified nodules in the tracheobronchial tree. Although chronic inflammation and trauma have been implicated, genetic factors remain unexplored.

Case presentation

This study enrolled two Mongolian siblings diagnosed with TO. The 38-year-old female patient presented with a 5-year chronic cough and acute onset of high fever and purulent sputum. Imaging examinations revealed bronchiectasis and diffuse tracheal wall calcification. Bronchoscopy showed tracheal mucosal granular hyperplasia, and pathological biopsy confirmed airway chronic inflammation and multifocal interstitial ossification. Her 38-year-old elder brother had a 6-year history of hypertension and one month of intermittent exertional chest tightness and wheezing. Chest CT demonstrated irregular tracheal wall thickening and luminal stenosis. Bronchoscopy detected diffusely distributed fragile airway nodules, and pathological examination verified bronchial mucosal metaplasia and interstitial ossification lesions. Both patients received standardized comprehensive symptomatic treatment including oral moxifloxacin and aerosolized budesonide and terbutaline during hospitalization. Clinical symptoms were significantly relieved after treatment. In follow-up lasting 4–6 months, only intermittent mild respiratory symptoms were observed without severe disease recurrence or adverse events.

Conclusion

This sibling case report of tracheobronchopathia osteochondroplastica (TO) suggests potential genetic factors underlying the pathogenesis of this disease.

Background

Tracheobronchopathia osteochondroplastica (TO) is a rare benign airway disorder characterized by cartilaginous or ossified submucosal nodules of unknown etiology that project into the tracheobronchial lumen^[1]. Most studies suggest its association with chronic inflammation, metabolic abnormalities, or local trauma, but direct genetic evidence is lacking^[2]. TO is predominantly sporadic, with approximately 400–600 cases reported worldwide, and no clear familial clustering has been documented to date^[3]. Herein, we detail two Mongolian siblings diagnosed with TO, aiming to explore potential genetic predisposition and enrich the clinical understanding of this rare disease.

Case 1 presentation

The patient is a 38-year-old Mongolian female, native to Hebukeerqin Mongolian Autonomous County, Xinjiang, China. She has no occupational exposure to dust, chemicals, or toxins, and no smoking history. She has a 5+-year history of chronic cough, managed with intermittent nebulized therapy for sputum clearance. A cesarean section was performed in 2014. Four days prior to admission, she developed fever, cough, and sputum production without apparent trigger, characterized by paroxysmal continuous coughing and yellow-green sputum that was easily expectorated. Her recorded home temperature reached 40°C. Following self-administered ibuprofen and oseltamivir tablets, fever subsided transiently, but intermittent fever, cough, and sputum production persisted.

A computed tomography (CT) scan performed at our institution (Karamay Central Hospital) revealed columnar bronchiectasis in the right middle lobe and left lower lobe, accompanied by irregular thickening of the bronchial walls ((Fig. 1)). Following admission, bronchoscopy demonstrated granular mucosal hyperplasia and protrusion in the trachea, with relative stenosis of the right middle lobe bronchus ((Fig. 2)). Pathological examination of biopsy specimens confirmed chronic bronchial inflammation with focal epithelial metaplasia, mild atypical hyperplasia, and multifocal interstitial ossification ((Fig. 3)). Pulmonary function tests (PFTs) were attempted but not completed due to poor cooperation; however, bedside spirometry showed no evidence of obstruction (forced expiratory volume in 1 second/forced vital capacity ratio > 0.8).

Case 2 presentation

This patient is the older brother of the previously described case. A 38-year-old Mongolian male, he is also a native of Hebukeerqin Mongolian Autonomous County, Xinjiang Uygur Autonomous Region, China. He has no occupational exposure to dust, chemicals, or toxins, but has a 20-year smoking history with an average daily cigarette consumption of less than 5. He has a 6-year history of hypertension, with the highest recorded blood pressure being 159/130 mmHg, currently managed by regular oral administration of Irbesartan Hydrochlorothiazide Tablets (0.15 g daily). The patient was admitted to the hospital mainly due to "intermittent chest tightness for 1 month, with symptoms worsening over 3 days". Over the past month, chest tightness recurred intermittently, mostly after physical exertion or during colds, accompanied by wheezing and exacerbation with activity. He had not received any prior medical treatment and first visited the People's Hospital of Xinjiang Uygur Autonomous Region.

Chest CT scan demonstrated irregular thickening of the tracheal wall with mild increased density and luminal stenosis (suggestive of inflammatory lesions requiring differentiation between tuberculosis and amyloidosis), patchy exudative opacities and linear streaks in the right middle lobe, left lingula, and bilateral lower lobes (consistent with inflammatory changes), and a tiny nodule in the right upper lobe posterior segment ((Fig. 4)). Bronchoscopy revealed diffusely distributed nodules from 2 cm below the glottis to the carina, which were friable and prone to bleeding on contact; the mucosa of bilateral bronchi at all levels showed congestion with scattered small nodules of similar characteristics, while the lumen remained patent ((Fig. 5)). Pathological examination confirmed focal squamous metaplasia of bronchial mucosal epithelium, multifocal calcification and ossification in the interstitium, accompanied by fibrous

tissue hyperplasia and scattered chronic inflammatory cell infiltration ((Fig. 6)). Pulmonary function tests were not completed due to poor cooperation, but bedside spirometry showed no evidence of obstruction (forced expiratory volume in 1 second/forced vital capacity ratio > 0.8).

Outcome and Follow-Up

Currently, there is no specific curative intervention for TO. Following hospital admission, both patients were administered oral moxifloxacin (0.4 g once daily) for suspected bacterial superinfection (based on elevated C-reactive protein and purulent sputum in Case 1, and inflammatory changes on CT in Case 2), budesonide (1 mg via nebulization twice daily) for airway inflammation, and terbutaline (5 mg via nebulization thrice daily) for symptom relief. Clinical improvement (resolution of fever in Case 1, alleviation of chest tightness and wheezing in Case 2) was observed, prompting discharge. During post-discharge follow-up (6 months for Case 1 and 4 months for Case 2), both patients reported intermittent cough but no recurrence of severe symptoms.

Discussion

TO is a rare benign airway disease characterized by the presence of bony or cartilaginous nodules beneath the mucosa of the trachea and bronchi. These nodules usually protrude into the airway lumen, leading to airway stenosis^[4]. The clinical manifestations of TO are highly variable. Patients can be asymptomatic or present with a range of nonspecific symptoms, including cough, hemoptysis, wheezing, and chest pain. These symptoms likely stem from airway stenosis and the compression exerted on the airway by the nodules^[5]. In certain cases, TO can be easily misidentified as other conditions like pulmonary infections, emphysema, calcified lesions resulting from pulmonary tuberculosis, papillomatosis, and airway calcification. Thus, making an accurate diagnosis is critically essential in order to prevent patients from undergoing needless surgeries or chemotherapy^[6].

Approximately 400 to 600 cases of TO have been reported worldwide. There are more male patients than female patients, with a male-to-female ratio of approximately 3:1. The middle-aged and elderly population (aged 40 to 60 years old) represents the high-risk group. However, cases among younger individuals have also been reported^[7]. In the currently published literature, most cases of Tracheobronchopathia Osteochondroplastica (TO) are sporadic, and there have been no reports related to a clear family history. Therefore, TO is generally regarded as a sporadic disease rather than a familial disease with a genetic predisposition^[3]. However, the two TO patients reported this time are siblings, and this phenomenon suggests that there may be a certain degree of genetic susceptibility to TO.

Currently, there's no definitive proof directly tying specific gene mutations to TO. However, multiple studies have suggested that certain genes may play a part in the development of this condition. For example, research has shown that the abnormal expression of genes related to airway cartilage development in the embryonic phase may be linked to the emergence of TO^[8]. Moreover, several studies have delved into genes associated with ossification and chondrification processes, including TNFSF11,

TNFRSF11B, and WNT3A^[9, 10]. Aberrations in these genes might be linked to the onset of TO. Nevertheless, as of now, no conclusive evidence directly connects specific gene mutations to TO. Thus, additional research is imperative to uncover the underlying genetic mechanisms.

We acknowledge limitations of this study: the lack of formal pedigree analysis and genetic sequencing, and the inability to fully exclude environmental confounders (e.g., unmeasured childhood exposures). However, the rarity of TO (estimated prevalence < 0.01%) makes familial clustering unlikely to be coincidental. This case report highlights the need for large-scale epidemiologic studies to explore the genetic basis of TO and for clinicians to consider familial predisposition when evaluating young patients with unexplained airway nodules.

Conclusion

The clinical manifestations of TO are extremely complex and diverse, and it is very easy to be misdiagnosed during the clinical diagnosis process. The special case of this pair of siblings being simultaneously affected reported this time strongly suggests that there may be a certain degree of genetic susceptibility to TO, providing new clues and directions for subsequent research on the pathogenesis of this disease.

Abbreviations

TO: Tracheobronchopathia osteochondroplastica

TNFSF11 : Tumor Necrosis Factor Superfamily member 11

TNFRSF11B : Tumor Necrosis Factor Receptor Superfamily member 11B

WNT3A : Wnt family member 3A

Declarations

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Author Contributions

Xue-long Jiang: Investigation, resources, supervision, writing-original draft.

Qin Wang: Investigation, methodology, writing-review and editing.

Shilin Ma: Data curation, methodology, writing-original draft.

Zhong-ming He: Conceptualization, investigation, methodology.

Jianping Li: Investigation, methodology, project administration, supervision.

Availability of data and materials

These data are considered confidential patient information and are not publicly available due to privacy concerns. However, access to anonymized data can be provided upon reasonable request from qualified researchers interested in further analysis for scientific purposes. Requests should be directed to the corresponding authors.

Ethics approval and consent to participate

Ethical approval was not required for this single case report, in accordance with the institutional policy.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of Interest

The authors declare no conflicts of interest.

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Figures

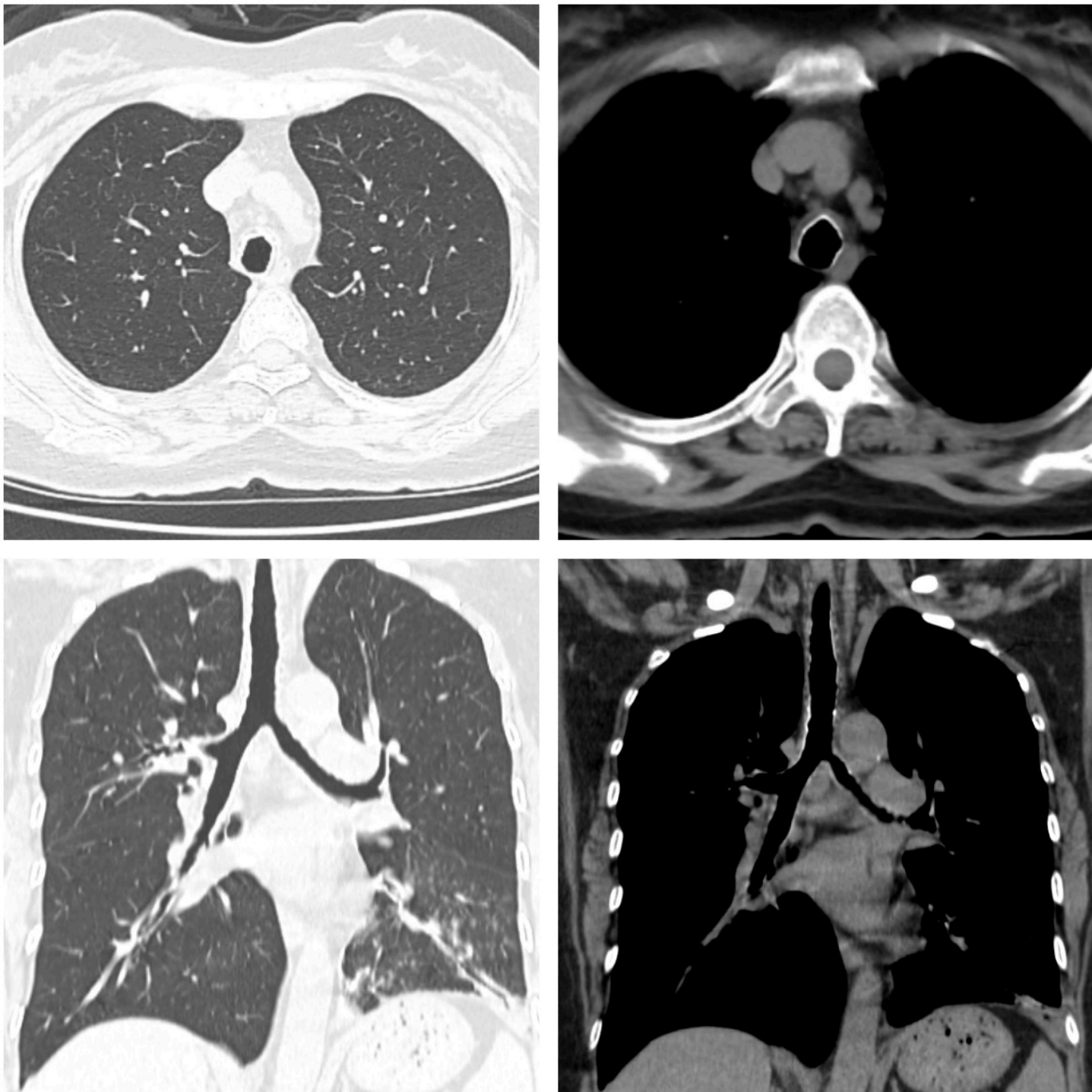


Figure 1

CT scan showing diffuse uneven thickening of the tracheal wall with calcification changes in some areas.

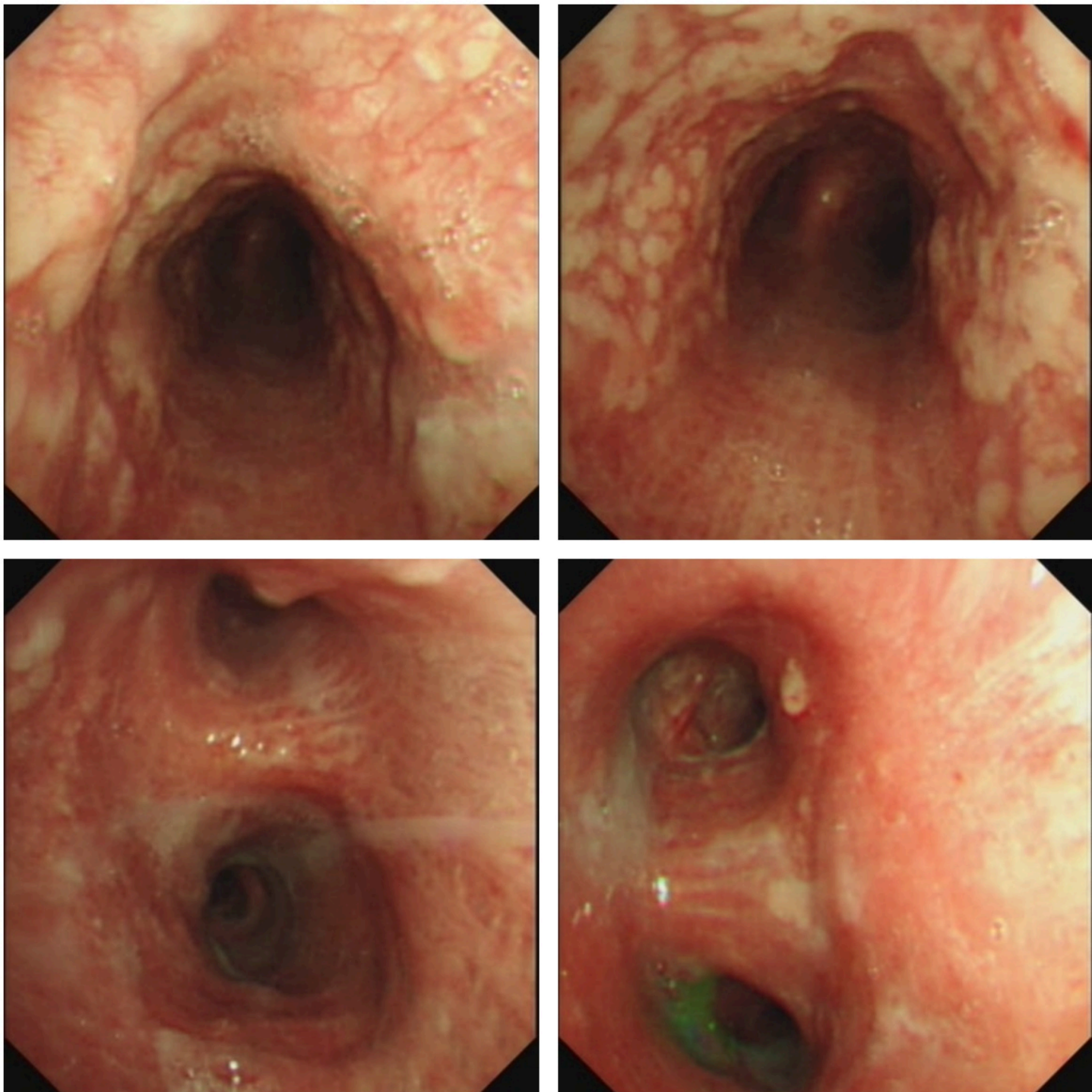
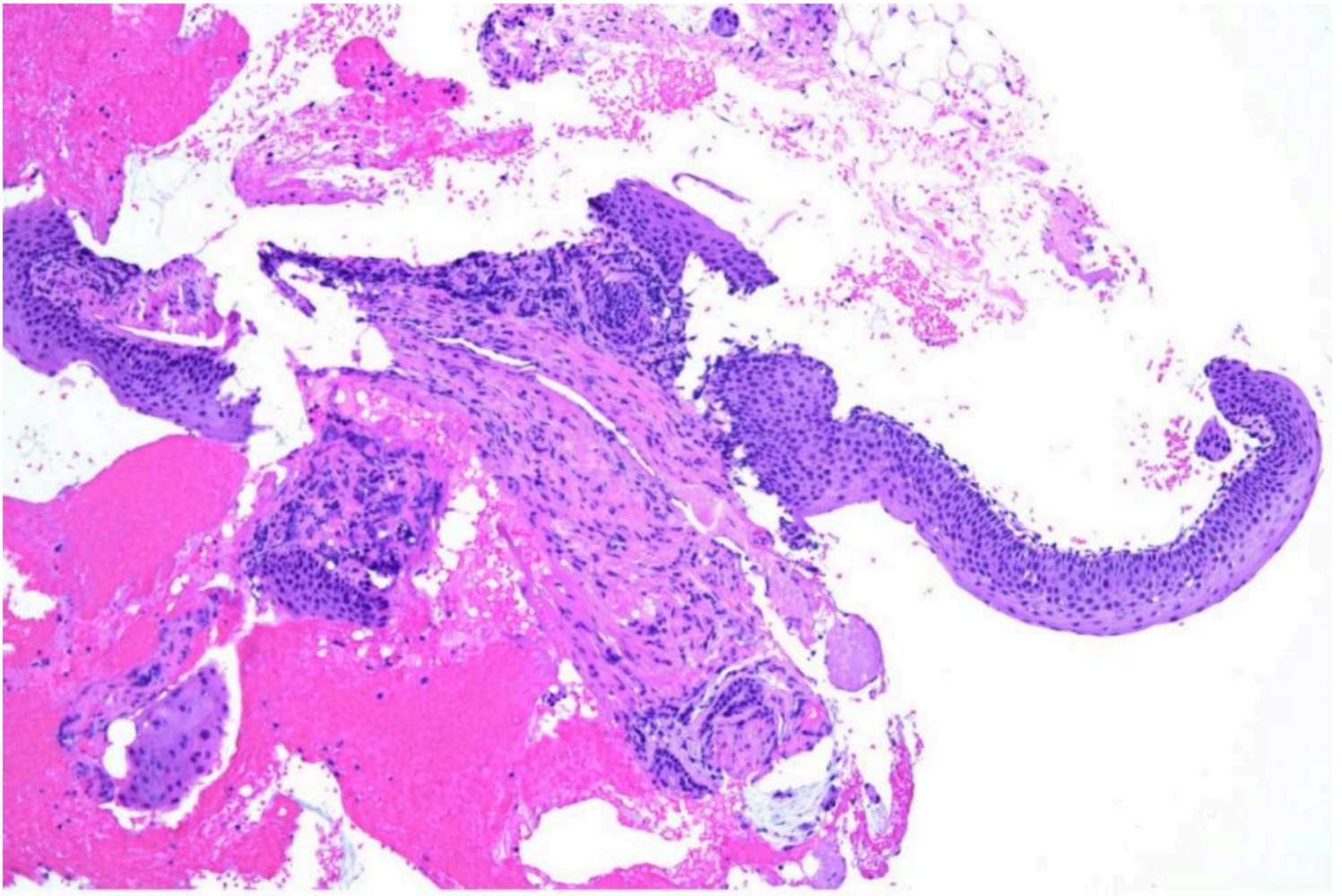


Figure 2

Bronchoscopic image of the tracheal mucosa exhibiting granular hyperplasia and elevation, a key endoscopic feature of TO correlating with submucosal cartilaginous/ossified nodule formation.



HE

Figure 3

Pathological section (HE staining) showing chronic inflammation of the bronchial mucosa with squamous metaplasia of the epithelium, mild cellular atypia in focal areas, and multifocal ossification in the interstitium. Biopsy confirms osseous/cartilaginous submucosal deposits.

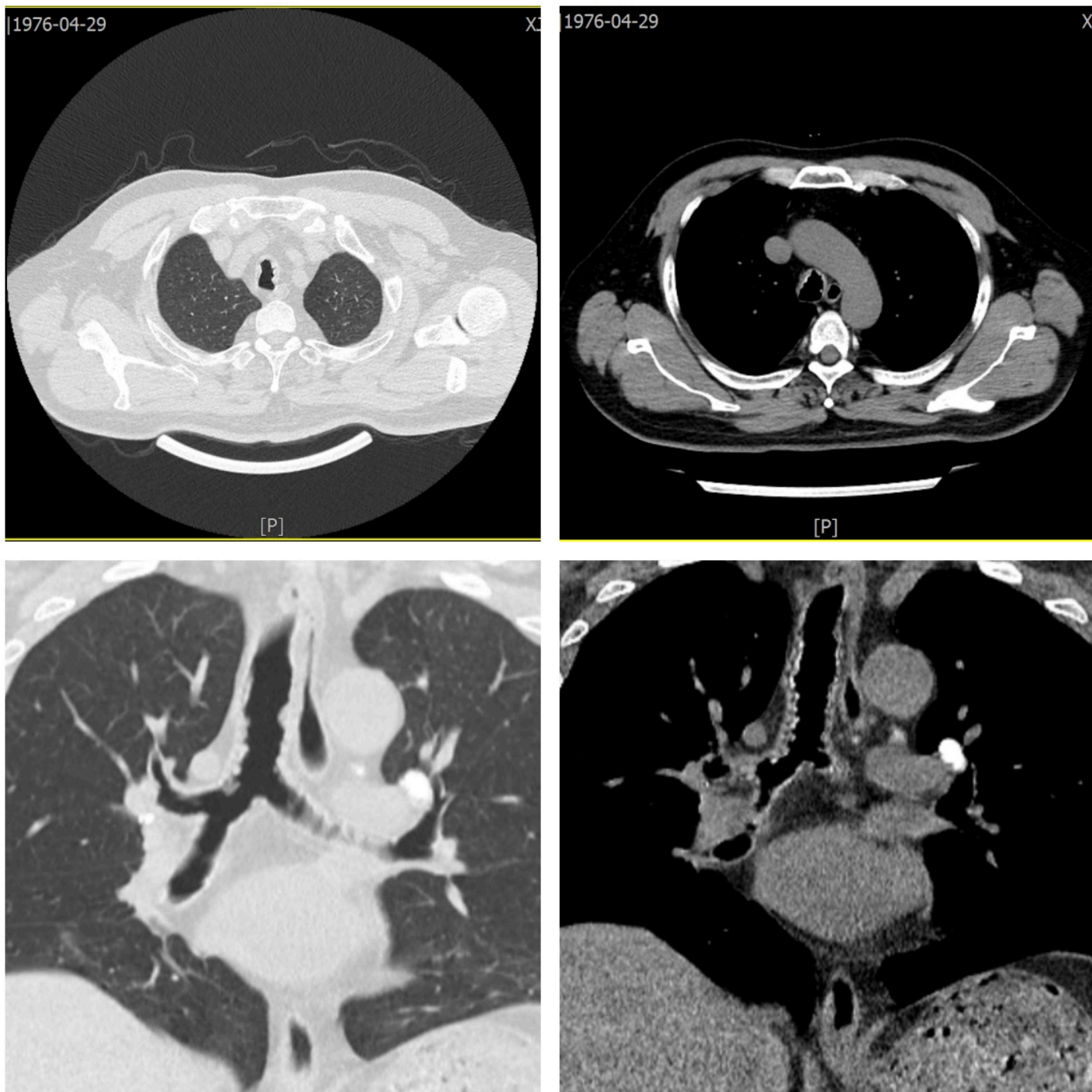


Figure 4

CT scan showing uneven thickness of the tracheal wall, diffuse mild increase in density, and varying degrees of luminal narrowing.

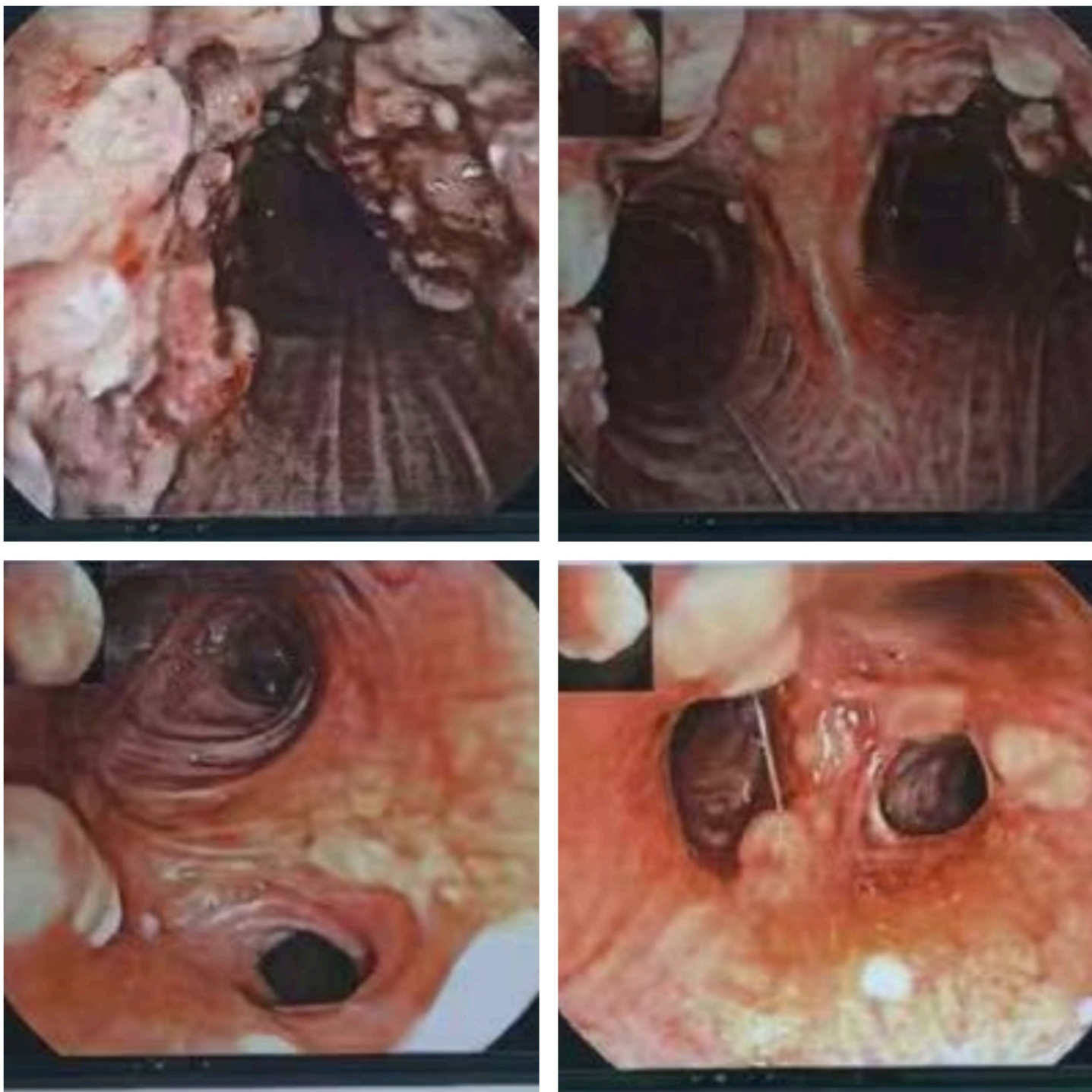


Figure 5

Bronchoscopic image showing "rock-hard" nodules with sparing of the posterior wall; diffusely distributed nodular lesions from 2 cm below the glottis to the tracheal carina, with lesional tissues being fragile and prone to bleeding upon minimal contact.

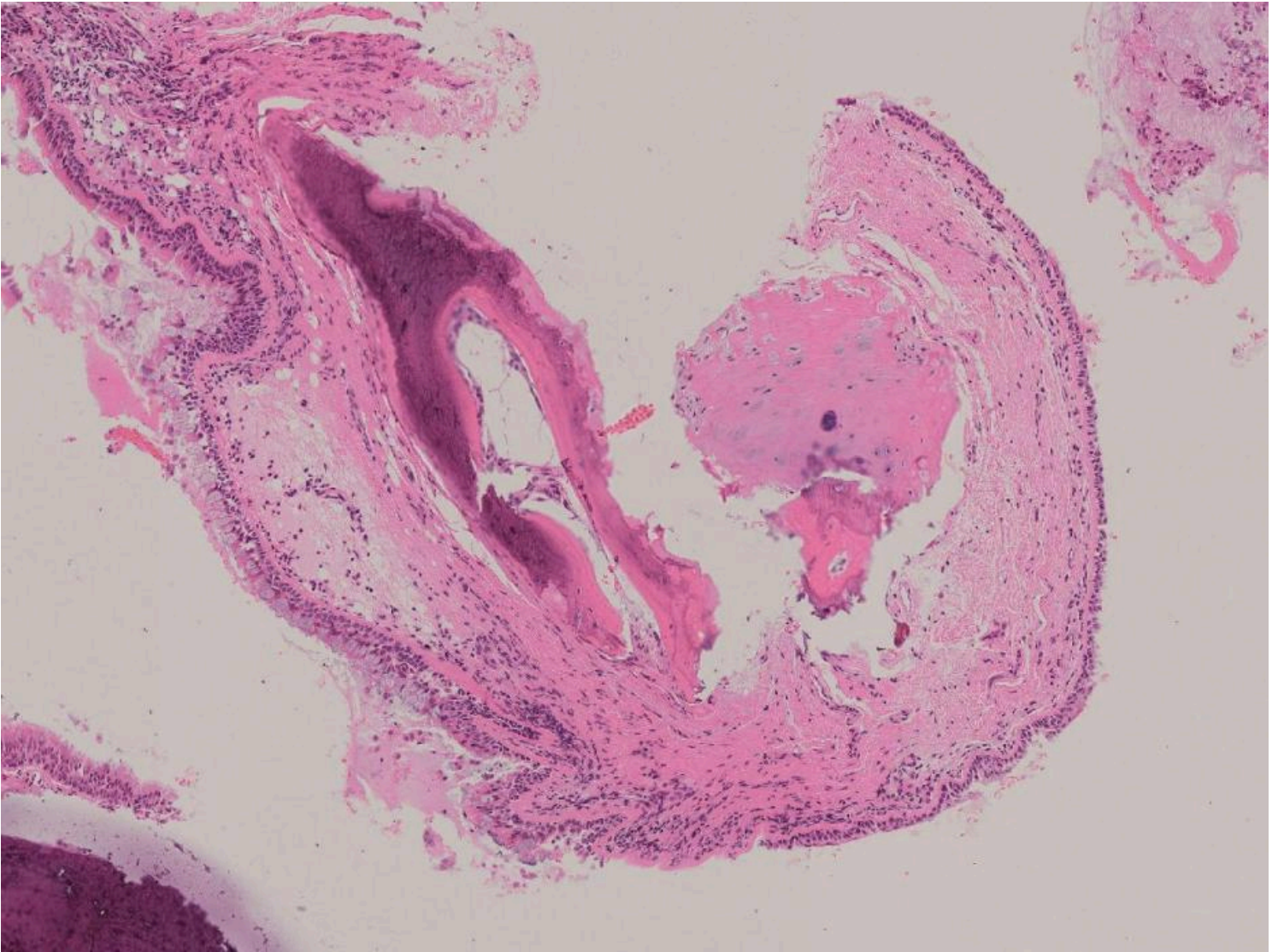


Figure 6

Pathological section showing focal squamous metaplasia of the bronchial mucosal epithelium, multiple scattered calcification and ossification foci in the interstitium, accompanied by fibrous tissue hyperplasia and scattered infiltration of chronic inflammatory cells. Biopsy confirms osseous/cartilaginous submucosal deposits.