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An uncommon cause of chronic cough: a case of tracheobronchopathia osteochondroplastica

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Abstract

Introduction. Tracheobronchopathia osteochondroplastica (TO) is an exceptionally rare disorder with unknown aetiology. Because its symptoms are nonspecific and radiologic findings may be subtle, TO is frequently overlooked, leading to repeated evaluations before the correct diagnosis is established.

Case presentation. A 67-year-old woman experienced a chronic cough lasting six months and recurrent respiratory tract infections. Initial imaging and spirometry were inconclusive, therefore multiple differential diagnoses were explored. Despite several computed tomography (CT) examinations, characteristic airway abnormalities were not recognized until retrospectively reviewed. Bronchoscopy revealed firm cartilaginous nodules throughout the trachea and main bronchi, arising from the cartilaginous rings and sparing the posterior membranous wall. Biopsy by forceps was technically challenging. Histological examination of the specimen revealed only mild chronic inflammatory changes without osseous or cartilaginous tissue. The combination of endoscopic findings, clinical presentation and retrospective imaging review supported the diagnosis of TO. The patient was managed conservatively, as no significant airway obstruction was present.

Conclusions. TO should be considered in patients with chronic cough, recurrent infections or other unexplained respiratory symptoms. Improved awareness among clinicians may enable earlier recognition, minimise unnecessary testing, and reduce the risk of complications.

Keywords: tracheobronchopathia osteochondroplastica, chronic cough, tracheal nodules, rare airway disease.

1. Introduction

Tracheobronchopathia osteochondroplastica (TO) is a rare, benign airway disorder involving the development of firm submucosal cartilaginous or ossified nodules that protrude into the tracheobronchial passageway [1,2]. Its incidence is estimated at only 0.01 to 4.2 per 100 000 people [2]. Although TO aetiology remains unclear, it is most commonly identified in middle-aged to elderly patients and often presents with nonspecific respiratory symptoms such as chronic cough, expectoration, dyspnoea, haemoptysis or recurrent infections, leading to frequent diagnostic delays. Radiologic findings may be subtle or misleading, therefore, bronchoscopy is currently considered the diagnostic gold standard [3,4]. Characteristic nodular protrusions are typically observed during airway endoscopy, where rigid whitish lesions arise along the cartilaginous airway walls but do not involve the posterior membranous segment [5]. Due to its variable and often mild clinical manifestations, TO may be misinterpreted as more common conditions, including asthma, chronic bronchitis or even bronchogenic malignancy [6]. We present a case that underscores the subtle clinical course of TO and the diagnostic challenges associated with the disease.

2. Case report

A 67-year-old woman presented with a six-month history of chronic cough, recurrent respiratory tract infections and frequent subfebrile fever. Her past medical history included hypertension, chest angina and anaemia. She had never smoked, reported no significant occupational or environmental exposures, and had no family history of chronic lung diseases. The patient's family physician

discontinued the angiotensin-converting enzyme inhibitor (Zofenopril) and switched her to an angiotensin II receptor blocker (Valsartan), but this did not lead to any improvement in her cough. Shortly thereafter, the patient developed yellowish sputum production.

Initial chest X-ray showed no focal lesions or infiltrates. Spirometry performed by a pulmonologist demonstrated mild obstruction without a decrease in FEV₁ (FVC 2.59 l – 97% [z-score -0.2]; FEV₁ 1.66 l – 74% [z-score -1.5]; FEV₁/FVC 63.98 – 84% [z-score -1.9]), with a negative bronchodilator response. As the findings were most compatible with acute bronchitis, budesonide treatment was initiated, and a computed tomography (CT) scan was scheduled to rule out bronchiectasis. First CT scan findings included post-infectious residual changes, bilateral S5 subsegmental atelectasis, isolated fusiform bronchiectasis in KS4/5, mucostasis. Bronchoscopy was recommended, but the patient refused the examination. Consequently, sputum cultures were obtained and the patient was scheduled for follow-up imaging. Moreover, because of the inability to rule out asthma, the patient was referred for bronchial hyperresponsiveness (BHR) testing, but she did not attend the appointment. Bronchodilators were prescribed, considering the obstruction caused by bronchiectasis.

For differential diagnostic purposes, the patient was referred to an otorhinolaryngologist, whose evaluation revealed no abnormalities, while gastroenterology assessment ruled out gastroesophageal reflux disease (GERD) and gastric biopsy confirmed chronic gastritis. During this period, the patient experienced several episodes of bacterial pneumonia requiring antibiotic therapy and eventually developed haemoptysis.

At the pulmonology follow-up visit, there was no clinical response to budesonide, and spirometry parameters remained unchanged. Serology for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* were negative. Sputum culture grew *Staphylococcus aureus*, antibacterial therapy was initiated, and the patient was scheduled for follow-up after several months. Repeated CT demonstrated new endobronchial changes while spirometry remained unchanged. Bronchoscopy was recommended again and this time was accepted by the patient. However the examination was not performed in the outpatient setting due to subsequent hospitalization for pneumonia complicated by sepsis.

Bronchoscopy performed during hospitalization revealed firm cartilaginous nodules throughout the trachea and bilateral bronchi, arising from the cartilaginous rings and sparing the posterior membranous wall (Figure 1). Although the nodules were difficult to biopsy, the samples were obtained. Bronchial secretions were obtained for microbiological culture, which grew *Candida kefyr*. Blood culture yielded *Streptococcus pneumoniae*. Histopathological

examination demonstrated scant material with mild chronic inflammatory changes, interpreted as reactive. Despite these nonspecific histological findings, the characteristic bronchoscopic appearance strongly suggested tracheobronchopathia osteochondroplastica.

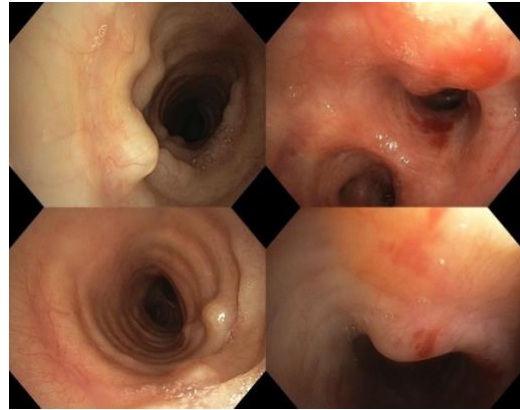


Figure 1. Bronchoscopy found firm cartilaginous nodules throughout the trachea and bilateral bronchi, arising from the cartilaginous rings

After a retrospective review of the CT images, it was noted that CT demonstrated thickening of the cartilaginous tracheal wall with irregular nodules, while the posterior membranous portion of the trachea was spared. Some of the observed nodules were calcified, whereas others were not.

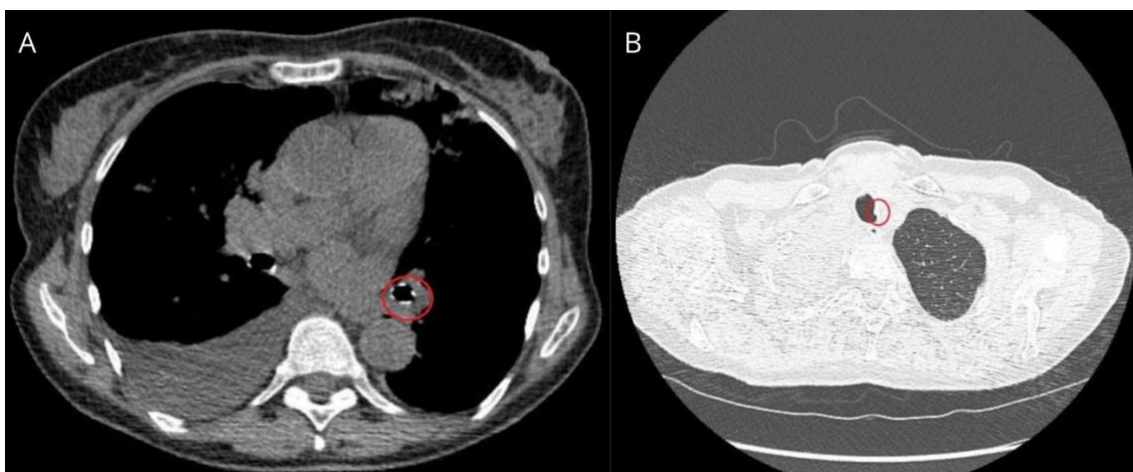


Figure 2. Computed tomography showing irregular nodules involving the tracheal wall with preservation of the posterior membranous wall, with calcified nodules in the left bronchus (A) and a small nodular prominence on the right tracheal wall (B).

The patient was informed of the TO diagnosis and was started on antibiotic and antifungal treatment for the ongoing infection. Upon completion of treatment, she was discharged with a conservative management plan under pulmonology follow-up, as no bronchial obstruction was present and interventional therapy was not indicated.

3. Discussion

Tracheobronchopathia osteochondroplastica (TO) is an uncommon and benign disease characterized by multiple submucosal cartilaginous or ossified nodules develop and project into the tracheobronchial airway, while the posterior membranous wall remains unaffected [1]. First described in 1932, TO is extremely rare – under 600 cases have been reported worldwide to date, with roughly 140 cases coming from Japan and about 80 from China [3,7]. Its detection varies considerably, as studies based on autopsies suggest a prevalence of 0.25-0.30%, whereas bronchoscopic examinations have identified it in 0.01-0.80% of cases [1,8]. Epidemiological data regarding sex distribution are inconsistent: some studies note a male predominance (male:female ratio 1.74:1) [3], whereas others report more female cases (ratio 2:3) [1], leaving the influence of sex on disease incidence uncertain. TO is predominantly observed in older adults, with the majority of diagnoses occurring between 55 and 70 years of age, although a few cases have also been identified in children [3,7].

The aetiology of TO remains unclear, but nodule formation is thought to result from calcium phosphate deposition, which induces aberrant proliferation of bone and cartilage and can lead to narrowing of the major airways [2]. Chronic airway inflammation has also been proposed as

a potential contributing factor. Support for this comes from a series of 15 patients in whom recurrent respiratory infections were consistently present and were thought to be related to selective IgA deficiency [1]. Reports have described cases occurring alongside malignant tumours such as skin and lung cancer, as well as an instance linked to a retro-sternal recurrent goiter, though the reasons for these relationships remain unclear. About 60% of cases reported occupational exposure to dust or irritant gases, but the relationship between TO and environmental factors remains unclear. Smoking was documented in 44.5% of cases, 55.5% had comorbidities, and only a single case of positive family history of TO has been reported. Molecular factors have also been speculated to play a role, with bone morphogenetic protein 2 and transforming growth factor beta 1 proposed as mediators of aberrant bone and cartilage formation in the airway. However, the available evidence for all of these associations is limited, and they remain theoretical rather than firmly established [1,3,9–13]. Clinical manifestations of TO are highly variable, and a substantial proportion of patients remain asymptomatic at the time of diagnosis. Many of those cases are identified incidentally during bronchoscopy performed for unrelated indications or during endotracheal intubation, where unexpected airway rigidity may be encountered [3,5]. Yet most patients present with one or more nonspecific symptoms [3]. Patients most commonly present with chronic cough, while other reported complaints include recurrent respiratory tract infections, sputum production, haemoptysis, voice changes, dyspnoea, chest tightness, and continuous or intermittent fever [3,4].

The diagnosis of TO remains challenging due to its nonspecific and often mild clinical presentation. Patients commonly undergo repeated evaluations for chronic cough, recurrent infections, or unexplained dyspnoea before characteristic findings are recognized. Published literature shows that the condition is often confused with more common respiratory diseases, including asthma, tuberculosis, and, on rare occasions, bronchogenic cancer [3,6]. In our case, the patient also underwent evaluation for several preliminary diagnoses while clinicians attempted to determine the underlying cause of her persistent cough. Studies show that radiological features of TO can be identified in approximately 82–97% of cases. While chest X-ray typically does not reveal any abnormalities, computed tomography (CT) scanning is considered the most accurate imaging technique for evaluating TO [4,10,14]. On CT, TO typically presents as thickening of the tracheal cartilaginous wall with irregular sessile nodules while consistently sparing the posterior membranous trachea. The nodules may be calcified or non-calcified and can occur either focally or diffusely along the trachea and even the proximal bronchi. These structural changes may partially narrow the airway lumen in the affected segments [5,6,10]. Despite this, it has been reported that about 6% of cases show no radiological abnormalities. However, several authors describe cases in which CT was initially interpreted as normal, but TO-related changes were retrospectively recognized when the images were reviewed again after the diagnosis had been confirmed by bronchoscopy or autopsy [3,4]. CT is also highly valuable for identifying complications such as bronchiectasis, atelectasis, or post-obstructive pneumonia, and it additionally contributes to the differential

diagnosis [5]. Radiological imaging can help differentiate TO from relapsing polychondritis and age-related changes [10]. However, unlike TO, relapsing polychondritis does not present with nodular lesions, while age-related calcifications typically involve the posterior and lateral tracheal walls. These calcifications are usually symmetric, linear, and generally do not cause luminal narrowing [6].

Bronchoscopy remains the definitive diagnostic method for TO [2,4]. During the examination, TO typically manifests as stalactite-like, pebble-like, or cobblestone nodules that may even create a tortuous “corkscrew-like” airway. These whitish, smooth, firm lesions arise from the cartilaginous tracheal rings and proximal main bronchi while sparing the posterior membranous wall [3,5]. Nevertheless, multinodular tracheobronchial changes can be characteristic of various diseases. Although amyloidosis, sarcoidosis, and papillomatosis may display similar endoscopic features, none of these conditions show the characteristic pattern of selective sparing of the posterior membranous tracheal wall [6]. Moreover, it is important to differentiate these findings from tuberculous granulomas, malignant tumours, lymphoma, and fungal infections [15]. Therefore, a definitive diagnosis is established when endobronchial nodules are biopsied during bronchoscopy and submitted for histopathological examination [2]. Histopathological findings of TO are heterogeneous, but the most common abnormalities include submucosal ossification, cartilage formation, and chronic inflammation [3,9]. TO nodules correspond to submucosal osteocartilaginous proliferations composed of variable mixtures of fibrotic tissue, cartilage, bone, and mineralized matrix, while the overlying respiratory epithelium may be normal

or demonstrate inflammatory changes, epithelial hyperplasia or squamous metaplasia [3,5]. Although some biopsies reveal only intact respiratory epithelium, the most characteristic feature described is squamous metaplasia associated with calcified cartilage or new bone formation. In some cases, mature osteomedullary tissue has also been identified [3]. Nevertheless, obtaining adequate tissue samples may be challenging because the nodules are often extremely firm and calcified. For this reason, many authors note that characteristic endoscopic and imaging features may be adequate for making the diagnosis, especially when biopsy is technically difficult or unlikely to yield diagnostic tissue [5].

Currently there are no standardized guidelines for the management of TO, and treatment remains generally symptomatic. Most patients receive conservative therapy aimed at relieving cough, managing infections, and improving breathing capacity [2–4]. This may include antibiotics, bronchodilators, oral anti-inflammatory agents, humidified air, oxygen or steam inhalation, mucolytics, chest physiotherapy, avoidance of airway irritants [2,3]. Inhaled corticosteroids may provide benefit in early-stage disease or in lesions with inflammatory cell infiltration, although optimal dosing and duration remain unclear [4,13]. Interventional procedures, such as argon plasma coagulation, radiofrequency ablation or surgical excision, can be considered for patients with more advanced disease or significant airway obstruction, but reported outcomes have been variable [2,4]. Overall, current management strategies focus primarily on symptom control and infection prevention. Further large-scale studies are required to establish standardized management strategies.

The prognosis of TO is generally favourable, as the disease is benign and often remains stable for many years. Progression is uncommon, and long-term follow-up studies report patients maintaining a stable condition for decades [5]. Moreover, no malignant transformation of the nodules has been reported. Direct mortality from this condition is very low, with only a few reported cases of TO-related deaths, presenting as recurrent infections resulting from progressive airway narrowing [3]. Nonetheless, some individuals may still experience complications such as tracheal or bronchial stenosis, exertional dyspnoea, or respiratory failure during acute infections due to further airway narrowing [5,6,16]. Difficulties with endotracheal intubation have also been documented, emphasizing the need for patient awareness and communication with anaesthesiology team [17].

4. Conclusions

Tracheobronchopathia osteochondroplastica should be considered in patients with chronic cough, recurrent respiratory infections, or otherwise unexplained symptoms, especially when nodular airway involvement with sparing of the posterior tracheal wall is observed. This case underscores the importance of endoscopic findings in establishing the diagnosis and highlights the need for increased clinician awareness to reduce diagnostic delays and unnecessary investigations.

References

1. Wang H, Li S, Chen P, Qin Q. Tracheobronchopathia osteochondroplastica: A case report and literature review. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2020;45(2):208–215. doi:10.11817/j.issn.1672-7347.2020.180804.

2. Rana A, Mezughi H, Malik SA, Mansoor K, Al-Astal A. Rare Manifestation of Idiopathic Tracheobronchopathia Osteochondroplastica: Misdiagnosed and Untreated Entity? *Cureus*. 2020;12(7):e9407. doi:10.7759/cureus.9407.
3. Devaraja K, Surendra VU. Clinicopathological Features and Management Principles of Tracheobronchopathia Osteochondroplastica - A Scoping Review. *Indian J Otolaryngol Head Neck Surg*. 2023;75(4):3798–3814. doi:10.1007/s12070-023-03998-6.
4. Li, D., Jin, F., Nan, Y., Jiang, H., Liu, Q., Liu, H., Xin, T. Multi-nodule of large airway: tracheobronchopathia osteochondroplastica. *Annals of Palliative Medicine*. 2020;10(2) doi:10.21037/apm-20-316.
5. Ribeiro GMRe, Natal MRC, Silva EF, Freitas SC, Moraes WC, Maciel FC. Tracheobronchopathia osteochondroplastica: computed tomography, bronchoscopy and histopathological findings. *Radiol Bras*. 2016;49:56–57. doi:10.1590/0100-3984.2014.0056.
6. Devaraja K, Sagar P, Chirom AS. Tracheobronchopathia osteochondroplastica: awareness is the key for diagnosis and management. *BMJ Case Rep*. 2017;2017:10.1136/bcr-220567. doi:10.1136/bcr-2017-220567.
7. Wang W, Hu H, Liu M, Wang J. Tracheobronchopathia Osteochondroplastica: Five Cases Report and Literature Review. *Ear Nose Throat J*. 2020;99(10):NP111–NP118. doi:10.1177/0145561319897982.
8. Prakash UBS. Tracheobronchopathia osteochondroplastica. *Semin Respir Crit Care Med*. 2002;23(2):167–175. doi:10.1055/s-2002-25305.
9. Luo T, Zhou H, Meng J. Clinical Characteristics of Tracheobronchopathia Osteochondroplastica. *Respir Care*. 2019;64(2):196–200. doi:10.4187/respcare.05867.
10. Dumazet A, Launois C, Lebargy F, Kessler R, Vallerand H, Schmitt P, et al. Tracheobronchopathia osteochondroplastica: clinical, bronchoscopic, and comorbid features in a case series. *BMC Pulm Med*. 2022;22(1):423–2. doi:10.1186/s12890-022-02225-2.
11. Quaglino F, Mazza E, Navarra M, Palestini N, Marchese V, Lemini R, et al. Tracheobronchopathia osteochondroplastica in recurrent retrosternal goiter. Surgical management. *Ann Ital Chir*. 2017;6:S2239253X17026731.
12. Tajima K, Yamakawa M, Katagiri T, Sasaki H. Immunohistochemical detection of bone morphogenetic protein-2 and transforming growth factor beta-1 in tracheopathia osteochondroplastica. *Virchows Archiv*. 1997;431(5):359–363. doi:10.1007/s004280050111.
13. Zhu Y, Wu N, Huang H, Dong Y, Sun Q, Zhang W, et al. A Clinical Study of Tracheobronchopathia Osteochondroplastica: Findings from a Large Chinese Cohort. *PLOS ONE*. 2014;9(7):e102068. doi:10.1371/journal.pone.0102068.
14. Jiang H, Yang X, Guo Y. Multi-Nodule of Large Airway: Tracheobronchopathia Osteochondroplastica, Two Cases Report and Literature Review. *Ear Nose Throat J*. 2024;103(4):NP226–NP228. doi:10.1177/01455613211051662.
15. An J, Yang H, Hu C, Cao L, Zhou Y, Xiao Q, et al. Multinodule abnormalities of the tracheobronchus: bronchoscopy findings and

clinical diagnosis. *The Clinical Respiratory Journal*. 2017;11(4):440–447. doi:10.1111/crj.12356.

16. Danckers M, Raad RA, Zamuco R, Pollack A, Rickert S, Caplan-Shaw C. A Complication of Tracheobronchopathia Osteochondroplastica Presenting as Acute Hypercapnic Respiratory Failure. *Am J Case Rep*. 2015;16:45–49. doi:10.12659/AJCR.892427.

17. Warner MA, Chestnut DH, Thompson G, Bottcher M, Tobert D, Nofftz M. Tracheobronchopathia osteochondroplastica and difficult intubation: case report and perioperative recommendations for anesthesiologists. *J Clin Anesth*. 2013;25(8):659–661. doi:10.1016/j.jclinane.2013.05.010.