

Nephroquiz 9: Tracheobronchopathia Osteochondroplastica Presenting With Dyspnea in a Patient With End-stage Renal Disease

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CASE

A 49-year-old nonsmoker woman suffering from end-stage renal disease (ESRD) in the setting of hypertension was referred to the pulmonology clinic as a part of consultations prior to kidney transplantation; an unexpected symptom of dyspnea was noted.

Apart from a history of elective caesarian section surgery 24 years earlier and essential hypertension for 8 years with the consequent ESRD, she had no remarkable medical history. Hemodialysis had been started 8 months before through a permacath eventlessly. Metabolic and consequent ESRD-related conditions were under control with standard care. Family history was negative for pulmonary diseases but included type 2 diabetes mellitus and atherosclerosis-connected myocardial infarction above the age of 60 in both parents.

Exertional dyspnea had started since 4 years earlier and reached disabling level in the past year. Chronic kidney failure and volume overload would be considered responsible for her dyspnea, specifically when concomitant rale would be heard sometimes in the lower half of her lungs when she came to hospital for dialysis. No other symptoms, such as cough, hemoptysis, wheezing, and sputum production, were found. General physical, cardiovascular, and respiratory system examinations were normal. Liver function tests were also normal. No abnormalities were witnessed in the coagulation profile. Routine laboratory findings

were indicative of ESRD and its sequelae. Cardiac echocardiography did not indicate any signs of heart failure. Left ventricular ejection fraction was 55%, the right heart looked good, and no significant valvular abnormality was reported.

The diagnostic plan to search for the situation behind her exertional dyspnea began with a chest radiography, which showed irregularly stenotic airways. An interferon- γ release assay for tuberculosis was performed after a positive purified protein derivative skin test, which turned out to be positive. However, tuberculosis was ruled out due to negative smear and culture obtained from broncho-alveolar lavage, which was obtained bronchoscopically, as well as polymerase chain reaction testing for tuberculosis.

Spirometry was performed and did not yield any findings compatible with obstructive or restrictive lung disease (forced expiratory volume in 1 second, 99%; ratio of forced expiratory volume in 1 second to forced vital capacity, 114%; and forced inspiratory flow 255 to 75%, 93%). However, a drop in respiratory indexes could have occurred because we did not have any previous pulmonary function test results from the patient. Next step would always be performance of fiberoptic bronchoscopy right after the chest computed tomography which showed some hits. Preliminary computed tomography report was indicative of multiple nodular irregularity, variable stenosis and calcification of tracheal wall, and calcification-like lesions in the left lung hilum

and both main bronchi (Figure 1).

Bronchoscopy made the final diagnosis; many submucosal nodules were seen from below of the vocal cords, down to the trachea and carina to all lobar airways. Surprisingly, the posterior tracheal wall was not spared. The largest nodule was 1.5 × 1 cm, approximately (Figure 2). Biopsy forceps took samples from hard-to-bite nodules. Microscopic examination of biopsied specimen revealed squamous metaplasia with ectopic bony tissue under the respiratory epithelium (hematoxylin-eosin and safran, × 400).

The endobronchial brushings and cytology were negative for malignancy and broncho-alveolar lavage did not suggest any specific pathogenic

microorganism such as fungi or acid-fast bacilli. Given the tuberculosis being ruled out and normal-range pulmonary function tests, the patient was introduced for registration to the kidney transplantation waiting list.

QUIZ

What are the clinical, laboratory, and histological manifestations of tracheobronchopathia osteochondroplastica?

Tracheobronchopathia osteochondroplastica (TO) is a rare idiopathic nonmalignant disorder of large airways characterized by submucosal osseous or metaplastic cartilaginous 1- to 3-mm nodules overlying the cartilaginous rings. Almost

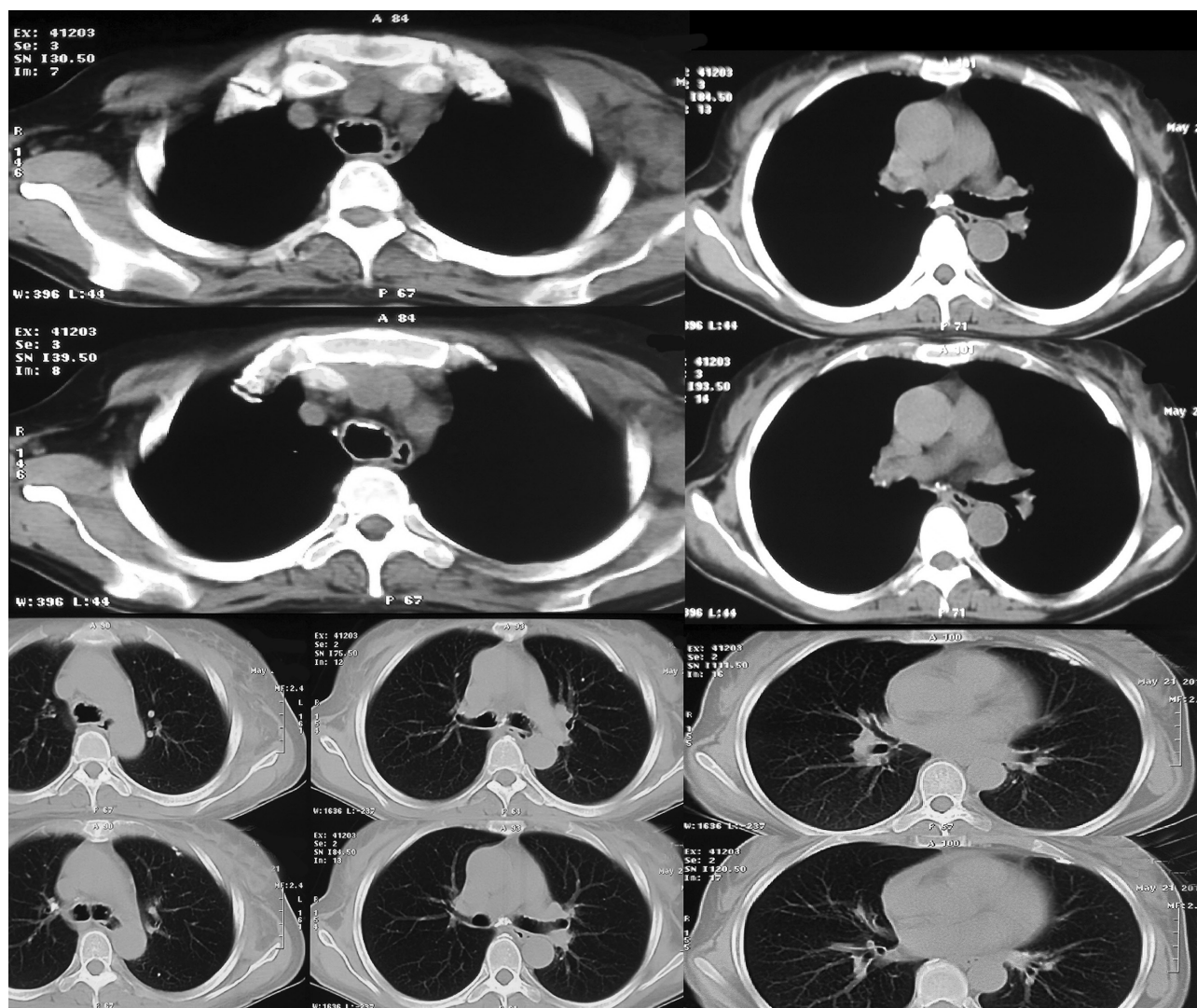


Figure 1. Chest computed tomography scan of the patient with tracheobronchopathia osteochondroplastica. Irregular nodular calcified nodules are extended from trachea (top left) and carina (bottom left) to left and right main bronchus (top right) and also distal airways (bottom right). Sizes of pictures have been changed in order to gain more accuracy.

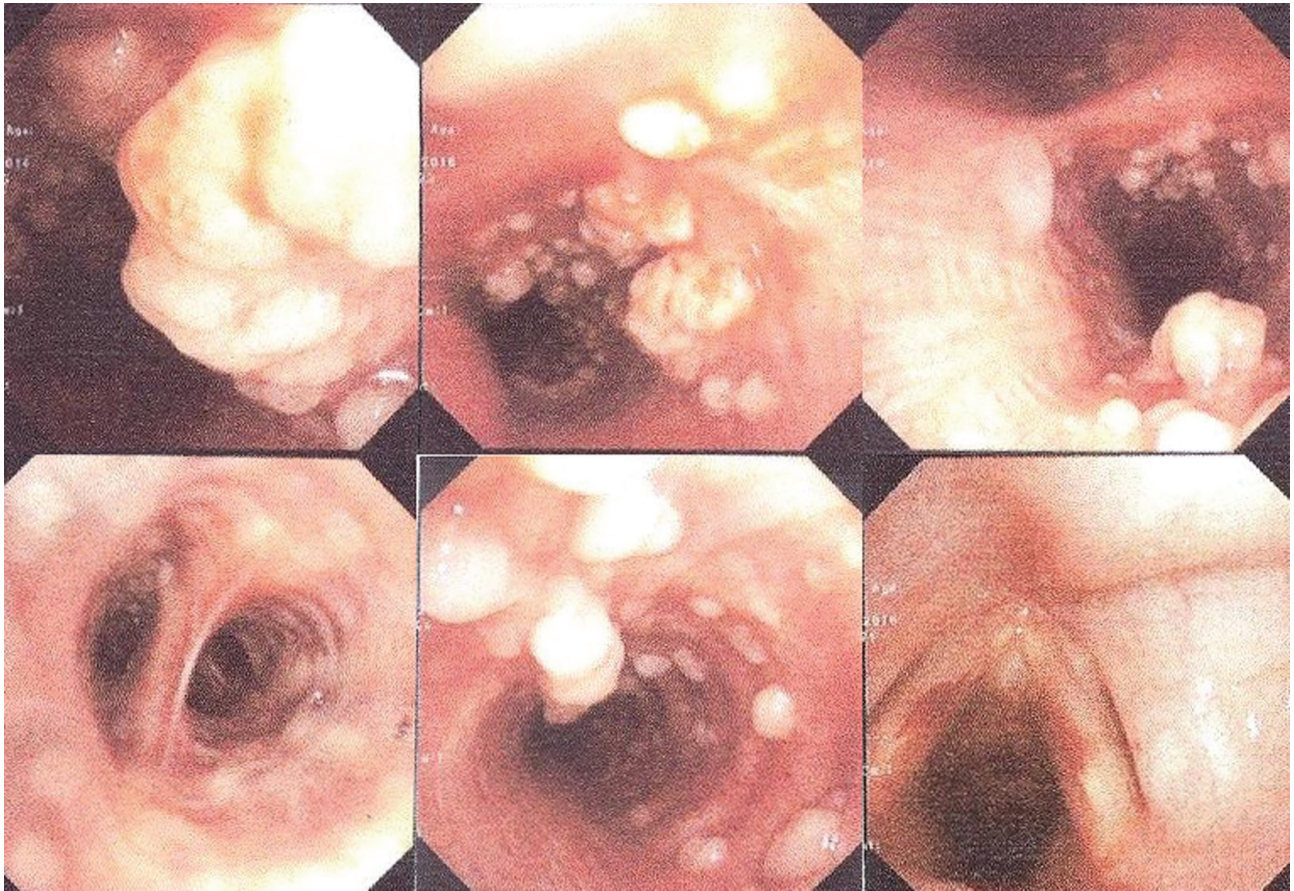


Figure 2. Bronchoscopic findings includes a large 1.5 × 1-cm nodule in the trachea (top right), multiple nodules above the carina (top middle and left), and smaller nodules in the right lower lobe (bottom left), left main stem bronchus (bottom middle), and vocal cord (bottom right).

always involving the anterior and lateral walls, nodules may be extended to main bronchus.¹ Chronic inflammation and bacterial or fungal superinfection may be caused by ecchondrosis and exocytosis nodules as well as mucosal metaplasia and stiffness. Airway obstruction can be caused by larger lesions which leads to presenting symptoms.² A chest computed tomography scan with a fiber bronchoscopy and pathological biopsy shows the clinical features supporting the ultimate diagnosis.

The disease may be often asymptomatic or associated with general and misleading symptoms making it difficult to estimate the exact prevalence. However, a low incidence of 0.01 to 4.2 per 100,000 inhabitants has been estimated, with no difference in sex distribution. The mean age at diagnosis has been reported to be 50 years.³⁻⁵ Dyspnea, hoarseness, persistent productive cough, wheezing, and hemoptysis have been linked to TO in the literature. In addition there are no absolute criteria

or symptomatic approach for the diagnosis. Cough and sputum production have been reported as the most prevalent symptoms in a cohort study.⁶

Tracheobronchopathia osteochondroplastica was described by Wilks in some details in 1867, and since then, approximately 400 cases have been reported worldwide. The clinical manifestations and diagnostic stories are very variant in every case.^{7,8} This report was a case of ESRD ready for kidney transplantation that was diagnosed with TO only with dyspnea. A vast majority of TO patients have at least 1 or more nonspecific respiratory symptoms including cough, dyspnea, hemoptysis, occasional wheezing, or rhonchi.^{6,9} In some cases, clinical situation may be more serious than thought. Severe illness has also been reported in a young man by Vikman and Keistinen, causing respiratory failure.¹⁰ The disease might be completely asymptomatic. Postmortem autopsies have shown very rare prevalence of the situation in some studies.¹¹ In

a few instances, difficult intubation has revealed the underlying TO. Madan and colleagues and also Warner and colleagues have reported discovery of stenotic upper airways due to TO after experience of a difficult intubation.^{12,13} A cohort study by Zhu demonstrated that chronic cough was the most common symptom in TO patients. Sputum production and dyspnea on exertion were next common symptoms among 22 patients.⁶ Repeated great airway infections due to insufficient airway toilet may be another manifestation.^{9,14} In our patient, the only sign was exertional dyspnea. She did not present any other symptoms, which is relatively uncommon in favor of other reports.

Differential diagnosis should be in mind to avoid early definitive diagnosis of TO. Tuberculosis-associated calcificating lesions, endobronchial sarcoidosis, endobronchial neoplasm, calcification of deep parts of tracheobronchial amyloidosis, papillomatosis, tracheobronchial calcinosis, and age-related changes of the trachea and bronchi should be ruled out before labeling a patient with TO due to their higher prevalence.^{11,15,16}

Different comorbid conditions have been discussed and reported in the literature to be related to TO. An infective association with accompanied by atypical microorganisms, such as chronic infections by atypical organisms including *Mycobacterium avium* or *Mycobacterium tuberculosis*, and *Klebsiella ozaenae*, has been proposed.^{9,17} Atrophic rhinitis and complicated or superinfected ozena may be precipitating conditions. Occupational exposure to silica resulting in pulmonary silicosis, end-stage primary tracheobronchial amyloidosis, and familial occurrence of TO leads us to more complex patterns of the disease associations.^{4,18,19} Mounier-Kuhn syndrome, which is characterized by abnormal dilatation of the trachea and main bronchi and also skin cancer in the scalp have also been reported in association with TO.^{20,21}

Regardless of whatever the precipitating factor may be, there is histopathologic proof that bone morphogenetic protein-2 operating in accompany with transforming growth factor- β 1 are the main nodule formation actors in the tracheobronchial submucosal.²² Bronchoscopy and biopsy is the final diagnostic instrument in TO, although providing a specimen with a flexible bronchoscope is probably difficult due to stiffness of the bony nodules as we have experienced.²³ The interesting fact about

our case was numerous continuation of very large bony nodules up to 1.5 cm in airways distally from the main bronchus to even lobar and segmental airways as demonstrated in Figures 1 and 2. Other reports remind us of involvement of main airways only and also sparing of posterior tracheal wall and minor nodules.^{3,4,7,8,10,12,13} We do not know if this overexpression may be associated with uremia and inflammatory state in ESRD or it is just the course of the disease or its variation among the Iranian population.

Management strategies for TO include administration of bronchodilators, invasive and early treatment of pulmonary infections, and bronchoscopic dilatation of airways.¹⁶

CONFLICT OF INTEREST

None declared.

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