

Endotracheal Tuberculosis and Aspergillosis Co-Infection Manifested as Acute Respiratory Failure: A Case Report

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Abstract

Background: Endotracheal and endobronchial tuberculosis are defined by microbiological and histopathological evidence of tuberculosis involving tracheobronchial tree, with or without parenchymal involvement. Tracheal tuberculosis is a rare and localized form of tuberculosis which can present itself with acute respiratory failure due to upper airway obstruction.

Case presentation: We present a case of a 62 year old female with a diagnosis of pulmonary tuberculosis, who was admitted to the emergency department of our hospital with severe dyspnea, which rapidly progressed to acute respiratory failure requiring tracheal intubation and mechanical ventilation. A four-drug anti-tuberculosis (TB) regimen, consisting of isoniazid, rifampicin, pyrazinamide and ethambutol, was started one month before and identification of a sensitive *Mycobacterium tuberculosis* strain was made at that time. During medical investigation, tracheobronchial tuberculosis and endotracheal aspergillosis co-infection were diagnosed by bronchoscopy and histological examination.

Conclusion: This uncommon case illustrates a severe clinical presentation of tracheobronchial tuberculosis with concomitant diagnosis of tracheal aspergillosis. It underlines the importance of a prompt diagnosis and treatment of tracheal tuberculosis and co-incidental infections in order to prevent serious complications, such as bronchostenosis and bronchomalacia. The bronchoscopic examination is the key for microbiological and histopathological confirmation of tracheobronchial involvement for both tuberculosis and aspergillosis. Corticosteroid therapy combined with anti-TB regimen remains controversial for endobronchial TB and its impact on patients' outcome is not well documented.

Keywords: Tracheobronchial tuberculosis; Endotracheal aspergillosis; Bronchostenosis; Bronchomalacia; Bronchoscopy

Background

Pulmonary tuberculosis is one of the major health problems worldwide. In Portugal, the incidence of tuberculosis has decreased in the last years, but it still remains higher than other countries from Western Europe [1].

Endotracheal or endobronchial tuberculosis (ETB) is a rare clinical situation and may occur with involvement of tracheobronchial tree, with or without pulmonary tuberculosis. It can affect any part and layer of the tracheobronchial wall and diagnosis is made by microbiological and histopathological examination [2]. The incidence of ETB ranges from 10 to 40% in cases with active pulmonary tuberculosis [3-5]. Diagnosis is frequently delayed, increasing the risk of complications such as erosion, stenosis, atelectasis or bronchiectasis [4]. The prompt diagnosis and treatment of tuberculosis is important to prevent ETB complications and also to prevent dissemination to other individuals.

Case Presentation

A 62 year old female who had been diagnosed with pulmonary tuberculosis one month before was admitted to the Emergency Room

(ER) of our hospital with symptoms of dyspnea, which rapidly progressed to acute respiratory failure requiring tracheal intubation and mechanical ventilation support.

She had a history of left bundle heart branch block, with an unremarkable past medical history; she had never smoked and serology for Human Immunodeficiency Virus (HIV) was negative.

She had symptoms of irritating cough starting several months before, which was treated with inhaled bronchodilators with minimal improvement. As chronic cough persisted, her physician referred her for pulmonary specialist consultation. A pulmonary-function test was performed and was suggestive of obstructive lung disease with a Tiffeneau index (FEV1/FVC) of 29% without reversibility after bronchodilator test. Chest computed tomography (CT) revealed a consolidation area in the right middle lobe, with several centrilobular micronodules. Specimens for microbiology investigation were collected and acid-fast bacilli staining in sputum was positive. The diagnosis of pulmonary tuberculosis (TB) was assumed and a four-drug anti-TB regimen consisting of isoniazid (INH), rifampicin (RMP), pyrazinamide (PZA) and ethambutol (EMB) was started. The sputum culture revealed a drug-sensitive *Mycobacterium tuberculosis* strain. Despite the beginning of therapy, she maintained persistent cough. One week before admission to the ER she started to complain of dyspnea and noisy breathing. At that time she had already been under anti-TB treatment for one month (Figure 1).

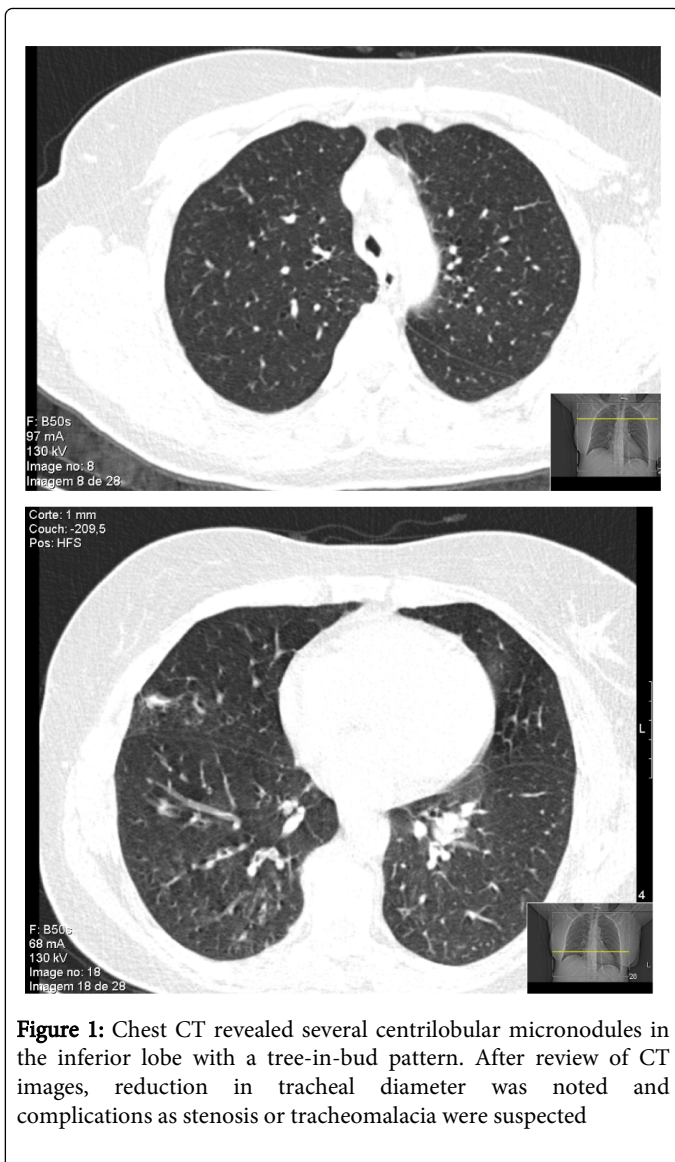


Figure 1: Chest CT revealed several centrilobular micronodules in the inferior lobe with a tree-in-bud pattern. After review of CT images, reduction in tracheal diameter was noted and complications as stenosis or tracheomalacia were suspected

On admission to the ER, the patient was afebrile and hemodynamically stable. Pulmonary auscultation revealed symmetrical respiratory sounds with bilateral crackles. Arterial blood gas (ABG) measurement revealed pH=7.19; PO₂=102.5 mmHg; PaCO₂=71.3 mmHg; HCO₃⁻=27.1 mmol/L; SO₂=96%; Lactates=0.95 mmol/L, with 100% oxygen mask; laboratory serum analyses were normal. Chest radiography (postero-anterior view) revealed lung opacity in the lower right lobe. Acid-fast bacilli (AFB) sputum smear remained positive. The patient worsened clinically, requiring intubation and invasive mechanical ventilation and she was admitted to Infectious Diseases Intensive Care Unit (ICU). Empiric antimicrobial therapy with amoxicillin/clavulanate and corticosteroid therapy with methylprednisolone were started; anti-TB therapy with INH, RMP, EMB and PZA were maintained. Rapid correction of respiratory acidosis was achieved and the patient was weaned successfully from mechanical ventilation 24 hours later. Corticosteroid therapy was changed to prednisolone 1 mg/kg/day.

During her stay in the Infectious Disease Department, the patient continued to experience recurrent episodes of irritating cough and

desaturation. A chest CT was performed and, compared with the previous CT performed two months prior, revealed a reduction of the consolidation area in the right middle lobe, but persisting several centrilobular micronodules with a tree-in-bud pattern and an increased number of centrilobular micronodules in the inferior lobe suggestive of an infectious process (Figure 1). A fiber optic bronchoscopy (FB) was performed and a white gelatinous material suggestive of caseum was observed in the trachea and at the opening of right main bronchus causing a 50% lumen obstruction; no morphological alterations on the right and left main bronchus were observed (Figure 2). During bronchoscopic intervention a biopsy was performed; examination of trachea specimens showed a positive AFB smear and histology revealed areas of dystrophic calcification in hyaline cartilage and abundant fungal structures of *Aspergillus spp.* Galactomannan antigen test in sputum was also positive. Antifungal therapy with oral voriconazole was added to therapeutic regimen. The patient did well, recovered from all respiratory symptoms and was discharged home. Sputum bacilloscopy and cultural exams were negative only after two months of anti-TB therapy.

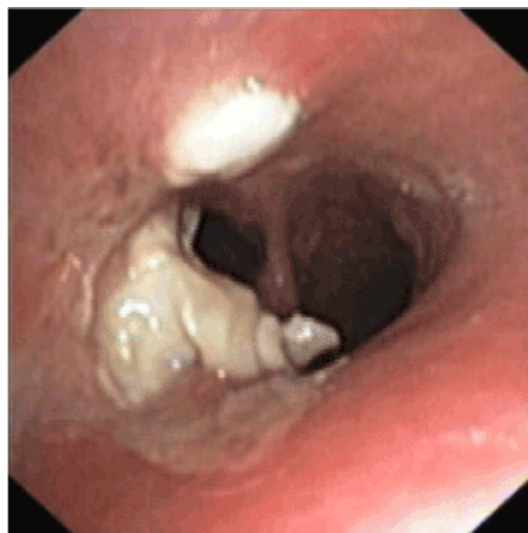


Figure 2: Caseum in tracheobronchial tree

One month after discharge, a follow-up FB was performed and revealed no white gelatinous material in the trachea (Figure 3), but two intraluminal granulomatous masses were observed and removed: one in the anterior wall of trachea with 2-3 mm, and another one on right main bronchus opening; no morphological or topographical changes in sub-segments were detected. Histopathologic examination of those lesions revealed granular tissue with lymphoplasmacytic *inflammatory infiltrate*, without evidence of tumour cells. A follow-up chest CT showed imagiological improvement with reduction in the number and dimension of micronodules (Figure 4). The patient was treated with a four-drug anti-TB regimen for the first three months and completed twelve months of anti-TB therapy.

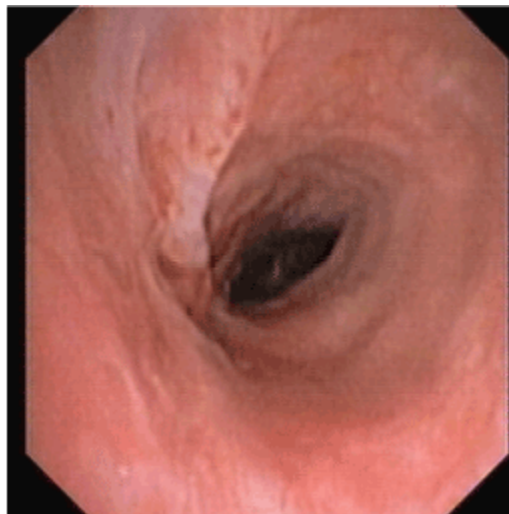


Figure 3: Tracheobronchial tree one month later



Figure 4: Reduction in the number and dimension of micronodules on follow-up chest CT one month after discharge.

After ten months of post-TB treatment, the patient had an episode of productive cough, dyspnea and fever with respiratory failure. After evaluation, a severe pneumonia and atelectasis were diagnosed. A rigid bronchoscopy (RB) was performed and revealed a tortuous trachea with reduction in diameter of the lower trachea and right main bronchus opening in 50%, which does not cause any resistance to the bronchoscope, but it returned to its original shape after the removal of the RB, which is suggestive of malacia. According to Pulmonary specialist consultation, prosthesis placement was not required.

Although symptoms such as irritating cough and noisy breathing progressively improved, the patient presented a severe obstructive syndrome requiring non-invasive ventilation with continuous positive airway pressure during the night.

Discussion

Tracheal and endobronchial tuberculosis (ETB) are rare forms of pulmonary tuberculosis which may lead to airway obstruction. Its diagnosis is challenging and requires a high awareness in specific clinical context.

Bronchostenosis may develop in 60 to 95% of cases of ETB. It is commonly seen in cases of delayed diagnosis and may occur despite adequate anti-tuberculosis therapy, when fibrostenosis and extensive granulation tissue already developed [4-7]. On the other hand, it may delay eradication of tubercle bacilli and patients can remain infectious over a longer period of time [5]. Severe bronchostenosis may cause pulmonary complications such as pulmonary infection, atelectasis, bronchiectasis and may induce severe respiratory failure and asphyxia. Although endoluminal tuberculosis leads to airway stenosis, it can also cause weakening of supporting cartilages, leading to a more collapsible airway [8]. The term tracheobronchomalacia is used when both trachea and bronchus are involved. Possible mechanisms implicated in tracheal weakness include pressure necrosis, disruption of blood supply and inflammation of the mucosa [9]. In this case, tracheal and bronchial walls were probably weakened by tuberculous disease process. Additionally, *Aspergillus spp.* was identified on histopathological examination of trachea specimens. The co-infection with aspergillosis may have contributed to tracheal and bronchial walls weakening, increasing the risk for the development of bronchomalacia due to tracheobronchial involvement of both TB and aspergillosis, to our knowledge, a previously non-described association. Endobronchial aspergilloma is also a rare presentation of pulmonary aspergillosis and usually appears as a mass causing bronchial obstruction on bronchoscopy and can be confirmed by histological examination [10].

Fiberoptic bronchoscopy (FB) is the gold standard to evaluate endotracheal obstructive lesions. The ETB can present itself with different bronchoscopic appearances including caseous, edematous, hyperemic, fibrostenotic, tumoral, granular or ulcerative lesions [4,7].

Computed tomography (CT) may demonstrate tuberculous endoluminal lesions. In addition, narrowed trachea, swollen larynx, and eroded cartilage eroded, may also be observed on chest CT. Quite often the whole length of the trachea is thickened and it may extend into the major bronchi. The thickening is usually irregular and the degree of narrowing can be quite significant at the location of the intraluminal granulomatous mass.

In this case report, ETB presented with progressive airway obstruction that evolved to acute respiratory failure; its diagnosis was delayed due to overlap of clinical manifestations and radiological findings with pulmonary TB. The diagnosis of endotracheal and endobronchial tuberculosis is often unexpected, and may be unnoted especially when patients have another pulmonary comorbidities. In fact, this patient complained of an irritating cough for three months before the diagnosis of pulmonary TB was made and even after the beginning of TB therapy she had recurrent episodes of dyspnea and noisy breathing until her admission into the ER with respiratory failure. After review of previous chest CT images, reduction in tracheal diameter was noted (Figure 1) and tracheomalacia was suspected. In this context, FB was performed and endobronchial tuberculosis was diagnosed with microbiological and histopathological confirmation. Despite the isolation of a drug-sensitive *Mycobacterium tuberculosis* strain in sputum, the AFB stain and culture became negative only two months after the beginning of anti-TB treatment.

No secondary cases were associated with transmission from our patient including in her family, which can be explained by a low level of tubercle bacilli in bacilloscopy and absence of lung cavitation.

As mentioned before, concomitant diagnosis of tracheal aspergillosis was not expected. A possible pathogenic mechanism is a initial saprophytic colonization with development of aspergillosis during corticotherapy, despite the short duration of corticosteroids previous to histological identification of *Aspergillus spp* (approximately 10 days). The resolution of both infections was achieved with anti-tuberculosis therapy and voriconazole for twelve months. Corticosteroid therapy was initiated at admission because of respiratory failure and stridor, and was maintained after the diagnosis of endobronchial tuberculosis, but it remains controversial as a prevention of bronchial stenosis [4,9].

Our patient presented clinical improvement with anti-TB and anti-fungal regimens, corticosteroids and bronchoscopic intervention which removed intraluminal masses. In some cases of ETB, insertion of airway stent in the affected tracheobronchial segments may be imperative to keep airway patency, however in our patient it was not required.

Conclusion

This case illustrates a severe clinical presentation of tracheobronchial tuberculosis with acute respiratory failure, with concomitant diagnosis of tracheal aspergillosis. This co-infection with the involvement of the tracheobronchial tree may have been responsible for the development of severe sequelae in this patient, including lower tracheomalacia and right bronchomalacia with persistent diameter reduction. The diagnosis of tracheobronchial tuberculosis and aspergillosis are usually unexpected and physicians should be aware of persistent symptoms as irritating cough and dyspnea.

The author's purpose in writing this case report was to highlight the importance of prompt diagnosis and treatment of ETB and co-incident infections in order to achieve eradication of tubercle bacilli and to prevent serious complications and long term sequelae associated with delay in diagnosis, such as bronchostenosis and bronchomalacia. As discussed above, the diagnosis of tracheal and endobronchial tuberculosis can be delayed due to its relatively uncommon occurrence, nonspecific clinical manifestations and misleading radiological findings; a high index of awareness is required for diagnosis. Bronchoscopic examination is the key for definitive diagnosis of ETB, allowing microbiological and histopathological confirmation and additional therapeutic interventions, including removing obstructing material. Corticosteroid therapy combined with anti-TB regimen remains controversial and its impact on patients' outcome is not well documented [4,9].

Consent

Written 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 of this journal.

Competing Interests

The authors declare that they have no competing interests.

Author's Contributions

SX have been involved in conception, sequence alignment and drafting of the manuscript.

NN have been involved in drafting the manuscript.

LS have made substantial contributions to intellectual content and interpretation of data.

AS have given final approval of the version to be published.

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