

Case report

The obstructive phenotype of chronic posttuberculosis disease - is there a role for the occupational exposure?

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Abstract

Tuberculosis (TB) disease is treatable, but the postTB lung disease in previously treated patients is a reality which must not be ignored. A case report of a 52-year-old male patient, heavy smoker (50 pack-years), alcoholic, with occupational exposure to chemical hazards (such as gaz oil vapors, distillate fuels and industrial solvents), physical hazards (thermal extremes, noise, vibration, UV radiation), ergonomic hazards (manual handling activities); and psychosocial hazards (e.g. overload, isolation from family and friends), was delayed diagnosed with severe extensive cavitary pulmonary TB disease in 1999, treated till 2001. The assessment of lung function was neglected before or after antiTB therapy ended, so COPD was ignored till 2009, when the patient was admitted in a Pneumology Hospital. Other long term postTB disorders, as left fibrothorax, bronchiectasis, cavitary open healing syndrome, were also identified. Chronic postTB lung disease (PTLD), centered on COPD, had unfavorable progressive evolution till September 2022, when premature death occurred. In conclusion, the obstructive phenotype of PTLD was delayed diagnosed and had multiple risk factors as tobacco smoking, occupational exposure and severe TB disease itself. A protocol for monitoring obstructive lung disorders among workers in oil industry, especially those diagnosed with TB disease, should be properly adapted through a collaborative approach between the occupational and the chest physician.

Keywords: *post-tuberculosis lung disease, COPD, smoking, occupational exposure*

Introduction

Secondary Pulmonary Tuberculosis (PTB) remains a great infectious threat to humanity, through its many victims (40 million people diagnosed between 2018 to 2022, with approximately 9 million case notifications and 1.5 million deaths every each year), as global trends of annual TB morbidity and mortality reveal [1].

Post Pulmonary TB syndromes are unfavourable consequences of post-TB lung damage, beyond completion of antiTB treatment, usually ignored and underdiagnosed, representing the hidden top of the iceberg and having an increased potential for chronic respiratory disability. The used umbrella term for chronic postTBP syndromes, posttuberculosis lung disease (PTLD), is referring to intrathoracic sequelae at different anatomic levels (lung parenchyma, pleural layers, bronchial tree, pulmonary vasculature) [2,3].

In the first international symposium of post-tuberculosis lung health, in 2020, minimum case definition of PTLD was considered as the 'evidence of chronic respiratory abnormality, with or without symptoms, attributable at least in part to previous (pulmonary) TB' [4], representing a kind of 'hidden TB epidemic' with attributable illness and deaths [5].

According to literature data from several clinical studies, almost a half of previous TB treated patients persist to have respiratory problems related to postTB lung damage, with irreversible anatomic changes in the lung and consequent loss of pulmonary function, inducing a chronic pulmonary impairment after tuberculosis (PIAT) [2,6].

PTLD itself is a global burden on the health system because millions of TB survivors experienced more or less complications. In a modelling study, Dodd et al estimated 172 million people surviving treated TB disease from 1980 to 2019, of which 155 million were still alive in 2020 [7].

In such a heterogenous and complex PTLD spectrum, any respiratory symptom in combination or not with imagistic markers of lung fibrosis, bronchiectasis, pleural thickening, nodular lesions, tuberculomas, open cavitary healing may be sufficient for an early diagnosis after contagious TB disease recovery [8].

PostTB chronic respiratory disability can be classified into restrictive, obstructive and mixed functional syndromes. Ventilatory dysfunction must be investigated and attested in all patients after ending antiTB therapy. Relapses of PTB can amplify the extension of TBP sequelae and the severity of ventilatory dysfunction, including bronchial obstruction.

The aim of this case report is to analyze the consequences of three episodes of recurrent pulmonary active TB disease on progressive irreversible pulmonary impairment and challenges for occupational rehabilitation.

Case report

A case of a 52-year-old male patient, heavy smoker (50 pack-years), alcoholic, who was admitted in February 2009, in Constanta Clinical Pneumology Hospital, for acute onset of a possible Pulmonary TB relapse considered on medium recurrent hemoptysis, subfebrility, night sweats, medium exertional dyspnoea and anterior left chest pain.

The occupational history revealed that the patient worked as roustabout on an oil platform for 18 years. In this job, he performed cleaning, greasing of hand tools, assembled and disassembled oilfield equipment, loaded and unloaded pipes, and assisted other oil rig workers to ensure by providing them the materials and equipment needed for their tasks. During these activities, the occupational exposure included chemical hazards such as gas oil vapors, distillate fuels and industrial solvents, physical hazards (thermal extremes, noise, vibration, UV radiation), ergonomic hazards (manual handling activities); and psychosocial hazards (e.g. overload, isolation from family and friends). The gases and vapours to which he has been exposed act as irritants and, obviously, can contribute to the lung function deterioration. In fact, the patient was on a continuous work disability since 1999, when pulmonary secondary TB was diagnosed.

The patient was known to have a personal medical history of 3 episodes of pulmonary active tuberculosis disease, with progressive extension of bilateral caseous excavated lesions and cavitary lesions in the left lung, from 1999 to 2001, when medical retirement was mandatory.

At the current hospitalization, smears and cultures for *Mycobacterium tuberculosis* were negative. Body mass index was 21.8 kg/cm², but there were 5 kg lost in weight in the last 12 months.

Chest X-ray showed fibro-nodular round and ovalar opacities localized in the upper 2/3 of the right hemithorax, left fibrothorax, with traction of the trachea, heart, mediastinum to the left and denudation of the vertebral spine, including an area of hypertransparency in the upper ½ of left hemithorax, suggesting upper left lobe (ULL) parenchyma destruction, flattened diaphragms as an indirect sign

of hyperinflation.

The imagistic inventory of postTB lung damage, after last antiTB therapy, performed by CT scan of the chest, revealed heterogenous sequelae consisting in left fibrothorax, open cavitary syndrome in upper left lung lobe, cylindrical bronchiectasis in upper right lung lobe (Figure 1).

Stage III GOLD of chronic obstructive pulmonary disease (COPD) was diagnosed by spirometry with forced expiratory volume in the first second (FEV1) of 1.39L (43.9%), forced vital capacity (FVC) of 2.11L (52.7%), FEV1/FVC ratio of 65.8%.

The patient underwent treatment with antibiotic (Cefixime 200 mg twice a day), inhaled combined triple therapy (Tiotropium 18 mcg and fixed combination of Budesonide/Formoterol 320/9 mcg), hemostatics, antitussive, with a favorable clinical evolution through the remission of the subfebrile syndrome and hemoptysis, and the improvement of

dyspnoea.

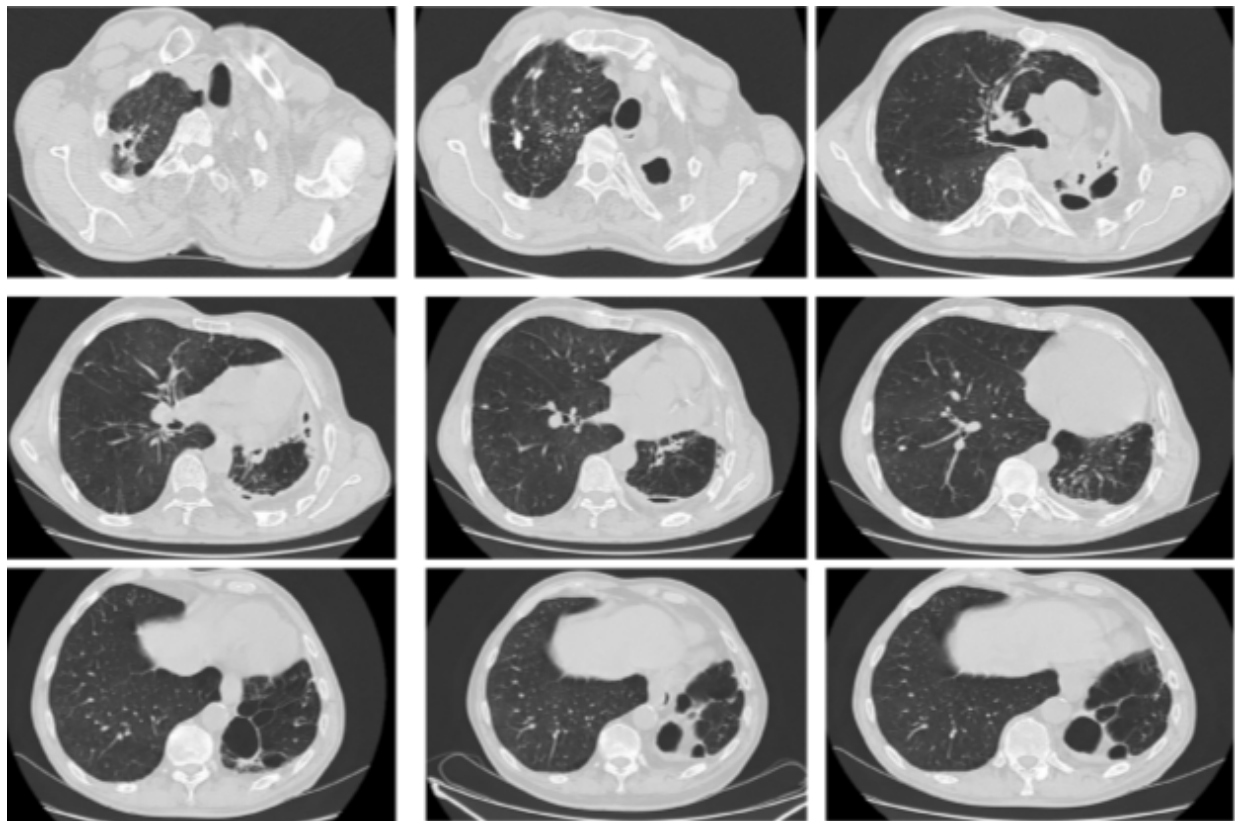
The evolution of the pulmonary impairment after tuberculosis was unfavorable along 13 years till death by acute myocardial infarction occurred in September 2022. It was a premature death at 65 year-old, after 23 years of prolonged respiratory illness caused by tuberculosis.

The last admission in hospital was in August 2022 for agravation of dyspnea and productive sputum with *Pseudomonas aeruginosa* identification in sputum.

The loss in lung function was important with decreased FEV1 from 1.39L in 2009 to 0.86L in 2022, FVC from 2.11L to 1.71L and FEV1/FVC ratio under 70%.

TLCO decreased dramatically in 7 months from 48% (13.02 mL/min/mmHg compare to normal range 20.16-34.05) in January 2022 to 37%, in August 2022, with low Kco (decreased from 48% to 39%).

Figure 1. Male patient, 65 year-old, investigated by CT scan of the chest which revealed: asymetry of the chest because of left fibrothorax, open healing cavitary syndrome in upper left lobe, cylindrical bronchiectasis in upper right lung lobe



Discussion

Risk-factors for PTLD occurrence include multiple TB episodes of disease, delayed diagnosis and treatment, drug-resistant spectrum of *Mycobacterium tuberculosis* bacilli, exposure to smoking or occupational dust or particles, poverty, outdoor and indoor pollution [9]. This case reported by us is eloquent from the perspective of delayed diagnosis of PTB and delayed therapy, heavy exposure to smoking (63 pack-year), occupational exposure to irritative respiratory noxes, poverty and alcoholism. His long term respiratory symptoms, which started after 1 year of TB treatment, were unfortunately ignored for almost consecutive 8 years by the patient and physicians as well. The previous exposure to occupational respiratory hazards was also ignored.

Any patient with a history of treated pleural or pulmonary TB should undergo a complex clinical, imaging, bronchological and functional systematic evaluation for the early identification of chronic postTBP disease. An occupational medicine examination should be also performed and exposure to respiratory hazards should require a stricter protocol of follow up. We have recently reviewed the most frequent agents and occupations associated with occupational COPD [10] and the main diagnosis challenges. For sure, in TB patients who were previously exposed to petroleum-derived vapours and fumes, the exact contribution of each of these factors to the bronchial obstruction is difficult to determine. The exploration of ventilatory function is mandatory in all patients completing anti-TB treatment, even in any carrier of TB sequelae, without history of treated TB disease, revealing possible ventilatory dysfunction. If we would have had at least the values of the spirometry before the TB episodes, we might consider occupation exposure as the most important factor. In fact, in Romania, in oil industry workers, bronchitis was rather frequent both in men and in women exposed to hydrocarbons and smoking [11]. In our reported case, the severe degree of airflow obstruction was combined with the extent of fibrotic parenchymal sequelae, with damage to the medium bronchial airways (bronchiectasis), with hemoptysis and colonisation of bronchiectasis with *Pseudomonas aeruginosa*. So, it is a peculiar obstructive phenotype of PTLD in a male patient with complex sequelae after treated PTB (fibrothorax, bronchiectasis, open healing cavitary syndrome), a heavy smoker with a serious chronic occupational exposure. Exposure to cigarette smoking is considered to act as a risk factor and confounder in the assessment of the severity of

oil industry's occupational disease related [11]. On the other hand, smoking has a central role in causing TB, other pulmonary infections, COPD and interactions between TB and COPD [12]. The association between exposure to active tobacco smoking and tuberculosis disease has been suggested since 1918 [13] and the negative impact of smoking is associated as well with alcohol chronic use, malnutrition, poverty and overcrowding [14].

Obstructive phenotype of PTLD is rarely pure in treated TB patients, because TB is a disease of all anatomical structures of the lung and lung injury is associated not only with progressive tissue damage, granuloma formation, necrosis, cavitation, but also with excessive inflammation, abnormal tissue repair and lung fibrosis [15]. The severity of TB disease is a risk factor for developing a chronic obstructive lung disorder as COPD and or bronchiectasis.

COPD and TB association among smokers is a major world public health issue, but pulmonary tuberculosis may induce itself airflow obstruction, even in the absence of smoking, either during the active phase of treatment or after treatment ended. The causal relation between TB history and chronic airflow obstruction was reported in previous century (1950s and 1960s) [16]. Among the long term consequences of TB disease, bronchiectasis is frequently reported and can be associated with COPD. Tuberculosis is the most frequent infectious cause of non cystic fibrosis (nonCF) bronchiectasis [17]. Non CF bronchiectasis is a very heterogenous disease with different clinical, radiological, bacteriological phenotypes [18]. Initial MTB positivity of smears and imagistic TB features suggestive for the presence of cavities and bilateral infiltration may reflect the severity of TB [19], PTLD, as well as PIAT [2,6]. So, pulmonary function tests are recommended to be used routinely in all treated TB patients in order to assess the loss of lung function, determining the lung restrictive, obstructive or mixed impairment.

Conclusions

Active tobacco smoking exposure increases both the risk of TB and COPD, causing long-term lung damage and airway obstruction. Tobacco smoking in association with severe extensive pulmonary tuberculosis disease and occupational exposure to respiratory hydrocarbons irritants can classify patients into a high risk category for developing COPD. According to the type, intensity and duration of the occupational exposure, as well as the severity of TB disease, a monitoring protocol should be properly

adapted through a collaborative approach between the occupational and the chest physician.

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