Ethiopian Medical Journal 2024, 62(1)
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ISSN 0014-1755 *eISSN 2415-2420* *Nigussie et al.*

Case Series

Pulmonary Tuberculosis Mimicking a Lung Cancer: a Case Series

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Abstract
Tuberculosis (TB) is an infectious disease that is caused by Mycobacterium tuberculosis. Despite TB being a preventable and curable disease, it still remains to be one of the leading causes of mortality worldwide and continues to be prevalent. TB can manifest in multiple systems, but its primary target is the lungs. Pulmonary TB can present differently depending on the patient's immune status and comorbidities. One atypical presentation of TB is lung mass, which can mimic lung malignancy and cause diagnostic delays.In this case series, we report on four cases in which TB was initially suspected to be lung malignancy. All four patients had lung masses on diagnostic imaging; microbiological testing was positive in only two of the patients and bronchoscopic abnormalities were seen in two of those. In two of the four cases, caseating granulomas were present on biopsy. All four patients attained clinical and radiologic resolution.In conclusion, despite years of knowledge and the prevalence of TB, atypical presentations can still cause diagnostic delays and unnecessary interventions. This case series provides examples of TB mimicking lung cancer, so considering TB as a differential diagnosis for patients presenting with a lung mass is crucial.

Keywords: *Tuberculosis, lung mass, Ethiopia*
Citation : *Nigussie M, Hagos G, Alemayhu M et al. Pulmonary Tuberculosis Mimicking a Lung Cancer: a Case Series. Ethiop Med J 62 (1) 73 -77*
Submission date : *24 September 2023 Accepted: 923 December 2023 Published: 1 January 2024*

Abbreviations

AFB- Acid- Fast Bacilli
BAL-Bronchoalveolar lavage
COVID- Coronavirus disease
CXR- Chest x-ray
DS- Disseminated
FNA- fine needle aspiration
HIV-Human immunodeficiency virus
LAP- Lymphadenopathy
LUL- Left upper lobe
MDR- Multidrug-resistant tuberculosis **MTB-** Mycobacterium tuberculosis **RUL**- Right upper lobe
SOB- shortness of breath
TB - Tuberculosis
WHO- World Health Organization

Introduction

Tuberculosis (TB) is a preventable and curable infectious disease caused by Mycobacterium tuberculosis. It is the second prevalent cause of death from infectious agents, after COVID-19, and 13th leading cause of death worldwide [1]. The highest prevalence is in Sub-Saharan Africa, India, and Southeast Asia. Ethiopia is one of the 30 high-TB burden countries, with incidence.

>100 per 100,000; which is why early diagnosis and intervention of TB is important [2-3].

TB is known for having multisystem manifestations although its primary target is the lungs. The most common presenting symptoms in TB diagnosed patients are cough greater than 2 weeks, fever, night sweat, fatigue, anorexia and weight loss [4]. Chest radiography findings vary as typical and atypical, with the former having findings of cavitary lesions, pulmonary consolidation, lymphadenopathy, pleural effusions. Atypical radiographic pattern like lung mass

occurs in 3.5 to 4.5% of pulmonary TB cases [5]. It contains caseous material encapsulated by multiple concentric layers of connective tissue without surrounding inflammation or spread.

Although lung masses can have benign etiologies as TB infection, diagnostic dilemma occurs in differentiating it from malignant causes. The overlap of clinical presentations as well as similarities in radiographic findings of lung cancer and tuberculosis necessitates use of histopathology to distinguish between the two [6].

In this case series, we described 4 cases of patients, age 21-41 years and presenting with respiratory and constitutional symptoms. All 4 patients presented with radiographic findings of pulmonary mass. Details of the diagnostic dilemma, clinical presentation, treatment as well as outcome will be presented in the case series.

Case presentation

Case –1

A-28-year-old male office worker and non-smoker presented with a dry cough of 04 months with associated right side chest pain, anorexia and unquantified weight loss. He had no history of TB treatment or contact with chronic cougher. Biochemical investigations were all within normal range. Chest x-ray (CXR) showed right lower lobe opacity and Chest CT showed 3cm x 3cm x 4cm peripheral (subpleural) mass on the posterior segment of right lung, and right hilar lymphadenopathy (LAP), the biggest measuring 2cm x 3cm. With preliminary diagnosis of lung cancer CT guided fine needle aspiration (FNA) cytology from the mass was done and results were inconclusive. Bronchoalveolar lavage (BAL) cytology and Gene Xpert, and trans-bronchial biopsy were non-yielding. For financial reasons, the patient was not investigated further. He was started on anti-TB treatment empirically. After 02 weeks of treatment he showed significant clinical improvement and at the end of the 6th month of anti-TB treatment, he had complete radiologic resolution.

Case –2

A 26 year old female nonsmoker with no contact history presented with dry cough of 03 months duration with associated unquantified weight loss. Biochemical investigations were unrevealing. CXR showed right upper lobe mass like consolidation . and Chest CT revealed right upper lobe (RUL) mass with multiple mediastinal LAP suspicious for lung cancer. Bronchoscopy showed right upper lobe bronchus fungating mass. BAL Gene Xpert showed rifampicin resistant mycobacterium TB (MTB) and endobronchial biopsy showed granuloma of epithelioid cells, giant cells and caseous necrosis. She was then referred to ALERT hospital for initiation of multi- drug- resistant (MDR) TB treatment regimen. On the 4th month of anti-TB, the cough subsided. Repeat Chest CT on the 4th month of treatment showed complete resolution of mass.

Case 3

A 28-year-old male physician presented with a cough productive of whitish sputum of 03 months, shortness of breath (SOB) on exertion, low grade fever, loss of appetite and weight. He smoked a few cigarettes per day for the 3 years before presentation. Biochemical investigations, sputum AFB, Gene X-pert were unremarkable. Chest CT showed 7.7cm x 7.1cm left upper lobe (LUL) mass with spicules and left hilar LAP. Bronchoscopy, done twice, showed narrowed LUL anterior segment bronchus. BAL cytology, BAL Gene X-pert, endobronchial biopsy results were negative. He had a left pneumonectomy and left hilar/para-aortic lymphadenectomy. The intraoperative finding was 10cm x 10cm LUL mass and multiple big hilar and para-aortic LAPs. Biopsy revealed granuloma with caseous necrosis. He was started on anti-TB regimen and symptoms resolved completely.

Case 4

A 41-years old male patient, with 5 pack year smoking history, presented with a dry intermittent cough of one month duration with associated headaches, sweating and a weight loss of 5 kg and loss of appetite. On examination at presentation he was sick looking and tachycardic (PR- 118- 122). Chest x-ray showed lung mass and CT revealed right hilar soft tissue attenuating mass compressing LUL bronchus resulting in narrowing and abutting but no invasion of the adjacent vessels with mediastinal enhancing LAP. There is LUL apicoposterior nodular interstitial septal thickening suspicious for tumor compression of left pulmonary vein resulting in focal pulmonary edema or lymphatic spread of a tumor. BAL showed atypical pleomorphic cells suspicious for malignancy. Endobronchial biopsy showed pseudostratified columnar epithelial lining underneath by granuloma and necrosis with area of mixed inflammatory cells. He was thus started on an anti-TB treatment regimen. Post treatment chest x-ray showed marked resolution of the mass lesion.

Table1. Summary of the clinical characteristics, radiologic presentations, microbiologic findings and treatment outcomes of the cases

S. No.	Age	Sex	Clinical Manifestation	Type of TB	HIV status	CT scan finding	Bronchoscopic finding	Biopsy Finding	Microbiologic	Treatment	Treatment Outcome
1	28	M	Dry cough Right side chest pain Anorexia and Unquantified weight loss	DS	NR	Peripheral (subpleural) mass on the posterior segment of right lung, with right hilar LAP	Non Yielding	None	None	Empirically started on anti-TB regimen	Cured
2	26	F	Dry cough Unquantified weight loss	MDR	NR	Right upper lobe mass with multiple mediastinal LAP	Right upper lobe bronchus fungating mass	Granuloma of epithelioid cells, giant cells and caseous necrosis	BAL Gene Xpert showed rifampicin resistant MTB	Started on MDR TB treatment regimen	Cured
3	28	M	Productive cough SOB on exertion, LGIF, Loss of appetite Unquantified weight loss	DS	NR	LUL mass with spicules and left hilar LAP	Narrowed LUL anterior segment bronchus	Granuloma with caseous necrosis	Non yielding	left pneumonectomy and left hilar/ paraaortic lymphadenectomy Started on anti-TB treatment	Cured
4	41	M	Dry cough Headache - Sweating - Weight loss - Loss of appetite - Smoker - Sick looking - Tachycardiic	DS	NR	RT hilar mass compressing LUL bronchus with mediastinal LAP	Not done	pseudostratified columnar epithelium with necrotic granuloma	Non-yielding	Started on anti-TB treatment	Cured

Discussion

TB is a well-known diagnostic mimicker with a multitude of presentations, one of them being a lung mass imitating malignancy. Pseudotumoral pulmonary TB occurs in 3.5% to 4.5% of immune competent patients even in TB endemic areas [5]. TB and lung cancer have been confused for quite some time as evidenced by a study carried out by Prytz et al. in 1976 on 91 cases of TB who underwent thoracotomy for a presumptive diagnosis of lung cancer [7]. On the other hand, although rare, TB and lung cancer can co-exist, be it through increased susceptibility for new infection or reactivation of a latent one due to the immunocompromised state of malignancy patients [8]. Such dilemmas lead to misdiagnosis, delayed treatment, unnecessary surgeries and further exacerbations of complications of pulmonary TB [9].

The aforementioned challenges partly can be attributed to the great overlap in symptomatology and features of presenting parenchymal infiltrates with lymphadenopathy in both Pulmonary TB and lung cancer [10-11]. Patients with pulmonary TB typically present with cough, chest pain, fever, night sweats and weight loss with infiltrates or cavities on chest imaging which is also seen in lung cancer cases [11]. Such non-specific clinical presentation combined with negative bacteriologic studies and atypical imaging results contribute towards the delay in diagnosis. A study conducted in Chinese PLA general hospital between 2011 and 2015 demonstrated overlapping chest CT findings including spiculation in both pulmonary TB and lung cancer cases [9]. In contrast, bronchoscopy with BAL or guided biopsy was shown to have better yield in reaching definitive diagnosis [12]. Nonetheless, biopsy histopathology studies remain to be the best definitive method of confirming the diagnosis, preferably excisional biopsy [13-14].

In light of the above literatures, accurately diagnosing atypical presentation of TB poses a great hurdle for clinicians, especially in resource limited developing countries. The aim of this case series is to characterize the clinical, radiologic and histologic findings as well as demonstrate diagnostic challenges of tuberculosis patients who were initially diagnosed as lung malignancy or had difficulty ruling out lung malignancy.

In this case series we report 4 cases who had presented with TB mimicking lung malignancy. Age of patients ranges from 21 to 41 years. In our study the cases presented with a constellation of symptoms

Cough and unquantifiable weight loss were the most common symptoms appreciated in all four patients. Other symptoms reported were loss of appetite in three patients; diaphoresis in two patients; headache, pleuritic chest pain and shortness of breath was reported by one patient each.

Although CT scan is an imaging modality commonly used to initially assess masses, evidence indicates chest CT leads to higher rates of misdiagnosis between TB and cancer as compared to head and neck CT and abdominal CT [14]. All of the above cases in this series had undergone chest CT scans which revealed a mass lesion with lymphadenopathies seen on hilar and/or mediastinal lymph nodes, and one of the cases having spicules along the mass. These findings were non-diagnostic and misleading towards the presumption of lung malignancy which warranted further investigation. Therefore, bronchoscopy was done in three of the cases and findings of two cases were revealing. One case revealed a fungating lesion while the other had narrowing of LUL anterior segment bronchus

In concurrence with similar literatures [12-14], definitive diagnosis of pulmonary TB in majority of the cases was reached through biopsy histopathology examination. Of the total cases, three of them had endo-bronchial biopsies performed. One of the cases initially had a non-revealing endo-bronchial biopsy, hence excisional biopsy was performed. All three cases' biopsy demonstrated caseating granulomatous inflammation. BAL from one of the biopsy confirmed case yielded a rifampicin resistant MTB, while the others were non-yielding.

As a result of the above findings, all patients were started on anti-TB medication as per the latest WHO standard. One case was diagnosed retrospectively after response to anti TB medication.

All of the study subjects achieved clinical and radiological resolution.

Conclusion

Despite long years of knowledge about tuberculosis, it still remains a diagnostic challenge due to its chameleon nature. These cases indicate the importance of considering TB in the differential diagnosis of patients presenting with lung masses particularly in the young. The findings also emphasize the need for better diagnostic tools due to its implication on proper management of the disease and reducing its burden. In addition, this calls for deeper

investigations towards understanding the prevalence of similar presentations of tuberculosis mimicking malignancies at both national and global level.

Conflict of interest- The authors have no conflict of interest to declare.

Ethical Clearance- Waiver was obtained from AAU CHS IRB office to publish the case series.

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