

## RESEARCH COMMUNICATION

# A Common Medical Error: Lung Cancer Misdiagnosed as Sputum Negative Tuberculosis

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### Abstract

**Objective:** To emphasize that delay in diagnosis of lung cancer can be caused by the wrong diagnosis of tuberculosis (TB) in TB endemic countries. This is of major concern as early-diagnosis of lung cancer can increase the chance of tumor resectability and timely chemo-radiotherapy may provide better quality of life. **Methods:** Proven lung cancer patients, who had received anti-tubercular treatment (ATT) since onset of current symptoms, were studied retrospectively during the period of Nov-07 to Nov-08. **Data-source:** Patient interview and medical records. **Results:** Total of 14 out of 70 patients received wrong diagnosis of TB and had received ATT [male-12, female-2; mean age-58.07±6.81; Non Small Cell Lung Cancer (NSCLC)-12, Small Cell Lung Cancer (SCLC)-2], 12 were smokers with median smoking pack-years of 44(15 to 112). Pre-referral sputum Acid fast Bacilli (AFB) was done in only 3 out of these 14 patients and sputum AFB was negative in these 3 patients. ATT was started on the basis of chest X-ray finding and clinical symptoms. Mean duration of ATT taken was 4.46±3.15 months. **Conclusion:** Due to high TB prevalence and radiological similarities, a large number of lung cancer patients initially get wrongly treated for TB. Also, clinicians associate lung cancer with high case-fatality and start ATT without detailed investigation. Altogether, this leads to delay in diagnosis and progression of disease.

**Key Words:** Diagnostic errors - lung neoplasms - pulmonary tuberculosis.

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### Introduction

World Health Organization (WHO) estimates, lung cancer (along with cancer of trachea and bronchus) to be the leading cause of mortality due to cancer in males in India. Smoking in women has markedly increased in the recent time. With increasing smoking behavior, lung cancer incidence is bound to grow. The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either low dose computerized tomography (LDCT), chest x-ray (CXR), sputum cytology, or a combination of these tests. Early detection of lung cancer might not improve the survival but can provide better quality of life to the patient and increase chances of resection.

India has a high prevalence of tuberculosis patients. Incidence of all form of tuberculosis in India is 168 per 100,000 per year and out of them 75 would be sputum smear positive for Acid fast bacilli (AFB) (WHO, 2008). Higher prevalence of tuberculosis and overlap of its clinical presentation with lung cancer creates a scenario where a significant number of early lung cancer patients may get wrongly labeled as TB (tuberculosis), more so in resource poor setup. This leads to a significant delay in diagnosis and management of lung cancer. We are

presenting this case series of lung cancer patients, as an attempt to quantify and emphasize the delay in diagnosis of lung cancer caused by wrong diagnosis of tuberculosis.

### Materials and Methods

We registered 70 cases of lung cancer in our medicine department out patient clinic between Nov-2007 and Nov-2008. As ours is a tertiary care referral hospital, most of the patients in this series were referred for evaluation of poor or no response to ATT and some for confirmation of diagnosis of lung cancer and further management. All the available records of the patients were analyzed and patients were interviewed for history of past treatment taken. The patient who do not have the tissue diagnosis were subjected for tissue sampling and patient who have the sampled tissue were subjected to review of slide by a senior pathologist from our institute. The data were subsequently analyzed.

### Results

The demographic and clinical profile of the studied patients is given in Table 1. A total of 14 out of 70 (20%) patients had received ATT for varying durations since onset of chest symptoms. Mean (±SD) duration of ATT

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**Table 1. Demographic and Clinical Profiles of the 14 Patients Presented in this Case Series**

No	Age	Sex	Smoker	Pack Years	Diagnosis	Duration ATT	Sputum AFB	Changes on Serial Chest X-ray (CXR)
1	58	M	Yes	62	NSCLC	10.0	Negative	Increase in size of opacity
2	57	M	No	0	NSCLC	6.0	Not Done	Increase in size of opacity
3	50	F	Yes	15	SCLC	2.0	Not done	Increase in size of opacity
4	65	M	Yes	93	SCLC	9.0	Negative	Metastasis to contralateral lung
5	60	M	Yes	25	NSCLC	9.0	Not done	Increase in size of opacity with metastasis to bone
6	68	M	Yes	100	NSCLC	6.0	Not done	Serial CXR not available. Records - increase in opacity
7	55	M	Yes	30	NSCLC	6.0	Not done	Serial CXR and radiological records not available.
8	56	M	No	0	NSCLC	3.0	Not done	Serial CXR not available. Records show no change
9	55	M	Yes	20	NSCLC	3.0	Not done	Serial CXR not available. Records show no change
10	59	M	Yes	80	NSCLC	2.5	Not done	Serial CXR not available. Records show no change
11	61	M	Yes	50	NSCLC	2.0	Not done	Serial CXR not available. Records show no change
12	64	M	Yes	112	NSCLC	2.0	Negative	Increase in size of opacity
13	62	F	Yes	25	NSCLC	1.5	Not done	Serial CXR not available
14	42	M	Yes	44	NSCLC	0.5	Not done	Serial CXR not done

taken was 4.46 (±3.15) months. In the majority of these patients sputum smear examination for AFB was not done and the ATT was empirically started on the basis of chest radiograph only. Routine three sputum AFB testing was done in only 3 out of 14 patients and was negative in all three. Six of our patients had taken a full course of ATT (6 month) before an alternate diagnosis was considered. 2 patients had taken ATT for less than 2 months, before diagnosis of TB was reconsidered. 10 out 14 patients in our series underwent bronchoscopy for tissue diagnosis and their bronchoalveolar lavage fluid was negative for AFB.

Studied patients were of the high risk group for lung cancer considering age, sex and smoking behavior. Mean age (±SD) was 58(±6.55) years, 12 were male and 2 female. 12 out of 14 patients were smokers with median (range) smoking pack-years of 44 (15-112).

Evaluation of serial chest X-rays of patients showed increase in size of opacity of 5 patients while continuing on ATT. One patient with SCLC (Small cell lung carcinoma) showed metastasis to contra-lateral lung while being continued on ATT. Case no. 5 had developed pain in left thigh while continuing ATT which on bone scan was found to be metastasis to upper end of left femur. Cases for which serial chest X-ray were not available, radiological records were reviewed and it showed increase in size of opacity on chest X-ray in one case. Only 2 out of 14 patients were started on ATT from a DOTS (Directly observed treatment short course) center, rest were under treatment with private physicians. CT scan of chest was

not ordered in any of the 14 patients at the beginning of presentation. It was ordered in 6 out of 14 patients as a part of work up of poor response to ATT and CT findings suggestive of malignant lesion of lung was one of the reasons for referral to our centre.

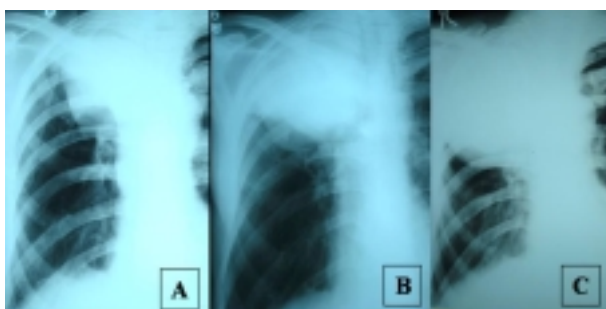
*Case Presentations*

**Case 1**

A 58-year-old male with history of 62 pack-years of smoking, presented to general physician with history of cough, blood in sputum and weight loss for past one month. CXR had shown opacity in RUZ (right upper zone). His three sputum smear, which was done at initial visit, was negative for AFB (Acid fast bacilli). Patient was diagnosed as sputum negative TB and started on ATT which was continued for 10 months despite no symptomatic improvement and progressively increasing opacity in serial chest radiograph (Figure-1A-C). Patient was referred to our institute for further evaluation and management. Here, Contrast enhanced Computed Tomography(CECT chest) showed 12x13 cm mass in (right upper lobe) RUL and RML (right middle lobe) which proved to be NSCLC (Non small cell lung carcinoma) on ultrasound-guided transthoracic biopsy. The TNM staging at that time suggested disease to be locally advanced (stage IIIB). Patient was treated with chemotherapy (paclitaxel+carboplatin) to which he showed partial response.

**Case 2**

A 57-year-old non-smoker male had presented to primary health center for insidious onset chest pain and shortness of breathing for past three months. CXR had shown opacity in left lung, on the basis of which, patient was started on ATT without sputum smear examination. After 6 months of ATT, patient was referred to our institute for no symptomatic improvement and increasing size of opacity on serial CXR. Patient CECT chest showed 10x10 cm mass in left lung with hilar and mediastinal lymphadenopathy. Fibreoptic bronchoscopy(F.O.B), showed infiltrative growth and edema in left main bronchus. Bronchoscopic biopsy proved it to be NSCLC.



**Figure 1. Serial CXR of Case 1 Taken at 0, 6 and 10 Months of ATT**

### Case 3

Another 50-year-old female with 15 pack-years of smoking history, presented to private hospital with history of cough and hemoptysis for last one month. Chest radiograph showed right hilar opacity. Sputum smear examination for AFB was not done and the physician started antitubercular treatment just on the basis of chest radiograph. When the patient did not show any improvement in symptoms, she was referred to our centre. The Patient was re-evaluated and a CECT chest revealed a RUL mass and right hilar lymphadenopathy. She was subjected to FOB which revealed infiltrative growth in right superior lobe bronchi and bronchoscopic biopsy was reported as SCLC (small cell carcinoma).

### Discussion

In developing countries, high prevalence along with clinical and radiological similarities of PTB (pulmonary tuberculosis) with lung cancer often may mislead clinicians to diagnose lung cancer as TB. Further, clinicians associate lung cancer with poor prognosis and high case-fatality rate and start ATT without confirmation of diagnosis, even when risk factors like smoking, male and elderly population, for example, are present.

Main source of diagnostic error was delay in investigating the opacities using CT scan/FOB (fiberoptic bronchoscopy) and forgotten art of reading chest radiographs in the age of CT and MRI, as in most the cases the opacities are very much suspicious of lung mass, especially in some follow up radiographs. Lack of utilization of these diagnostic modalities can be attributed to their high cost and limited availability in big cities and tertiary care centers in developing countries.

#### *Error reduction strategy:*

In the developing world where TB prevalence is high, therapeutic ATT trial for suspicious lung opacities would remain as an acceptable practice but we must reach a consensus on the time limit for the therapeutic trial of ATT, beyond which the diagnosis of TB must be reconsidered for poor or no response. In this direction, a prospective case series of 107 patients of cutaneous tuberculosis concluded that if patient does not respond to 5 weeks of ATT, they are unlikely to respond with further treatment and diagnosis should be reviewed. (Ramam et al., 2007) If we apply this suggestion for reviewing the diagnosis if no or poor response to therapeutic trial of ATT at 5 weeks in pulmonary tuberculosis cases, 85% (12/14) of patients would have benefited in the form of early diagnosis of lung cancer in our case series.

The best and cost effective way to reduce errors will be to investigate all patients suspected of TB and having risk factors for lung carcinoma with 3 sputum AFB as well as sputum cytology for malignant cells. The practice of sputum AFB should be done in all patients without fail as advised in Revised National Tuberculosis Control Program (RNTCP) guideline (RNTCP, 2005). Any patient with suspected mass on chest X-ray should undergo CECT chest as missing a diagnosis of malignancy is less likely on CT and any atypical presentation or mass should have

*Lung Cancer Misdiagnosed as Sputum Negative Tuberculosis* tissue diagnosis. Current RNTCP guidelines which are being followed in DOTS centers across India, does not detail about the management for poor response to ATT in sputum negative PTB (RNTCP, 2005). We need further studies to determine the magnitude of false positive diagnosis of sputum negative PTB in field conditions and factors behind it. Once those are identified, a corrective strategy can be designed.

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