

Association of Pulmonary Tuberculosis with Lung Carcinoma: An Epidemiological Study

Abstract

Introduction: Tuberculosis (TB) is a serious public health problem in developing countries, with India bearing highest burden. Lung cancer (LC), especially adenocarcinoma, is also increasing all over the world, with India having highest mortality in males due to lung cancer. Both diseases do co-exists producing diagnostic dilemma and treatment controversies. We intended to explore the incidence of both diseases at a tertiary cancer centre. **Materials and Methods:** This longitudinal study was conducted between 2014 to 2017. Diagnosis and treatment of TB were according to DOTS protocol. For lung cancer biopsy was mandatory for diagnosis. **Results:** Our study was conducted on 42 patients at the Department of Radiotherapy, R.G. Kar Medical College. In 19 of the 42 patients, the diagnosis of TB and LC occurred simultaneously, whereas, in 23, the occurrence was sequential. Fifteen (35.7%) patients reported having had TB twice. TB treatment was given as Category 1 of DOTS in 21 patients (50%) and Category 2 in 15 (35.7%). In 6 (14.3%) patients, the data on treatment regimen were either not provided or unavailable. Regarding carcinoma lung management, 50% of patients were purely treated as palliative intent. Twenty percent of patients received chemotherapy with platinum doublet. Thirty percent of patients were given best supportive care. **Conclusion:** The symptoms of TB and lung carcinoma overlap with each other. If we get any patient with lung cancer not much improving after anticancer treatment, diagnosis of TB should be kept in mind. Similarly, in any diagnosed case of pulmonary TB, development of lung cancer should be considered if not improved with anti-tubercular treatment.

Keywords: Lung carcinoma, pulmonary tuberculosis, simultaneous and sequential

Introduction

Tuberculosis (TB) is a serious public health problem in developing countries. Medical science is getting improved day by day, and still, the odds of treatment against TB are also developing, for example, emergence of multidrug resistant. India is the highest TB burden country, with the World Health Organization statistics for 2011 giving an estimated incidence figure of 2.2 million cases of TB for India out of a global incidence of 9.6 million cases.^[1]

Lung cancer is a deadly type of cancer seen worldwide and in India. There were 1.8 million new lung cancer cases estimated to occur in 2012.^[2] In India, lung cancer constitutes 6.9% of all new cancer cases and 9.3% of all cancer-related deaths in both sex; it is the most common cancer and cause of cancer-related mortality in men.^[3] Risk of developing lung cancer increases in the presence of a chronic inflammation, pulmonary fibrosis due to TB,

and TB scar tissue.^[4,5] Lung cancer and its treatments result in immunosuppression which attracts the bacillus to infect the victim.^[6]

Simultaneous or sequential occurrence of TB in lung cancer patients affects the prognosis.^[7-9] In addition, one study demonstrated that the association between TB and lung cancer varies in different ethnic groups and in different regions; it is important to know the characteristics of these cases in India.^[6] Therefore, the objective of this study was to describe the clinical characteristics of patients with pulmonary TB and lung cancer.

Aims and objective

The study was performed to reveal epidemiology and treatment outcome in pulmonary TB with lung cancer and how are these two mutually affected. The study period was from November 2014 to October 2017. The study was conducted at the Department of Radiotherapy, R.G. Kar Medical College, Kolkata.

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Materials and Methods

This was a longitudinal study, involving prospective data collection, conducted to determine the characteristics of patients with TB and lung cancer who were treated in R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India. The study involved patients diagnosed with TB and lung cancer, either simultaneously or sequentially.

For each and every patient, a standardized protocol was followed:

1. We searched for the demographic data of the patients, and all relevant data for pulmonary TB and lung carcinoma were collected, e.g., occupation, residence, and history of prolonged exposure to polluted air or not
 2. We took a detailed history of each and every patient, including family history and smoking history
 3. Thorough examination was done for assessing performing status of the patients, and any other significant findings were noted
 4. We also reviewed the reports, and what was the treatment done for diagnosed pulmonary tuberculosis (PTB) cases, i.e., according to Directly Observed Treatment Short Course (DOTS).
- The diagnosis of pulmonary TB was based on consensus criteria:^[10]
 1. Positive Ziehl–Neelsen staining for acid fast bacillus (AFB) (two positive smears)
 2. A positive smear and a positive culture for *Mycobacterium tuberculosis*
 3. Positive Ziehl–Neelsen staining for AFB and radiological findings consistent with pulmonary TB
 4. A single positive culture for *M. tuberculosis*
 5. Epidemiological, clinical, and radiological findings consistent with pulmonary TB, associated with a favorable response to treatment with antitubercular drugs.

The diagnosis of lung cancer was based on the histopathological findings.

The data were entered into Microsoft Excel spreadsheets, after which they were processed and analyzed with the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, USA). We carried out a descriptive analysis of the study variables. Quantitative data are presented as mean \pm standard deviation and qualitative data are expressed as *n*.

Results

The diagnosis of lung cancer and TB was classified by timing as follows:

- Group 1: Pulmonary TB occurred before 2 months of diagnosis of lung carcinoma, and during our study, the TB was in active phase, possibility of scar cancer^[11,12]
- Group 2: Pulmonary TB and lung cancer occurred

simultaneously within 2 months of diagnosis of any of the disease

- Group 3: Pulmonary TB occurred after 2 months of diagnosis of lung cancer.

We took two groups, i.e., Group 1 and Group 3 both in one arm as sequential.

Group 2 was considered as simultaneous occurring of both diseases in concern.

The study involved 42 patients diagnosed with TB and lung cancer and registered in our outpatient department between November 2015 and October 2017. The epidemiological characteristics of the patients are shown in Table 1. In 19 of the 42 patients, the diagnosis of TB and lung cancer occurred simultaneously, whereas, in 23 patients, the occurrence was sequential as stated in our criteria. Fifteen (35.7%) patients reported having had TB twice. The diagnosis of TB was established by the following methods: smear microscopy of spontaneous sputum, in 10 patients; culture of spontaneous sputum, in 6; smear microscopy of induced sputum, in 7; bronchoalveolar lavage (BAL) culture, in 5; PCR positivity for *M. tuberculosis* in BAL samples, in 9; and clinical and radiological findings consistent with TB, in 5. TB treatment was as follows: Category 1 of DOTS in 21 patients (50%) and Category 2 of DOTS in 15 (35.7%). In 6 (14.3%) patients, the data on treatment regimen were either not provided or unavailable.

Table 1: Epidemiological characteristics of the study population (n=42)

Epidemiological characteristics	Number of patients (n=42)
Age (years)	
Mean	65
Range	With SD 10
Gender	
Male	18
Female	24
Residence	
Urban	32
Rural	10
Performance status	
ECOG 0-1	14
ECOG 2-3	28
Stage	
I-II	2
III	5
IV	35
Histopathology	
Adenocarcinoma	36
Squamous cell carcinoma	6
Others	0
Smoking	
Positive	34
Negative	8

ECOG: Eastern Cooperative Oncology Group, SD: Standard deviation

Only 2 (4.7%) patients reported noncompliance with TB treatment, 5 (11.9%) patients died, and 24 (57.1%) patients were discharged as cured. No treatment outcome data were available for 11 (26.2%) patients. The mean age of lung cancer diagnosis was 65 ± 10 years. Of the 42 patients, 35 (83.33%) patients presented with distant metastases at diagnosis; of them, 71% were diagnosed with LC and TB simultaneously.

The following LC treatments were performed:

- Twenty-one patients, i.e., 50% of patients, were purely treated as palliative intent. Of them, 20% received palliative RT (30 Gy in 10#). The rest 30% of patients received palliative chemotherapy containing 4–6 cycles of platinum doublet combination with injection cisplatin 100 mg/m², intravenous (IV) D1, and injection etoposide 100 mg/m² IV D1–D3
- Twenty percent of patients received chemotherapy with platinum doublet combination with injection cisplatin 100 mg/m², IV D1, and injection etoposide 100 mg/m² IV D1–D3, followed by concomitant chemoradiation with a radiation dose 50 Gy in 25# over 5 weeks along with weekly cisplatin injection 40 mg/m².
- Thirty percent of patients were kept in best supportive care, considering the performance status, tolerance, age, etc.

The epidemiological characteristics of our study population is shown in Table 1 ($n = 42$).

Discussion

In this study, we described the characteristics of 42 patients developing TB and lung cancer, either simultaneously or sequentially. TB was diagnosed before lung cancer in most of the patients (23), and in none of the cases, lung cancer was diagnosed before TB. Non-small cell lung cancer, especially adenocarcinoma, was the most common histological type. The relation of pulmonary TB and LC was first described in 1810, and it was demonstrated histologically a few years later.^[13] Several studies on this association have been published, most of which are case series and case–control studies.^[6–13] However, the cause of development of lung cancer in TB patients is still not clear, whether it can be explained with some biologically plausible theory. One hypothesis would be that inflammation associated with infections can contribute to carcinogenesis.^[3] Reactive oxygen or nitrogen species produced by activated neutrophils can bind to the DNA, inducing genetic damage and neoplastic transformation.^[14,15] Alterations of the fragile histidine triad gene in patients with chronic pulmonary TB may result in lung carcinogenesis.^[16,17] During the development of bacillary nidus, carcinogens tend to act more on the hyperactive area. Even metaplastic changes occur in the epithelium of the hyperactive area.^[18] The cases described here are similar to those reported in previous studies.^[6–13] Adenocarcinoma was the most common histological type followed by squamous cell carcinoma in our study.

TB may present before lung cancer in most of the cases due to reversible causality bias, i.e., due to the development of cancer immunity decreases, so the latent TB infection perhaps which was present before may get activated.^[13,19] Around 81% of the cases in our study were smokers, so it may look like a confounding factor. Although, after cessation of smoking, TB itself stands as a risk factor for lung carcinoma, it increases the risk around 2.5 times.^[20] A meta-analysis supported this evidence, showing that the association between TB and lung cancer was not due to the effects of smoking, because, when considering only nonsmoking patients, there was a 1.78-fold increase in lung cancer risk among patients with TB. That same meta-analysis^[7] demonstrated that the association between TB and lung cancer was not due to the time since the diagnosis of TB. Because the initial symptoms of these two diseases are similar, it should be considered that there can be a delay in the diagnosis of either condition, and consequently, patients can present with either LC or TB at a more advanced stage.^[21,22] In a recent, retrospective case–control study^[11] involving 36 patients with lung cancer, 10 (27.8%) were diagnosed with TB and cancer concomitantly, whereas 26 (72.2%) were diagnosed with TB after being diagnosed with cancer. In a case series conducted in Japan,^[23] the diagnoses were concomitant in six patients, TB was diagnosed before lung cancer in five cases, and lung cancer was diagnosed before TB in the remaining five. It is also possible that TB was diagnosed before lung cancer more frequently because of a reverse causality bias, i.e., an occult cancer can reduce immunity and lead to reactivation of latent TB. Therefore, TB can present clinically before lung cancer.^[12,19]

Limitations

- In Berksonian bias for hospital based studies, patients with an index diagnosis are more likely to be diagnosed with another disease than those who are without an index diagnosis. For instance in our study, patients with TB, at follow-up chest X-ray, are more prone to be diagnosed with cancer than those who are not diagnosed with TB.^[24]
- Some cases were lost to follow-up.

Conclusion

We should advise the TB-diagnosed patients to avoid lung carcinogens, such as tobacco smoking, as much as possible, because these agents contribute to a substantial increase in lung cancer risk. In conclusion, the present study demonstrated that most of the patients with TB and lung cancer were smokers, and that TB was diagnosed either before or simultaneously with lung cancer. Family history of TB is also an important epidemiological factor. Association of lung cancer, especially adenocarcinoma, is increasing in female gender. The presence of indoor air pollution or residence (urban area) also affects the development of lung cancer. Hence, we can warn those patients or their relatives beforehand. Non-small cell lung cancer, especially adenocarcinoma, was the most common histological type we got in our study.

Hence, if we get any patient with lung cancer not much improving after anticancer treatment, diagnosis of TB should be kept in mind. Similarly, in any diagnosed case of pulmonary TB, development of lung cancer should be considered if not improved with antitubercular treatment.

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Conflicts of interest

There are no conflicts of interest.

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