Original Article-I

Simultaneous Presentation Of Pulmonary Tuberculosis And Lung Cancer: Experience From A Regional Cancer Centre

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ABSTRACT

Background: **Prevalence of pulmonary tuberculosis is very high in India. Lung cancer is the most common cancer in males in Delhi and because of close similarity in clinical and radiological features of lung cancer and tuberculosis many of lung cancer patients have had received empirical anti tubercular treatment (ATT) before a diagnosis of lung cancer was established. True incidence of pulmonary tuberculosis in lung cancer is not known. Tuberculosis in lung cancer may get reactivated following chemotherapy and/or radiation therapy. Simultaneous presentation of tuberculosis and lung cancer independent of treatment with immunosuppresants, however, is rare.**

Material and Methods: At our center we evaluated records of 580 lung cancer patients seen over a period of 5 years to see incidence of pulmonary tuberculosis in lung cancer. Patients who had been worked up for pulmonary tuberculosis like sputum or bronchoalveolar lavage (BAL) for AFB smear or culture were identified.

Results: Two hundred and ninety eight of these patients were worked up for pulmonary tuberculosis. Twelve patients in the present study had documented evidence of simultaneous existence of pulmonary tuberculosis (acid fast bacilli positive sputum and or culture positivity) and lung cancer. Radiologically, no separate active tubercular lesion was identified except in one patient who had left upper zone fibro parenchymal lesion. Fibrosis and calcification on chest X-rays (CXR) suggestive of old tuberculosis were evident in 7 patients. Eight patients died of progressive lung cancer within 3 months of diagnosis, 4 patients became acid fast bacilli (AFB) negative after 2 months of anti tubercular therapy. Diagnosis of lung cancer was delayed in 4 patients as they were receiving anti tubercular therapy after detection of AFB in sputum.

Conclusion: Recognition of tuberculosis is important not only because it is curable but also due to the fact that its presence interferes with radiological assessment to chemotherapy and radiotherapy. Sputum acid fast smear may be done more frequently in patients of lung cancer in countries where tuberculosis has high prevalence. The true incidence may be still higher and newer techniques e.g. PCR based and others may help in knowing true incidence of co existence of lung cancer and pulmonary tuberculosis.

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INTRODUCTION

Lung cancer is the most common cancer in males in Delhi.[1] Pulmonary tuberculosis may occur before, during or late in the course of lung cancer.[2,9] Local and systemic effects of tumour as well as the immunosuppression induced by anticancer treatment predisposes the patients of lung cancer to opportunistic infections including tuberculosis. However, true incidence of pulmonary tuberculosis in lung cancer is not known.

Prevalence of tuberculosis in India as judged by standard PPD tuberculin test is 60-80%.[10] In

majority of patients tubercular infection remains dormant; and clinically apparent tuberculosis develops in approximately 10% of infected patients soon after primary infection or years later due to reactivation.

In most reported cases tuberculosis developed following treatment with chemotherapy and/or radiation therapy in lung cancer patients.[9,11] Gettler et al[12] reported a case of simultaneous presentation of Mycobacterium Kansasii infection and small cell lung cancer illustrating reactivation of latent infection independent of either chemotherapy and radiation therapy. Author claimed it to be the first documented case of simultaneous mycobacterial infection and primary lung cancer independent of immunosuppressive therapy.

At our center we evaluated records of 580 lung cancer patients seen over a period of 5 years to see the incidence of pulmonary tuberculosis in lung cancer.

MATERIAL AND METHODS

Case records of all the lung cancer patients seen from January 1991 to December 1995 in Medical Oncology department were analyzed to look for documented evidence of pulmonary tuberculosis. Five hundred and eighty cases with diagnosis of lung cancer were registered during this period. Two hundred and ninety eight of these patients were also worked up for pulmonary tuberculosis either at our institute (174) or outside (124) with reports available for review. The work up included any or combination of; sputum AFB, sputum culture, examination of BAL fluid, and ESR examination.

The cases were subjected for these tests if they had either of the followings-

(i) Past or family history of tuberculosis and or productive cough (ii) Fever (iii) Hemoptysis (iv) Strong clinical suspicion, or (v) As per practice if bronchoscopy has been done then examination of BAL

RESULT

Twelve of these patients had evidence of pulmonary tuberculosis. Ten had acid fast bacilli (AFB) positive smear (four had positive culture also). Two patients who had negative smear were positive for culture suggesting active tubercular infection. None of the patients at the time of documentation of tubercular bacilli in sputum has had any chemotherapy or radiation therapy for their lung cancer. The clinical profile of these patients is being presented. Important issues relevant to chemotherapy and radiation therapy for such coexistence are discussed.

CLINICAL DETAILS

The clinical features of all the 12 patients are summarized in table – 1.

DISCUSSION

The prevalence of tuberculosis in India is about 60-80%. Majority of patients have subclinical infection and about 10% will develop clinically detected disease. This is in contrast to developed countries where prevalence rate is 2-3%. Pulmonary tuberculosis in India is one of the major public health problem. It has been estimated that nearly 15 million new cases are diagnosed each year in India out of which 90% have pulmonary tuberculosis. It causes 2 million deaths each year world over.[10]

Reactivation of latent tubercular infection in patients with lung cancer seems to be the cause of tuberculosis in such patients. Latent infection of tuberculosis may be activated by local and systemic effects of lung tumour or following chemotherpay and radiation therapy. Lung cancer is known for its various hormonal secretions and cortisol is one of them. Although reactivation is proposed as the likely explanation for occurrence of tuberculosis during the course of lung cancer or at its inception; a possibility of fresh pulmonary infection cannot be ruled out. As regarding the reason for reactivation no satisfactory explanation is available. It is possible that microorganisms may conceal their true antigen from immune system but years later, during suboptimal functioning of immune system reactivation may occur.[13]

Many reported coexistence of tuberculosis and lung cancer following radiation therapy and/

TABLE-1
SUMMARY OF CLINICAL PRESENTATION

S.N.	Age/ Sex	Symptoms	CXR	Bronchoscopy	Histology	Sputum AFB	Treatment	Course	Survival
1.	55-M	Chest Pain Fever	Rt LL Mass Rt. Hilar node	Normal	Adeno Ca	Smear+ve Culture NA	ATD Supportive	Progression	3 months Died
2.	58-M	Hemoptysis Fever Lt. Pleural Effusion	Lt. LL Collapse Lt. Hilar Mass	Growth. Lt Lower bronchus	SCLC	Smear-ve Culture+ve	ATD Cyclo Adriamycin VCR x 2	Progressive Disease	2 months Died
3.	45-M	Dysphagia	Lt. LL Mass SVC syndrome Pericardial Effusion	NA	SCC	Smear+ve Culture NA	RT to chest 20 Gy/5 fract, ATD	Progressive Disease	2 months Died
4.	50-M	Hemoptysis	Lt. Hilar Mass	NA	SCC	Smear+ve Culture NA	RT to chest 20 Gy/5	Partial Response	4 months Died
5.	63-M	Fever	Lt. MZ mass 7 x 6cm	Normal	Adeno Ca	Smear+ve Culture--ve	Cyclo 500mg x 3 RT	Partial Response	6 months Alive
6.	65-M	Chest Pain Fever	Rt. MZ mass Lt. Apical Fibrocavitary Lesion	External Compression Rt. LL bronchus	SCC	Smear+ve Culture+ve	Did not get treated	Progressive Disease	3 months Died
7.	50-M	Hemoptysis Fever	Lt. MZ cavity 6 x 6cm	NA	SCC	Smear+ve Culture+ve	RT to chest 20 Gy/5 Fract ATD	Partial Response	9 months Died
8.	62-M	Hemoptysis	Rt. MZ mass Hilar node	Extensive compression RL bronchus	SCLC	Smear+ve Culture--ve	ATD+Chemo + RT	CR	10 months Alive
9.	49-M	Dysphagi SVC syndrome	Growth Rt. Pl. effusion	Growth main bronchus	Adeno Ca	Smear--ve Culture+ve	ATD+RT	Progression	3 months Died
10.	57-M	Memoptysis	Lt. Hilar Mass	NA	SCC	Smear+ve	ATD+chest wall Died	PR	8 months
11.	64-M	Chest Pain	LL Mass	Normal	SCC	Smear+ve Culture+ve	ATD+Supportive	Progression	2 months Died
12.	40-F Fever 2	Chest Pain nodules	Bilat Multiple lung	NA	SCLC	Smear+ve Culture+ve	ATD+Chemo	Progression	3 months Died

Abbreviation :

M-Male, Rt-Right, Lt-Left, LL-Lower Lobe,-ve-Negative, +ve-Positive, NA-Not Available, ATD-Antitubercular Drugs, Cyclo-Cyclophosphamide, VCR-Vincristine, SVC-Superior Vena Cava Syndrome, SCLC-Small Cell Lung Cancer, SCC-Squamous Cell Carcinoma, RT-Radiation Therapy, Fract-Fraction.

or chemotherapy. Negata et al[9] analyzed the pattern of infections in 304 patients who died of lung cancer. In 9 patients lung cancer was complicated with Mycobacterial infection. In retrospect fever, new infiltrates on CXR and pleural effusion were thought to be due to tuberculosis. Four of these 9 patients had evidence of pre-existent tuberculosis in the form of old scarring suggesting reactivation of tuberculosis. Zventina et al described 4 patients of Mycobacterial Kansasii infection complicating lung cancer following chemotherapy or radiation therapy. [11] They reported that structural changes induced by either the chemotherapy or radiation therapy predisposes the patient to reactivation of latent Mycobacterium Kansasii infection. Tamura et al reported series of 25 patients of lung cancer having pulmonary tuberculosis, 14 of which had concurrent tuberculosis.[14]

The overall clinical presentation of active pulmonary tuberculosis with lung cancer is dominated by manifestations of lung cancer. The radiological finding characteristic of either disease is not specific enough to differentiate between the two processes. Because aggressive tumour behavior of lung cancer leads to early death in many of these patients, tuberculosis may be overlooked. In some of these patients tubercular process is recognized as terminal flaring up of chest infection.[9]

The exact incidence of tuberculosis in lung cancer is difficult to assess clinically because of many reasons; sputum acid fast bacilli positivity is between 31-82% in pulmonary tuberculosis, radiologically it is also difficult to diagnose tuberculosis once patient presents with lung cancer, and tuberculin test using PPD is not very useful in this group of patients due to their old age and immunosuppression.[15,16]

In the present series of the 12 positive patients 6 had fever, 4 had hemoptysis, and 2 had SVC syndrome and dysphagia. Radiologically 7 of our patients had evidence of old scarring on X-ray with or without calcification. CAT scan in a patient revealed areas of breakdown and cavitating lesion within the mass lesion. This patient had squamous cell histology which is known to cavitate.[17] All these patients were started on anti tubercular drugs. In 4 patients AFB negative sputum smear was documented after 2 months of anti tubercular therapy. Eight patients died of progressive lung cancer within 3 months of diagnosis; their sputum smear status could not be restudied. Among the cases whose sputum was negative for AFB survival was between 6 - 10 months. The overall clinical manifestation, radiological manifestations and prognosis in these patients were dominated by lung cancer. Impact of chemotherapy and radiation therapy could be monitored in only 4 patients, in whom gross residual disease persisted and tubercular lesion could not be recognized separately.

Of the 12 patients discussed here, acid fast-smear was positive in 10 patients and 2 patients had negative smear but positive culture. All were typical M *tuberculi* infection. Unlike central America where M *Kansasii* infection is endemic. In India M *tuberculi* is the most likely pathogen.

A considerable delay in the diagnosis of lung cancer is likely when sputum smear shows Mycobacteria. Failure of anti tubercular drugs to resolve the lesion radiologically leads to further investigations in these subset of patients. In 4 of these patients diagnosis of lung cancer was considered only after failure of 2-3 months of anti tubercular drugs.

With chemotherapy now having an impact on survival of small cell carcinoma and non small cell lung cancers; in those cases where tuberculosis and lung cancer coexist, we are likely to see tubercular residual lesions mimicking residual lung tumour. [18] The assumption that this lesion is a metastatic or recurrent neoplasm should not be made unless other diseases including tuberculosis are ruled out before institution/ continuation of anticancer chemotherapy.

The impact of radiation therapy to such lesions where tubercular bacteria and lung cancer coexist is interesting. Radiation therapy probably is not lethal to Mycobacteria. On the contrary, the resultant necrosis and local effects of tumour

provide a fertile culture medium for growth of these organisms.[11]

Up to 50% of Mycobacteriosis in lung cancer could be due to atypical Mycobacteria.[3,8] Differentiation of Mycobacterial tuberculosis from atypical Mycobacterial infection is of crucial importance as atypical Mycobacteriosis is known to be resistant to anti tubercular drugs and may require alternate therapy and /or surgery.[6]

Pattern and course of coexistence of pulmonary tuberculosis and lung cancer in India may be variable and is presented in table-II.

tubercular lesion which can be effectively treated. The true incidence may be still higher and newer techniques PCR based and others may help in knowing true incidence of co existence of lung cancer and pulmonary tuberculosis.

Present report suggest that mycobacterium tuberculosis may coexist with lung cancer at its beginning more frequently than described. Infections are one of the leading cause of death in patients with neoplastic diseases and mycobaterial infection is one of them. We feel sputum smear evaluation for AFB at diagnosis and at frequent intervals during the course of lung cancer at least in endemic zones should be done.

TABLE-II

CLINICAL COURSE OF COEXISTING TUBERCULOSIS AND LUNG CANCER:

1. Rapidly progressive lung cancer; Tuberculosis masked by lung cancer and remain unrecognized.
2. High prevalence of tuberculosis in India and positive acid fast sputum smear may delay the diagnosis of lung cancer.
3. Tuberculosis unrecognized; during therapy with chemotherapy and /or radiation therapy patient develops fever, pleural effusion or cavitary lesion.[8,9] Of note; up to 2-16% of squamous cell carcinoma cavitate without associated infection.[16]
4. Tuberculosis manifesting radiologically as residual lesion mimicking residual tumour in patients with chemotherapy and radiation therpay. Sputum or bronchoalveolar lavage may demonstrate acid fast bacilli.
5. Disssemination of mycobacteriosis causing miliary tuberculosis in an already immunocompromised individual. Such dissemination may follow chemotherapy and radiation therapy.

The true incidence of co existence of these two may be higher and better laboratory techniques particularly PCR based should be helpful in detecting true incidence.

CONCLUSION

The present study highlights the co existence of pulmonary tuberculosis and lung cancer. Study also stress upon that there should be a high index of suspicion in detecting tuberculosis in lung cancer patients. The detection of this is all the more important in a country like ours where prevalence and incidence of tuberculosis is high. A new or persistent lesion on chest x ray may be wrongly diagnosed as disease progression indicating treatment failure whereas, in fact this may be a

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