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KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Lung cancer diagnosed with *Mycobacterium tuberculosis* or nontuberculosis mycobacteria concomitantly

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SUMMARY

Lung cancer diagnosed with *Mycobacterium tuberculosis* or nontuberculosis mycobacteria concomitantly

Introduction: *The concomitant occurrence of disease of Mycobacterium tuberculosis or nontuberculosis mycobacteria (NTM) and lung cancer has been reported in previous studies. We aimed to determine characteristics of the patients with lung cancer diagnosed with M. tuberculosis or NTM concomitantly.*

Materials and Methods: *From 2010 to 2015, the patients diagnosed with lung cancer and M. tuberculosis or NTM concomitantly were enrolled in the study. Patient data were collected retrospectively.*

Results: *Concomitant M. tuberculosis or NTM and lung cancer were diagnosed in 17 cases (1.2% of total lung cancer cases, 0.9% of total tuberculosis cases). M. tuberculosis was isolated from 11 (64.8%) patients and NTM disease was from 6 (35.2%) patients. Squamous cell carcinoma was the most common histological type. Tumoral stage was often advanced as stage III- IV (76.5%). Bronchial lavage smear positivity foracid-fast bacilli was found only in 4 (23.5%) patients. Tuberculosis treatment therapy was started only in 4 (23.5%) patients who had bronchial lavage smear positivity for acid-fast bacilli. So tuberculosis treatment was delayed for other 13 (76.5%) patients with bronchial lavage smear negative for acid-fast bacilli. Seven out of 17 (41.1%) patients died.*

Conclusion: *Physicians should consider concomitant M. tuberculosis or NTM when managing lung cancer. Tuberculosis patients may be mis diagnosed as lung cancer or vice versa.*

Key words: *Lung cancer, Mycobacterium tuberculosis, nontuberculosis mycobacteria*

ÖZET

Akciğer kanseri ile eş zamanlı teşhis edilen *Mycobacterium tuberculosis* veya nontüberküloz mikobakteri infeksiyonları

Giriş: *Akciğer kanseri ile Mycobacterium tuberculosis veya nontüberküloz mikobakteri (NTM) eş zamanlı birlikteliği daha önceki çalışmalarda gösterilmiştir. Bu çalışmada akciğer kanseri ile M. tuberculosis veya NTM eş zamanlı birlikteliği görülen hastaların karakteristik özelliklerinin saptanması amaçlandı.*

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Materyal ve Metod: *2010-2015 yılları arasında akciğer kanseri ile M. tuberculosis veya NTM eşzamanlı birlikteliği görülen hastalar çalışmaya dahil edildi. Hasta bilgileri retrospektif olarak toplandı.*

Bulgular: *Akciğer kanseri ile M. tuberculosis veya NTM eş zamanlı birlikteliği 17 olguda (tüm akciğer kanseri olgularının %1.2'si, tüm tüberküloz hastalarının %0.9'u) saptandı. M. tuberculosis 11 (%64.8) hastada ve NTM 6 (%35.2) hastada izole edildi. Skuamöz hücreli akciğer kanseri en sık görülen histolojik tipti. Tümörler en sık ileri evrede idi (Evre III-IV, %76.5). Bronşiyal lavaj (BL) aside dirençli bakteri (ARB) sadece 4 (%23.5) hastada tespit edildi. Tüberküloz tedavisi sadece bu ARB (+) olan 4 (%23.5) hastaya başlandı. Böylece BL ARB (-) olan 13 (%76.5) hastaya TB tedavisi başlanmadı. On yedi hastanın 7 (%41.1)'si öldü.*

Sonuç: *Doktorlar akciğer kanseri hastalarını değerlendirirken M. tuberculosis veya NTM birlikteliğini akıllarında tutmalıdır. Tüberküloz hastaları yanlışlıkla akciğer kanseri tanısı alabilir veya tam tersi de olabilir.*

Anahtar kelimeler: *Akciğer kanseri, Mycobacterium tuberculosis, nontüberküloz mikobakteri.*

INTRODUCTION

Lung cancer (LC) is the most deadly type of cancer. *Mycobacterium tuberculosis* is also important cause of morbidity and mortality, especially in developing countries (1). The concomitant occurrence of diseases of pulmonary tuberculosis (TB) and LC has been reported in previous studies (2-8). Some scientists suggested that TB leads to development of cancer; others state that TB and cancer are antagonists. Also relationship between LC and nontuberculosis mycobacteria (NTM) disease was found in previous studies (9,10).

It has been suggested that inflammation and pulmonary fibrosis caused by TB can induce genetic damage, which can increase LC risk (11-13). Infection-induced immunosuppression can be cause of LC in patients with TB (14). Also, cancer-induced or chemotherapy-induced immunosuppression can be reasons of TB reactivation in patients with solid tumors (15). In the present study, we aimed to determine characteristics of the patients with LC diagnosed with *M. tuberculosis* or NTM concomitantly and radiological characteristics and bronchoscopic locations of LC, the types and stages of LC and to calculate mortality rate in one-year.

MATERIALS and METHODS

The study involved patients diagnosed with *M. tuberculosis* or NTM and LC concomitantly between 2010-2015. This was a retrospective study involving 1325 patients with a confirmed diagnosis of LC by cytological and histopathological evaluation of bronchial lavage (BL) specimens or endobronchial biopsy specimens.

The diagnosis of pulmonary TB was based on consensus criteria (16): positive Ziehl-Neelsen staining for AFB and/or a single positive culture for *M. tuberculosis*. NTM disease was diagnosed by finding NTM bacteria in BL.

The diagnoses of LC and *M. tuberculosis* or NTM were classified as simultaneous when the diagnoses of *M. tuberculosis* or NTM and LC occurred concomitanly or when the time between the two diagnoses was < 2 months.

The patients' characteristics, radiological, bronchoscopic and microbiological features were recorded retrospectively.

Tumor staging has been made according to the seventh edition of the "TNM classification of (IASLC) malignant tumours" (17).

Mortality rate in one-year was calculated.

RESULTS

During the study period (2010-2015) a total of 1325 patients have been diagnosed with LC and 1776 patients with TB at our hospital.

Concomitant *M. tuberculosis* or NTM and LC were diagnosed in 17 cases (1.2% of total LC cases, 0.9% of total TB cases). *M. tuberculosis* was isolated from 11 (64.8%) and NTM disease was from 6 (35.2%) patients. NTM species could not be identified because of technical problem at that time. All of the patients were men. Patients age were ranging between 49 and 85. The mean age was 69.

Radiological view of 15 patients could be reached. Radiologic findings revealed mass lesion (10 cases, 66.7%), consolidation (7 cases, 46.7%), acinar infiltration (7 cases, 46.7%), nodular infiltration (7 cases, 46.7%), pleural effusions (7 cases, 46.7%), atelectasia (4 cases, 26.7%), fibrotic infiltrates (4 cases, 26.7%), ground glass appearance (3 cases, 20%), lymphadenopathy (3 cases, 20%), cavitary infiltration (3 cases, 20%), pericardial effusion (1 case, 6.6%) (Figure 1). Lesions were mostly unilateral and in the right lung (10 cases, 66.7%). Multilobar involvement were found in 8 cases (53.3%).

If a subtype of non-small cell carcinoma case could not be determined it was called non-small cell carcinoma others. Squamous cell carcinoma was the most common histological type diagnosed with TB concomitantly (41.2%) (Table 1). Small cell carcinoma was diagnosed in 5 (29.4%) patients.

Tumoral stage was of ten advanced as stage III-IV (53%) for non-small cell carcinoma, extensive disease IV (23.5%) for small cell carcinoma (Table 2). So, 76.5% of all LC were advanced. Four out of 6 NTM patients were in stage III-IV (66.6%), 9 out of 11 TB patients were in stage III-IV (81.8%) (Table 3).

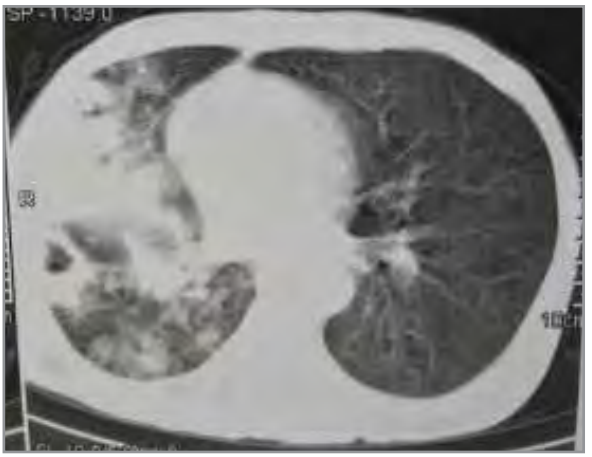

Figure 1. Cavitary infiltration and consolidation in the right lung.

Table 1. Frequency of lung cancer types

Type of lung cancer	Frequency (%)
Squamous cell carcinoma	7 (41.2)
Small cell carcinoma	5 (29.4)
Non-small cell carcinoma (others)	3 (17.6)
Adenocarcinoma	2 (11.8)
Total	17 (100)

Table 2. Tumoral stage distribution

	Frequency (%)
Non-small cell carcinoma	
Ia	1 (5.9)
Ib	1 (5.9)
IIb	1 (5.9)
IIIb	2 (11.8)
IV	7 (41.2)
Small cell carcinoma	
Limited disease	1 (5.9)
Extensive disease IV	4 (23.5)

BL smear positivity for AFB was found only in 4 (23.5%) patients. BL smear was negative for AFB in 13 (76.5%) patients. BL culture for TB was positive in all the patients.

Anatomically, the bronchoscopic findings were located primarily in the right main bronchus in 5 (29.4%) patients, and the right upper lobe bronchus in 4 (23.5%) patients (Table 4).

Seven out of 17 (41.1%) patients died in one year. Two out of 6 NTM patients (33.3%) and 5 out of 11 TB patients (45.4%) died in one year.

Both *M. tuberculosis* and NTM was diagnosed mostly with squamous cell carcinoma concomitantly (Table 5). Four out of 5 patients with small cell carcinoma (80%) was diagnosed concomitant with *M. tuberculosis*, only 1 of them (20%) was with NTM. None of the patients with adenocarcinoma was found with NTM concomitantly.

Table 3. Distribution of *Mycobacterium tuberculosis* and NTM patients according to tumoral stage

	Mycobacterium tuberculosis	NTM
Non-small cell carcinoma		
Ia	1	-
Ib	1	-
IIb	-	1
IIIb	1	1
IV	4	3
Small cell carcinoma		
Limited disease	-	1
Extensive disease IV	4	-
Total	11	6

NTM: Nontuberculosis mycobacteria.

Table 4. Anatomical location of tumors

	Frequency (%)
Right main bronchus	5 (29.4)
Right upper lobe bronchus	4 (23.5)
Right lower lobe bronchus	2 (11.8)
Trachea	2 (11.8)
Left upper lobe bronchus	2 (11.8)
Left main bronchus	1 (5.9)
Left lower lobe bronchus	1 (5.9)
Total	17 (100)

Table 5. Distribution of NTM and *Mycobacterium tuberculosis* patients according to lung cancer subtypes

	Squamous cell carcinoma	Adenocarcinoma	Non-small cell carcinoma (others)	Small cell carcinoma
Mycobacterium tuberculosis	4	2	1	4
NTM	3	-	2	1
Total	7	2	3	5

NTM: Nontuberculosis mycobacteria.

DISCUSSION

In present study, concomitant *M. tuberculosis* or NTM and LC were diagnosed in 1.2% of total LC cases, and in 0.9% of total TB cases. We consider that these ratioswould be higher, if physicians had thought about the possibility of concomitant *M. tuberculosis* or NTM when managing LC. Because then they would investigate BL in all patients to prove TB. These findings similar to the literature that the frequency of LC accompanying pulmonary TB is around 1% and that of active pulmonary TB accompanying LC is closeto 4% (18). Watanabe et al. published analysis of 758 of LC and coexistence of cancer and TB was found in 2.1% of cases (19,20). The frequency of concomitant development of LC is 25-fold in patients with pulmonary TB compared to the expected incidence of LC in healthy individuals, which appears to indicate a higher morbidity rate of LC in patients affected by pulmonary TB (18). Some research showed that scars, which remain after healing of tuberculoses' lesion, could cause development of LC (21). Although it was previously believed that patients with pulmonary TB are less likely to be affected by LC, the reverse may be true (18).

In this study, most commonly seen radiologic findings were mass lesion (66.7%), consolidation (46.7%), acinar infiltration (46.7%), nodular infiltration (46.7%), pleural effusions (46.7%), respectively. Lesions were mostly unilateral and in the right lung (66.7%) and also multilobar (53.3%). Bronchoscopic findings were located primarily in the right bronchial system (64.7%).

Squamous cell carcinoma was the most common histological subtype in our study (41.2%) that was similar to the studies of Morales-Cardia et al. Varol Y et al (22,23). But, adenocarcinoma was the most common subtype in other series (20,24).

Both *M. tuberculosis* and NTM was diagnosed mostly with squamous cell carcinoma concomitantly. Most of the patients with small cell carcinoma (80%) was diagnosed concomitant with *M. tuberculosis*. None of the patients with adenocarcinoma was found with NTM concomitantly.

In this study, LC stage was advanced (76.5%). Similar results were reported in previous studies (22,23,25,26).

In our study, NTM was isolated from 35.2% of the 17 patients and *M. tuberculosis* was from 64.8% of them. NTM patients were in advanced stage (66.6%) that was similar to the study of Tamura et al. (9). Relationship between LC and NTM was found in previous studies (9,10). Tuberculosis patients were also in advanced stage (81.8%). So LC in the TB group were in far-advanced.

In present study, 41.1% of patients died in one year. 33.3% of NTM patients and 45.4% of TB patients died in one year. The difference in mortality rates between TB and NTM patients might be due to presence of more advanced LC in TB group than NTM group. Leung et al. have suggested that TB is independently associated with subsequent mortality due to LC (27). Patients with LC diagnosed with TB had worse prognosis than those with LC without TB (28).

TB treatment was started only in 4 (23.5%) patients at the beginning who had BL smear positivity for AFB. The other 13 patients with BL smear negative for AFB were referred to onchology department without TB treatment. So TB treatment was delayed for these patients. These findings are reverse to that of Agrawal who suggested that large numbers of the bronchogenic carcinoma patients were mis diagnosed as a case of TB, this leads to significant delay in diagnosis and progression of cancer and results in poor outcome and lower survival (29). But according to present study, TB patients were also mis diagnosed as only LC and that contributed diagnostic and treatment delay in TB. So once LC has been diagnosed, possible presence of concomitant TB should be kept in mind.

Our study has certain limitations. Primarily, due to the retrospective nature of the study, we relied on electronic medical records as our source of patient data.

CONCLUSION

Physicians should consider concomitant *M. tuberculosis* or NTM when managing lung cancer. TB patients may be mis diagnosed as LC or vice versa.

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