Original Article

Lung Cancer In Former Tuberculosis Patients at Arifin Achmad General Hospital, Riau Province

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Abstract

Background: There is ongoing discussion over the connection between lung cancer and pulmonary tuberculosis (TB). Future lung cancer cases in Indonesia, which has the second-highest TB case burden, are a cause for concern. The purpose of this study is to ascertain the connection between TB and LC at Arifin Achmad General Hospital in the province of Riau.

Method: From 2015 to 2018, we looked back on lung cancer patients at Arifin Achmad General Hospital in Riau Province who had received pulmonary tuberculosis and anti-tuberculosis treatment (ATT).

Results: From 203 patients, 24 patients (11.8%) had histories of TB. The patients' ages were from 41 years to 60 years. The most prevalent pathological findings were adenocarcinoma in 13 patients (54.0%). The most common cancer stage was advanced stage IIIB in 7 patients (29.2%).

Conclusion: The cases of TB infections were apparent in lung cancer patients, approximately around 11% of lung cancer cases. Therefore, it is necessary to assess the history of TB in lung cancer patients.

Keywords: anti-tuberculosis treatment, lung cancer, pulmonary tuberculosis

INTRODUCTION

Indonesia is the 2nd country with the highest burden of tuberculosis (TB) all around the world.[1] From 2020 to 2021, there an 18% increase in the incidence of TB, from 819 000 to 969 000. [1,2] By increased case of TB there is also a problem that estimated also increased case of lung cancer (LC).[3,4] This is due to the fact that several studies have shown an increase in the risk of LC among former TB patients. Polymorphic microbiomes may cause tumor-promoting inflammation and contribute to cancer, according to a new cancer signature discovered in 2022.[5]

Due to a paucity of evidence, the risk of TB to LC in Indonesia is currently debatable. In 2022, there are 13.007 new cases of TB in Riau based on Riau

Goverment data. This large number of cases is certainly a concern because the risk of LC after TB infection is linked to this data, so there is the potential for lung cancer cases in Riau to increase due to TB infection.

This study aims to outline the patient TB with a higher risk of LC in patients seen at the Arifin Achmad General Hospital as referral goverment hospital in Riau Province for LC in the Riau Province.

METHOD

A cross-sectional research methodology was used in this retrospective study. From 2015 to 2018, we gathered information from the medical records kept at Arifin Achmad General Hospital. This study population were all patients with lung cancer at Arifin Achmad General Hospital.

The following conditions had to be met for a patient to be included in the study: (1) TB history; (2) anti-TB treatment received prior to lung cancer diagnosis; (3) LC diagnosis based on anatomical pathology findings; and (4) positive and negative Ziehl-Neelsen staining for acid-fast bacillus in sputum smear. Patients who matched two out of four criteria were included in the study. There is a chance that LC was mistakenly diagnosed as TB, so in order to rule this out, we check the patient diagnoses using histological examination of the relevant medical records.

The following patients are excluded from this study: (1) those who have TB and LC co-infections and (2) extra pulmonary TB. The research received ethical clearance from Ethical Review Board for Faculty of Medicine, Riau University No. B/214a/UN19.5.1.1.8/UEPKK/2019.

RESULTS

Table 1 demonstrate characteristics of patients that included in this study. Male are dominant in this study by 91% compared to female (9%). The patients were dominated by elderly patients, 40–60 years old in 79.16% and >60 years old in 16.67%.

Table 1. Patients Characteristics (n=24)

Characteristics	n (%)
Sex	
Male	22 (91.00%)
Female	2 (9.00%)
Age (years old)	
<40	1 (4.17%)
40–60	19 (79.16%)
>60	4 (16.67%)
Sputum Smear	
Positive	12 (50.00%)
Negative	12 (50.00%)
Anti Tuberculosis Drug	
Category 1	13 (54.17%)
Category 2	11 (45.83%)
Type of LC	
Adenocarcinoma	13 (54.00%)
SCC	9 (37.50%)
SCLC	2 (8.33%)
Stage of LC	
I	1 (4.17%)
III a	5 (20.83%)
III b	9 (37.50%)
IV a	2 (8.33%)
IV b	7 (29.17%)
Time of diagnosis with TB before LC	
<5 years	20 (83.33)
5–10 years	3 (12.5)
>10 years	1 (4.17)

Note: SCC=Squamous Cell Carcinoma; SCLC=Small Cell Lung Carcinoma

Both AFB Sputum smear are equal positive (microbiologically TB) and negative (clinically TB). Most patients receive Category 1 of Anti Tuberculosis Drug (ATD) by 54.17% followed by Category 2 by 45.83%. For the pathological type of lung cancer, it was dominated by dominated by adenocarcinoma (54%), SCC (37.5%) and SCLC (8.33%).

For the stage of LC dominated by Stage IIB (37.5%) followed by IVb (29.17%), IIIa (20.83%), IVa (8.33%), and I (4.17%). Most of the LC patients had history of TB less than 5 years (83.33%), followed by 5 – 10 years after TB infection (12.5%) and more than 10 years (4.17%).

DISCUSSION

Studies looked into TB as an LC risk factor associated with aging. Younger individuals had a greater incidence of LC and TB. The Indonesian Society of Respirology (ISR) states that male patients who are over 40, have smoked in the past, are exposed to industrial hazard compounds, and have symptoms are at high risk for lung cancer (LC).[6] However, younger individuals were shown to have a higher likelihood of coexisting TB and LC.[7]

Regardless of smoking history or other factors, a meta-analysis revealed that TB at a younger age is a risk factor for developing LC. Additionally, the risk was higher in nations with high TB prevalence, upper-middle class economies, especially in the East Asian and Pacific region.[3] Due to common radiologic findings and symptoms such coughing, expectoration, fever, hemoptysis, and weight loss, TB and LC may be misdiagnosed.[8,9]

In this study, the incidence of cancer after TB infection was higher in the productive age group of 40-60 years (79%) and males (96.67%). So that this evidence supports the ISR statement that age >40 years, especially those with exposure are at risk of lung cancer, in this study also supports that patients with a history of TB also need more attention because it has the potential to increase the risk of lung cancer in the future. Therefore, it is expected that a history of TB needs to be a concern and become the basis for lung cancer screening.

Compared to other studies in Surabaya, similar incidences were dominated by men with an age range between 40-60 years. The type of lung cancer was also similarly dominated by adenocarcinoma at 90.8% in the Surabaya study and 54% in this study. For the staging itself, the study in Surabaya was dominated by NSCLC stage IV at 77.6% and in this study, it was dominated by stage IIb at 37.5%.[10]

In this study, only 1 person was found to have a long history of TB of more than 10 years, and other case reports have also found cases of post-TB squamous cell carcinoma after 30 years of treatment. This opens up the possibility that the effects of TB infection, which can lead to lung cancer, can also last for a long period of time.[11]

In our study, we found that duration <5 years post-TB dominated the incidence. In a meta-analysis, the incidence of lung cancer increased after 2 years of TB

diagnosis (HR=5.01; 95% CI=3.64-6.89) but decreased thereafter. However, this does not rule out the possibility that after >2 years we still find the incidence of lung cancer after infection from TB.[12]

Cancer formation is complex; however, it has been demonstrated that persistent inflammation can promote the growth and spread of tumors.[13] Tuberculosis induced chronic inflammation may lead to genetic changes in lung parenchyma cells. Through infected macrophages, TB can cause cell dysplasia and squamous cell aggregation. This held true for latent TB as well, which causes persistent inflammation and infection, increasing the risk of LC. [10,11]

Mycobacterium tuberculosis causes inflammation in the lung tissues by elevating inflammatory cytokines such INF-y, IL-1, IL-2, IL-12, and TNF.12,13 Patients with latent TB had an increased chance of developing LC (HR=2.69; P=0.17). No one who had isoniazid prophylaxis among 135 TB contacts got cancer. Because of this, reducing chronic inflammation requires treating TB, especially latent TB.[4]

Tuberculosis may raise the risk of cancer since it also has an immunosuppressive effect in the body through naturally existing regulatory T cells. By exposing cells to reactive oxygen and reactive nitrogen intermediates when it enters macrophages, TB may potentially cause cellular DNA damage. DNA damage, cytokinesis defects, and an increased frequency of apoptotic and necrotic cells were all seen in TB patients. Repeated tissue injury results in the creation of fibrotic scar tissue, which can induce fibrosis and increase the risk for tumor growth.[14–17] Tuberculosis induces a cytokine storm and lung epithelial cell proliferation through the production of cytokines by macrophages, dendritic cells, and alveolar type II pneumocytes.[18–20]

Potentially, bacterial toxin or other compounds produced by the mutagenesis of epithelium, which might disrupt the mechanisms that preserve genomic integrity or damage DNA, or stress cells in other ways that indirectly reduce the fidelity of DNA replication, could cause tumors.[5]

The limitation in this study was only conducted in one hospital. Arifin Achmad General Hospital is a referral health facility in Riau province. Interpretation data in this study needs further evaluation and examination to be implemented in minor policies.

CONCLUSION

This descriptive study showed LC for former TB patients in Arifin Achmad General Hospital dominated by male, age between 40–60 years old, received 1st category of ATD, adenocarcinoma, stage IIIb of LC, and had history of TB less than 5 years.

Suggestion for next study is multi-center study to analyze risk of LC in former TB patients in Indonesia, due to Indonesia is 2nd highest burden TB case in the world. We need to determine so macro-policy could implement to help post TB infection to have screening for risk of LC.

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