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Histopathological profile and radiological features of lung cancer with and without a history of pulmonary tuberculosis at dr. Zainoel Abidin Hospital, Banda Aceh

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ABSTRACT

Introduction: Lung cancer is one of the types of malignancies that is the leading cause of cancer deaths worldwide. In Indonesia, the incidence of lung cancer is quite high, with pulmonary TB as a risk factor that can increase the risk of lung cancer in the future. This study aims to describe the histopathological profile and radiological picture of lung cancer patients in patients with and without a history of pulmonary TB at dr. Zainoel Abidin Hospital Banda Aceh.
Methods: This study uses retrospective methods and univariate analysis. The subjects of this study are lung cancer patients at dr. Zainoel Abidin Hospital from January 2022 to December 2023.
Result: The results of this study showed that of the 184 patients, 6.5% of them had lung cancer with a history of pulmonary TB, while the other 93.5% had lung cancer without a history of pulmonary TB. Of the two groups of lung cancer, the majority of patients were aged 51-60 years (32.6%), male (83.7%), still working (81%), from Aceh (99.5%), and Muslim (99.5%). Most lung cancer patients were diagnosed at stage IV (86.4%), with Squamous Cell Carcinoma being the most common type of histopathology (57.1%). In lung cancer patients with a history of pulmonary TB, post-TB lesions are often found, such as fibrosis (83.3%), calcification (50%), cavitation (33.3%), pleural thickening (16.7%), and atelectasis (8.3%).
Conclusion: Efforts to prevent lung cancer, especially in patients with a history of pulmonary TB, need to be continued so that the risk of developing lung cancer can be reduced.

Keywords: Lung cancer, pulmonary tuberculosis, histopathological profile, radiological features.
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INTRODUCTION

Lung cancer is a form of lung malignancy caused by genetic changes in the epithelial cells of the respiratory tract, causing uncontrolled growth of abnormal cells. Based on data from the World Health Organization (WHO), in 2020 lung cancer was the leading cause of death from cancer, reaching 1.8 million deaths. Indonesia is the 4th country with the highest number of lung cancer cases in the world.[1] According to the Global Burden of Cancer (GLOBOCAN) in 2018, lung cancer is the most common malignancy in Indonesia.[2]

Indonesia is the country with the 2nd highest number of TB cases globally after India, and is included in the High Burden Countries category (HBC) for cases of pulmonary TB.[3] Data from the Aceh Health Profile in 2022 showed an increase, namely with an incidence rate of 10,896 cases compared to 2021 of 7,170 TB cases in Aceh Province.[4] Pulmonary TB is one of the risk factors for the development of lung cancer. Post-TB scars can damage blood vessels and lymphatics, leading to lymphostasis and carcinogenesis, which may trigger the malignancy process.[5] A cohort study showed that the incidence of lung cancer was higher in patients with a history of pulmonary TB than in patients who did not have a history of pulmonary TB, namely 269 compared to 153 cases per 100,000 people per year. Chronic inflammation caused by *Mycobacterium tuberculosis* infection can trigger lung cancer.[6] The risk of lung cancer increases among patients with a history of pulmonary TB, particularly in young pulmonary TB patients from countries with a high burden of TB.[7]

Research on the relationship between TB and lung cancer has been widely conducted in various countries; however, no similar studies have been carried out in Aceh. The high incidence of TB and lung cancer indicates a serious health problem in Aceh. Therefore, it is important to know whether the high incidence of TB is related to the increased incidence of lung cancer in Aceh, as well as to identify the most common histopathological types.

METHODS

This research is a descriptive study with a retrospective approach, based on secondary data derived from patient medical records. This study was conducted at the Medical Records Installation of dr. Zainoel Abidin General Hospital (RSUDZA) Banda Aceh.

The study was conducted from July to September 2024. The population in this study comprised all lung cancer patients hospitalized at RSUDZA Banda Aceh from January 2022 to December 2023. The sample included patients from this population who met the inclusion and exclusion criteria. The inclusion criteria of this study were lung cancer patients aged ≥ 18 years, both with and without a previous history of pulmonary TB. The exclusion criteria in this study were lung cancer patients currently undergoing treatment for pulmonary TB (coexisting of pulmonary TB) and lung cancer patients with incomplete medical records, specifically those lacking radiology and histopathology data. This study employed a nonprobability sampling technique using the total sampling method, in which all eligible patients during the study period were included. The sample size comprised 184 lung cancer patients, both with and without a history of pulmonary TB, who were hospitalized at RSUDZA Banda Aceh from January 2022 to December 2023.

RESULTS

Table 1 showed the distribution of lung cancer patients based on a history of pulmonary tuberculosis (TB). Out of a total of 184 patients, 12 patients (6.5%) have a history of pulmonary TB, while 172 patients (93.5%) do not have a history of pulmonary TB.

Based in table 2, the results showed that of the 184 patients who were the study samples, most lung cancer patients were in the 51-60 age group, with 41.7% having a history of pulmonary TB and 32% without a history of pulmonary TB. The majority of patients were male, with 83.3% of those with a history of pulmonary TB and 83.7% of those without a history of pulmonary TB. Most of the patients were employed, with 83.3% of patients with a history of pulmonary TB and 80.8% of those without a history of pulmonary TB working. In terms of region, nearly all patients were from Aceh (99.5%). Regarding religion, the majority of patients were Muslim (99.5%), with one patient identified as Christian.

Most lung cancer patients were in stage IV (86.4 %), both with a history of pulmonary TB (58.3%) and without a history of pulmonary TB (88.4%), indicating that most patients were diagnosed at an advanced stage. In terms of histopathology, Squamous Cell Carcinoma was the most common, which was 50% in patients with a history of pulmonary TB and 57.4% in patients without a history of pulmonary TB. Meanwhile, Adenocarcinoma was also often found, which was 41.7% in patients with a history of pulmonary TB and 38.4% in patients without a history of pulmonary TB. The least histopathological type was Large Cell Carcinoma which was found in 1 patient. Overall, these data indicate that the majority of lung cancer patients are in an advanced stage with the majority of histopathological types being Squamous Cell Carcinoma and Adenocarcinoma.

Based on radiological images, all patients, both with and without a history of pulmonary TB, had lung masses (100%). Pulmonary consolidation was found in 88.3 % of patients with a history

Table 1. Prevalence of lung cancer with and without a history of pulmonary tuberculosis

Lung Cancer	%	%
With History TB	12	6.5
Without History TB	172	93.5
Total	**184**	**100**

Table 2. Sociodemographic characteristics of lung cancer patients

Variables	Lung Cancer				Total	%
	With History TB	%	Without History TB	%		
Age						
18-30	0	0	5	2.9	5	2.7
31-40	1	8.3	15	8.7	16	8.7
41-50	0	0	32	18.6	32	17.4
51-60	5	41.7	55	32	60	32.6
61-70	4	33.3	48	27.9	52	28.3
≥ 71	2	16.7	17	9.9	19	10.3
Gender						
Man	10	83.3	144	83.7	154	83.7
Woman	2	16.7	28	16.3	30	16.3
Occupation						
Work	10	83.3	139	80.8	149	81
Not Working	2	16.7	33	19.2	35	19
Region						
Aceh	12	100	171	99.4	183	99.5
Non-Aceh	0	0	1	0.6	1	0.5
Religion						
Islam	12	100	171	99.4	183	99.5
Christian	0	0	1	0.6	1	0.5
Buddha	0	0	0	0	0	0

Table 3. Clinical characteristics of lung cancer patients

Variables	Lung Cancer				Total	%
	With History TB	%	Without History TB	%		
Staging						
NSCLC						
I	0	0	1	0.6	1	0.5
II	0	0	0	0	0	0
III	4	33.3	13	7.6	17	9.2
IV	7	58.3	152	88.4	159	86.4
SCLC						
Limited	0	0	0	0	0	0
Extensive	1	8.3	6	3.5	7	3.8
Histopathology						
Adenocarcinoma	5	41.7	66	38.4	71	38.6
Squamous Cell Carcinoma	6	50	99	57.4	105	57.1
Large Cell Carcinoma	0	0	1	0.6	1	0.5
Small Cell Carcinoma	1	8.3	6	3.5	7	3.8
Radiology						
Mass						
Yes	12	100	172	100	184	100
No	0	0	0	0	0	0
Consolidation						
Yes	10	83.3	59	34.3	69	37.5
No	2	16.7	113	65.7	115	62.5
Multiple Nodule						
Yes	1	8.3	27	15.7	28	15.2
No	11	91.7	145	84.3	156	84.8
Infiltrat						
Yes	1	8.3	42	24.4	43	23.4
No	11	91.7	130	75.6	141	76.6
Fibrosis						
Yes	10	83.3	17	9.9	27	14.7
No	2	16.7	155	90.1	157	85.3
Calcification						
Yes	6	50	2	1.2	8	4.3
No	6	50	170	98.8	176	95.7
Cavity						
Yes	4	33.3	3	1.7	7	3.8
No	8	66.7	169	98.3	177	96.2
Pleural Thickening						
Yes	2	16.7	6	3.5	8	4.3
No	10	83.3	166	96.5	176	95.7
Atelectasis						
Yes	1	8.3	13	7.6	14	7.6
No	11	91.7	159	92.4	170	92.4

of pulmonary TB and 34.3% of patients without a history of pulmonary TB. As many as 8.3 % of patients with a history of pulmonary TB had multiple nodules, compared to 15.7% in patients without a history of pulmonary TB. Infiltrates were found in 8.3 % of patients with a history of pulmonary TB and 24.4% of patients without a history of pulmonary TB. Fibrosis was dominant in patients with a history of pulmonary TB (83.3 %), compared to patients without a history of pulmonary TB (9.9%). Calcification was seen in 50% of patients with a history of pulmonary TB and only 1.2 % in patients without a history of pulmonary TB. Cavities were found in 33.3 % of patients with a history of pulmonary TB and only 1.7% of patients without a history of pulmonary TB. Pleural thickening was found in 16.7 % of patients with a history of pulmonary TB and 3.5% in patients without a history of pulmonary TB. While atelectasis was found in 8.3 % of patients with a history of pulmonary TB and 7.6% in patients without a history of pulmonary TB.

DISCUSSION

The results of this study indicate that the occurrence of lung cancer with a history of previous TB was 12 people (6.5 %), while 93.5% of lung cancers did not start with pulmonary TB. The same results were obtained by the study by Nadira et al. in Surabaya which stated that the incidence of lung cancer with a history of pulmonary TB was 7.3 %.[8] The presence of lung cancer with a history of TB was also studied in Taiwan by Liao et al. and produced a prevalence of 2.79%.[9] Previous research indicates that scar-related lung cancer is a rare condition, accounting for only 7% of all lung cancer cases. A study conducted in South Africa reported that at least one in five lung cancer patients exhibited pulmonary scarring on radiological imaging, likely linked to the high prevalence of pulmonary tuberculosis (TB) in the region. The high burden of pulmonary TB contributes to the development of scar-related lung cancer and the increasing number of lung cancer cases overall. Patients with a history of pulmonary TB are twice as likely to develop lung cancer in the future.[10]

In this study, lung cancer with and without pulmonary TB was most commonly found in patients aged 51-60 years (32.6 %). This is in line with research conducted by Chairudin et al. which showed that the highest proportion of lung cancer sufferers was in the 51-60 year age group (35.5%).[11] According to the Indonesian Lung Doctors Association, male patients over 40 years of age who smoke and are often exposed to industrial pollution have a high risk of developing lung cancer.[12] A study by An et al. in Korea reported that younger patients with pulmonary TB have a higher risk of developing lung cancer compared to older patients. Specifically, the risk of lung cancer was found to be higher in individuals under 60 years of age than in those over 60.[13]

In this study, it was found that men were more dominant in lung cancer patients with and without a history of pulmonary TB (83.7 %). This is in line with WHO data which states that lung cancer cases occur more in men (17.1 per 100,000 population) than in women (5.5 per 100,000 population).[2] This may be due to higher levels of exposure to risk factors in men, such as exposure to air pollution due to work and outdoor activities, as well as smoking habits.[13] Cigarette smoke contains carcinogens that can cause damage to respiratory epithelial cells and stimulate tumorigenesis. Chronic cell damage can trigger abnormal cell growth, which ultimately increases the risk of lung cancer.[14] Based on occupation, region, and religion, it was found that the majority of lung cancer patients, both with and without a history of pulmonary TB were still employed (81%), came from Aceh (99.5%), and were Muslim (99.5%).

The study results showed that the majority of lung cancer patients, both with and without a history of pulmonary TB, were diagnosed with stage IV NSCLC. Specifically, 58.3% of lung cancer patients with a history of pulmonary TB and 88.4% of those without a history of pulmonary TB were diagnosed with stage IV. Stage III NSCLC followed, with 33.3% of lung cancer patients with a history of pulmonary TB and 7.6% of those without a history of pulmonary TB diagnosed at this stage. This is consistent with the study by Sutandyo et al., which found that 69.7% of lung cancer patients were diagnosed at stage IV.[15] Similarly, the research by Nastiti et al. showed that 77.6% of lung cancer patients with a history of pulmonary TB were diagnosed with stage IV, while 13.2% were diagnosed with stage III.[8]

Based on histopathological type, Squamous Cell Carcinoma is the most common histopathological type found, followed by Adenocarcioma, Small Cell Carcinoma, and Large Cell Carcinoma. In lung cancer patients with a history of pulmonary TB, there were 6 patients with Squamous Cell Carcinoma (50%), 5 patients with Adenocarcinoma (41.7%), and 1 patient with Small Cell Carcinoma (8.3%). Meanwhile, in lung cancer patients without a history of pulmonary TB, there were 92 patients with Squamous Cell Carcinoma (57.6%), 66 patients with Adenocarcinoma (38.4%), patients with Large Cell Carcinoma (0.6%), and 6 patients with Small Cell Carcinoma (3.5%).

From the data obtained, it is known that in both groups, Squamous Cell Carcinoma is the most common type of lung cancer. The same results were obtained from the study by Chauhan et al. namely there were 25.5% of lung cancer patients with Squamous Cell Carcinoma and 15.3% of patients with Adenocarcinoma.[16] The high incidence of Squamous Cell Carcinoma lung cancer in this study can be influenced by certain factors, such as Squamous Cell Carcinoma is more common in men, influenced by high cigarette and alcohol consumption, cancer in the final stages, and larger tumor size.[17] While Adenocarcinoma is more common in women and in non-smokers.[15] Patients with Squamous Cell Carcinoma tend to experience cough, fever, bacterial and fungal infections, and have higher leukocyte counts compared to patients with Adenocarcinoma. The results of the study indicate that infections and inflammation play a more significant role in the development of Squamous Cell Carcinoma than in Adenocarcinoma.[17] This may also explain why lung cancer patients with a history of pulmonary tuberculosis were more commonly found to have Squamous Cell Carcinoma in this study.

It was observed that all lung cancer patients exhibited mass-like lesions. Consolidation and multiple nodules were more commonly seen in lung cancer patients without a history of pulmonary TB. Lesions associated with previous TB, such as fibrosis, were more frequently found in patients with a history of pulmonary TB, indicating a link between fibrosis and changes in lung tissue caused by prior TB infection. Calcifications, cavities, and pleural thickening were less commonly observed overall but were more frequently found in patients with a history of pulmonary TB. In summary, consolidation, multiple nodules, and infiltrates were more prevalent in lung cancer patients without a history of pulmonary TB, while fibrosis, calcifications, cavities, and pleural thickening were more often seen in those with a history of pulmonary TB.

The formation of masses in lung cancer results from DNA damage that transforms normal cells into carcinoma cells, caused by exposure to carcinogens such as cigarette smoke. This damage disrupts cellular repair mechanisms or apoptosis,

allowing uncontrolled cell proliferation. Carcinogens can also activate proto-oncogenes, such as EGFR, and deactivate tumor suppressor genes, accelerating the growth of malignant cells and leading to the development of tumor masses.[18]

Consolidation refers to lung density that occurs when the alveoli are filled with substances such as pus, fluid, or blood due to infection. It appears as an area of opacity on chest radiography.[19] Multiple nodules can form as part of primary lung neoplasms, which originate directly from lung tissue, such as epithelial, mesenchymal, or lymphoid tissues. These neoplasms can produce multiple nodules simultaneously, detectable as multiple nodules on CT scans.[20] Infiltrates in lung cancer can be caused by infections or side effects of treatments such as chemotherapy. Impaired immune function in cancer patients increases the risk of respiratory tract infections. Chemotherapy can also induce lung damage, such as inflammation or fibrosis, leading to the formation of infiltrates. This condition is typically observed as ground-glass opacity on CT scans.[21]

Fibrosis or scarring of the lungs, forms as a result of inflammation and wound healing, characterized by the accumulation of connective tissue. This condition can be caused by exposure to hazardous materials such as asbestos and silica, as well as lung infections or inflammation, including TB and pneumonia. Fibrosis often appears as residual damage from pulmonary TB, even when treatment is optimal. Additionally, fibrosis can increase the risk of lung cancer in the same area through a process known as "scarsinoma." In this process, excessive cell regeneration during healing triggers abnormal cellular changes that may become malignant, thereby elevating the risk of tumor formation, particularly at the site of prior TB infection.[22]

Calcification is often a remnant of prior infections, such as TB or fungal infections, appearing as healed granulomas that signify chronic lesions. In lung cancer patients without a history of TB, calcification may result from tumor tissue degeneration caused by necrosis. This process can be triggered by the secretion of parathyroid hormone-related protein by tumor cells, leading to calcium deposition in the tumor area. Lesions with calcification are generally considered benign if the calcification is evenly distributed in the lesion's center, has well-defined margins, and remains unchanged for more than two years.[23]

Cavities resulting from TB form due to chronic inflammation during active infection, where the body's inflammatory response to TB bacteria leads to lung tissue damage, including necrosis that creates cavities. Once the infection resolves, these cavities may persist for a prolonged period. Post-TB cavities are often found in the upper lobes of the lungs, characterized by thick walls, irregular shapes, and the presence of air or fluid on imaging, typically accompanied by surrounding fibrosis. These cavities pose a risk of serious complications, such as lung cancer, and can persist for years after TB treatment is completed.[5]

Pleural thickening in lung cancer can result from malignant pleural effusion (MPE), which involves the accumulation of fluid containing cancer cells, triggering inflammation in the pleura.[24] In patients with a history of TB, pleural thickening often arises from prolonged inflammation during active TB infection. Even after TB resolves, scarring can lead to permanent pleural thickening. On imaging, pleural thickening typically appears as an opacity covering a significant portion of the chest wall, often causing obliteration of the costophrenic angle or extending to the lung apex.[25]

Atelectasis refers to the collapse of lung tissue caused by bronchial obstruction. In lung cancer, atelectasis is often due to bronchial obstruction by a tumor, leading to lung collapse in the affected area. On imaging, atelectasis typically appears as linear or dense areas.[26] In patients with a history of TB, atelectasis may occur due to fibrosis and airway narrowing following recovery. Fibrosis leads to lung volume loss and pulls surrounding structures, contributing to lung collapse.[27]

Generally, the most common lesions found in lung cancer patients with a history of pulmonary TB, compared to those without such a history, were fibrosis (83.3%), calcifications (50%), and cavities (33.3%). This aligns with the findings of Deshpande et al., who reported that treated pulmonary TB patients exhibited fibrosis (90%), calcifications (74%), and cavities (21%).[28] Pleural thickening and atelectasis are also common markers of prior pulmonary TB. In this study, pleural thickening was observed in 16.7% of lung cancer patients with a history of pulmonary TB, and atelectasis was observed in 8.3%, both of which were higher compared to patients without a history of pulmonary TB. These findings are consistent with previous studies, which reported pleural thickening percentages of 22% and 33.33% in patients with a history of pulmonary TB.[25,28]

LIMITATIONS

The study faced several limitations. First, challenges were encountered in accessing complete medical records, as not all patient records could be retrieved, and some available records contained incomplete data, rendering them unusable for inclusion in the study sample. Second, among patients with a history of pulmonary tuberculosis (TB), many records lacked information on the initial year of TB diagnosis, complicating efforts to assess the relationship between the timing of TB diagnosis and the progression of lung cancer. Lastly, the available radiological data for some patients were not obtained at the initial diagnosis of lung cancer, potentially introducing bias in the interpretation of radiological findings.

CONCLUSION

Based on the conducted study, the following conclusions can be concluded thatthe prevalence of lung cancer is higher in patients without a history of pulmonary TB (93.5%) compared to those with a history of pulmonary TB (6.5%). The majority of patients are aged 51-60, male, employed, from Aceh, Muslim, and diagnosed with stage IV lung cancer. The most commonly found histopathological type is Squamous Cell Carcinoma, both in patients with and without a history of pulmonary TB. Radiological findings reveal that all patients presented with lung masses. Patients with a history of pulmonary TB more frequently showed signs of fibrosis, calcifications, cavities, atelectasis, and pleural thickening on imaging.

DISCLOSURES

Conflict of Interest

There is no conflict of interest related to the materials or methods used in this study.

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Ethic Approval

The authors had obtained approval from the dr. Zainoel Abidin General Hospital for the data used in this case report.

Author Contribution

All authors equally did case identification, manuscript drafting, and revision.

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