Primary Pulmonary Sarcoma Coinfected with Pulmonary Tuberculosis: A Case Report

Dea Putri Audina 1*, Sita Laksmi Andarini 1, Hana Khairina Putri Faisal 1, Prasenohadi Prasenohadi 1, Jamal Zaini 1, Herawati Hidajat 2

1 Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia – Persahabatan National Respiratory Hospital, Jakarta Indonesia.
2 Department of Pathology Anatomy, Persahabatan Hospital, Jakarta Indonesia.

*Corresponding author:
Dea Putri Audina
Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia – Persahabatan National Respiratory Hospital, Jakarta Indonesia
drdeaputriaudina@gmail.com

INTRODUCTION

Approximately 4.8 million individuals worldwide were diagnosed with pulmonary tuberculosis (TB) in 2020 and 59% of these cases have been confirmed through bacteriological testing. This number has increased by about 2% since 2019, but the figure has not changed since 2005. In 2020, Indonesia ranked as the 3rd largest contributor, demonstrating the most significant disparity between the estimated number of cases and those that were reported [1]. The country had recorded a minimum of 420,994 new cases of TB in 2017 [2].

TB was discovered by Dr. Robert Koch, who identified the disease as being caused by Mycobacterium tuberculosis.

This infectious ailment stands as one of the oldest and it continues to impose a significant burden on public health [1]. TB infection can also develop into tubercle granulomatous tumors, spheres, and avascular known as tuberculoma. About 7-9% of patients with the disease often have it evolve into tuberculoma. Mycobacterium tuberculosis inoculated in bronchioles forms an immunological complex involving local alveolar macrophage and developing granuloma. The granuloma was transformed into a tuberculoma by growing in size and encapsulated with soft tissue and caseosa necrotic in the middle [3].

Lung tuberculoma commonly presents as a solitary lung nodule (SLN), appearing in imaging as well-defined...
round or oval solitary nodules measuring around <30 mm in size. The solitary lung nodule can both be benign (pulmonary hamartoma, hemangioma, and tuberculosis) and malignant (squamous cell carcinoma, adenocarcinoma, and bronchoalveolar carcinoma). Some studies concluded that the larger the size, the more it becomes malignant. However, distinguishing between benign and malignant SLN remains a challenge [3].

Soft tissue sarcoma is a malignancy capable of occurring at any age and can manifest anywhere in the body, spanning from head to toe due to its origin within the mesenchymal layer [4,5]. This diverse origin contributes to the existence of more than 50 distinct sarcoma subtypes, each defined by unique histopathological features [5]. Approximately 12,020 new cases of sarcoma were discovered in the US in 2014 with a total of 4,740 death cases being reported. This is a rare disease that accounts for approximately 1% of all malignancies in the country [4]. A specific variant, pulmonary sarcoma carcinoma (PSC), is a rare malignancy with a poor prognosis. This type of cancer represents 0.1-0.4% of lung disease [6].

WHO divides PSC into 5 subgroups, namely pleomorphic carcinoma, spindle cell carcinoma, large cell carcinoma, carcinosarcoma, and pulmonary blastoma [6]. Sarcoma is aggressive with a high ability to metastasize and does not respond very well to chemotherapy, radiotherapy, and neoadjuvant therapy. These factors contribute to the poor prognosis. However, the knowledge concerning this malignancy remained limited [5,6].

The coexistence between TB and malignancy, specifically sarcoma, remains uncertain. Cicenas et al. [8] reported that 2.1% of TB cases were accompanied by lung malignancy in Lithuania from 1990 to 2015 [7,8]. The coexistence between lung carcinoma and TB was simultaneously reported to be around 2% and was observed in the upper lobe [9]. Finally, the case of TB coexistence with sarcoma which is primarily considered TB infection mimicking lung malignancy was illustrated.

CASE PRESENTATION

A 62-year-old man presented the emergency ward (EW) with the chief complaint of experiencing shortness of breath 3 months ago. This condition became worsened within 3 days before admission. Furthermore, it was accompanied by intermittent left chest pain since 5 months ago. The patient also complained of yellow phlegm productive cough and a history of blood streak on sputum spanning 5 months. There was a loss of weight of about 10 kg within 5 months, along with the presence of Night sweats. Additionally, the disease of nausea with no vomiting was also felt. The patient was an active smoker who consumed approximately 2 cigarettes a day for 45 years (Severe classification of Brinkman index). There was no previous history of lung and systemic diseases such as diabetes mellitus, hypertension, cerebrovascular disease, or heart complications. The patient was a construction worker for more than 40 years and worked without using any personal protective equipment.

Physical examination during the first day of admission showed moderate sickness with comatos mentis consciousness. The vital signs observed were a respiratory rate of 22 breaths per minute, along with an oxygen saturation of 89% on room air and 96% while receiving oxygen through nasal cannula at a rate of 3 liters per minute. The patient body mass index was 17.6kg/m2. During a thoracic examination, an asymmetrical movement of the thorax was noted, with diminished expansion observed on the left hemithorax. Tactile fremitus was reduced on the left side in comparison to the right. Percussion yielded a dull sound on the left hemithorax, and auscultation showed decreased vesicular breath sounds in the same region, without wheezing or crackles detected in either hemithorax. Finally, no other abnormalities were discovered during the general physical examination.

A blood gas analysis was conducted while the patient was receiving 3 liters of oxygen per minute through a nasal cannula. The results showed a pH, pCO2, pO2, HCO3, total CO2, BE, and oxygen saturation of 7.452, 29.2 mmHg, 73.7 mmHg, 20.6 mmol/L, 21.5 mmol/L, -3.6 mmol/L, and 95.8%, respectively. There was a slight increase in leucocytes 12,850/mm3, accompanied by low albumin levels of 2.6 g/dL. A rapid molecular test (GenExpert) was conducted with a sputum sample on the 4th day of admission, and positive *Mycobacterium tuberculosis* sensitive to rifampicin was detected. Chest x-ray indicated left lung atelectasis, as presented in Figure 1A, while a CT scan of the thorax performed with contrast on May 12th, 2022 showed atelectasis in the left lung lobe. A suspected mass located intra or peri the left main bronchus was identified, approximately measuring 3x2.5 cm in size. Additionally, an obstruction was observed in the left main bronchus, as shown in Figure 2.

The patient underwent a bronchoscopy diagnostic procedure on June 7th, 2022. During this procedure, a mass that was non-bleeding in nature was observed to completely close the left main bronchus, as shown in Figure 3. Both forceps biopsy and cryo-biopsy were performed in an attempt to obtain tissue samples for analysis. The pathological anatomy results on 9th June 2022 were inconclusive, with no viable cells detected. Subsequently, the patient received a diagnosis of lung TB and was prescribed a fixed dose of anti-TB drugs (FDC), requiring the daily consumption of 3 tablets. Each tablet contained 150 mg of Rifampicin, 75 mg Isoniazid, 400 mg Pyrazinamide, and 275 mg Ethambutol. Despite the administration of this tailored treatment, the sensation of dyspnea persisted.

The patient resides more than 100 km away from the hospital. Due to this distance-related issue, the relatives visited the outpatient clinic at Persahabatan Hospital every month to provide updates on the current
Figure 1. Serial chest X-rays since the patient was admitted to Persahabatan Hospital showed no improvement from the 1st admission on (A) May 21st; (B) June 15th; (C) July 6th; and on the 2nd admission on (D) August 4th, 2022.

Figure 2. CT-Scan thorax with contrast on May 12th, 2022 revealed atelectasis throughout the left lung lobe, a suspected mass intra or peri left main bronchus with the approximate size of 3x2.5 cm and obstructed left main bronchus.

Figure 3. Bronchoscopy showing a mass that completely closed the left main bronchus.

Figure 4. (A). Gross visual of the spontaneous like mass phlegm; (B). Pathological anatomy sample from the sputum sample found a malignant tumor cell focus with a differential diagnosis of pleomorphic sarcoma differential diagnosis sarcomatoid carcinoma. The arrow is shown to focus on nucleated, pleomorphic, hyperchromatic, and spindle cell tumors.

condition and disease for evaluation. However, conducting a CT scan evaluation was not feasible. Meanwhile, the specific treatment for TB was continued. On the 3rd month of anti-TB therapy, the patient came into the emergency department with chief complaints of increasing shortness of breath. Subjectively, there was a feeling of no improvement despite taking drugs for 3 months, with shortness of breath and fatigue still experienced. The patient was then admitted to the inpatient ward. During the first day of the second admission, there were symptoms of moderate sickness while maintaining compos mentis consciousness. The vital signs showed a respiratory rate of 23 breaths per minute, along with an oxygen saturation of 88% on room air and 95% when receiving oxygen through nasal cannula at a rate of 3 liters per minute. Body mass index was decreased to 14.1 kg/m2. Additionally, the thoracic examination showed results that were consistent with those observed during the initial admission. Chest x-ray was conducted (Figure 1D) but no differences were observed compared to the previous evaluation. Despite the plan to repeat the bronchoscopy and CT scan, the patient declined these procedures.

The blood gas analysis results, obtained while administering 3 liters per minute of oxygen through a nasal cannula, showed pH, pCO$_2$, pO$_2$, HCO$_3$, total CO$_2$, BE, and oxygen saturation of 7.415, 28.7 mmHg, 77.4 mmHg, 18.5 mmol/L, 19.4 mmol/L, -6.2 mmol/L,
and 95.7%, respectively. On day 5 of admission, phlegm with a solid consistency unlike usual was coughed up. The sample was collected and sent to the pathological anatomy laboratory. Upon examination, the sample exhibited extensive necrotic tissue with focus nucleated, pleomorphic, hyperchromatic, and spindle cell tumors, as seen on Figure 4. The final diagnosis highlighted the presence of malignant tumor cell focus with a differential diagnosis of pleomorphic sarcoma and sarcomatoid carcinoma. On day 7 of admission, the condition improved and the patient was discharged. There was a plan to begin chemotherapy in an outpatient setting. However, within 1 month of being diagnosed with sarcoma, the patient was reported dead.

DISCUSSION

An immune response was triggered when Mycobacterium tuberculosis was inhaled into the airways and reached the respiratory bronchioles and alveolus. The ability of Mycobacterium tuberculosis to cause an infection depends on the number of pathogens and the response of the host. In cases where the number of pathogens was not enough to cause the infection, they become eliminated by the macrophages as a nonspecific immune system. However, when their count exceeds the ability of macrophages to phagocytes, these pathogens can survive the immune response and multiply intracellularly. This led to the creation of an immune response in the form of a barrier around the infected area and forming granulomas [10].

Malhotra et al. [9] stated that lung carcinoma was more often observed in males than females. It was also reported that the incidence of lung cancer was considered low in the population aged < 40 and increased with the age range of 75-80. A 62-year-old man was identified, and the complaint presented was a chronic respiratory disease that can lead to a malignancy diagnosis.

In this case report, the patient had classic TB disease such as a productive cough for more than two weeks, a history of blood streak in sputum, loss of appetite, weight loss, and chest pain. Since the disease was chronic, it overlapped with those of lung malignancy which included shortness of breath, chest pain, chronic cough, and hemoptysis [6,10]. Based on the disease and the gen expert examination, anti-TB drugs were administered for three months until the patient was reported deceased. Anti-TB treatment for TB rifampicin sensitivity was divided into the intensive phase for 2 months and the continual phase for 4 months, giving a total treatment duration of 6 months. Bacterial TB can be evaluated clinically, bacteriologically, and radiologically. Based on the clinical appearance, monthly evaluation of the body weight, the response to the anti-TB drugs, and any side effects experienced, were essential. Bacteriological evaluation typically occurs during the 2nd month of treatment when the results still come positive. Reevaluation was conducted in the 3rd month, followed by another assessment in the 6th month of treatment. Finally, radiological evaluation was recommended on the 2nd and 6th [10].

The prevalence of TB coexistence with malignancy remains unknown. Compared to a previous study by Cicenas et al. [8], an investigation in Turkey also showed a higher prevalence of TB coexistence with lung malignancy cases, which was approximately 4% [7,8]. A study conducted at the National Cancer Institute stated that patients with TB had a higher risk of developing lung cancer and had also been treated with anti-TB drugs for 3 months [11]. However, a lack of improvement was evident in Figures 1A to D, which showed the chest X-ray results. Based on this scenario, it became imperative to entertain the possibility of malignancy, particularly when there was a dearth of progress in both imaging and clinical evaluations.

TB and malignancy stand out as two of the most widespread global health concerns, but they often face the risk of being misdiagnosed. This risk is particularly heightened in patients with malignancies who exhibit atypical symptoms and conditions, compounded by the constraints of diagnostic tests. Therefore, these individuals may be mistakenly identified as having TB [12]. This problem is not exclusive to malignancy. For example, a study reported about 91 patients with suspected lung malignancy who received surgery and were proven to have pulmonary lung TB as the final diagnosis. Another investigation also stated there were 26 cases out of 70,000 patients with bacteriologically proven pulmonary TB but not malignancy. The shared signs and disease of TB and malignancy make the diagnostic process challenging, often referred to as a diagnostic chameleon due to its elusive nature. This complexity arises from the disease overlap, and the differentiation between the two conditions becomes intricate. However, diagnosing pulmonary TB can be facilitated through a simple microbiological test, such as a rapid molecular test for TB [13]. The present case shows a coexistence of TB and malignancy in the same period.

Sarcoma includes epithelial and mesenchymal tissue elements that differentiate it from other non-small cell lung carcinoma types. Due to the rarity of sarcoma, studies and knowledge about lung sarcoma were limited, hence, it became difficult to identify the specific treatment for PSC which was also known as resistant to chemotherapy and radiotherapy [14]. Patients with PSC were usually diagnosed at later stages and had no opportunity for surgery [6,14].

Pulmonary sarcoma carcinoma predominantly affects males, often correlating with a significant Brinkman smoking history in the moderate to severe range. Survival rates exhibit variation, yielding a median survival period of 21 months. The pattern of metastasis in this
cancer mirrors other lung cancer types, extending to sites such as the contralateral lung, adrenal glands, pleura, brain, bones, and liver. Characteristic CT scan results for PSC commonly encompass peripheral masses, prevailing over central masses. The upper lobes serve as a more frequent location for lesions, which are typically sizable and well-defined. Plain CT scan images frequently show dense connective tissue, accompanied by substantial necrotic areas. The presence of peritoneal masses, coupled with local or distant metastases invading the chest wall or pleura, is a recurrent observation. However, intratumoral calcification remains a rarity. CT scan offers advantageous tumor identification benefits. It is important to note that while CT scans aid in identifying tumors, the gold standard for diagnosing malignancy lies within histopathological and immunohistochemical examinations [6]. In the presented case, malignancy was diagnosed through the examination of spontaneous sputum phlegm. This examination unveiled a focus on malignant tumor cells, prompting a differential diagnosis encompassing pleomorphic sarcoma and sarcomatoid carcinoma.

In this case, the patient cannot come physically into the outward clinic monthly due to the distance problems and has been evaluated and observed clinically by the relatives. However, the CT scan was not conducted monthly or every 3 months. Gierada et al. [15] stated that follow-up for solid lung nodules with sizes greater or equal to 6 mm on initial screening was evaluated with a CT scan at 6 months. Meanwhile, at a size range between 6 to <8 mm, a 3rd month of PE/CT was performed no later than in 3rd month. Therefore, a CT scan assessment should be performed no later than in 3rd month.

CONCLUSIONS

Since lung malignancy coexisted with lung TB, it should be considered in TB patients, specifically in the male population age older than 40 with a smoking history and no improvement despite taking anti-TB drugs. Therefore, close observation, which involved regular evaluation through monthly or quarterly chest CT scans, was required.

DECLARATIONS

Competing of Interest
The authors declared no competing interest in this study.

Acknowledgment
Not applicable.

REFERENCES