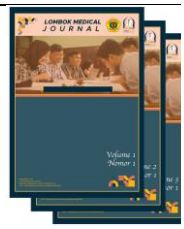
LMJ 4(2) (2025)

Lombok Medical Journal

http://journal.unram.ac.id/index.php/LMJ



Pulmonary Tuberculosis Complicated by Pneumonia, Pneumoconiosis, Fungal Infections, and Drug-Induced Liver Injury (DILI): A Case Report

Ni Kadek Mega Suryantini[1*], Gemilang Khusnurrokhman[2] ,Salim Said Thalib[3], Suryani Padua Fatrullah[4]

[1] Faculty of Medicine, University of Mataram, Mataram, Indonesia

[2,3,4] Pulmonology and Respiratory Department, Medical Faculty Mataram University/West Nusa Tenggara Province General Hospital, Indonesia

DOI: https://doi.org/10.29303/lmj.v4i2.5564

Article Info
Received **: 30 Oktober 2024**
Revised **: 02 Desember 2024**
Accepted **: 22 April 2025**

Abstract: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. According to the World Health Organization (WHO), TB is one of the top 10 causes of death in the world. TB is divided into pulmonary TB and extrapulmonary TB. There were 10.4 million cases of TB globally in 2017, and it is estimated that there will be 845.000 new cases of pulmonary TB in Indonesia in 2019. In 2018 approximately seven million new and relapsed TB cases were reported worldwide. The death rate due to TB may reach 1.5 million cases. TB patients can develop several complications before, during or after treatment, including coughing up blood, pneumothorax, respiratory failure, and heart failure. TB patients may have several comorbidities, including pneumonia, pulmonary mycosis, pneumoconiosis, and drug induced liver injury (DILI). Pneumoconiosis is an occupational lung parenchymal disease that results from prolonged dust inhalation. It can progress to progressive massive fibrosis, followed by severe lung function decline. According to the WHO, there are 1.1 million deaths by occupational diseases worldwide, with 5% being pneumoconiosis with exposure from an industrialization process causing occupational diseases. The International Labor Organization (ILO) states that pneumoconiosis is an occupational lung disease suffered by many workers. Early diagnosis is needed to determine the management that can be given to prevent other complications.

Keywords: Tuberculosis, pneumonia, pneumoconiosis, pulmonary mycosis, drug induced liver injury (DILI)

Citation: Suryantini, K.M.,Gemilang, K., Thalib, S.S., & Fatrullah, S.P. (2025). Pulmonary Tuberculosis Complicated by Pneumonia, Pneumoconiosis, Fungal Infections, and Drug-Induced Liver Injury (DILI): A Case Report . *Lombok Medical Journal*, 4(2) 45-52. DOI : https://doi.org/10.29303/lmj.v4i2.5564

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis (MTB). These bacteria are acid-resistant and rod-shaped, called acid-resistant bacilli. Most MTBs are found to infect the lung parenchyma, which causes pulmonary TB. Still, these bacteria also can infect other organs (extra-pulmonary TB), such as lymph nodes, pleura, bones, and other extra-pulmonary organs (Kementerian Kesehatan Republik Indonesia, 2020). Tuberculosis bacterial infection is currently the leading cause of death from a single infectious pathogen disease (Luies & Preez, 2020). Mycobacterium tuberculosis bacteria have infected nearly 1/3 of the world's population (Natarajan et al.,

Email: kadekmega18@gmail.com

2020). Globally, the mortality and prevalence of TB are 47% and 42% respectively (Weldemhret, 2023). According to the World Health Organization (WHO), TB is one of the top 10 causes of death in the world (Rodriguez-Takeuchi et al., 2019). Several groups have a higher risk of developing TB disease, such as people with HIV infection, environment, malnutrition, smoking, high alcohol consumption, diabetes mellitus, children, and health workers (Narasimhan, et al., 2013). TB symptoms vary based on lesion location and include a persistent cough more than 2 weeks (often with sputum or blood), shortness of breath, chest pain, and general symptoms of weight loss, loss of appetite, malaise, fever, chills, and night sweats (Kementerian Kesehatan Republik Indonesia, 2020). Anti-tuberculosis drugs are the most important component of TB treatment to prevent further spread of the bacteria that cause TB (Kementerian Kesehatan Republik Indonesia, 2020) (Kementerian Kesehatan Republik Indonesia, 2023).

Pneumonia is an acute inflammation in the lung parenchyma caused by pathogenic infections (bacteria, viruses, parasites, and fungi), excluding Mycobacterium tuberculosis (Kementerian Kesehatan Republik Indonesia, 2023). Diagnosis of pneumonia is based on anamnesis, physical examination, supporting examination (radiology and laboratory). Radiological examination infiltrates/opacity/consolidation/air bronchogram is found coupled with an acute onset of cough, shortness of breath, chest pain, changes in sputum characteristics or purulent, body temperature more than 38◦C (axillary) or a history of fever, on physical examination can be found signs of consolidation, bronchial breath sounds, and rhonchi and leukocyte count >10.000 cells/µL or <4500 cells/µL with increased rod neutrophils or immature granulocytes (Kementerian Kesehatan Republik Indonesia, 2023).

Pneumoconiosis is an occupational lung parenchymal disease caused by prolonged dust inhalation and can develop into progressive massive fibrosis followed by severe lung function decline (PDPI, 2021a). According to the International Labor Organization (ILO), pneumoconiosis is a disease caused by dust accumulating in the lungs, causing the dust to become fibrous (Sinaga et al., 2020). Some of the risk factors that affect the incidence of pneumoconiosis include age, work duration (the longer the work duration, the greater the accumulation of dust particles in the lungs), personal protective equipment such as masks, and smoking history (Ulfahimayati et al., 2021). Clinical manifestations in patients with pneumoconiosis can be respiratory symptoms such as cough with phlegm that tends to persist, shortness of breath, especially during activities and chest pain (Sinaga et al., 2020). There are three major criteria in helping the diagnosis of pneumoconiosis, namely significant mineral dust exposure accompanied by a latent period, the presence of specific features, especially in radiological abnormalities, and the absence of other diseases that resemble pneumoconiosis (Sinaga et al., 2020). Management of pneumoconiosis is carried out with symptomatic therapy and reduces the possibility of complications that will arise (Ulfahimayati et al., 2021).

Pulmonary mycosis is one of the respiratory disorders caused by infection, colonization, or hypersensitive reactions to fungi. Pulmonary mycosis can also be referred to as fungal pneumonia (PDPI, 2021a). Inhalation of fungal particles is the main infection route, often causing respiratory disease, with or without systemic spread (Wilson et al., 2024). The clinical manifestations of fungal pathogen infections in the respiratory tract include pneumonia, characterized by fever, cough, and radiographic findings of lower respiratory tract disease (Heung et al., 2023). Candida growth in respiratory secretions usually indicates colonization and rarely needs antifungal treatment. Airway colonization with Candida is linked to bacterial colonization and pneumonia, which mainly occurs in immunocompromised patients after hematogenous spread. Chest CT scan often show multiple pulmonary nodules. Diagnosis is confirmed by isolating the organism from bronchoalveolar lavage (BAL) and histopathological evidence of invasive disease (Pappas et al., 2016).

Drug-Induced Liver Injury (DILI) refers to liver damage, including to hepatocytes and other liver cells, caused by commonly used medications. It is related to drug metabolism (Andrade et al., 2019). The causes of DILI are related to dose, duration of consumption, and direct toxicity or drug metabolites (Katarey & Verma, 2016). According to The American DILI Network (DILIN), antibiotics were involved in 45.4% of cases. In addition to drug classes, herbal supplements, foods, cardiovascular agents (9.8%), central nervous system agents (9.1%), antineoplastic agents (5.5%), and analgesics (3.7%) can also be causative. In addition, drugs that are often involved in causing acute liver failure are anti-tuberculosis therapy drugs (Katarey & Verma, 2016). Anti-tuberculosis drugs are the most common cause of DILI in China and India (Andrade et al., 2019).

Case Presentation

A 33-year-old man presented with complaints of shortness of breath that was felt to be aggravated 3 hours before admission to the hospital. The shortness of breath appeared suddenly and became progressively worse. The shortness of breath was felt worse during activity and felt slightly reduced at rest. Complaints are accompanied by a cough with thick white phlegm about

one month ago. The cough is not accompanied by mucus or blood. Other complaints include a history of fever, decreased appetite, and weight loss. The patient has been diagnosed with Pulmonary TB and has completed treatment for 6 months in 2023. The patient was again diagnosed with pulmonary TB and has been taking anti-tuberculosis drugs for the last 4 months (since April, 2024). The patient had worked as a gold miner laborer for 4 years and has now quit. The patient admitted that sputum examination was never positive at the beginning of treatment until the end of treatment in 2023 and 2024. During work, the patient admitted that he rarely used personal protective equipment such as masks or helmets. The patient has a history of smoking for 16 years and a history of drinking alcohol.

The patient has undergone several supporting examinations including sputum culture with the results obtained 10-15/HPF leukocytes, 0-3/HPF epithelium, and organisms in the form of Candida Albicans. In addition, a blood culture examination was carried out with the result that no organism growth was found.

In the laboratory examination results obtained platelets 118000/uL, hematocrit 43%, blood glucose 127 mg/dL, urea 41 mg/dL, BUN 19.16 mg/dL, creatinine 0.9 mg/dL, eGFR 97.00 mL/min/1. 73, SGOT 388 U/I and SGPT 282 U/I (4/8/2024), SGOT 42 U/I and SGPT 107 U/I (12/8/2024), SGOT 30 U/I and SGPT 48 U/I (15/8/2024), total bilirubin 1,2 mg/dL, direct bilirubin 0.69 mg/dL, anti-HIV rapid non-reactive, HBsAg rapid non-reactive. In the leukocyte count, the dominant type of neutrophils was 91.5%, neutrophils# 7.31 10^3/uL

Figure 1. Thorax X-Ray

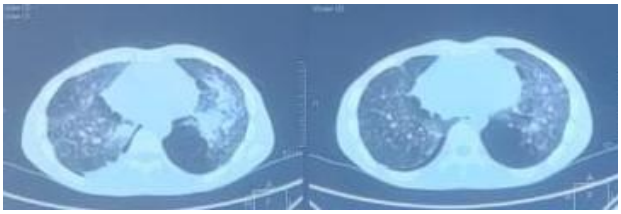


Figure 2. Non-Contrast HRCT Scan Thorax

Discussion

The patient has been diagnosed with pulmonary TB and has been on anti-tuberculosis drug treatment since April 2024 with a dose of 1x3 tablets. However, based on the anamnesis of the patient, a sputum examination has been carried out, but no positive results have been obtained. By the history and physical examination of the patient in accordance by the clinical manifestations of pulmonary TB, namely there are symptoms of chronic cough, fever, decreased appetite, decreased body weight. In the results of the thoracic examination at the West Nusa Tenggara Province General Hospital, an X-ray picture was obtained that supported TB, namely in the thoracic photo there was

consolidation in the supra-parahilar right and left lungs and in the CT scan results obtained tree in bud pattern in both lungs dominant in the superior-medial lobe of the right lung and superior lobe of the left lung. Patients in this case fall into the category of relapse cases with a history of treatment. A relapse case is a patient who has previously received anti-tuberculosis drugs and at the end of treatment, was declared cured or completed treatment, and is currently diagnosed with a re-episode of TB (due to reactivation or a new episode caused by reinfection). In this case, the patient had been diagnosed with TB in 2023 and had completed 6 months of treatment. When admitted to the hospital (4 September 2024 the patient was already in the continuation phase of TB treatment (PDPI, 2021b) (Kementerian Kesehatan Republik Indonesia, 2020).

The patient came to the hospital with complaints of increasingly severe shortness of breath, then the patient had a history of fever, and a cough with thick white phlegm that had been experienced for a long time leading to suspicion of pneumonia. Diagnosis of pneumonia is based on anamnesis, physical examination, and supporting examination. Where the clinical symptoms and signs experienced by the patient support the acute onset of pneumonia symptoms and signs, namely the presence of shortness of breath and cough, there is a history of fever, in laboratory results the dominant increase in neutrophils indicates a secondary infection. On radiologic examination of thoracic photographs, consolidation was found in the right supra-parahilar, left lung, fibrosis in the right parahilar-paracardiac, suprahilar and on CT Scan, consolidation with air bronchogram was found in the apical-posterior segment of the superior lobe, medial segment of the lobe medius and superior segment of the inferior lobe of the right lung; apico-posterior segment of the superior lobe of the left lung and lingual segment. The patient also had a sputum culture examination with the results of 10-15 leukocytes/HPF. The patient also has risk factors for comorbidities in the form of pulmonary TB, and the patient has a history of smoking for 16 years.

In patients with clinical symptoms accompanied by sputum examination results that indicate Candida albicans organisms, it can be diagnosed with pulmonary mycosis type candidosis. Pulmonary mycosis is a lung disorder caused by infection, fungal colonization, or hypersensitivity reactions to fungi. The treatment plan that can be given to patients is antifungal therapy in the form of nystatin or fluconazole (PDPI, 2021a).

The patient was also diagnosed with pneumoconiosis. Pneumoconiosis is an occupational lung parenchymal disease caused by prolonged dust inhalation and can develop into progressive massive fibrosis followed by severe lung function decline (PDPI, 2021a). To confirm the diagnosis of pneumoconiosis based on three major criteria, namely the presence of significant exposure to mineral dust which is the suspected cause of pneumoconiosis and is accompanied by a latent period, the presence of a specific picture of the disease in radiological abnormalities, and the absence of other diseases. Based on anamnesis, the patient worked as a gold miner laborer for 4 years. During work, it is known that patients rarely use personal protective equipment such as masks and the duration of mining is uncertain. Clinical manifestations that appear in patients are cough with phlegm that tends to persist and shortness of breath, especially when doing activities. The radiology showed fibrosis in the right parahilar-paracardiac, suprahilar, and left paracardial. Management of pneumoconiosis is carried out with symptomatic therapy and reduces the possibility of complications arising. Use masks to prevent, regular health checks, controlling dust levels in the work environment. Efforts that can be made to prevent exposure include the use of personal protective equipment such as masks and helmets, periodic health checks, and controlling dust levels in the work environment (Ulfahimayati et al., 2021). In addition, maintaining health by avoiding smoking will worsen respiratory conditions (Sinaga et al., 2020). Encourage patients to perform rehabilitation exercises to improve lung function and alleviate symptoms (Qi et al., 2021).

Based on the patient's occupational history as a gold mine worker, the type of pneumoconiosis the patient may have is silicosis. Silicosis is a common pneumoconiosis that occurs in workers who are highly exposed crystalline silica during work, particularly in mining (Liu *et al.*, 2023) Exposure to inhaled crystalline silica can occur from natural stones such as granite or marble, engineered or artificial stones with a silica content >90%, concrete, and sand (Hua, Cool and Green, 2023). Silicosis leads to impaired lung function and common respiratory symptoms like shortness of breath, cough, sputum production, hemoptysis, chest pain, along with complications such as tuberculosis, respiratory infections, and pneumothorax (Liu *et al.*, 2023).

In the laboratory examination results when the patient first entered the hospital, the results of the SGOT/AST 388 U/I and SGPT/ALT 282 U/I levels were obtained, so there was a suspicion that the patient had a condition called DILI. DILI related to the metabolism of the drug (Andrade et al., 2019). The patient did not show any reaction such as a rash but was only seen in the laboratory results. It is known based on previous study results that there are several drugs that can cause DILI and the patient is taking including isoniazid and pyrazinamide in the treatment of pulmonary TB. In this case the patient is classified as idiosyncratic DILI (indirect or unpredictable), the condition determined by

the interaction of environmental, host factors, and drugs, occurs in less than 1 in 10.000 exposed individuals and has a long latency period, ranging from several days to months (Katarey & Verma, 2016). Based on the Council for International Organizations of Medical Sciences (CIOMS) and modified by the Food and Drug Administration (FDA) Drug Hepatotoxicity Steering Committee, the diagnostic criteria for DILI are hepatocellular DILI characterized by alanine aminotransferase (ALT) levels ≥3 times the normal limit and alkaline phosphatase (ALP) ratio ≥5 times the normal limit, cholestatic DILI is characterized by ALP ≥2 times the normal limit, and mixed DILI is characterized by ALT ≥3 times the normal limit, ALP ≥2 times the normal limit, and ALT/ALP ratio <5 but >2 times the normal limit. However, none of the patients met the criteria for DILI. The diagnosis is confirmed by ruling out other liver disease causes, evaluating relationhip between drug use and abnormal liver tests, identifying signs of typical drug reactions, and observing liver function improvement after stopping the drug. In this patient, the suspicion of DILI was due to anti-tuberculosis drugs because when a temporary cessation of anti-tuberculosis drugs consumption was carried out for several 10 days, the patient's SGOT and SGPT values decreased and had reached normal values, SGOT 30 U/I and SGPT 48 U/I, so the suspicion of DILI was due to consumption anti-tuberculosis drugs and the need for a re-experiment in administering anti-tuberculosis drugs to see the next treatment response. So, management of DILI cases is with immediate discontinuation of the causative drug as soon as DILI is suspected. If the suspicion of DILI is due to the consumption of anti-tuberculosis drugs, stop the hepatotoxic drugs, namely rifampicin, isoniazid, and pyrazinamide (RHZ). If clinical and laboratory symptoms return to normal (bilirubin, SGOT, SGPT), start giving rifampicin doses slowly up to the total dose. During this time, continue to pay attention to clinical and laboratory examinations until the total dose of rifampicin; if clinical and laboratory symptoms are normal, add isoniazid with slowly increasing doses up to the total dose (according to body weight). In jaundiced patients, it is recommended not to include pyrazinamide in the drug guide. If rifampicin cannot be tolerated, the recommended combination is 2HES/10 HE, if isoniazid cannot be tolerated, the recommended combination is 6-9RZE, and if pyrazinamide is discontinued in the intensive phase, the RH mixture in the continuation phase is extended to 9 months (Kementerian Kesehatan Republik Indonesia, 2020).

Conclusion

Patient's pulmonary TB case was classified as a relapse case. Pneumonia and pulmonary mycosis by the patient is seen in the clinical manifestations of acute infection and fungal infection and pneumoconiosis is suspected as a result of prolonged dust inhalation due to work and can develop into progressive massive fibrosis followed by severe lung function decline where the patient is a gold miner laborer who has worked for 4 years. DILI experienced by the patient may be caused by several drug mechanisms previously consumed by the patient such as one of them, namely anti-tuberculosis drugs in the form of isoniazid and pyrazinamide so that the management given is temporary suspension of anti-tuberculosis drugs. It is important to be able to provide education to patients related to the condition, risk factors, and treatment given so as not to cause a worse prognosis in the future.

References

Andrade, R. J., Chalasani, N., Björnsson, E. S., Suzuki, A., Kullak-Ublick, G. A., Watkins, P. B., Devarbhavi, H., Merz, M., Lucena, M. I., Kaplowitz, N., & Aithal, G. P. (2019). Drug-Induced Liver Injury. *Nature Reviews Disease Primers*, *5*(1), 1–22. Available from: https://doi.org/10.1038/s41572-019-0105-

Heung, L.J. *et al.* (2023) 'Immunity to Fungi in The Lung', *Seminars in Immunology*, 66, pp. 1–34. Available from: https://doi.org/10.1016/j.smim.2023.101728

Hua JT, Cool CD, Green FHY. Pathology and Mineralogy of the Pneumoconioses. Seminars in Respiratory Critical Care Medicine. 2023;44(3):327–39. Available from: https://doi.org/10.1055/s0043-1764406

Katarey, D., & Verma, S. (2016). Drug-Induced Liver Injury. *Clinical Medicine*, *16*(6), 104–109. Available from: https://doi.org/10.7861/clinmedicine.16-6-s104

Kementerian Kesehatan Republik Indonesia. (2020). *Pedoman Nasional Pelayanan Kedokteran Tata Laksana Tuberkulosis*. Kementerian Kesehatan Republik Indonesia

Kementerian Kesehatan Republik Indonesia. Keputusan Menteri Kesehatan Republik Indonesia Tentang Pedoman Nasional Pelayanan Kedokteran Tatalaksana Pneumonia Pada Dewasa Nomor HK.01.07/Menkes/2147/2023 (2023)

Kementerian Kesehatan Republik Indonesia. Surat Edaran Nomor HK.02.02/III.1/936/2021 Tentang Perubahan Alur Diagnosis Dan Pengobatan

Tuberkulosis Di Indonesia, Kementerian Kesehatan RI 1 (2021)

Liu X, Jiang Q, Wu P, Han L, Zhou P. Global Incidence, Prevalence and Disease Burden of Silicosis: 30 years' Overview and Forecasted Trends. BMC Public Health. 2023;23(1):1–8. Available from: https://doi.org/10.1186/s12889-023-16295-2

Luies, L., & Preez, I. du. (2020). The Echo of Pulmonary Tuberculosis: Mechanisms of Clinical Symptoms and Other Disease-Induced Systemic Complications. Clinical Microbiology Reviews, 33(4), 1–19. Available from: https://doi.org/10.1128/CMR.00036-20

Narasimhan, P. ., Wood, J. ., MacIntyre, C. R. ., & Mathai, D. . (2013). Risk Factors for Tuberculosis. *Pulmonary Medicine*, 1–11. Available from: https://doi.org/10.1155/2013/828939

Natarajan, A., Beena, P. M., Devnikar, A. V., & Mali, S. (2020). A Systemic Review on Tuberculosis. *Indian Journal of Tuberculosis*, *67*(3), 1–17. Available from: https://doi.org/10.1016/j.ijtb.2020.02.005

Pappas, P.G. *et al.* (2016) 'Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America', *Clinical Infectious Diseases: IDSA Guideline*, 62(4), pp. e1–e50. Available from: https://doi.org/10.1093/cid/civ933.

PDPI. (2021a). *Panduan Umum Praktik Klinis Penyakit Paru dan Pernapasan*. Jakarta: Perhimpunan Dokter Paru Indonesia.

PDPI. (2021b). *Tuberkulosis: Pedoman Diagnosis dan Penatalaksanaan di Indonesia*. Jakarta: Perhimpunan Dokter Paru Indonesia.

Qi, X. M., Luo, Y., Song, M. Y., Liu, Y., Shu, T., Liu, Y., Pang, J. L., Wang, J., & Wang, C. (2021). Pneumoconiosis: Current Status and Future Prospects. Chinese Medical Journal, 134(8), 898–907.Availablefrom:https://doi.org/10.1097/CM9.0000000000001461

Rodriguez-Takeuchi, S. Y., Renjifo, M. E., & Medina, F. J. (2019). Extrapulmonary Tuberculosis: Pathophysiology and Imaging Findings. Radiographics, 39(7), 2023–2037. https://doi.org/10.1148/rg.2019190109

Sinaga, N. N. P., Hutagalung, P., & Andriana, J. (2020). Waspada Pneumokoniosis Pada Pekerja di Industri Pertambangan. *Jurnal Kedokteran*, *8*(1), 935–945.

Ulfahimayati, Deddy, H., Masrul, B., & Fenty, A. (2021). Kejadian Pneumokoniosis Pekerja Tambang Batu Bara di PT. A Kota Sawahlunto dan Faktor-Faktor yang mempengaruhi. *Jurnal Respirologi Indonesia*, *41*(1), 51–63.

Weldemhret, L. (2023). Burden of Pulmonary Tuberculosis and Challenges Related to Tuberculosis Detection in Ethiopia. *Journal of Infection in Developing Countries*, *17*(5), 578–582. Available from: https://doi.org/10.3855/jidc.13169

Wilson, M.J. *et al.* (2024) 'Pulmonary Endemic Mycoses', *Clinical Medicine, Journal of the Royal College of Physicians of London*, 24(1), pp. 1–4. Available from: https://doi.org/10.1016/j.clinme.2024.100014.