



CASE STUDY

LUNG ADENOCARCINOMA COMPLICATED BY HYDROPNEUMOTHORAX AND PERICARDIAL EFFUSION WITH IMPENDING CARDIAC TAMPONADE: A RARE CASE REPORT FROM A RURAL HOSPITAL IN KETAPANG REGENCY

Gede Ardi Saputra^{1*}, Kesih Kalua¹, Herick Alvenus Willim¹, Eva Lydia Munthe²

¹Rumah Sakit Umum Daerah Dr. Agoesdjani, Ketapang, Indonesia

²Departemen Pulmonologis, Rumah Sakit Umum Daerah Dr. Agoesdjani, Ketapang, Indonesia

*Correspondence email : belejebeleje@gmail.com

ABSTRAK

Lung cancer is the most common cancer found today. One of the lung cancers that is often found is lung adenocarcinoma. Lung adenocarcinoma has been associated with pulmonary complications such as hydropneumothorax and pleural effusion and cardiac complications such as cardiac tamponade and pericardial effusion but is very rare. In this case, we present a rare case report from a rural hospital, a 52-year-old woman had worsening shortness of breath for 1 month, accompanied by chest pain and weight loss. A chest x-ray examination uncovered a right pleural emission, and after that, thoracentesis was performed. Cytological examination of pleural liquid uncovered lung adenocarcinoma. A chest CT scan revealed hydropneumothorax and pericardial effusion. The patient was given an emergency chest tube and pericardiocentesis surgery. In conclusion, lung cancer is regularly found when looking at a few recently developing respiratory issues or disintegration of pre-existing conditions. Pleural emission regularly happens in lung malignancies. In this case, hydropneumothorax occurred due to repeated thoracentesis of a massive pleural effusion. Pericardial effusion is rare, thought to be due to metastases to the pericardium and obstruction of lymphatic drainage, requiring pericardial fluid analysis.

Keywords: Hydropneumothorax; Pericardial effusion; Adenocarcinoma; Complication

АБСТРАКТ

Рак легких является наиболее распространенным видом рака на сегодняшний день. Одним из часто встречающихся видов рака легких является аденокарцинома легких. Аденокарцинома легких связана с такими легочными осложнениями, как гидропневмоторакс и плевральный выпот, а также с сердечными осложнениями, такими как тампонада сердца и перикардиальный выпот, но встречается очень редко. В этом случае мы представляем редкий отчет из сельской больницы: у 52-летней женщины в течение 1 месяца ухудшалась одышка, сопровождавшаяся болью в груди и потерей веса. Рентгенография грудной клетки выявила правый плевральный выброс, после чего был проведен торакоцентез. Цитологическое исследование плевральной жидкости выявило аденокарциному легких. КТ грудной клетки выявила гидропневмоторакс и перикардиальный выпот. Пациенту была проведена экстренная грудная дренажная трубка и операция перикардиоцентеза. В заключение следует отметить, что рак легких регулярно обнаруживается при рассмотрении нескольких недавно развившихся респираторных проблем или распада ранее существовавших состояний. Плевральная эмиссия регулярно происходит при злокачественных новообразованиях легких. В этом случае гидропневмоторакс произошел из-за повторного торакоцентеза массивного плеврального выпота. Перикардиальный выпот встречается редко, считается, что он вызван метастазами в перикард и обструкцией лимфатического дренажа, что требует анализа перикардиальной жидкости.

Ключевые слова: Гидропневмоторакс; Перикардиальный выпот; Аденокарцинома; Осложнени

INTRODUCTION

Lung cancer is a malignancy that originates from the growth of cells in the lung parenchyma and bronchi. Lung cancer is the most often diagnosed cancer globally, representing around 12.4% of all cancer cases worldwide. It is also the primary cause of cancer-related fatalities.^{1,2} Based on the 2020 World Cancer Insights Report, lung cancer is the leading cause of cancer-related deaths, estimated to claim the lives of 1.8 million individuals worldwide. The five-year survival rate for lung cancer is below 12–15%.² By 2023, it is projected that approximately 238,340 individuals will be diagnosed with lung cancer, and around 160,000 people will die from lung cancer annually in the United States.^{1–3} The number had a significant surge in the subsequent decades, primarily attributed to the rise in the number of male and female smokers. This study will examine the aetiology, pathophysiology, and features of lung cancer, with a focus on the role of the multidisciplinary team in its management.^{3,4}

Lung cancer incidence is on the rise not only in wealthy nations but also in low-income countries. Recent data indicates that approximately 49.9% of unutilized contaminations are examined in developing countries. The incidence of lung cancer in Indonesia increases every year.^{3–5} In addition, the age of those affected is decreasing. Lung cancer has a significant prevalence and ranks as the third most prevalent cancer in Indonesia. Conversely, lung cancer is first among males. According to data from the World Health Organization (WHO), in 2020, there were 34,783 diagnosed cases of lung cancer in Indonesia, and the number of deaths attributed to lung cancer was 30,843 individuals.^{1–3}

We show the case of a 52-year-old lady analyzed with lung adenocarcinoma who displayed side effects of shortness of breath and was found to be enduring from pericardial emanation and hydropneumothorax. The patient's treatment plan focuses on managing hydropneumothorax and pericardial effusion with close monitoring after the procedure.

CASE PRESENTATION

A 52-year-old woman experienced shortness of breath, which had become increasingly severe one month before seeking treatment. The shortness of breath continued throughout the day and got worse. Patients also complain of chest pain and decreased appetite. The patient experienced a weight loss of 8–10 kg six months before treatment. The patient denied any previous history of pulmonary disease. Despite never having smoked, the patient's social history revealed decades of frequent exposure to firewood smoke while cooking. The patient arrived conscious, with blood pressure 90/75 mmHg, pulse 95 x/m, respiratory rate 32 x/m, axillary temperature 36.7°C, oxygen saturation 98% using an NRM 10 l/m nasal cannula, and body weight 32 kg.

A chest exam showed chest movement that wasn't even, the use of accessory muscles during breathing, weak vocal fremitus in the right lung, chest retraction, dullness in the right lung at ICS level 4, and a gradual loss of breath sounds in the right lung. However, there was no increase in JVP. The electrocardiography (EKG) examination revealed a low QRS voltage and electrical alternans (Figure 1).

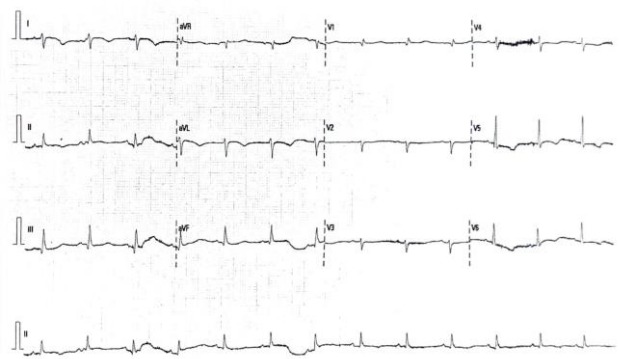


Figure 1. EKG showed low QRS voltage and electrical alternans

A chest radiology examination revealed right pleural effusion, atelectasis, and infiltration in the left perihilar (Figure 2).

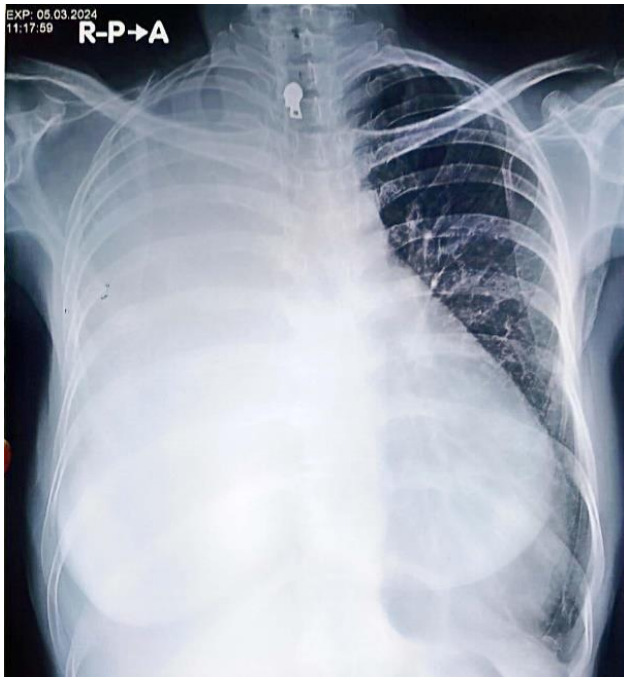


Figure 2. Chest X-Ray of the PA position showed right pleural effusion.

The patient underwent thoracentesis, the first of which obtained 1000 cc of clear, yellowish-colored fluid. The patient experienced clinical improvement after the procedure. Next, we performed three thoracentesis procedures using a total of 2000 cc of fluid, followed by a pleural fluid cytology examination, CT scan, and echocardiography.

Laboratory examination showed an increase in erythrocytes of 5.21 million μL (3.80–5.20 million μL) and an increase in platelets of 566,000 μL (150.000–440.000 μL); other laboratory results showed normal results. The results showed a decrease in MCV 70.8 fL (80 to 100 fL), a decrease in MCH 23.6 pg (26 to 34 pg), an increase in SGOT 115 /L (35), and a decrease in creatinine 0.45 mg/dL (0.60 to 1.10 mg/dL).

Cytological examination of pleural fluid was suggestive of lung adenocarcinoma. A chest CT scan with contrast revealed a right hydropneumothorax (Figure 3a), with an estimated fluid volume of 300 ml, and a suspected mass measuring 5.2 x 4.4 x 5.3 cm in the upper lobe of the right lung. The middle lobe and inferior lobe of the right lung appeared to collapse. The patient has a mild

left pleural effusion, with an estimated volume of 20 ml, a moderate-severe pericardial effusion, and visible lymph nodes at 2L (0.8x0.7cm), 2R (0.6x0.7cm), 5 (1.3x1.1cm), 6 (1.2x0.7cm), and 7 (1.7x1cm) (Figure 3b).

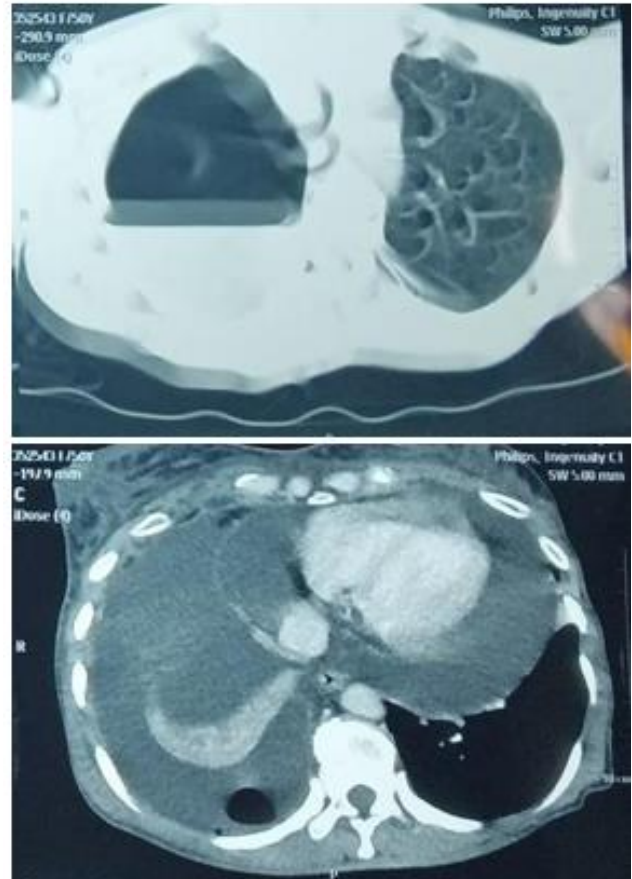


Figure 3. Chest CT scan showed right hydropneumothorax (a) and pericardial effusion (b).

Following the diagnosis of hydropneumothorax, the patient underwent emergency WSD surgery (Figure 4a), resulting in the collection of positive undulating serous xanthochrome fluid within a range of +/- 500 cc. Repeated chest X-ray examination after installing a WSD on the right lung showed that the envelope on the right hemithorax was relatively reduced, and the right pneumothorax was somewhat gone (Figure 4b).



Figure 4. The patient after the installation of the chest tube procedure (a) and right pneumothorax relatively reduced (b).

The patient underwent an echocardiography procedure before the pericardiocentesis procedure. An echocardiography test showed that both the left and right ventricles had normal systole, the global normokinetic LVH concentration was normal, and there was a lot of fluid around the heart that showed signs of impending tamponade (Figure 5). Based on these considerations, it is necessary to carry out immediate pericardiocentesis.

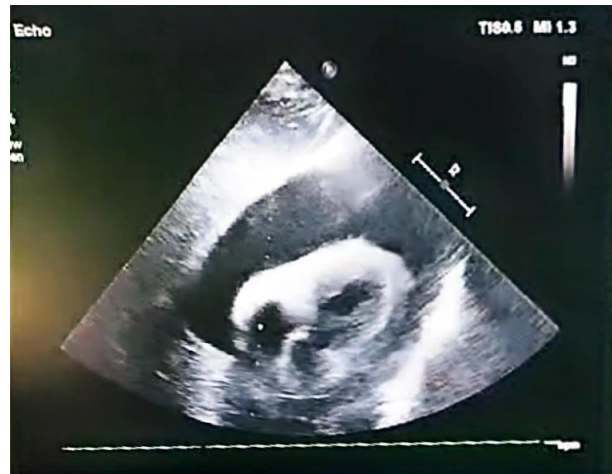


Figure 5. Echocardiography showed pericardial effusion.

The patient maintained a bed rest position of 45° and experienced a decrease in symptoms of chest pain and shortness of breath; muscle movements assisting breathing decreased; blood pressure increased to 112/98 mmHg; pulse 85x/m; breathing 22x/m; oxygen saturation 98%; and nasal cannula 3 lpm. Pericardial effusion appeared relatively reduced after the pericardiocentesis procedure (Figures 6a, 6b). On the first day of pericardiocentesis treatment, we obtained 172 cc of red fluid in the first 8 hours, 47 cc in the second 8 hours, and 31 cc of reddish clear fluid in the third 8 hours. We treated the patient for 12 days. We then referred the patient to a center that has complete facilities to treat lung adenocarcinoma.



Figure 6. The patient after the pericardiocentesis procedure (a) and echocardiography showed the pericardial effusion relatively reduced (b).

DISCUSSION

We present the case of a 53-year-old woman who spent decades cooking with firewood smoke. The patient complained of worsening shortness of breath one month before treatment. The patient experiences continuous shortness of breath throughout the day, which worsens without any external influence. Patients also complain of chest pain that gradually worsens but does not spread, as well as a decrease in appetite. The patient experienced a weight loss of 8–10 kg for 6 months before treatment. The patient denied any history of diseases such as asthma, tuberculosis, and diabetes mellitus.

The patient arrived conscious, with unstable vital signs and a body weight of 32 kg. On physical examination, the lymph hubs within the neck and chest were not substantial. The respiratory examination shows asymmetrical chest movement. The trachea isn't displaced. The right side experiences reduced lung development, reduced vibration, and vocal fremitus. The correct side of the chest also exhibits generalized delicacy. The auscultation examination revealed dullness in the right lung at ICS level 4, a reduction in breath sounds in the right lung, and no rise in JVP. Electrocardiography (ECG) shows low QRS voltage and electrical alternans. We believe that the immersion of the heart in pericardial fluid is the cause of the nonspecific ECG findings. Radiological findings revealed a right pleural effusion accompanied by atelectasis, as well as an infiltrate in the left perihilar.

We removed pleural fluid three times using thoracentesis, removing a total of 2000 cc of fluid. The cytopathological examination of the pleural fluid revealed several groups of suspicious cells, including large epithelial distribution, round oval nuclei, pleomorphic, hyperchromatic, and coarse chromatin. Some of these cells contained real nuclei and sufficient cytoplasm, while others formed a glandular structure with a background of cell distribution, mononuclear inflammation, macrophages, and blood foamy cells. In addition, smears of atypical cells revealed metastatic lesions. A chest CT scan with contrast revealed a right hydropneumothorax with an estimated fluid volume of 300 ml, along with a suspected mass in the superior lobe of the right lung. The middle lobe and inferior lobe of the right lung appear collapsed. Furthermore, moderate-severe pericardial effusion was found.

Lung cancer is divided into two groups: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). This classification is based on the infinitesimal appearance of tumor cells. These two cancers develop and spread, and they have distinct medicines and forecasts. SCLC represents a small percentage of lung cancers, approximately 10–15%.^{2,8} This type of

lung cancer is the most aggressive of all, grows rapidly, and has a poorer outlook. Cigarette smoke exposure strongly correlates with SCLC. SCLC rapidly metastasizes to numerous areas within the body and is most frequently found after it has spread widely. NSCLC is the most common type of lung cancer, making up approximately 85% of all cases, and has a significantly higher prognosis. The type of cells present within the tumor determines the three primary types of NSCLC: adenocarcinoma, large cell carcinoma, and squamous cell carcinoma.^{8,9}

The most common NSCLC is adenocarcinoma. Most adenocarcinomas occur in the lungs' outer or fringe regions. The malady, moreover, tends to spread to adjacent lymph hubs. Lung adenocarcinoma is classified into four sorts: to be specific, adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), invasive adenocarcinoma, and other sorts of adenocarcinoma.⁷⁻¹⁰ AIS may be a subtype of adenocarcinoma that regularly happens in different areas within the lungs, spreads along the alveolar dividers, and frequently looks like pneumonia on X-ray pictures. The frequency is increasing, and it occurs more often in women. Patients with AIS cancer tend to have a better prognosis when removed early compared with other lung cancers.⁶⁻⁹

Smoking is the primary factor responsible for the development of lung adenocarcinoma. Cigarette smoke includes several carcinogens, and the likelihood of primary or secondary exposure rises in direct proportion to the level of exposure.^{4,8,9} Our diligent individual did not engage in smoking, but had been consistently exposed to the smoke emitted from burning fuel when cooking for many years. Although adenocarcinoma is commonly linked to smoking, it is important to note that nonsmokers, particularly women, might also be vulnerable to this form of cancer. Additional risk factors include a familial predisposition to lung cancer, as well as exposure to other substances such as combustion gases, silica, asbestos, radon, and heavy metals. The most prevalent cause of tumor progression in

NSCLC, occurring in 52% of cases, is genetic alterations within the p53 gene.⁶⁻⁸

In a lung adenocarcinoma case, local spread may include coordinate spread to the pleura, stomach, pericardium, or bronchi; progressed infection may include the mediastinum, incredible vessels, trachea, esophagus, spine, or spread to adjacent clears out.¹⁷⁻¹⁹ Lymph node metastases start from the peribronchial lymph nodes, then move to the mediastinal or subcarinal lymph nodes, and after that to the contralateral lung. Far-off metastases incorporate spread to the contralateral lobe, pleural nodules, threatening pleural or pericardial effusion, or far off sites such as the brain, bone, or liver.¹¹⁻¹⁵

This persistent, local spread is characterized by malignant pleural effusion (MPE). Lung cancer is the primary cause of MPE, accounting for 8-15% of cases, followed by breast cancer and lymphoma.^{10,14} Approximately 15% of patients with non-small cell lung cancer (NSCLC) have malignant pleural effusion (MPE). The prognosis for patients diagnosed with MPE is often a survival period of 3 to 12 months after the initial diagnosis. Malignant pleural effusion (MPE) is defined by the existence of cancerous cells in the fluid around the lungs, and it is estimated to have an annual incidence of approximately 150,000 cases. Approximately 90% of lung cancer cases exhibit an ipsilateral pleural association. Contralateral pleural effusion is found in 10 percent of patients. While small cell carcinoma cells directly enter the pleura, non-small cell lung cancer indirectly disrupts pleural lymphatic function.⁸⁻¹³

Chest X-ray examination is the initial diagnostic procedure for suspected cases of MPE. This examination is capable of identifying pleural effusion volumes over 200 cc. However, in patients with malignant pleural effusion (MPE), the volume of pleural effusion typically falls between the range of 500 to 2,000 cc. The primary features of MPE include the presence of nucleated cells (50-70%), eosinophils, erythrocytes with a pH of 7.3, lymphocytes among the nucleated cells, and glucose levels below 60 mg/dL.^{10,13,14}

Aspiration of pleural fluid may increase the risk of pneumothorax or hydropneumothorax. In any case, lung cancer rarely exhibits de-novo events within the context of discussion and fluid, or even within the pleural depression itself. The assessed frequency is around 0.03-0.05% for essential lung cancer.¹⁶ The precise component of pneumothorax caused by lung cancer is not well caught. Several ideas have been put forward, such as the rupture of necrotic neoplastic tissue within the pleural depth, the rupture of necrotic tumor nodules, or the necrosis of metastases that have spread sub-pleurally. In this case, repeated thoracentesis caused hydropneumothorax. Previous studies have reported an incidence of hydropneumothorax associated with thoracentesis of 5.2–26% without using ultrasound and 0.61–5% using ultrasound.^{15,16}

Hydropneumothorax is a medical emergency, where there's fluid within the pleural depression that causes lung tissue to break down. The most common causes of hydropneumothorax in patients experiencing thoracentesis are the coordinate cut when embedding the needle or catheter, the presentation of discuss through the needle or catheter into the pleural depth, and the inability of the ipsilateral lung to completely grow after waste of expansive amounts of liquid.^{10,14} When the lung is unable to expand, brief parenchymal pleural fistulas form, causing fluid to spill into the pleural cavity. The patient was then managed by installing an intercostal drainage to remove fluid and air.^{18,20}

Pericardial effusion can appear in various forms. Our patient's primary complaint was shortness of breath. However, some patients may exhibit symptoms of cardiac tamponade, such as increased pulse, low tension, pulsus paradoxus, jugular vein distention, and heart sound disorders. Diagnosis necessitates a heightened level of suspicion because to the potential variability in presentation.^{5,14} Physical examination features can potentially indicate the presence of cardiac tamponade, however they may not be present in cases of minor effusions. Additional non-specific

observations include an enlarged heart seen on chest x-rays and irregular electrical patterns or weak signal complexes on an electrocardiogram (ECG). Echocardiography continues to be the primary imaging method used for diagnosis, revealing the presence of effusion, with or without tamponade.¹⁸⁻²²

In Western countries, pericardial effusion is generally idiopathic, but can also be caused by malignant diseases such as lung cancer, breast cancer, and lymphoma/leukemia. Up to 50% of cases often have lung cancer as the primary tumor affecting the pericardium. In our patient's case, the pericardial effusion was caused by lung adenocarcinoma.^{3,17} Almost 10-12% of cancer-related autopsies typically reveal pericardial effusion, which often goes unnoticed. Pericardial metastases, lymphatic drainage obstruction, chemotherapy drugs, or radiotherapy can cause the formation of pericardial effusion in malignant patients. The ability to differentiate these causes depends on the results of pericardial fluid analysis. The pericardial effusion found in our patient was thought to be caused by intrapericardial tumor metastasis, but pericardial effusion analysis was not investigated due to limited resources.^{17,18}

We adjust the pericardial effusion treatment based on the clinical symptoms and the effusion size. We found that our patient was experiencing impending tamponade and hemodynamic instability, necessitating pericardiocentesis. Patients who have unstable vital signs may consider percutaneous or open pericardiotomy.^{17,19} The prognosis for malignant pericardial effusion is very poor, especially in patients who have a history of cancer before symptoms appear. This may be influenced by the severity of the disease. At monthly follow-up visits, perform echocardiography and chest X-rays to monitor for recurrent fluid collections. Our patient was immediately referred to a center that has complete facilities for the treatment of adenocarcinoma.^{18,19}

By the time of diagnosis, most lung cancers are already progressing, making the prognosis exceptionally dire. Lung cancer has a five-year

survival rate of only 12%. The 5-year survival rate for arrange 1 is 70-85%. At advanced stages of the disease, the survival rate significantly decreases to less than 30%. For distant metastases, the 5-year survival rate is less than.^{5,21} Therefore, the current focus is on lung cancer screening and prevention. A multidisciplinary group approach can help reduce lung cancer frequency and prevalence. We should educate the public about smoking habits, occupations that involve smoke, exposure to particulate matter (like asbestos), and the implementation of appropriate safety precautions. People who have high-risk factors should consider lung cancer screening. A lung CT scan can presently be utilized to screen people over 50 a long time of age who have different chance components for lung cancer.^{18,22}

CONCLUSION

The larger part of lung cancers is analyzed, whereas exploring a few unused respiratory indications or compounding of a pre-existing respiratory condition. Pleural effusions frequently occur in lung malignancies. In this case, hydropneumothorax occurred due to repeated thoracentesis of a massive pleural effusion. In lung malignancies, pericardial effusion is rare. In this case, it appears to be due to metastases to the pericardium and obstruction of lymphatic drainage, requiring pericardial fluid analysis

ACKNOWLEDGMENT

I would like to thank everyone involved

DECLARATIONS

GAS and KK designed the study and collected data. GAS, KK, and HAW prepared the manuscript. GAS, KK, HAW, and ELM reviewed the manuscript. The final manuscript was approved by all authors.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2023. Atlanta; American Cancer Society: 2023.
2. National Institute of Health. Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC). 2022.
3. Asmara OD, Tenda E, Singh G, et al. Lung Cancer in Indonesia. *Journal of Thoracic Oncology*. 2023;18(9):1134-1145. DOI: <https://doi.org/10.1016/j.jtho.2023.06.010>
4. Li C, Lu H. Adenosquamous carcinoma of the lung. *Onco Targets Ther*. 2018;11:4829-4835. DOI: <https://doi.org/10.2147/OTT.S164574>
5. Rami PR, Call S, Dooks C, et al. Lung cancer staging: a concise update. *Eur Respir J*. 2018;51(5) DOI: <https://doi.org/10.1183/13993003.00190-2018>
6. Majmundar N, Shao B, Assina R. Lung adenocarcinoma presenting as intramedullary spinal cord metastasis: Case report and review of literature. *J Clin Neurosci*. 2018;52:124-131. DOI: <https://doi.org/10.1016/j.jocn.2018.03.030>
7. Sung H, Ferlay J, Siegel RL. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71: 209-249. DOI: <https://doi.org/10.3322/caac.21660>
8. Cheng Y, Wang Q, Li K. Overall survival (OS) update in ALTER 1202: anlotinib as third-line or further-line treatment in relapsed small-cell lung cancer (SCLC). *Annals of Oncology* 2019; 30: v711 DOI: <https://doi.org/10.1093/annonc/mdz264.002>
9. Kolbas I, Evman S, Tezel C. Spontaneous pneumothorax in the elderly: a sign of malignancy? *Asian Cardiovasc Thorac Ann* 2019; 27: 294-297. DOI: <https://doi.org/10.1177/0218492319831840>
10. Kort S, Keizer MB, Schouwink H, et al. Diagnosing Non-Small Cell Lung Cancer by Exhaled Breath Profiling Using an Electronic Nose: A Multicenter Validation Study. *Chest*. 2023;163(3):697-706 DOI: <https://doi.org/10.1016/j.chest.2022.09.042>
11. Si X, Li Z, Wang H. Management of anlotinib-related adverse events in patients with advanced non-small cell lung cancer: experiences in ALTER-0303. *Thorac Cancer* 2019;10: 551-556. DOI: <https://doi.org/10.1111/1759-7714.12977>
12. Sappington D, Helms S, Siegel E, et al. Diagnosis of lung tumor types based on metabolomic profiles in lymph node aspirates. *Cancer Treat Commun*. 2018;14:1-6. DOI: <https://doi.org/10.1016/j.ctarc.2017.08.002>
13. Jiang G, Chen C, Zhu Y, et al. [Shanghai Pulmonary Hospital Experts Consensus on the Management of Ground-Glass Nodules Suspected as Lung Adenocarcinoma (Version 1)]. *Zhongguo*. 2018;21(3):147-159.

14. Paliwal P, Rajappa S, Santa A, et al. Clinical profile and outcomes of patients with Stage IV adenocarcinoma of lung: A tertiary cancer center experience. *Indian J Cancer*. 2017;54(1):197-202. DOI: <https://doi.org/10.4103/0019-509X.219595>
15. Sun YL, Gao F, Gao P, et al. [Diagnostic value of contrast-enhanced CT scans in identifying lung adenocarcinomas manifesting as ground glass nodules]. *Zhonghua Zhong Liu Za Zhi*. 2018;40(7):534-538.
16. Japuntich SJ, Krieger NH, Salvas AL, et al. Racial Disparities in Lung Cancer Screening: An Exploratory Investigation. *J Natl Med Assoc*. 2018 Oct;110(5):424-427. DOI: <https://doi.org/10.1016/j.jnma.2017.09.003>
17. Yang S, Yu X, Fan Y, et al. Clinicopathologic characteristics and survival outcome in patients with advanced lung adenocarcinoma and KRAS mutation. *J Cancer*. 2018;9(16):2930-2937. DOI: <https://doi.org/10.7150/jca.24425>
18. Jao K, Tomasini P, Kamel-Reid S, et al. The prognostic effect of single and multiple cancer-related somatic mutations in resected non-small-cell lung cancer. *Lung Cancer*. 2018 Sep;123:22-29. DOI: <https://doi.org/10.1016/j.lungcan.2018.06.023>
19. Imazio, Deerrari G. Cardiac tamponade: an educational review, *European Heart Journal. Acute Cardiovascular Care*. 2021;10(1):102–109. DOI: <https://doi.org/10.1177/2048872620939341>
20. He B, Yang Z, Zhao P, et al. Cytopathologic analysis of pericardial effusions in 116 cases: Implications for poor prognosis in lung cancer patients with