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CASE REPORT: COMPREHENSIVE MANAGEMENT OF PATIENTS WITH LUNG CANCER SUSPECTED OF BRAIN METASTASES ACCOMPANIED BY PNEUMONIA

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Abstract: Case Report: Comprehensive Management of Patients with Lung Cancer Suspected of Brain Metastases Accompanied by Pneumonia. *Worldwide, the most frequently diagnosed cancer is lung cancer. The chief complaints of the disease are dyspnea and chest discomfort. Lung cancer causes an immunodeficiency state in the body, which can lead to infection. Lung cancer is also known to complicate cerebrovascular disease, causing an infarction or stroke. This case report aims to elucidate the etiology of lung cancer-associated infection and cerebrovascular disease and effectively detect and heal the disease. A 58-year-old man came with his family to the emergency department of Abdoel Moeloek Hospital, Lampung Province with complaints of shortness of breath that worsened, accompanied by complaints of cough and pain in the right chest. The doctor conducted a detailed examination and then the doctor diagnosed the patient with community-acquired pneumonia because of immunodeficiency from lung squamous cell carcinoma, hemiparesis dextra, dysarthria due to cerebrovascular disease, and malnutrition. The doctor administered oxygen and a nebulizer to the patient. Subsequently, he was hospitalized for symptomatic therapy and antibiotic treatment.*

Keywords: *Cerebrovascular disease, community-acquired pneumonia, lung cancer, smoking.*

Abstrak: Laporan Kasus: Penatalaksanaan Komprehensif pada Pasien Kanker Paru yang Diduga Metastasis Otak yang Disertai Pneumonia. Kanker paru merupakan penyakit keganasan nomor satu di dunia. Manifestasi utama dari penyakit ini adalah rasa tidak nyaman di dada dan sesak napas. Kanker paru menyebabkan keadaan imunodefisiensi yang dapat menyebabkan infeksi. Kanker ini juga diketahui berhubungan dengan penyakit cerebrovaskular, menyebabkan serangan jantung atau stroke. Laporan kasus ini bertujuan untuk menjelaskan etiologi infeksi terkait kanker paru-paru dan penyakit serebrovaskular, serta metode untuk mendeteksi dan mengobati kondisi ini secara efektif. Pria setengah baya berusia 58 tahun diantar oleh keluarganya ke unit gawat darurat RSUD Abdoel Moeloek Provinsi Lampung kerena menderita sesak napas yang semakin parah, disertai batuk dan nyeri dada sebelah kanan. Setelah memeriksa riwayat medis pasien secara rinci, pemeriksaan fisik, dan pengujian lebih lanjut, dokter mendiagnosis pasien dengan pneumonia yang didapat dari komunitas karena defisiensi imun akibat karsinoma sel skuamosa paru, hemiparesis dextra, disartria akibat penyakit cerebrovascular, dan kekurangan gizi. Dokter memberikan oksigen dan nebulizer pada pasien. Dia kemudian dirawat di rumah sakit untuk terapi simtomatik dan pengobatan antibiotik.

Kata Kunci: *Community-acquired pneumonia*, kanker paru, merokok penyakit serebrovaskuler.

INTRODUCTION

Lung cancer has continuously been the most common type of cancer worldwide since 1985, both in terms of how frequently it occurs and how many people it causes to die. Globally, lung cancer is the leading cause of cancer-related deaths (17.6%) and accounts for the largest percentage of new cancer cases (12.4%) (Dela et al., 2011). Over 234,000 new cases of lung cancer and over 154,000 lung cancer-related deaths occur in the US each year, according to the American Cancer Society. Based on the 2020 Global Cancer Statistics report, lung cancer maintained its position as the primary cause of cancer-related mortality globally, resulting in around 1.8 million deaths (Siddiqui et al., 2023).

One subtype of non-small cell lung cancer (NSCLC) is squamous cell carcinoma of the lung, also known as squamous cell lung cancer. People attribute this shift to cigarette smoking habits, but there's no definitive evidence to support it. Squamous cell lung cancers frequently manifest in the center region of the lung or the primary airway, such as the left or right bronchus. Smoking is the main factor that causes cellular change. Approximately 80% of male cases and 90% of female cases demonstrate the correlation between smoking and lung cancer. (Sabbula et al., 2024)

Pneumonia survival rates were significantly lower in NSCLC patients compared to non-cancer and other cancer patients. Pneumonia is a significant cause of hospital stays for patients with non-small cell lung cancer (NSCLC) and presents a separate risk factor for in-hospital death and readmission requirements. (Patel et al., 2020). On the other hand, lung cancer is increasingly being recognized as a systemic issue linked to diabetes, obesity, and hypertension, all of which are known risk factors for heart disease. It has been proposed that lung cancer is associated with an increase in cardiovascular risk, namely the risk of coronary heart disease and stroke. (Bignami et al., 2018). In this case report, we describe a patient undergoing ongoing lung cancer treatment who also has community-acquired pneumonia, with hemiparesis dextra, and dysarthria due to cerebrovascular disease.

CASE REPORT

A 58-year-old man was brought to the emergency room of Abdoel Moeloek Regional General Hospital in the province of Lampung by his family on March 20, 2024. The patient claims that his shortness of breath has deteriorated since 4 days ago, after beginning one year ago. Further investigation revealed that the patient had been suffering from a phlegm-filled cough for a year, which had deteriorated in 4 days. The phlegm is yellowish in color. For a year, the patient also reported having pain in his right chest, which intensified in a week and moved to his back.

The patient had a history of tuberculosis and was now on anti-tuberculosis medication. Due to the complaints not improving, the patient received a CT scan in July 2023, which revealed a possible lung tumor. The pathology anatomy of the bronchoscopy revealed a squamous cell carcinoma type of lung tumor, which verified the diagnosis. The patient received six cycles of chemotherapy with carboplatin and paclitaxel, beginning in August 2023. The most recent thorax CT scan with contrast revealed that the patient was stable. (figure 1).

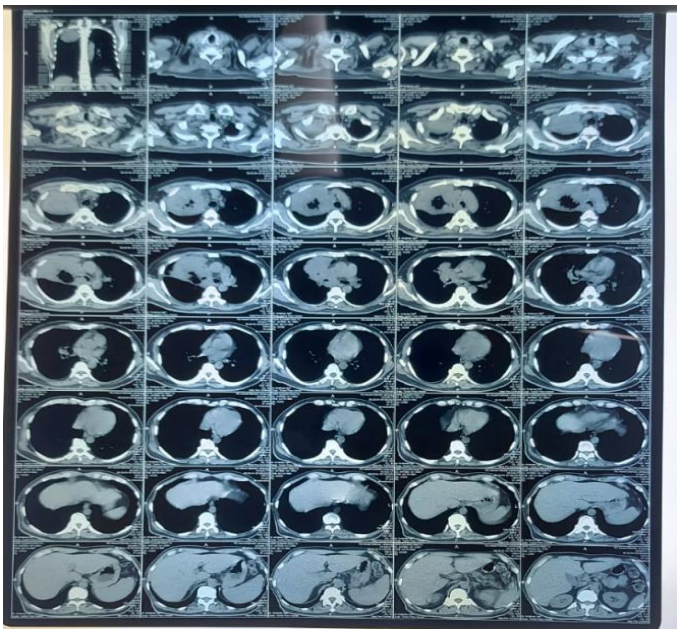

Figure 1. A stable condition Thorax CT Scan with contras

Upon physical examination on the day of admission, his overall health appeared to be moderately compromised. Consciousness: 139 beats per minute, blood pressure of 102/63 mmHg, and somnolence. With an oxygen 3 lpm nasal cannula, the saturation was 96%, the temperature was 36.9 °C, and the respiratory rate was 28 breaths per minute.

Examining the thoracic area reveals that the right chest wall moves less in both static and dynamic situations; palpation reveals a difficult-to-examine fremitus tack; the right basal hemithorax experiences weakened percussion; auscultation reveals a weak vesicular sound in the right hemithorax, bronchovesicular sounds in the left hemithorax, rales in both hemithorax and no wheezing. In the midclavicular line, the ictus cordis can be felt between the V ribs; the border of the heart is within normal limits. In the neck area, the jugular venous pressure rises to 5+1 cmH20. On a head examination, the tongue was tilted to the left. The physical examination of the abdomen was within normal limits, but the extremities were difficult to examine.

Additional examinations include laboratory and radiological ones. On March 20th, 2024, there were decreased hemoglobin (9,9), lymphocytes (10), potassium (3,0), increased leukocytes (21,500), and neutrophils (84), giving the impression of acute infections. We also performed a blood gas analysis, interpreting it as hypercapnia and hyperoxemia (table 1).

Table 1. Laboratory Examinations on March 19-20th 2024. The interpretation were Anemia, Leukocytosis, Shift to the left, Hypokalemia Hypercapnia, and Hyperoxemia

	RSAM 20/3/2024	Normal range
Complete Blood Counts: Hb/Ht/ WBC/ Platelets	**9.9*** /38 / **21.500***/396.000	13,2-17,3/40-52/3.800-10.600/150.000-440.000
Differential count Neutrophils/Lymphocytes/Monocytes/Eosinophils /Basophils	**84*/10***/0/0/0/6	50-70/25-40/2-8/0-1/2-4/3-5
Na/K/Ca/Cl	139/**3.0*/**9.6/101	135-147/3,5-5,0/8,95-105
Ureum / Creatinine	67/0.97	18-55/0,6-1,2
Random Blood sugar test	106	70-200
Albumin	2.9	3.5-5.2
SGOT/SGPT	33/22	0-35/0-35

	19/03/2024	Normal Range
pH	7,35	7,35 – 7,45
pCO2	**50.5***	35 – 45
pO2	**192***	80,0 – 108,0
HCO3-	28.3	23,0 – 29,0
TCO2	30	24,0 – 30,0
BEecf	+3	
O2 sat	99 %	
AaDO2	101.375	
FiO2 needed	**0,23 (NK 1 lpm)**	

On the day of admission, an x-ray showed an opacity on the superior lobe of the right hemithorax and another opacity on the lower lobe with a clear border. Both hemithoraxes also showed infiltration, which meant there was a lung tumor and pneumonia on both sides (Figure 2). The USG examination also confirmed the presence of a tumor (Figure 3). We performed a noncontrast brain CT scan because the patient was sleepy on the day of admission. The scan revealed a lacunar infarction in the left basal ganglia area, an ischemic-like hypodense lesion in the right occipital subcortical EC, and significant atrophy, particularly in both parietal areas. On March 1st, 2024, a brain CT scan confirmed the diagnosis of atrophy cerebri.

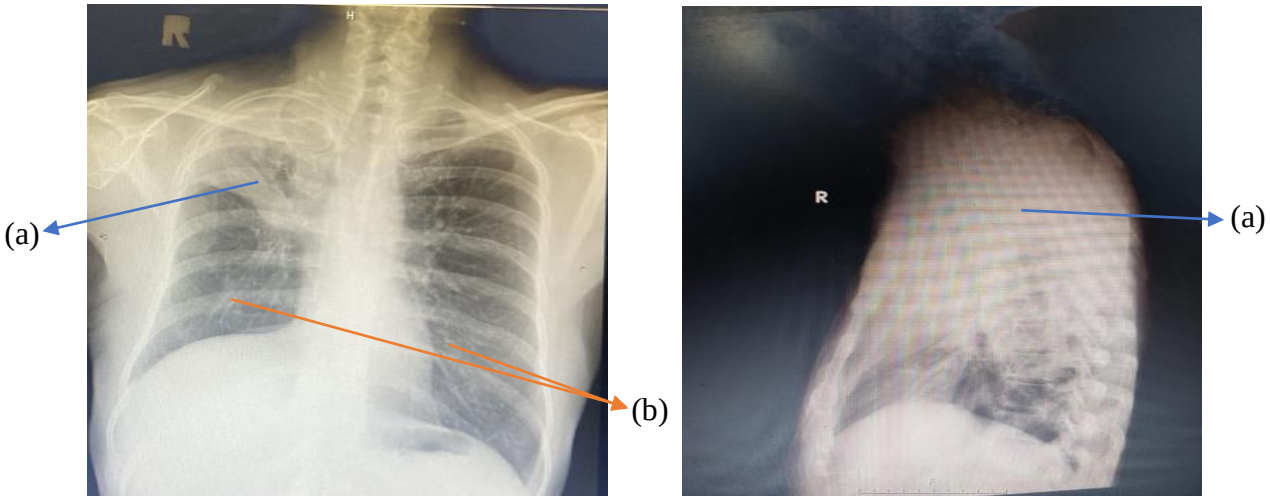

Figure 2. A Chest X-ray serial examination, (a) opacity on the superior lobe of the right hemithorax and (b) Bilateral lung infiltrate

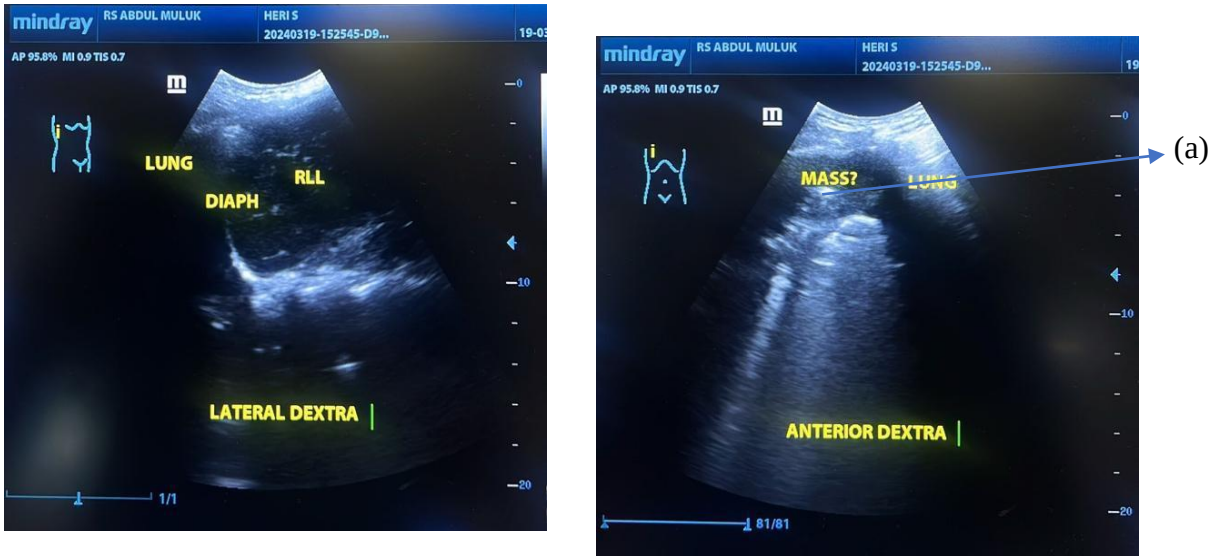

Figure 3. An Ultrasonography examination, (a) a tumor on the anterior dextra lung

We have determined the patient's clinical diagnosis to be community-acquired pneumonia based on the patient's history, physical examination, and supporting examinations. The community-acquired pneumonia secondary to immunodeficiency due to lung carcinoma type squamous cell carcinoma, hemiparesis dextra, dysarthria due to cerebrovascular disease, and malnutrition.

The hospitalized patient received symptomatic therapy, which included Oxygen 3 lpm nasal cannula, levofloxacin injection 750 mg/24 hours, nebulizer ipratropium bromide 0,52 mg + salbutamol sulfate 3,01 mg/6 hours, paracetamol 3 x 500 mg, NAC 3 x 200 mg, and KCL drip 1 flash in natrium chloride 0,9% 500 ml/24 hours.

DISCUSSION

Patients with lung cancer are more likely to interact with other illnesses. An immune system should be able to recognize and eliminate cancerous cells. Tumors have evolved multiple strategies to elude host immune-mediated monitoring. These strategies may include the activation of defective T-cell signaling, the expansion of local immunosuppressive microenvironments, and the overexpression of inhibitory immunological checkpoints. (Budisan et al., 2021). Age, family history, exposure to secondhand smoke, and work-related exposure to metals, minerals, or asbestos are additional risk factors for lung squamous cell carcinoma. (Sabbula et al., 2024). Therefore, we should carefully treat lung cancer patients and manage any potential complications.

Excessive lung cell proliferation, which damages healthy tissue and may spread to other organs, is a hallmark of lung cancer (Heo et al., 2020). With the highest death rate, this illness is the second most common malignancy diagnosed globally, after breast cancer (Hana and Faizah, 2023). Tuberculosis (TB) is caused by Mycobacterium tuberculosis (MTB), which primarily localizes in the lungs. 2020 saw TB overtake COVID-19 as the infectious disease with the second-highest global death rate. Following India, Indonesia continues to have the world's highest TB burden. (WHO, 2023). While both tuberculosis and lung cancer have significant incidence and fatality rates, it is extremely uncommon for these two illnesses to coexist. Previous research has extensively publicized case reports involving tuberculosis and lung cancer. Currently, there is no solid evidence linking tuberculosis to lung cancer incidence. However, researchers have proposed theories to elucidate the potential processes underlying these two illnesses. The most likely explanations are that either TB raises the incidence of lung cancer, lung cancer triggers MTB reactivation, or the two conditions coexist without any connection (Ho and Leung, 2018). According to one study, other theories explain how the two diseases could coexist. First, a carcinoma that develops in the TB region causes the disease's former focal lesions to reactivate. The evolution of TB scarring into cancer is the next step. While they might happen at similar times, lung cancer and tuberculosis are unrelated diseases. Last is TB-related secondary cancer infection.

The close relationship between lung cancer symptoms and x-ray images of lesions makes it take longer to diagnose people who have had tuberculosis in the past. When the cancer stage has progressed, a new diagnosis is established (Parker et al., 2018). There is currently no research on the coexistence of tuberculosis and lung cancer in Indonesia, despite the publication of several case reports.

It is well known that several infectious infections are linked to lung cancer. Lung cancer may arise as a result of the persistence of microbes in the lung due to mechanisms like systemic inflammatory pathways. It's commonly known that lung cancer infection causes chronic inflammation that predates tumor growth and has a big impact on how well a treatment works. In fact, bacterial and viral illnesses can trigger inflammatory signaling pathways and inflammatory cells (Budisan et al., 2021).

Prolonged inflammation has been linked to the development of lung cancer. Proinflammatory chemicals like prostaglandins, chemokines, and cytokines accumulate and infiltrate, which are its defining features. These elements have the ability to promote several different processes, including angiogenesis, metastasis, and cell division. According to recent studies, three different types of membrane receptors—Toll-like receptors (TLRs), pattern recognition receptors (PRRs), and clusters of differentiation—can identify proinflammatory cytokines, microbes, microbial products, signaling molecules, proteins, and nucleic acids. Moreover, advancements in metastasis and alterations in the tumor microenvironment (TME) have been noted by researchers. Direct exposure to microbial oncogenes, toxins,

and reactive oxygen species (ROS) produced by microbial activity can result in mutations. Furthermore, the dysregulation of processes governing cell cycle control, apoptosis, and proliferation leads to carcinogenesis. Therefore, improving knowledge of the part microbes play in inflammation-induced cancer may ultimately result in the development of antimicrobials to stop the start or spread of cancer (Budisan et al., 2021).

Even after cigarette use was reduced, there was still a connection between tuberculosis and lung cancer. In TB patients, the risk of cancer was 2.5 times greater. Prior studies carried out in Korea showed that nonsmokers had a lower risk of lung cancer, while smokers and TB patients had a higher risk than ex-smokers. The study did find, however, that although the risk rates for smokers and non-smokers were similar, tuberculosis may be a risk factor for the development of lung cancer in non-smokers (Nugroho and Wati, 2020). Even in cases where a clinical and microbiological diagnosis of tuberculosis has been made, a CT scan designed specifically to identify lung cancers should be used to evaluate patients who have high-risk factors for lung cancer, such as being older than 55 and smoking more than 30 packs annually (Liu et al., 2017).

Pneumonia is a common presenting symptom for patients with lung cancer and a major cause of morbidity and death during the course of the disease. The complex pathophysiology of infection is influenced by co-morbidities, iatrogenic immunosuppression, and the underlying illness. This can include opportunistic infections resulting from immunosuppression in lung cancer cases, diseases caused by tumor obstruction of the airways, and infective COPD exacerbations (Patel et al., 2020).

Community-acquired pneumonia, or CAP, is one of the leading causes of mortality and morbidity worldwide. According to the Global Burden of Disease report from 2017, pneumonia is estimated to be the cause of 2.6 million deaths globally. The bulk of these deaths (75%) happen in two age groups: adults over 70 years old (1.13 million deaths) and children under five years old (809,000 death cases). Two-thirds of deaths due to pneumonia occur in countries in the Sub-Saharan Africa region, South Asia, and Southeast Asia. In Southeast Asia, 14% of deaths occur among children under five and 60% among the elderly. According to Basic Health Research data (Riskesdas) from 2018, the prevalence of pneumonia in Indonesia, as determined by medical professionals' diagnoses, is 2%; this represents an increase from 1.8% in 2013. Pneumonia is in the top 10 hospital admissions by the proportion of cases; most were men (53.95%), with a crude fatality rate (CFR) of 7.6%, the highest compared to other diseases (Patel et al., 2020).

The American Thoracic Society and the Infectious Diseases Society of America Patients displaying clinical symptoms of community-acquired pneumonia (CAP) should be carefully characterized using the criteria for defining severe community-acquired pneumonia (table 2). Patients must meet one major criterion or at least three minor criteria (Patel et al., 2020).

Table 2. Criteria for CAP

Minor Criteria
Respiratory rate ≥ 30 breaths/min
Pa_{O2}/FI_{O2} ratio ≤ 250
Multilobar infiltrates
Confusion/disorientation
Uremia (blood urea nitrogen level ≥ 20 mg/dl)
Leukopenia (white blood cell count < 4,000 cells/µl)
Thrombocytopenia (platelet count < 100,0000/µl)
Hypothermia (core temperature < 36**°**C)

Hypotension necessitates aggressive fluid resuscitation
Major criteria
Respiratory failure necessitates mechanical ventilation
Septic shock with a need for vasopressors
Infiltrate increases > 50%

When treating community-acquired pneumonia without coexisting medical conditions, the first course of treatment is either monotherapy using a macrolide (such as azithromycin, clarithromycin, or erythromycin) or, if the patient prefers take-home medication, doxycycline. On the other hand, patients who have beta-lactam (high-dose amoxicillin or amoxicillin-clavulanate, cefuroxime, and cefpodoxime) and macrolide in addition to fluoroquinolone (high-dose levofloxacin, moxifloxacin, and gemifloxacin) should also have comorbidities like lung cancer, liver disease, alcohol use disorder, diabetes mellitus, and smoking. In this case, we administer levofloxacin to the patient. For emergency requirements, the patient is given oxygen and a nebulizer (Ho and Leung, 2018).

Numerous investigations have linked pulmonary problems to advanced age. Studies have indicated that older patients with advanced lung cancer who received cytotoxic chemotherapy have an increased risk of developing bacterial pneumonia. Pneumonia following surgery was more common in lung cancer patients 64 years of age or older. The compromised physical health of the elderly puts them at a higher risk of contracting pneumonia due to multiple factors. One major factor that contributes to pneumonia is immune system dysfunction. Aspiration pneumonia can occur in older patients who have difficulty swallowing due to aspirated oropharyngeal secretions entering the lung (Jung et al., 2017).

For both patients receiving cytotoxic chemotherapy as part of their treatment and those with lung cancer in general, smoking was a common risk factor for the development of pneumonia. Research clearly links smoking to poorer diets, higher alcohol use, decreased physical activity, and lower socioeconomic position. Research has established a link between smoking and community-acquired pneumonia. Smoking alters cilia loss, increases goblet cells, hypertrophies mucous glands, and impairs alveolar macrophage function. As a result, the bronchus has a large and permanent population of bacteria. An immunological response is elicited by cytokine release and oxidative stress. As a result, the mucosal epithelium of the bronchi becomes more inflammatory and prone to infection. Nicotine can inhibit the action of natural killer (NK) cells. Normally, NK cells trigger the body's defences against viral infections. Smoking increases the risk of postoperative pulmonary problems, including hospital stay duration, admission rate to the critical care unit, and hospital mortality. Smoking is an independent risk factor for cancer patients to develop post-operative pneumonia (Lugg et al., 2017). Quitting smoking can reduce the risk of problems following surgery. In our investigation, we did not find any difference in the incidence of pneumonia between current and former smokers. To fully comprehend the effects of patients with lung cancer quitting smoking prior to therapy, more research is required. Pneumonia may arise from cancer therapy in patients with advanced-stage lung cancer. The majority of medications used in chemotherapy inhibit immune system activity (Lugg et al., 2017). Immunosuppressive substances include pyrimidines, alkalizing medications, folic acid, and purine antimetabolites. Pneumonia was more common in lung cancer patients with advanced staging, according to (Heo et al., 2020).

CONCLUSION

Lung cancer has a high likelihood of interacting with other diseases and causing complications that can increase morbidity and mortality. Chronic

inflammation caused by previous infections and risk factors such as smoking increases the likelihood of infection and worsens symptoms in patients. Immunosuppressive conditions may also contribute to the onset of infections that accompany lung cancer in patients.

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