

CASE REPORT: A 30-year-old Woman with Multiple-Sites Metastasis Lung Adenocarcinoma and Coronavirus-19 Disease (COVID-19)

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Abstract

Background: Adenocarcinoma is the most common Non-Small Cell Lung Cancer (NSCLC) in non-smokers in Indonesia. It often metastasizes in multiple sites. Metastasis is a negative predictor for prognosis in lung adenocarcinoma. In this covid pandemic era we present a case of a 30-years-old woman with adenocarcinoma and multiple-sites metastasis, and Coronavirus-19 Disease (COVID-19).

Case: A 30-year-old woman came to our hospital with multiple complaints of hearing loss, visual loss, and occasional shortness of breath. The patient had a history of wild-type EGFR adenocarcinoma and has been treated with 4 cycles of gemcitabine. She also presented with a lump in her neck. Further examination revealed multiple metastasis tumours in her brain, right eye, neck, and spine. Pleural fluid examination also showed a malignant pleural effusion. Nasopharyngeal swab using reverse transcriptase-polymerase chain reaction (rt-PCR) method revealed that she also suffers from COVID-19 with positive swab result. Despite adequate treatment, she rapidly deteriorates and passed away in hospital.

Discussion: Management in this patient is complex due to multiple complications and limitation of management given in COVID-19 isolation ward. She presented with multiple equally complicated metastasis, in which treatment priority should be carefully assessed. Despite treatment by multiple specialists, her problems still persist and proved to be fatal.

Conclusion: Although metastasis is common in adenocarcinoma, multiple metastasis is uncommon, and this case highlights the need of careful management priority in such patients in COVID-19 pandemic setting.

Keywords: Adenocarcinoma, Multiple Metastasis, Lung Cancer, COVID-19

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1. Introduction

Lung malignancy is the second most common cancer diagnosis by sex, after prostate cancer for men and breast cancer for women. In 2012 around 1.6 million people died from lung cancer worldwide, the majority in developing countries (63% in men, 57% in women). The death rate in men is almost 1.4 times higher in developed countries¹. Lung adenocarcinoma is the most common primary lung cancer in America. Adenocarcinoma is included in the category of NSCLC and has a strong relationship with smoking habits. Although incidence and mortality have decreased, the disease remains the leading cause of cancer death in the United States. Adenocarcinoma of the lung usually develops from the mucous glands and represents about 40% of all lung cancers. Adenocarcinoma is the subtype most commonly diagnosed in people who have never smoked. Adenocarcinoma of the lung usually occurs in the periphery of the lung, and in many cases, may be found in scars or areas of chronic inflammation².

Clinical complaints that occur in lung cancer can be caused by the tumour itself (cough, chest pain and bloody cough), tumour obstruction in the bronchi (wheezing, stridor, atelectasis, or dyspnea), tumour growth into the pleura (pleural pain, pleural

effusion), and metastases (hoarseness, dysphagia, paresis, back pain)³. Lung cancer management must involve a multidisciplinary team that includes surgeons, oncologists and radiotherapists. The choice of therapy is not only influenced by the histological type, stage, and appearance of the patient, but also by looking at non-medical conditions such as the facilities owned by the hospital and the patient's economic ability⁴.

Since the first reports of cases from Wuhan, a city in China's Hubei Province, in late 2019, cases have been reported on all continents⁵. Globally, the number of cases and deaths of COVID-19 as of 2 January 2022 has increased, the number of new cases globally increased sharply by 71% compared to the previous week, while the number of new deaths decreased by 10%. As of 2 January, a total of 289 million cases and more than 5.4 million deaths have been reported globally. Comorbid conditions increase a person's susceptibility to suffering from severe COVID-19 infection. These comorbid conditions include hypertension, chronic obstructive pulmonary disease, diabetes mellitus and cardiovascular disease. Immunocompromised conditions such as autoimmune and non-autoimmune diseases, patients taking immunosuppressant drugs

with organ transplants, and people with cancer also increase their susceptibility to severe COVID-19⁶. The clinical presentation of COVID-19 with cancer is no different than that of patients without cancer. Patients generally experience fever, chills, myalgia, respiratory symptoms, painful swallowing, and/or disturbances of smell and taste. Although the clinical spectrum of COVID-19 is heterogeneous, patients with active malignancy experience more severe disease and higher mortality⁷.

The main goal of lung cancer management during the COVID-19 pandemic is to minimize the risk of exposing patients and staff to infection while managing life-threatening disease. This can be achieved by keeping doctor, clinic or hospital visits to a minimum. Patients visiting the hospital should be screened for symptoms of COVID-19 and undergo a SARS-CoV2 diagnostic test if symptoms are found. If possible, patients undergoing invasive procedures or systemic chemotherapy and immunotherapy should be tested for COVID-19 infection⁸.

2. Case

A 30-year-old patient came with the chief complaint of shortness of breath. The patient came with complaints of shortness of breath after previously trying to swallow

tablets. Choking vomit. History of shortness of breath before intermittent, PND (-), DOE (-), orthopneu (-), and shortness of breath not related to activity, shortness does not depend on time. The patient admits that there is a dry cough when shortness of breath occurs. In addition, the patient also has chest pain on the left side, does not radiate, pain occurs when tightness and coughing. The patient has decreased appetite without nausea and vomiting. The patient has lost 10 kg in weight in the last 3 months. In the last 3 months, the patient felt that there was a decrease in hearing, starting with the right ear, until gradually it became both ears and the more you come here, the more you can't hear anything. The patient also complained that the right eye was also dim at first, so now he can only see until people move. The patient was referred from Panti Waluya Hospital with Bronchogenic Carcinoma for diagnosis. The patient entered the ER and was hospitalized in the incovit room because the results of the eclia were reactive and the PCR swab was positive.

Based on physical examination found a decrease in oxygen saturation of 92% with room air. The patient was given 4 lpm NC. The general physical examination was found to be within normal limits. In this patient, a laboratory examination was carried out

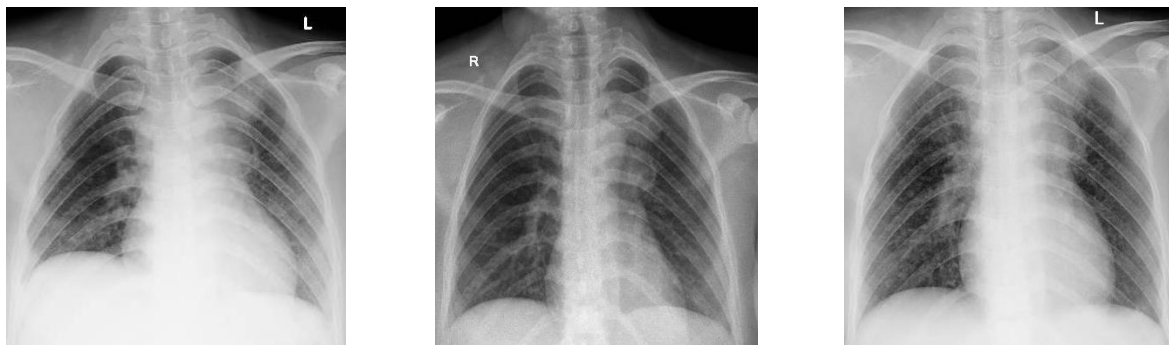


Figure 1 & 2. Plain chest radiograph shows bilateral infiltration when the patient got Covid-19 day 1 compared by day 10 (result: improvement chest x-ray).

Figure 3. Plain chest radiograph on a month after shows a mass in the left paratracheal.

which concluded that there was anaemia and decreased albumin. In this patient, an analysis of pleural fluid was also performed and a reddish liquid with a transudate LDH was obtained accompanied by an increase in total protein. In this patient, a chest x-ray (Figure

1 – 3) was examined and the results showed a mass in the left paratracheal. Chest CT scan (Figure 5 – 7) showed a left pulmonary nodule with regional lymphadenopathy and multiple nodules in both lungs and lytic lesions.

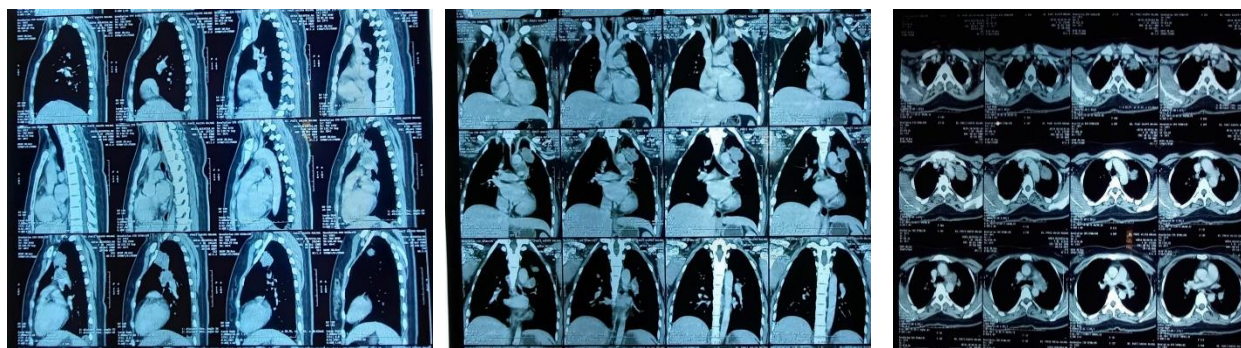
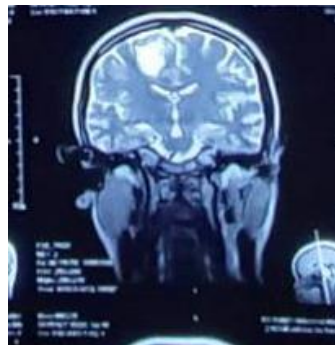


Figure 5, 6, 7. Chest CT scan shows that there is lung mass in the upper left of chest.

The patient was also subjected to an MRI of the head (Figure 8 & 9) which showed brain metastases and the tumour pressed against the oculi bulb causing blindness.



The patient also complained of recurrent back pain and an MRI examination of the whole spine was performed. From the examination can be found results of metastatic bone disease and fractures in VL1.



Figure 8 & 9. MRI showed brain metastases and tumour pressing on the oculi bulb causing blindness.

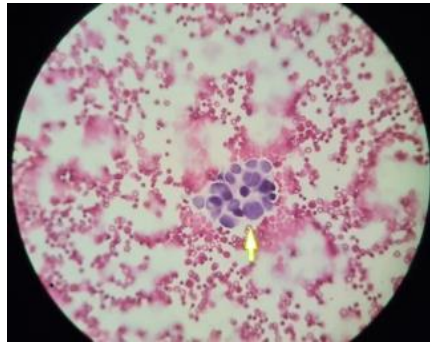
The patient was examined by fiber optic bronchoscopy (Figure 10) which found a mass encroachment on the left bronchial segment 6. In addition, washing and brushing

were carried out and examined in the Anatomical Pathology laboratory.



Figure 10. FOB examination showed a mass encroachment on the left 6th segment bronchus

On histopathological examination, an adenocarcinoma was found (Figure 11). After finding the results of adenocarcinoma on the



FOB results, an EGFR examination was carried out and found an EGFR mutation with wild type status.

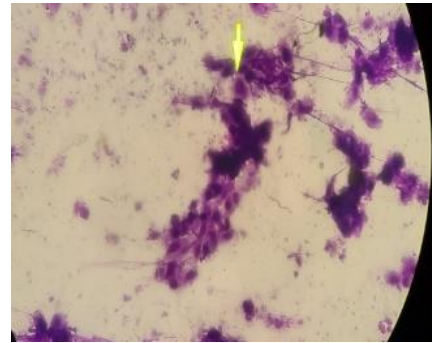


Figure 11. (left) Anatomical pathology of pleural effusion fluid. (Right) Anatomical pathology and neck lump. Samples from pleural effusion and FNAB showed an adenocarcinoma.

3. Discussion

In this case, it was reported that a 30-year-old woman came with complaints of shortness of breath. Dyspnea is a common symptom experienced by 19%-51% of patients with advanced lung cancer⁹. In theory, the pathophysiology and mechanism of breathlessness in lung cancer is complex and multifactorial and may include impaired ventilation, increased ventilation needed or a combination of both¹⁰. Patients also reported hearing loss. Primary metastases to the internal auditory canal are rarely reported, representing only 0.3% of etiologies¹¹.

On initial physical examination, it was found to be within normal limits. In theory, the patient usually experiences shortness of breath; Physical examination may reveal use

of accessory muscles of respiration (scalenus muscles, intercostal muscles) and nostril breathing. In addition, based on the central tumour location, patients may develop distal atelectasis and post-obstructive pneumonia. With pleural effusion, examination reveals dull percussion and decreased or absent breath sounds on the effusion side¹².

Previously, this patient had a PCR swab test for SARS-CoV-2 and found a positive result. According to the literature, patients with lung cancer have the highest risk of death from SARS-CoV-2 infection. Lung cancer represents a clinical scenario characterized by an increased risk of pulmonary complications, severe lung injury and high mortality from COVID-19, due to pathophysiological, clinical and treatment-

related risk factors. A significant interaction of factors frequently associated with lung cancer, including smoking-related lung damage, significant cardiovascular and respiratory comorbidities, and older age, leads to a higher severity of SARS-CoV-2 infection. Patients with lung cancer share the severity of lung and alveolar architecture damaged by previous thoracic surgery or radiotherapy and/or malignant airway obstruction which may also predispose to more severe infections^{13, 14}.

In this patient, a laboratory examination was carried out which concluded that there was anaemia and decreased albumin. Anaemia is a common clinical condition in malignancy, which can be caused by blood loss, impaired erythropoiesis due to inadequate production or effectiveness of erythropoietin, decreased iron availability or decreased circulating erythrocyte life span¹⁵. The main reasons for low albumin levels in patients with cancer are still unclear, but various mechanisms have been proposed. For example, cancer cells can produce cytokines, such as interleukin-6 (IL-6), which modulate albumin production¹⁶.

In this patient, an analysis of pleural fluid was carried out and a reddish liquid with a transudate LDH was obtained accompanied by an increase in total protein. In theory, in 5-

10% of cases, the pleural effusion is a transudate. Transudative effusions are more likely when lymphatic drainage is obstructed by a tumour and in atelectasis caused by bronchial obstruction or congestive heart failure. Malignant cells can also be found in transudative effusions¹⁷.

In this patient, a chest x-ray was examined and the results showed a mass in the left paratracheal. Chest CT scan showed a left pulmonary nodule with regional lymphadenopathy and multiple nodules in both lungs and lytic lesions. The patient was also subjected to an MRI of the head which showed brain metastases and the tumour pressed against the oculi bulb causing blindness. Lung cancer is the most common cancer that metastasizes to the brain, and intracranial disease can be found in 30% of patients with lung cancer¹⁸. The patient also complained of recurrent spinal pain and had an MRI examination of the whole spine. From the examination can be found results of metastatic bone disease and fractures in VL1. This is in accordance with the literature where pain is usually the first symptom of lung cancer with bone metastases in 80% of patients. Patients with bone metastases complain of pain at several points with wide variations in pattern and severity. Many factors are involved in bone metastatic pain

but most pain is related to osteoclastic bone resorption. Tumour cells can cause an imbalance of osteoblasts and osteoclasts, thus interfering with bone reconstruction. There are two types of bone metastases in lung cancer, namely osteolytic metastases and osteogenic metastases. Among all cases, most lung cancer metastases are osteolytic metastases caused by osteoclasts¹⁹.

The patient was examined by fiber optic bronchoscopy which found a mass encroachment on the left bronchial segment 6. In addition, washing and brushing were carried out and examined in the PA lab. Found a picture of adenocarcinoma. After finding the results of adenocarcinoma on the FOB results, an EGFR examination was carried out and found an EGFR mutation with wild type status. According to a literature review, lung adenocarcinoma is broadly classified into 4 types, namely adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), invasive adenocarcinoma, and variant adenocarcinoma. Lymph node metastases may occur in the peribronchial lymph nodes before moving to the mediastinal or subcarinal lymph nodes and then to the contralateral lung. Distant metastases include extension to the contralateral lobe, pleural nodule, pleural effusion, or distant sites such

as the brain, bone, or liver. NSCLC can have mutations in the epidermal growth factor receptor (EGFR), which makes it sensitive to tyrosine kinase inhibitors, as well as anaplastic lymphoma kinase (ALK) fusion oncogene rearrangements^{20, 21}. EGFR stands for of the epidermal growth factor receptor. EGFR is a protein found in healthy cells. When a cancer cell tests positive for EGFR, it means that the gene contains a mutation and is sending the wrong instructions to the cell, allowing the cancer to grow and spread. EGFR-TKI is approved for second-line treatment of EGFR wild-type (EGFR-wt) non-small cell lung cancer (NSCLC). However, the results of a randomized trial conducted to compare EGFR-TKI with chemotherapy did not show any survival benefit²².

4. Conclusion

A 30-year-old woman was referred with complaints of shortness of breath, intermittent coughing and decreased hearing since 7 years ago. Blurred vision in the right eye since 1 year ago. The patient underwent a PCR swab and tested positive. Based on chest X-ray examination found a tumour in the lung. After carrying out additional investigations, the results of an anatomical pathology, namely adenocarcinoma, were

obtained. The patient was given conventional chemotherapy and had his mutation EGFR status checked and a wild type was found. The patient underwent a thorough examination and found metastases to the brain, bones, pleura and ears. The patient died 4 months after the diagnosis was confirmed after a worsening. The management of these patients is complex due to the multiple complications and limited treatment in the COVID-19 isolation wards. This patient exhibits multiple organ spread, in which case the priority of treatment should be carefully assessed. Despite treatment by several specialist fields, the patient's problems still remain and become fatal. This case is interesting to report because multiple metastatic lung adenocarcinoma and COVID-19 are rare. The combination of these cases greatly increases patient mortality.

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