

STAGE 4 LUNG CANCER WITH BRAIN AND PERICARDIAL METASTASES WHICH ARE FIRST CONSIDERED AS PULMONARY TUBERCULOSIS INFECTION AND HEART FAILURE

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Abstract: Lung cancer and pulmonary tuberculosis become a global problem in the world. The similarities of clinical symptoms and radiological appearances often complicates diagnosis especially in TB endemic countries. A 43-year-old man presented with shortness of breath for 6 months, accompanied by intermittent cough mixed with blood streaks. He had been taking anti-tuberculosis for 2 months, but there's no improvement. On physical examination, ronchi were heard in the lower 2/3 of the right lung and heart sounds diminished. Motoric movement of the left hand was difficult to grasp hard. A contrast-enhanced CT scan of the head revealed hyperdense multiple nodules. Chest X-ray showed cardiomegaly with right lung consolidation and a primary malignant right lung mass accompanied by pericardial effusion at thoracic CT scan. Cytology and EGFR examination of pericardial effusion found adenocarcinoma metastasis with exon 18 and 21 mutations. Evaluation of clinical symptoms and radiological examination during tyrosine kinase inhibitor (TKI) therapy showed improvement. Lung cancer can resemble pulmonary tuberculosis in various manifestations. Adenocarcinoma with positive EGFR mutations is more commonly found in Asians. Cytology and EGFR examination of pericardial effusion became the basis of diagnosis in this case. He was given TKI therapy. Re-evaluation must be carried out in patients who do not improve with antibiotics or anti-tuberculosis. Patient reported a good response after consuming EGFR-TKI.

Keywords: lung cancer, tuberculosis, tyrosine kinase inhibitors

INTRODUCTION

Lung cancer is a type of cancer that begins in the lungs. According to the World Health Organization (WHO) in 2015, lung cancer was the highest cause of death in the world.¹ In 2017, an estimated death rate about 155,870 cases in US.^{2,3} Meanwhile, Indonesia has a mortality rate of 103,100 cases in men and 92,200 cases in women.⁴

Lung cancer typically doesn't cause signs and symptoms in its earliest stages. Signs and symptoms of lung cancer typically occur when the disease is advanced. Lung cancer can cause a number of complications in the lungs and other parts of the body. Symptoms of complications in the lung such as persistent cough, haemoptysis, shortness of breath, unexplained tiredness and weight loss, an ache or pain when breathing or coughing, and hoarseness. Another serious complications of lung cancer is that it may spreads to other parts of the body (metastasis) like pleural effusion, lymph node, adrenal glands, pericard, brain, liver and bones.^{1,2}

The high rate of lung cancer mortality due to late diagnosis because symptoms usually only occur when the cancer has become too advanced to cure and high rates of tuberculosis (TB) cases, especially in developing countries. A retrospective study in India on 76 patients with lung cancer, found 39.47% had received previous anti-tuberculosis therapy, thus affecting the delay in diagnosis of lung cancer.⁵

The classification of lung cancer is divided into two groups, namely small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is divided into squamous and non-squamous cell carcinoma types. Non-squamous carcinoma consists of adenocarcinoma, large cell carcinoma, and NSCLC not otherwise specified (NOS). Adenocarcinoma is the most common type of lung cancer.⁶

The appearance of lung cancers can mimic infections like tuberculosis in the form

of consolidation accompanied by air bronchogram, ground-glass appearance, or military type. These are the most common cause of misdiagnosis of a lung cancer.^{7,8}

In this case report, we will discuss a case of stage 4 lung cancer with brain and pericardial metastases, which are first considered as pulmonary tuberculosis infection and heart failure.

CASE REPORT

Mr. A, 43-year-old, came to Ulin General Hospital Banjarmasin with complaints of shortness of breath since 6 months, and felt increasingly since the last 3 days especially during activity, accompanied by abdominal cramps to the waist and spread to the back. He felt pain like being pricked at both chests. Complaints of cough with blood streak. Patient had loss appetite and body weight about 10 kg in the past 6 months. He had felt the weakness of his left hand for the last 3 months. He has history of working in oil palm processing since the last 10 years and history of smoking for about 20 years, 4-6 packs/day. Patient was diagnosed with pulmonary TB and received anti-tuberculosis for 2 months before admitted to Ulin Hospital (figure 1) but the patient did not feel any improvements.



Figure.1. Previous CXR when patient first considered as Pulmonary Tuberculosis and Heart Failure

Patient physical examination found tachycardia, tachypnea, and 98% oxygen saturation with 2 liter per minute oxygen

nasal canul. Ronchi were heard in the lower 2/3 of the right lung field and heart sounds were diminished. Motoric movement of the left hand was difficult to grasp hard. Laboratory tests found hypochromic microcytic anemia (Hb 8.8 g/dl), granulocytosis (87.1%), and high CEA values (17.72 ng/ml). Chest X-ray revealed cardiomegaly with right lung consolidation and Thoracic CT scan showed a primary malignant right lung mass which infiltrates the mediastinum, accompanied by pericardial effusion (figure 2). From Head CT scan was found abnormalities in the form of multiple nodules, 19.7 mm in right parietal vertex and 7.9 mm in left posterior parietal, suggesting of metastatic nodules (figure 3).

A pericardiocentesis was performed and 1050 mL of hemorrhagic fluid was removed. Cytology and EGFR examination of pericardial effusion found adenocarcinoma metastasis with positive EGFR exon 18 and 21 mutations. He was given Gefitinib, a tyrosine kinase inhibitors (TKI) 250 mg per day.

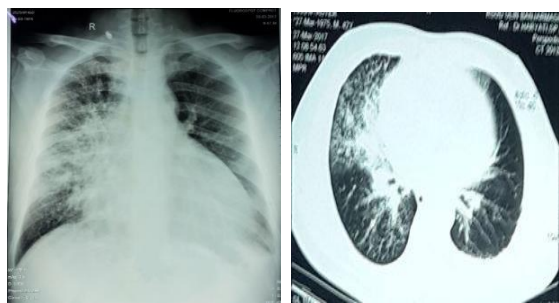


Figure 2. (a) Chest X-ray showing cardiomegaly and right lung consolidation; (b) Thoracic CT scan showing a primary malignant right lung mass.

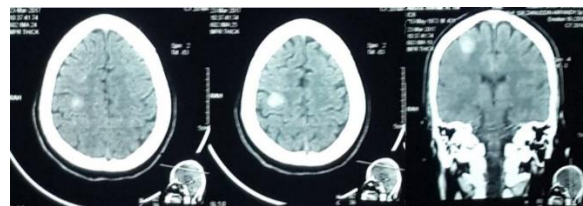


Figure 3. Head CT showing hyperdense nodules in right parietal vertex and left posterior parietal.

Evaluation of clinical symptoms, chest X-ray, thoracic and head CT scan during therapy showed improvements. Chest X-ray after 4 months therapy showing improvement of right lung consolidation and a normal heart size (figure 4). Meanwhile, thoracic CT scan showing reduced bronchovascular patterns from right bronchogenic carcinoma (figure 4) and head CT scan after 5 months therapy also showing reduced size of metastatic lesions (figure 5).



Figure 4. (a) Chest X-ray after 4 months therapy showing improvement of right lung consolidation and a normal heart size; (b) Thoracic CT scan evaluation showing reduced bronchovascular patterns from right bronchogenic carcinoma.



Fig.5. Head CT scan after 5 months therapy showing reduced size of metastatic lesions.

DISCUSSION

Lung cancer and tuberculosis have many similarities like they both are very common, have high prevalence, involve lung parenchyma and above all, characterised by similar symptoms. But, there are many differences between these two entities like they have different etiologies and different management. Delay in the diagnosis and treatment of lung cancer results in poorer outcome and lower survival.⁹

Lung cancer can resemble pulmonary tuberculosis in various manifestations on clinical features and radiological. Symptoms such as fever, cough, expectoration, hemoptysis, weight loss and anorexia are common to both tuberculosis and lung cancer.^{6,9,10} Meanwhile, from lung cancer radiological features can be found consolidated appearance or infiltrates resembling pneumonia, opacity in the form of ground-glass appearance, and miliary type.¹¹

In this case, chest X-ray examination of the patient found an increase in bronchovascular patterns with cardiomegaly, so that it was suspected early as a specific process tuberculosis and heart failure. Due to high TB prevalence and radiological similarities, a large number of lung cancer patients initially get wrongly treated for tuberculosis based on radiological picture alone so chest CT scan with contrast is a better choice than chest radiograph in patients suspected with malignancy.¹¹

The 85-90% of lung cancer cases have risk factor with a history of smoking.^{12,13} In cigarettes, it is estimated that there are approximately 400 dangerous substances.¹⁴

Carcinogenic toxic substances in cigarettes such arsenic, polycyclic aromatic hydrocarbons, N-Nitrosamines, nickel, cadmium, etc.¹⁵ In our case, the patient has risk factors such as smoking habits with a Brinkman index of 960-1440.

Adenocarcinoma is the most common type of lung cancer, with epidermal growth factor receptor (EGFR) mutations more commonly found in Asians (50%).⁶ The most common mutations are 19 (45%) and 21 (40%).^{6,16} Normally, EGFR is found on the surface of cell epithelium and involved in regulating various oncogenic functions such as cell proliferation, survival, differentiation, neovascularization, invasion and metastasis.¹⁶ Epidermal growth factor (EGF), transforming growth factor (TGF)- α or other, bind to the tyrosine kinase (TK) domain, resulting in activation and receptor transphosphorylation of the Grb2 and Sos proteins, which recruit Ras and phosphatidylinositol 3-kinase (PI3K), leading to the formation of two major signalling pathway branches, Ras / mitogen-activated kinase-like protein (MAPK) and PI3K/Akt. These networks cause proliferation, immunity to apoptosis, and angiogenesis (figure 6).¹⁷

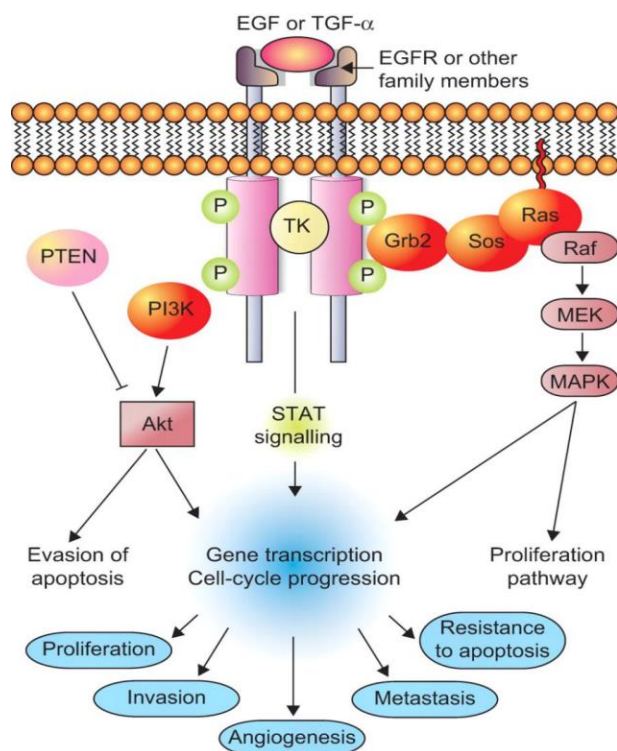


Figure 6. Epidermal growth factor receptor (EGFR) pathway.¹⁷

The majority of lung cancers are discovered because of the development of distant metastases, with the most common location is the brain.^{10,18} Another study found that 8.1% of patients with malignancy had pericardial involvement and 2.7% experienced pericardial effusion.¹⁹

The incidence of brain metastases in patients with lung cancer is approximately 25%, with only 5% surviving beyond the first year after diagnosis. They originate from cancer cells that have spread through the bloodstream. Due to an increase in intracranial pressure as well as the number, localisation, and rate of growth of brain metastases, they are associated with the onset of many clinical signs and symptoms, including headaches, sometimes with vomiting or nausea, seizure, cognitive dysfunction and motoric dysfunction.²⁰ In this case, patient felt weakness of his left hand for the last 3 months and brain CT scan showed

hyperdense multiple nodul that suggesting of metastatic nodules.

Beside brain metastasis, patient had malignant pericardial effusion. An malignant pericardial effusion forms when cells from either a lung cancer or another type of cancer spread to the pericardial space. As fluid accumulates in the pericardium, the increase in intrapericardial pressure affects diastolic filling of the heart, leading to decreased cardiac output. Symptoms may arise gradually or rapidly, depending on fluid accumulation rate. Pericardiocentesis is usually needed to establish aetiology, the malignant nature of pericardial effusion being confirmed by identification of malignant cells at cytological examination.¹⁹

Cytology and EGFR examination result from pericardiocentesis at this patient showed adenocarcinoma metastasis with positive EGFR exon 18 and 21 mutations and became the basis of diagnosis in this case.

The patient was given a tyrosine kinase inhibitors (TKI) therapy, but the role of EGFR-TKI in brain metastases is still unclear and usually considered as an exclusion criteria in previous clinical studies.¹⁸ A retrospective study by Hao Bai et al in 148 NSCLC patients with positive EGFR mutations and also experienced brain metastases given by Gefitinib and Erlotinib, found that there was a good response in terms of objective response rate (ORR) of 36.5% and disease control rate (DCR) of 87.2%. In addition, the median progression-free survival (PFS) was found to be 11.2 months and the overall survival (OS) was 13.6 months. This study showed that EGFR-TKI has promising anti-tumor activities against brain metastases in NSCLC patients with positive EGFR mutations.¹⁸ In this case, the patient had a good response from clinical and radiological features, and in terms of brain metastasis which was assessed from the head CT scan post-evaluation of EGFR-TKI administration for approximately 5 months.

CONCLUSION

Early diagnosis of lung cancer is a difficult challenge. Re-evaluation must be carried out in patients who do not improve with antibiotics or anti-tuberculosis. The interesting thing about this case report is the clinical and radiological response of brain metastases after consuming EGFR-TKI, becomes a promising new hope in the future.

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