

CASE REPORT

Risk Factors and Challenging Management of Lung Adenocarcinoma in Young Adult Women: Case Series

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ABSTRACT

Introduction: Lung cancer found in young age is relatively rare with a percentage of cases only 1.4% of overall lung cancer cases in the world.

Case: We reported two cases of lung adenocarcinoma in young women aged less than 30. The first case was lung adenosquamous carcinoma in a 28-year-old woman, a passive smoker, who had a family history of cancer. She had the mutation of epidermal growth factor receptor (EGFR) exon 19 deletion and received 1st generation of tyrosine kinase inhibitor. Since the patient was diagnosed at advanced stage with poor performance status, she died within 2 months after being diagnosed. The second case was lung adenocarcinoma in a 23-year-old woman. The patient was a passive smoker and had a history of cancer in the family. She was diagnosed at an advanced stage but with good performance status. The patient underwent chemotherapy with Pemetrexed-Platinum in 6 cycles and 15 cycles of radiotherapy.

Conclusion: Lung cancer at a young age is more common in non-smoking female with the histopathology type adenocarcinoma. Non-specific early symptoms become a problem in the early enforcement of lung cancer at a young age. Many cancer-related issues occur in young cancer patient such as premature death, increased dependence on parents, difficulty in school and work due to medication, and reproductive disturbance.

INTRODUCTION

The incidence of lung cancer is more common in men than women with median age at diagnosis 71 years old. Lung cancer at a young age is rare and less than 3.5% of patients are younger than 45 years old. In the last two decades, there was a shift in the proportion of lung cancer from men to women. These changes cannot be fully explained by differences in smoking habits between the two genders. Studies found that histology of lung cancer in adolescents and young adults was dominated by non-small cell lung cancer (NSCLC), and adenocarcinoma was more common in young patients.¹⁻³

The incidence of lung cancer at a young age is rare, therefore in this article we reported two case series in women under 30 years old. Various aspects were discussed including epidemiology, risk factors, and management.

CASE

Case 1

Balinese female patient, 28 years old, complained left chest pain radiating to back and right leg. She also complained dyspneu on effort and dry cough. The patient was an employee of an insurance company and was

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an employee of an insurance company and was planning for her wedding. She was a passive smoker and had a history of cancer in her family. Her maternal grandparents suffered from liver cancer and already died. Chest computed tomography (CT) scan revealed malignant solid mass with central necrotic in the left lung which destroyed the left rib and invaded the chest wall, multiple nodules on both lungs, multiple lymphadenopathy, and multiple subcutaneous nodules (Figure 1). Biopsy showed an adenosquamous carcinoma with exon 19 deletion epidermal growth factor receptor (EGFR) mutation. Tyrosine kinase inhibitor was given for only 10 days because her condition was getting worse. She finally died within 2 months after being suspected to have lung cancer. During the diagnostic and therapeutic procedure of cancer, she experienced emotional disturbances and depression. The patient only received support from his mother, while his future husband was in another province.

Case 2

Balinese female patient, 23 years old, complained chronic productive cough, chest pain, and anorexia. She was an employee in pharmaceutical company. She was a passive smoker and had a history of cancer in her family. Her maternal grandfather was diagnosed with lymphoma.

Chest CT scan suggested a lung mass in right middle lobe, with multiple lymphadenopathies and right pleural effusion (Figure 2). Biopsy showed adenocarcinoma with wild type EGFR mutation. 6 cycles Platinum-Pemetrexed chemotherapy were administered and showed a partial response. 7 months after the last chemotherapy, she complained chest pain and cough. Clinical and radiograph evaluation concluded that her cancer was progressed, and then underwent 15 series of radiotherapy. Her condition improved after receiving radiation. The patient survived a year and 8 months until this report was made.

The patient also had psychological problems similar to the first case at the time of diagnosis and treatment. Sadness was what she felt when diagnosed with lung cancer because she had just graduated from college, wanted to pursue a career, and do many things. The patient denied her illness and felt hopeless, especially when experiencing cancer pain and the side effects of cancer therapy. She also had attempted suicide. Luckily she had people who supported her, including her family and other cancer patients who were also undergoing cancer therapy. She shared experiences with other cancer patients. Currently she works for an online shop but does not want to be in a relationship or get married because she wants to focus on the treatment and her family.

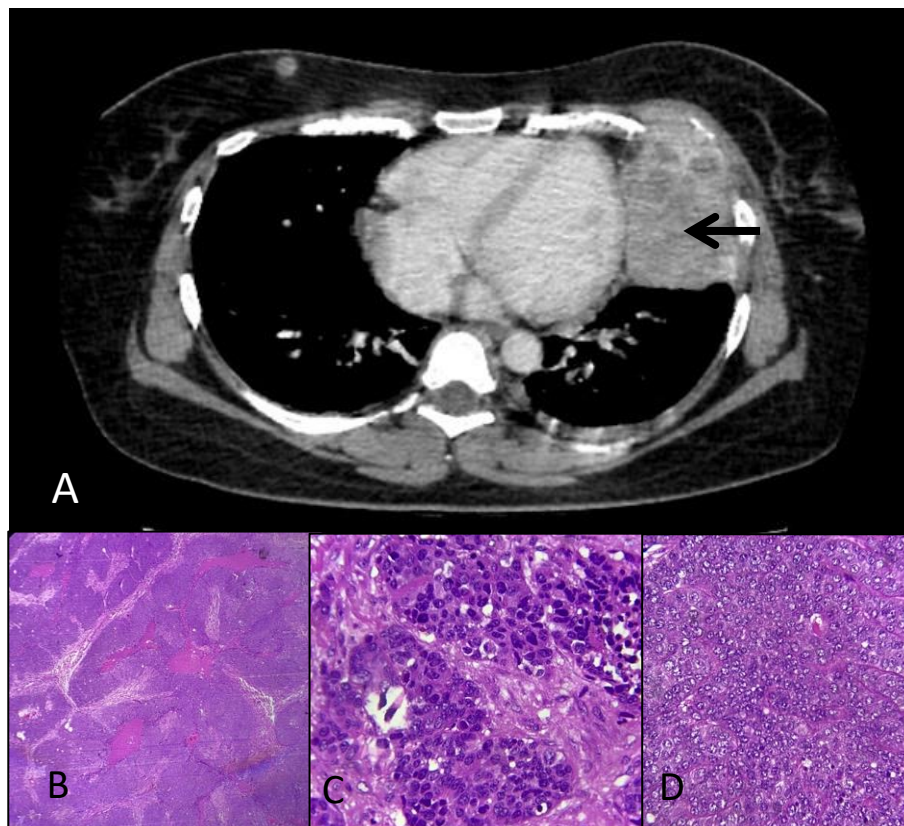


Figure 1. A) Chest CT scan showed lung mass (black arrow) in the left lung; B), C), D) Histopathology examination showed adenosquamous carcinoma infiltrated to visceral pleura and invaded the lymphovascular. Areas of adenomatous hyperplasia of carcinoma were seen in lung tissue.

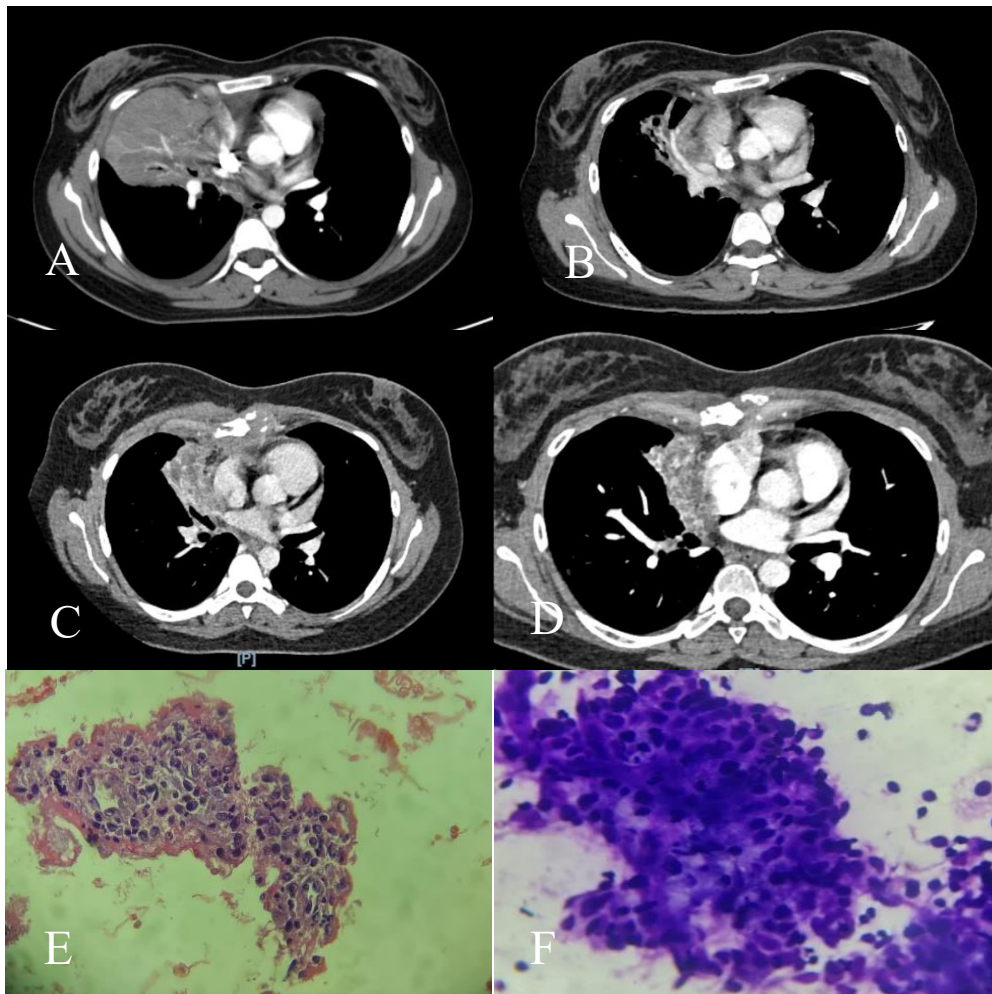


Figure 2. A) Chest CT scan revealed lung mass in right medial lobe and minimal pleural effusion. B) The lung mass size reduced after administration of 4 cycles doublet chemotherapy. C) The lung cancer progressed 7 months after chemotherapy, and radiotherapy was given to the primary tumor. D) Chest CT scan showed a reduced lung mass 1 month after radiotherapy was given. E) & F) Cytomorphology examination showed adenocarcinoma.

DISCUSSION

Lung cancer in young adult patients is uncommon. Based on Cancer Statistics 2016 and database of Surveillance, Epidemiology, and End Results (SEER), approximately 13,000 deaths from lung cancer occur in young adults.¹ Several studies showed that the incidence in adolescents and young adults (aged 15-40 years old) is about 1.4%.^{2,3} Lung cancer is the most common cancer in men, but based on studies in 40 countries, the age-specific lung cancer incidence rates generally decreased. The incidence rate of lung cancer in women varies with the tendency to show a stable or slow decreasing incidence rate. Changes in the pattern of incidence rates are caused by an increase in the incidence of adenocarcinoma in women.^{2,4-6} The patients in this case were diagnosed with lung cancer predominantly adenocarcinoma at young age (before 30 years old), and both of them were female.

Possible risk factors

The risk of lung cancer can be evaluated from several things, including age, gender, genetic predisposition to cancer, tobacco use, and exposure to toxic and carcinogenic agents. Lung cancer at a young age is associated with a genetic predisposition. Gene mutation causes the transformation of normal cells into cancer cells. Various studies have reported oncogenic genomic changes in young lung cancer patients compared to older people.⁵⁻⁸ A study conducted by Chen reported that 92.3% of young lung cancer patients diagnosed with adenocarcinoma had treatable genomic changes. The frequency of anaplastic lymphoma kinase (ALK) translocations, EGFR, and Kirsten rat sarcoma viral oncogene homologue (KRAS) mutations were 37.6%, 34.3%, and 6.1% respectively. Young patients also had a high prevalence of rare genomic changes, such as HER2, ROS1, and MET compared to older patients.⁸

EGFR mutations are associated with the type of adenocarcinoma in lung cancer. Various studies of these mutations in young patients showed discrepancies. PIONEER study suggested that EGFR mutations cannot be associated with age.⁵ However, there was another study which stated that the exon 19 deletion EGFR mutation was more prevalent in young people, while L858R was more prevalent in old age.^{7,8} Uncommon mutation (exon 20) was said to be more prevalent at a young age. In addition, a study mentioned that poor prognostic factor such as TP53 was more prevalent at a young age.⁹ Gene fusion, including ALK, ROS, and RET rearrangements are more common at a young age. ALK rearrangement was the most common at a young age, which was around 10-34%. The frequency of ROS1 rearrangement was around 0-6.9% at a young age, whereas RET rearrangement varies between 1.4% and 9.3%.⁵ The first patient showed an exon 19 deletion EGFR mutation which in the literature was said to be more common at a younger age. Meanwhile, for the second patient, the oncogenic genomic changes were unknown because genomic profiling was not performed due to financial problem.

Women are more likely diagnosed with adenocarcinoma compared to men at a younger age, have inherited cancer from family, and have less cigarette exposure. Smoking is known as one of the causes of lung cancer in both men and women, but various studies have shown that women are more likely to develop lung cancer than men. This happens because women have different genetic and molecular related to cancer compared to men. Several genetic variations related to lung cancer in non-smoking populations include cytochrome P450 polymorphisms, family 1, subfamily A, polypeptide 1 gene which can cause interference with DNA repair, overexpression of X-linked gastrin releasing peptide receptor, and p53 mutations.¹⁰ Disturbances in DNA repair capacity (DRC) have been investigated as a cause of the development of cancer. DRC is decreased in women with lung cancer compared to men with lung cancer and healthy women as controls. The decrease in DRC was found to be similar in female smokers and non-smokers with lung cancer, indicating that the reduced DRC is independent or not influenced by the carcinogenic effect of smoking. Several studies have analyzed the presence of germ line polymorphisms in genes associated with increased susceptibility to cancer and its active products (cytochrome P450 1A1 = CYP1A1) and detoxification of carcinogenic chemicals found in cigarette smoke (glutathione S-transferase M1 = GSTM1 and T1 = GSTT1).¹¹

Studies found an increased risk of lung cancer in non-smoking female patients with CYP1A1 polymorphisms (MspI CC and I1e462Val) as much as 1.7

and 2.8 times respectively. After an analysis based on exposure to environmental tobacco smoke (ETS), it was found that the risk of lung cancer associated with both polymorphisms was increased in individuals with lower exposure to ETS, compared to individuals exposed to ETS at least once per week. The GSTM1 homozygous null genotype was statistically significantly associated with an increased risk of lung cancer in women who did not smoke but were exposed to high levels of ETS. Both cases had history of cancer in their family and exposure to high levels of ETS. These factors can increase the risk of lung cancer in female young adults.^{11,12}

Challenging management

In general, the management of lung cancer is based on the type of tumor histology, biological or molecular markers, clinical stage and/or tumor pathological stage, patient performance status, and drug availability in health facilities. In adenocarcinoma patients, gene mutations or biomarker markers are examined, hence targeted therapy can be given. Advanced stage patient with unknown or negative mutation status are given systemic chemotherapy. The first patient received targeted therapy although she eventually died 2 months after being diagnosed with lung cancer. The other patient was given chemoradiotherapy and still lives in good condition. Both patients had severe psychosocial problems due to their cancer.

Young adult is a developmental stage characterized by rapid alteration in emotional and cognitive growth. This is challenging for young adults who are undergoing cancer therapy. Cancer diagnosis and therapy disrupt daily life, give physical pain, lower energy, alter the physical appearance, limit body function, give pressure about death or mortality, and eventually lead to existential issues. Young patients have additional problems dealing with cancer, including facing premature death, increasing dependence on parents, having difficulty in school and work due to medication, and reproductive disturbance. Healthy growth and development in young people require identity development, thus they need healthy peer relationships. Isolation due to cancer in young adults are commonly reported. Young cancer patients feel lonely and isolated, while normally they should be busy interacting socially, pursuing a career, or getting married.^{13,14}

Young adults with cancer who actively seek support show a positive attitude towards therapy. Studies reported that family support is the most important factor to positive adjustment. Others showed the important role of friends, including healthy peers and other adolescent, and young adult cancer survivors. The first case showed symptoms of emotional disturbance and depression. Pain was one factor that made it worse in addition to the lack

of support from the closest people. The second case also had psychological problem and even attempted suicide. However, she managed her problem by actively seeking support from her family and healthy peers sharing her cancer experiences.^{13,14}

CONCLUSION

The incidence of lung cancer at a young age is rare. A number of potential risk factors have been proposed. Women are more likely diagnosed with adenocarcinoma compared to men at a younger age, have inherited cancer from family, and have less cigarette exposure. Lung cancer at a young age is associated with a genetic predisposition. Gene mutation causes the transformation of normal cells into cancer cells, and EGFR mutation is one of them.

In general, the management of lung cancer is based on the type of tumor histology, biological or molecular markers, clinical stage, patient performance status, drug availability, and financial support. Young adult is characterized by rapid alteration in emotional and cognitive growth. This is challenging for them while undergoing cancer therapy. Isolation due to cancer in young adults are commonly reported and can lead to depression and even suicide attempts. Young adults with cancer who actively seek support show a positive attitude towards therapy.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The author stated there is no conflict of interest in this study.

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Authors' Contributions

Write manuscript, collect data of patient: IAJK, LKAWK, NWC, HS, NPSW, NBA. Review and revision: IAJK, NWC. All authors contributed and have approved the final version.

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