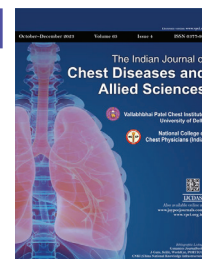


CASE REPORT

Lung Adenocancer in Pregnancy and Review of the Literature

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ABSTRACT

The incidence of tumors during pregnancy comprises 0.1% of all malignant tumors. Breast cancer, cervical cancer, melanoma, ovarian cancer, leukemia, and lymphoma are the most common malignant tumors that occur during pregnancy. The less common cancers include gastrointestinal, urological, and lung cancers. The patient was 34 years old, 30 weeks of gestation, and a nonactive cigarette smoker, but exposed to passive cigarette and biomass smoke. She was diagnosed with hemoptysis two days ago. On physical examination, respiratory sounds decreased at the left baseline. Computerized tomography (CT) of the chest revealed a 32 × 79 mm mass lesion with irregular borders in the basal anterior of the left lung. A fiberoptic bronchoscopic examination was performed, and biopsies that were taken from the patient's airways with mucosal irregularity in the basal posterior of the left lung were consistent with adenocarcinoma. Estimated glomerular filtration rate (EGFR), anaplastic lymphoma kinase (ALK), and proto-oncogene tyrosine-protein kinase-1 (ROS-1) mutations were not detected. No brain metastases were detected. After delivery, two cycles of cisplatin–gemcitabine chemotherapy were administered. Multiple metastases were detected in the scalp, cervical, and thoracic regions. Due to neck pain caused by cervical metastasis, palliative radiotherapy was applied. During chemotherapy, the patient started to have severe headaches, and brain magnetic resonance imaging (MRI) was repeated for this reason. Multiple metastatic lesions were found in the brain MRI, and palliative cranial radiotherapy was started. The patient, whose chemotherapy was completed for six cycles, died 8 months after the diagnosis. Lung cancer can be diagnosed during pregnancy, and its prognosis is poor. This should be kept in mind by clinicians.

Keywords: Case report, Gravidity, Hemoptysis, Lung neoplasms, Metastasis, Prognosis.

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ABBREVIATIONS USED IN THIS ARTICLE

ALK = Anaplastic lymphoma kinase; CT = Computerized tomography; EGFR = Estimated glomerular filtration rate; ESMO = European Society for Medical Oncology; MRI = Magnetic resonance imaging; NSCLC = Non small cell lung cancer; PET = Positron emission tomography; ROS-1 = Proto-oncogene tyrosine-protein kinase-1; TTF-1 = Thyroid transcription factor 1.

INTRODUCTION

Lung cancer is the type of cancer that causes the most deaths for both sexes. Diagnosis during pregnancy is rare and constitutes less than 1% of pregnancy-related cancers.¹ Its incidence increases in smokers and advanced-age pregnancies.² With the increasing trend of smoking in the young population, its incidence is also increasing at younger ages, and the majority of these cases are stages III or IV lung cancer with a poor prognosis.³

We present a 36-year-old, 30-week pregnant, passive smoker who was diagnosed with lung adenocarcinoma, had severe biomass exposure, and received chemotherapy and radiotherapy after pregnancy.

This case was reported due to the rare occurrence of lung cancer in a pregnant patient exposed to biomass and passive smoking.

CASE DESCRIPTION

A 36-year-old, 30-week pregnant patient applied to the chest diseases clinic with chest pain and shortness of breath for 6 months and hemoptysis mixed with sputum that started two days ago. The patient, who lived in a rural area, had passive smoking and biomass

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exposure and was in her 13th pregnancy. The patient had no other disease in her medical history.

Physical examination showed that blood pressure was 120/70 mm Hg, respiratory rate was 14/minute, heart rate was 78/minute, and fever was 36.7°C. In auscultation, lung sounds at the left basal were found to be decreasing. Heart sounds were rhythmic.

Lymph nodes were not palpable. Her admission blood tests revealed anemia, hyponatremia, hypokalemia, and hypocalcemia (Table 1).

In the thorax computerized tomography (CT), which was taken while preserving the abdominal area, a bilobular mass lesion of approximately 32 × 79 mm in diameter with irregular borders adjacent to the left anterobasal fissure, extending from the lateral aorta to the thoracic pleura, was observed. In addition to the aortopulmonary and subcarinal lymph nodes, some of which reached 20 mm in diameter, 2 subpleural nodules in the right upper lobe posterolateral and 1 nodule in the right superior basal segment that may be compatible with metastasis were observed (Fig. 1).

In the bronchoscopic evaluation, mucosal irregularities were detected, and a biopsy taken from the posterior left lower lobe revealed lung adenocarcinoma. Tumor cells were positive for thyroid transcription factor 1 (TTF-1) (Fig. 2), napsin A, cytokeratin 7, and negative with estrogen receptor, mammoglobin, and Pax-8. Estimated glomerular filtration rate (EGFR), anaplastic lymphoma kinase (ALK), and proto-oncogene tyrosine-protein kinase-1 (ROS-1) mutations were not detected.

The patient, who was accepted as stage IV lung cancer, delivered a healthy baby by cesarean section 1 week after the diagnosis, and fetal lung maturation was provided with steroids 24–48 hours

before delivery. After delivery, the patient was administered two cycles of cisplatin–gemcitabine chemotherapy. Despite treatment, new metastases were detected in the cervical and thoracic regions. Palliative radiotherapy was applied to the patient, who had neck pain. Palliative cranial radiotherapy was started when metastatic lesions were found in the brain MRI of the patient, who started to have headaches. Afterward, six cycles of chemotherapy were completed. She died 8 months after the diagnosis.

DISCUSSION

As it is known, there are many factors that play a role in the etiology of lung cancer. Women who smoke and never smoke have a higher risk of lung cancer than men. In addition, passive smoking, heating, and cooking methods that cause indoor air pollution, family history of cancer, and menstrual and reproductive factors are also effective in the formation of lung cancer.⁴

About 50% of the world's population and 90% of rural households, especially in developing countries, use biomass fuel as the primary local energy source for heating and cooking. Carcinogens produced by biomass fuel burning are a significant cause of lung cancer, especially in women.⁵ In a study conducted in Turkey, it was reported that exposure to biomass may cause lung cancer as well as various lung diseases.⁶

Pregnancy-associated lung cancer is defined as lung cancer detected during pregnancy and within 1 year after birth. In a retrospective analysis by Yang Lei et al.,² including clinical manifestations, treatments, and outcomes, the median age of 77 pregnancy-related lung cancer cases reported up to 2021 was 34. 20% of the patients had a history of smoking. The most common symptoms were coughing, shortness of breath, and chest pain.²

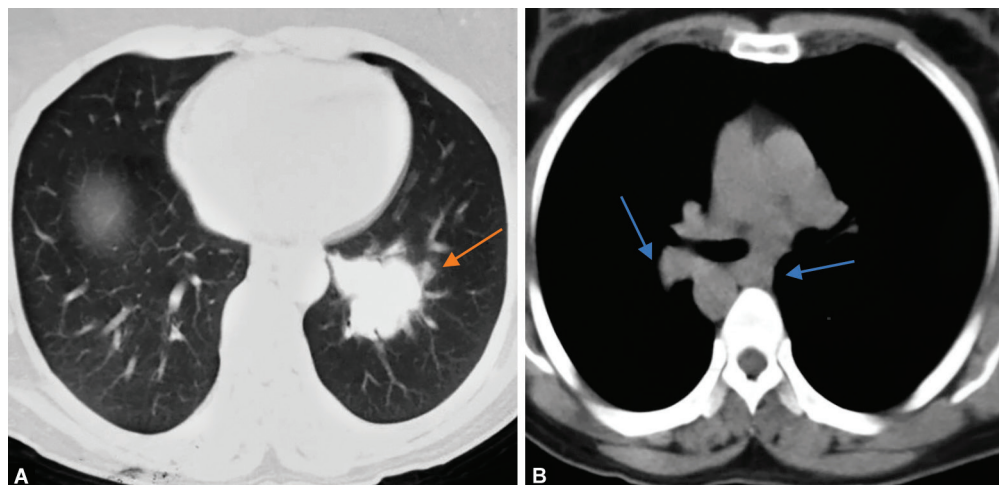
Lung cancer symptoms that develop during pregnancy can be confused with symptoms related to both pregnancy-related physiological and nonpregnant lung diseases during this period. Since lung cancer is rare at this age, it may cause delays in diagnosis. In the previous study, the time from symptom onset to hospital admission was approximately 2 months. The most common histopathological cancer type in pregnant women was nonsmall cell lung cancer, and most of them were stage IV.²

Guidelines are published by the relevant associations on which criteria should be used in the diagnosis, treatment, and follow-up

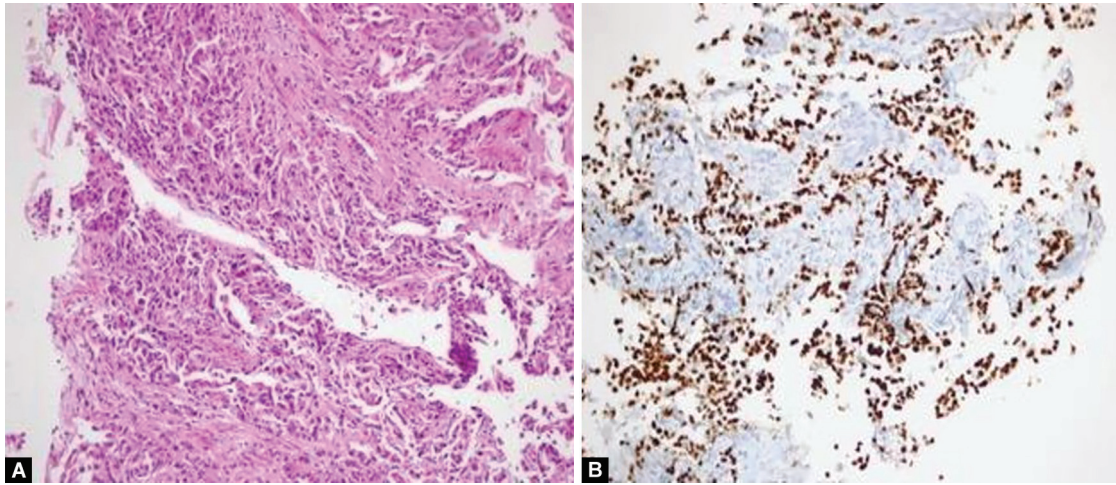
Table 1: Laboratory results at admission

Labs (unit)	Normal range	Value
Hemoglobin	12–15 gm/dL	9.80 gm/dL
White blood cell count	3.9–11.7 k/ μ L	6.18 k/ μ L
Red blood cell count	3.85–5.16 million/ μ L	3.35 million/ μ L
Na ⁺	135–145 mEq/L	131 mEq/L
Na ⁺	3.5–5.5 mEq/L	3.37 mEq/L
Ca ⁺⁺	8.6–10 mg/dL	8.4 mg/dL
AST	8–46 U/L	9 U/L
ALT	0–35 U/L	7 U/L
Blood urea nitrogen	5–24 mg/dL	3.6 mg/dL
Creatinine	0.4–1.4 mg/dL	0.44 mg/dL

ALT, alanine amino transferase; AST, aspartate aminotransferase; Ca⁺⁺, calcium; K⁺, potassium; Na⁺, sodium



Figs 1A and B: Thorax CT. (A) A 32 × 79 mm, irregularly circumscribed mass lesion was observed in the left lung; (B) Aortopulmonary, subcarinal lymph nodes



Figs 2A and B: Adenocarcinoma in needle biopsy. (A) H&E $\times 200$; (B) TTF1 $\times 200$. H&E, hematoxylin-eosin; TTF1, thyroid transcription factor-1

phase of a pregnant woman with suspected cancer.^{7,8} Registries are created worldwide to provide the best personalized management plan for patients diagnosed with cancer during pregnancy.¹

It should be aimed at ensuring that the staging tests performed during pregnancy do not harm the pregnant woman or the fetus. Delaying or not performing an imaging study may be more harmful to the pregnant woman and fetus than the examination itself. In each case, examinations should be requested by considering the profit-loss ratio.⁹

Ultrasound and magnetic resonance imaging (MRI) are the preferred tests during pregnancy. However, methods using ionizing radiation may contribute to the definition of diagnosis and treatment when the benefits outweigh the potential risks to the fetus. These risks are low if dose-limiting protocols are followed and the frequency of administration is not high.⁹

Exposure to ionizing radiation may concern many pregnant women and clinicians, as it is teratogenic. The most sensitive time is between 5 and 17 weeks of pregnancy. Although imaging methods such as chest X-ray and thorax CT are relatively more reliable in cases other than these periods, a multidisciplinary team should evaluate their application during pregnancy.¹⁰ Positron emission tomography (PET) and CT examinations should be delayed until after pregnancy.¹¹

Lung cancer treatment in pregnant women follows the same course as in nonpregnant women. A multidisciplinary team should manage the treatment of pregnant women with cancer. In addition to the benefits of surgery, chemotherapy, and radiotherapy applied during pregnancy, it should be aimed at having no side effects on both mother and child health.

The main parameters affecting the choice of treatment are gestational age, type, and stage of cancer, the possibility of transplacental transfer of the drug, and the risk of teratogenicity. If the disease is diagnosed in the early stages, the patient's opinion about the continuation of the pregnancy is also essential. Depending on the gestational age, surgery, radiotherapy, and chemotherapy are possible during pregnancy.¹¹

Chemotherapy can be used in the second and third trimesters, with a 3-week treatment-free interval before delivery, up to week 35 of pregnancy. Delivery should be delayed for 2–3 weeks following the administration of chemotherapy.¹¹

Antimetabolites (e.g., gemcitabine and pemetrexed) should be avoided during pregnancy.⁷ Although the mainstay of treatment

is chemotherapy, targeted therapies and immunotherapy are becoming more and more important.¹²

Oncogene mutations are more common among non small cell lung cancer (NSCLC) cases that occur during pregnancy. Protein kinase inhibitors gefitinib, erlotinib, and osimertinib are standard first-line treatments in NSCLC cases with an EGFR (epidermal growth factor receptor) activating mutation. Non small cell lung cancer with ALK rearrangement is less common than NSCLC with an EGFR mutation and is usually treated with crizotinib or alectinib. European Society for Medical Oncology (ESMO) clinical practice guidelines recommend the combination of carboplatin and paclitaxel for the treatment of NSCLC during pregnancy but do not recommend the use of protein kinase inhibitors due to a lack of available data.¹²

In the histopathological examination, the tumor cells of our patient were positive for TTF-1, napsin A, cytokeratin 7, and negative for estrogen receptors. In addition, EGFR, ALK, and ROS-1 mutations were found to be negative.

Chemotherapy is excreted in human milk, and although its oral bioavailability is low, neutropenia in breastfed infants during cancer treatment has been described in case reports. A 3-week interval between the last administration of most nonplatinum chemotherapeutic agents and breastfeeding is recommended for safety reasons. Platinum derivatives have a longer half-life and can be detected in breast milk 3 weeks after the last exposure. In addition, both chemotherapy and cancer may adversely affect the bacterial and metabolic composition of breast milk.¹¹

The final survival analysis in 2021 was performed on 64 patients diagnosed with lung cancer with follow-up information, and the mean survival time was found to be 16 months. In addition, no significant difference was found between the patients who received treatment during pregnancy and those who received treatment after pregnancy.²

Our patient was diagnosed in her third trimester, and her treatment was started with gemcitabine-cisplatin treatment after delivery. No side effects were detected except for the treatment-related grade-2 alopecia. She died 8 months after the diagnosis.

CONCLUSION

There is no data in the literature regarding a case diagnosed with lung cancer during pregnancy and exposed to biomass without smoking.

The lung cancer prognosis in pregnancy is very poor and rare. The clinician should not hesitate to use radiological methods for diagnosis in this rare case. Since inhalation of biomass fuel contents has an important role in the etiology of lung cancer, it is recommended that women be kept away from these exposures.

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