



## Maternal and fetal outcomes in pregnant women with lung cancer: a case report

### Maternalni i fetalni ishodi kod trudnica obolelih od karcinoma pluća

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#### Abstract

**Introduction.** Lung cancer (LC) during pregnancy is rare, rarer than other types of malignancy. We present the case of a pregnant patient with advanced-stage LC, highlighting the diagnostic approach, pregnancy management, delivery, and postpartum course. **Case report.** A 46-year-old primiparous patient, 30 weeks pregnant with *in vitro* fertilization, was admitted to the hospital with right-sided chest pain and cough. The patient was a former smoker with a 15-year history of smoking. Due to the patient's general condition and reported symptoms, an X-ray and computed tomography of the chest were performed. A massive necrotic lobulated tumor was revealed in the right lobe of the lung, involving the pleura and almost the entire lung parenchyma. A tru-cut biopsy of the lesion in the right lung was immediately performed. Histopathological examination of the biopsy specimen revealed a poorly differentiated neuroendocrine tumor of the small cell LC. At 32 weeks of gestation, signs of fetal hypoxemia were diagnosed, and the pregnancy was terminated by elective cesarean section. A male fetus weighing 1,550 g was born, with an Apgar score of 7/8, and after stabilization was referred to the Institute for Neonatology, Belgrade, Serbia. The placenta was sent for histopathological examination, and metastatic poorly differentiated neuroendocrine carcinoma was confirmed. The patient was presented to the Gynecological, Pulmonology, and Oncologic Councils, and radiotherapy was initiated immediately after delivery, but unfortunately, she died 7 days after delivery. **Conclusion.** The diagnosis and treatment of LC in pregnancy is challenging. That includes timely detection, treatment decisions and efficacy, as well as the potential risks for the fetus.

#### Keywords:

biopsy, needle; diagnosis; lung neoplasms; pregnancy; radiotherapy; treatment outcome.

#### Apstrakt

**Uvod.** Karcinom pluća (*lung cancer* – LC) tokom trudnoće je redak, ređi od drugih vrsta maligniteta. Prikazujemo trudnicu sa uznapredovalim LC, sa posebnim osvrtom na dijagnostički pristup, vođenje trudnoće, porođaj i postporođajni tok. **Prikaz bolesnika.** Prvorotkinja, starosti 46 godina, u 30. nedelji trudnoće nakon vantelesne oplodnje, primljena je u bolnicu zbog bola u grudnom košu sa desne strane i kašlja. Bolesnica je bila bivši pušač, sa 15-godišnjom istorijom pušenja. Zbog opšteg stanja i prijavljenih simptoma, urađeni su rendgenski snimak i kompjuterizovana tomografija grudnog koša. U desnom režnju pluća otkriven je masivni nekrotični lobulirani tumor, koji je zahvatao pleuru i skoro ceo plućni parenhim. Odmah je izvršena *tru-cut* biopsija lezije u desnom plućnom krilu. Histopatološkim pregledom biopsije uzorka utvrđen je slabo diferencirani neuroendokrini sitnoćelijski LC. U 32. nedelji gestacije dijagnostikovani su znaci fetalne hipoksemije i trudnoća je prekinuta elektivnim carskim rezom. Rođen je muški fetus, težine 1 550 g, Apgar skora 7/8 i posle stabilizacije upućen je na Institut za neonatologiju, Beograd, Srbija. Placenta je poslata na histopatološki pregled, i potvrđen je metastatski slabo diferenciran neuroendokrini karcinom. Bolesnica je prikazana na ginekološkom, pulmološkom i onkološkom konzilijumu i radioterapija je započeta odmah posle porođaja, ali je, nažalost, preminula 7 dana posle porođaja. **Zaključak.** Dijagnoza i lečenje LC u trudnoći predstavljaju poseban izazov. To podrazumeva rano otkrivanje, odluke o lečenju i njegovu efikasnost, kao i rano otkrivanje potencijalnih rizika za fetus.

#### Ključne reči:

biopsija iglom; dijagnoza; pluća, neoplazme; trudnoća; radioterapija; lečenje, ishod.

## Introduction

The incidence of malignant diseases during pregnancy is around 0.1%<sup>1</sup>. Lung cancer (LC) during pregnancy is rare, with only 133 cases reported in the literature from 1953 to 2024<sup>2</sup>. The incidence of LC is on the rise due to the rising number of smokers and the trend of delayed childbearing. Among all cancers in pregnancy, it carries the highest mortality rate (64.3%) and increases the risk of placental abnormalities, preterm birth, and low birth weight<sup>2,3</sup>. Diagnosis is usually made at an advanced stage of the disease<sup>1</sup> due to nonspecific symptoms that are often overlooked by both pregnant patients and their physicians, leading to delayed diagnosis and a poor prognosis<sup>3,4</sup>. Distant metastases are often present, and in rare cases, metastases may also be found in placental tissue, which can negatively affect fetal outcomes<sup>1</sup>.

We present the case of a pregnant patient with advanced-stage LC (stage IV), highlighting the diagnostic approach, pregnancy management, delivery, and postpartum course.

## Case report

A primigravida, 46-year-old medical worker and radiologist, in the 30th week of pregnancy, achieved through the fourth attempt at *in vitro* fertilization (donor egg), presented to the Clinic for Gynecology and Obstetrics "Narodni Front" Belgrade, Serbia, due to right-sided chest pain radiating to the spine, tachycardia, and shortness of breath. The pain and shortness of breath had been present for the past 2 weeks, while tachycardia had been ongoing for several months

(treated with Presolol® 10 mg prescribed by a primary care internist). The patient also reported an occasional dry cough but denied other respiratory symptoms. She denied weight loss (with a total weight gain of 3 kg during pregnancy). She was a former smoker with a history of smoking for 15 years (20 cigarettes *per day*), but had quit a year prior.

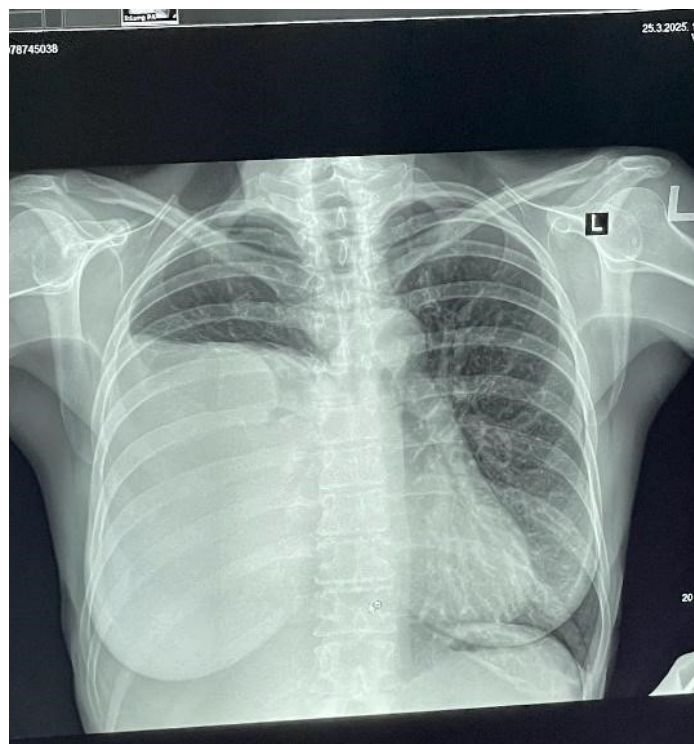
Upon hospital admission, clinical, ultrasound, and laboratory evaluations were performed.

Laboratory results included: leukocytes  $9.8 \times 10^9/L$  [reference range (RR):  $3.4\text{--}9.7 \times 10^9/L$ ]; hemoglobin 98 g/L (RR: 119–157 g/L); platelets  $593 \times 10^9/L$  (RR:  $158\text{--}424 \times 10^9/L$ ); C-reactive protein 147.9 mg/L (RR: less than 5 mg/L); potassium 5.0 mmol/L (RR: 3.5–5.1 mmol/L); lactate dehydrogenase 789 U/L (RR: 0–241 U/L); D-dimer 0.5 mg/L (III trimester cut-off 2.12 mg/L); erythrocyte sedimentation rate 70 mm/h (RR: less than 50 mm/h). After consultation with an internist, due to the patient's general condition and reported symptoms, a chest and heart X-ray was indicated.

The chest X-ray showed a massive right-sided effusion up to the anterior margin of the second rib, with the effusion shadow superimposed on a clearly contoured oval-shaped tumor shadow in the right hemithorax (Figure 1).

Due to these X-ray findings and the patient's symptoms, urgent further diagnostics were performed, including a computed tomography (CT) scan of the chest.

CT imaging showed a very large lobulated necrotic tumor in the right lung in continuity with the rib, extending into the pleura, and involved almost the entire right lung parenchyma. Only the apical segment of the upper lobe (segment I) and a small part of the posterior segments of the middle and lower lobes remained unaffected. After contrast



**Fig. 1 – X-ray image of the heart and lungs of a woman at 30 weeks of gestation showing massive right pleural effusion extending to the anterior margin of the second rib, with a well-defined oval tumor shadow in the right hemithorax and involving almost the entire right lung parenchyma.**

administration, the lesion demonstrated heterogeneous opacification and contained several central microcalcifications, measuring approximately  $15 \times 14 \times 17$  cm [anteroposterior  $\times$  transverse  $\times$  craniocaudal (AP  $\times$  LL  $\times$  CC)]. The tumor caused a marked shift of the mediastinal structures toward the left. It demonstrated compression and infiltration of the right pulmonary artery, the right main bronchus and its branches, with suspected involvement of the superior *vena cava*. A loculated pleural effusion containing clear fluid, measuring up to 1.5 cm in thickness, was present. In addition, a small thrombus was identified within the right pulmonary veins, resulting from compression by the tumor. Enlarged mediastinal lymph nodes were noted: 2R –  $15 \times 11$  mm, 4R –  $12 \times 10$  mm. Bilateral reactive axillary lymph nodes were present, measuring up to  $13 \times 10$  mm. No evidence of tumor infiltration was identified in the remaining lung parenchyma. Cross-sections through the upper abdomen revealed multiple hypodense hepatic lesions, the largest located subcapsularly in segments II/III, measuring  $22 \times 17$  mm, with central contrast enhancement. Additionally, a  $3 \times 2$  cm osteolytic soft-tissue lesion was identified in the L1 vertebral body, consistent with a probable metastatic deposit.

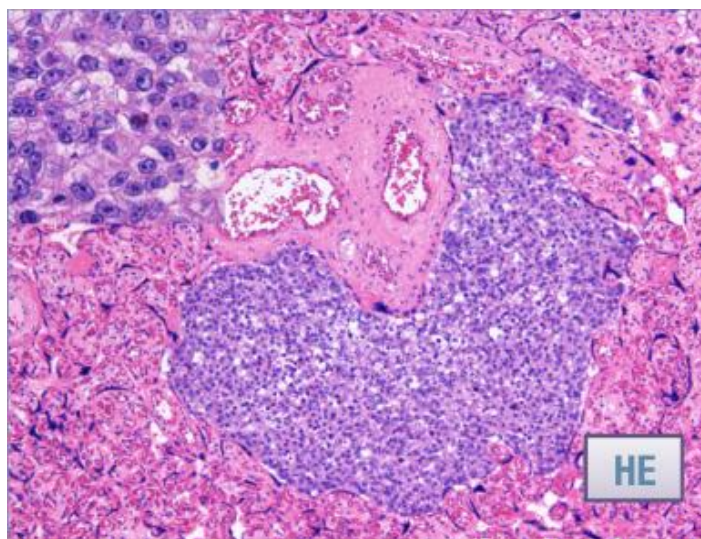
A tru-cut biopsy of the lesion in the right lung was indicated and subsequently performed. Histopathological (HP) examination of the biopsy revealed: Histology and immunohistochemistry (IHC): tumor cells are CK AE1/AE3+ cytoplasmic dot-like, CD56 diffuse ++, synaptophysin diffuse+++, Pax7+, TTF-1-, vimentin -, CD99-, Nkx 2.2-, ERG1 -, Fli1-, pRb IHC nuclear expression observed in about 50% of tumor cells, Ki-67 shows nuclear immunopositivity in about 40% of tumor cells. The described morphological changes and IHC profile of the tumor cells are consistent with small cell LC (Figure 2).

With the HP findings, the patient was presented to the Gynecological Council at Obstetric and Gynaecology Clinic “Narodni Front”, the Pulmonology Council of the Clinic for Pulmonology, University Clinical Center of Serbia, Belgrade, Serbia, and the Lung Council at the Institute for Oncology and Radiology of Serbia, Belgrade.

A discussion was held with the patient regarding the possibility of preterm termination of the pregnancy. Corticosteroid therapy was prescribed to promote artificial maturation of the fetal lungs, aiming to allow the earliest possible start of treatment for the underlying disease [systemic chemotherapy according to the EP protocol (includes etoposide and cisplatin), which the above-mentioned councils were initially reluctant to apply to a pregnant patient].

Additional diagnostics were performed to prepare for the treatment of the underlying disease: magnetic resonance imaging (MRI) of the brain showed an expansive lesion in the left cerebellum, mostly cystic with a small solid component, surrounded by a wide zone of perilesional edema, most likely secondary deposit and less likely of other etiology, along with signal alteration in the pons of unclear etiology. MRI of the cervical and thoracic spine indicated polydiscopathy with protrusions of the disc-osteophyte complex at the C4–5 intervertebral space dorsolaterally on the right, with mild irritation of the right C5 nerve root, and at C5–6 dorsally circumferentially with minor caudal migration of disc material medially and paramedially bilaterally, compromising the C7 nerve roots bilaterally, in close relation to the ventral aspect of the spinal cord without intramedullary myelopathy and with relative spinal canal stenosis (AP diameter  $\sim 9$  mm), along with spondylosis and early spondyloarthritis. MRI of the abdomen showed multiple focal liver lesions highly suspicious for secondary deposits.

The patient was closely monitored at the Department of High-Risk Pregnancy, Clinic for Gynecology and Obstetrics “Narodni Front” from March 25, 2025, to April 10, 2025. Ultrasound showed a mildly growth-restricted fetus (small for gestational age) without visible anomalies, in breech presentation, amniotic fluid index (AFI) 100 mm, placenta located on the posterior wall, 27 mm thick, grade II maturity by Grannum with central cord insertion. Doppler indices of uteroplacental and fetoplacental circulation were normal. The biophysical profile was normal (8/8). Daily ultrasound monitoring and non-stress cardiotocography were performed.



**Fig. 2 – The immunohistochemical profile of the patient is consistent with small cell lung cancer (HE staining, magnification  $\times 60$ ).  
HE – hematoxylin-eosin.**

The patient received antibiotic, symptomatic, supportive, and corticosteroid therapy and was evaluated by an internist, hematologist, and anesthesiologist.

At 32 weeks of gestation, a sudden decrease in AFI to 50 mm was diagnosed, with changes in fetoplacental and fetal circulation (cerebro/umbilical ratio < 1), indicating fetal hypoxemia. Given the conception *via* assisted reproductive technology, the diagnosis of LC, and the breech presentation of the fetus, it was decided to terminate the pregnancy by elective cesarean section.

The patient was medically, hematologically, and anesthesiologically prepared, and on April 10, 2025, an elective cesarean section was performed at 31+6 weeks of gestation. A viable male infant was delivered, weighing 1,550 g, with Apgar scores of 7/8. After stabilization in the neonatal Intensive Care Unit, the infant was transferred to the Institute for Neonatology, Belgrade, Serbia.

In the postoperative period, while the patient was in the Intensive Care Unit, she received one unit of blood of the appropriate blood type due to severe anemia, which she tolerated well. Prophylaxis for deep vein thrombosis and thromboembolic complications was administered, along with antibiotic and antiulcer therapy. The placenta was sent for HP examination.

Placental HP examination revealed the following macroscopic findings: the placenta measured 200 × 180 × 30 mm, with preserved fetal surface, a paramarginal cord insertion (150 mm), and a three-vessel cord. More than 70% of the placental tissue showed grayish-yellow areas. Histology and IHC showed synaptophysin diffusely positive, chromogranin A diffusely positive, CD56 positive, TTF-1 positive, Ki-67 ~80%, and CK7 focally positive. The conclusion stated that the findings were metastatic in nature and consistent with small cell LC.

On April 14, 2025, the patient was discharged from the Clinic in stable general condition with normal gynecological and ultrasound findings. In coordination with the team of physicians from the Institute for Oncology and Radiology of Serbia, the patient was presented to the Council the following day to plan the initiation of therapy for the underlying disease.

The patient passed away on April 17, 2025, after one round of radiation therapy to the affected part of the spinal column.

## Discussion

Epidemiological data on cancer mortality show a decreasing trend for most malignant diseases across Europe, owing to the progress in prevention, screening, and treatment. However, mortality from LC is increasing, particularly among women<sup>5</sup>. LC is the second most common cancer in the world and has the highest mortality rate<sup>6</sup>. It is the second most common cancer in men after prostate cancer, and the fourth most common cancer in women after breast cancer, colorectal cancer, and thyroid cancer<sup>2</sup>. Malignancy is the second leading cause of death among women aged 25 to 39 years<sup>6</sup>.

Cancer during pregnancy is rare, with an incidence of approximately 1 in 1,000 pregnancies. These numbers are expected to increase in the coming decades due to delayed childbearing<sup>6,7</sup>. The most common cancers diagnosed during pregnancy are breast cancer, cervical cancer, hematological malignancies (such as lymphomas and acute leukemias), and melanoma<sup>7</sup>.

Early diagnosis is extremely important. The 5-year survival rate varies greatly depending on the stage of diagnosis, ranging from 57% for localized disease to only 5% for patients with metastatic disease<sup>8</sup>. The two most effective strategies for reducing LC mortality are reducing tobacco use and exposure to tobacco smoke<sup>9</sup> and early diagnosis through LC screening programs<sup>10</sup>.

Smoking remains the leading risk factor for LC, considering that 18.4% of the population in the European Union still smokes. Smoking cessation is therefore a key strategy for the prevention and management of LC. Tobacco control policies such as increasing tobacco taxes, creating smoke-free environments, educating the population, especially women and pregnant women, organizing health campaigns, and providing accessible smoking cessation counseling are expected to have a significant impact on public health<sup>11</sup>.

Clinical screening studies, including the 2020 study by De Koning et al.<sup>9</sup> published in the *New England Journal of Medicine*, have shown that low-dose CT effectively reduces mortality, shifts LC diagnosis toward earlier stages of the disease, and improves survival rates and quality of life<sup>9, 12–14</sup>.

The diagnosis of malignant tumors during pregnancy has attracted increasing attention due to its relatively higher prevalence and its negative impact on outcomes for both the mother and the newborn.

The incidence of LC during pregnancy is lower compared to breast cancer, cervical cancer, and Hodgkin lymphoma, but it has been increasingly documented over the last two decades<sup>2</sup>. The first case of LC during pregnancy was described in 1953 by Barr<sup>15</sup>, and more than 90 additional cases have been reported since then<sup>2–4</sup>.

LC during pregnancy has been rarely reported, but an increase in incidence over the past 20 years is expected due to a higher number of young female smokers<sup>1, 4</sup>. In pregnant women, LC is usually diagnosed at an advanced stage, most commonly stage III or IV, due to nonspecific or absent symptoms<sup>2–4</sup>. The most commonly reported nonspecific symptoms include chest pain, cough, sputum production, and shortness of breath. Diagnosis during pregnancy is often limited due to potential risks to the fetus or embryo. Because of this, these symptoms are often attributed to pneumonia or asthma, which delays accurate diagnosis and treatment<sup>1, 4</sup>.

A study by Zhou et al.<sup>4</sup> from 2023 analyzed 93 cases of LC during pregnancy between 1953 and 2022. The average age of the pregnant women was 34 years, and the average gestational age at diagnosis was 26 weeks. Unfortunately, nonspecific symptoms such as cough, shortness of breath, and chest pain, as seen in our patient as well, often lead to

delayed diagnosis and disease progression to advanced stages. Metastatic disease was identified in 35.5% of all cases. All reported cases had a long history of nicotine exposure. HP analysis showed that 81 cases were non-small cell LC, with placental metastases detected in 35.6% of cases. Metastases were also diagnosed in two newborns <sup>4</sup>.

Non-small cell LC accounts for approximately 85% of LCs and is more commonly associated with older populations, with smoking as the primary risk factor <sup>16</sup>.

Metastatic transmission of LC to the fetus and placenta is rare, with 11 reported cases of placental metastases and 3 cases of fetal metastases described in the literature <sup>1-4</sup>. In 27% of cases, mothers died within the first 24 hrs after delivery, while in 33.3% of cases, survival was approximately 12 months <sup>4</sup>. Our patient died 7 days after delivery. Similar results were reported in a study by Jacobson et al. <sup>2</sup>.

There is currently no established protocol for the diagnosis and treatment of LC during pregnancy. According to available guidelines, oncological therapy during pregnancy is generally avoided. Chemotherapy is often avoided because pregnancy can change drug metabolism and because of potential toxicity to the fetus. The general risks associated with chemotherapy include premature birth, low birth weight, transient neonatal tachypnea, and temporary neonatal leuko-

penia <sup>17, 18</sup>. Chemotherapy and radiotherapy are typically initiated after delivery <sup>1, 18-20</sup>.

In general, the golden rule in treating pregnant women with cancer is that treatment should not differ from treatment given to non-pregnant patients <sup>21</sup>. The main goal of treatment during pregnancy is to improve maternal survival by treating the underlying disease while continuously protecting the fetus from the harmful effects of therapy.

## Conclusion

Delayed childbearing and long-term smoking habits have contributed to an increase in lung cancer incidence over the past 10 years. The diagnosis and treatment of lung cancer during pregnancy are challenging. It involves early detection, making treatment decisions, and balancing the health of the pregnant woman, effective tumor treatment, and the potential risks to the fetus. A multidisciplinary approach is essential to achieve the best possible outcome for both the patient and her pregnancy.

## Conflict of interest

The authors declare no conflict of interest.

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Received on March 16, 2026

Revised on April 21, 2026

Revised on May 13, 2026

Accepted on May 27, 2026

Online First July 2026