CASE REPORT

EXPERIMENTAL ONCOLOGY

https://doi.org/10.15407/exp-oncology.2025.01.096

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CHOLANGIOCARCINOMA IN TWIN PREGNANCY: A CASE REPORT

Cholangiocarcinoma during pregnancy is a very rare condition. We present the case of a 35-year-old pregnant woman with intrahepatic cholangiocarcinoma. To our knowledge, this is the first case of cholangiocarcinoma in a patient with twin pregnancy. At 25 weeks of gestation, surgical intervention was performed: right-sided hemihepatectomy, lymphadenectomy D3, and diaphragmatic peritoneumectomy on the right side. At 33 weeks of pregnancy, a cesarean section was performed. Currently, the patient is receiving chemotherapy. A multidisciplinary approach should be a standard workup in making decisions regarding the treatment strategy for a pregnant patient with a cancer diagnosis.

Keywords: cholangiocarcinoma, pregnancy, case report.

According to the world literature, the incidence of malignant tumors during pregnancy is 1 case per 2000—3000 pregnancies, and in recent years, there has been observed a tendency toward an increase [1—3]. The most frequently occurring cancers during pregnancy include breast, cervical, and ovarian cancers, melanoma, and lymphoma [1—4]. Cholangiocarcinoma represents less than 1% of all malignancies and about 10—15% of all primary liver cancers [5]. This is an uncommon and very aggressive malignancy with a median survival of 3 to 6 months [6, 7]. Cholangiocarcinoma during pregnancy is an extremely rare condition with limited cases reported in the literature, therefore, very limited data are available on the diagnosis, progression, and pregnancy-related outcomes of this malignancy.

Currently, there are no clear guidelines and recommendations in the world and Ukraine regarding the management of pregnant women with cancer, therefore decisions regarding each case should be made individually with the help of a multidisciplinary team, taking into account the risks for the mother and fetus.

Case presentation

Patient K., a 35-year-old gravida, was admitted to the Department of Operative Gynecology with a diagnosis of metastatic hepatic adenocarcinoma

Citation: Dronova VL, Dronov OI, Lyalkin SA, Mokryk OM, Teslyuk RS. Cholangiocarcinoma in twin pregnancy: A case report. *Exp Oncol*. 2025; 47(1): 96-101. https://doi.org/10.15407/exp-oncology.2025.01.096

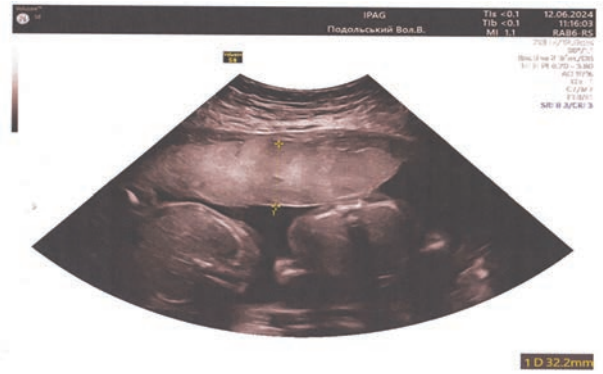


Fig. 1. Ultrasound examination. Progressing pregnancy at 22 weeks + 1 day. Diamniotic, dichorionic twins

of Segment 6 (Sg6). Pregnancy I, 22—23 weeks. Twins: dichorionic diamniotic.

From the anamnesis: The patient has her first, desired twin pregnancy. From the 16th week of gestation, the patient presented with pain in the right hypochondrium, which worsened after eating and active fetal movements. An ultrasound scan of the abdominal cavity was performed. The lesion in Sg6 of the liver was detected. At the 16th week of pregnancy, a biopsy of this neoplasm was performed. According to the results of the pathohistological study, the morphological picture and the results of the immunohistochemistry correspond to adenocarcinoma originating from the gastrointestinal tract or the pancreatobiliary system. The patient has a complicated heredity: her father and paternal grandfather died of gastric cancer.

The following examinations were performed:

1) Fetal ultrasound, which confirmed a progressive pregnancy at 22 weeks + 1 day (Fig. 1). Diamniotic dichorionic twins. No pathological changes were detected in the fetuses.

2) CT scan of the chest cavity with i.v. enhancement, which did not reveal signs of inflammatory and neoplastic changes.

3) MRI of the abdominal cavity with i.v. enhancement: Sg6 liver tumor with invasion to veins, capsule, delayed enhancement, minimally prestenotically dilated subsegmental bile ducts — it was impossible to exclude mass-forming cholangiocellular carcinoma. Periportal lymphadenopathy. No gastrointestinal or pancreatic neoplasms were detected. Moderately enlarged spleen. Right-sided ureterohydronephrosis (uterine compression).

In the parenchyma of liver segment Sg6, there is a nodular solid tumor measuring 68 × 50 × 62 mm. It invades the segmental Glisson's capsule of Sg6, infiltrates the liver capsule, exhibits high cellular density, restricts diffusion (ADC 0.75), and demonstrates a delayed contrast accumulation. The posterior subsegmental Glisson's capsule 8 and small branches of the right hepatic vein (RHV) are involved along the upper edge of the mass. The subsegmental bile ducts of Sg6 are minimally prestenotically dilated. A small avascular cyst in Sg6 — 4 mm. In the remaining parenchyma, the liver exhibits a homogeneous MR signal. Below the portal vein, in the area between the head of the pancreas, the duodenum, and the inferior vena cava, an enlarged lymph node measuring 24 x 17 mm with a heterogeneous structure is observed. The portal and hepatic veins show no signs of thrombosis. The intrahepatic bile ducts are not dilated, demonstrating a classic pattern of convergence.

4) Esophagogastroduodenoscopy: erythematous gastropathy. Duodenogastric reflux.

5) Oncomarkers: CA 72-4 — 3.16 U/mL (reference range < 6.0); CA — 242 < 0.5 U/mL (reference range < 20); CA 19 — 9 < 1.2 U/mL (reference range < 37); carcinoembryonic antigen — 4.88 ng/mL (reference range < 2.5).

The AFP level was not tested because the patient was pregnant and with twins.

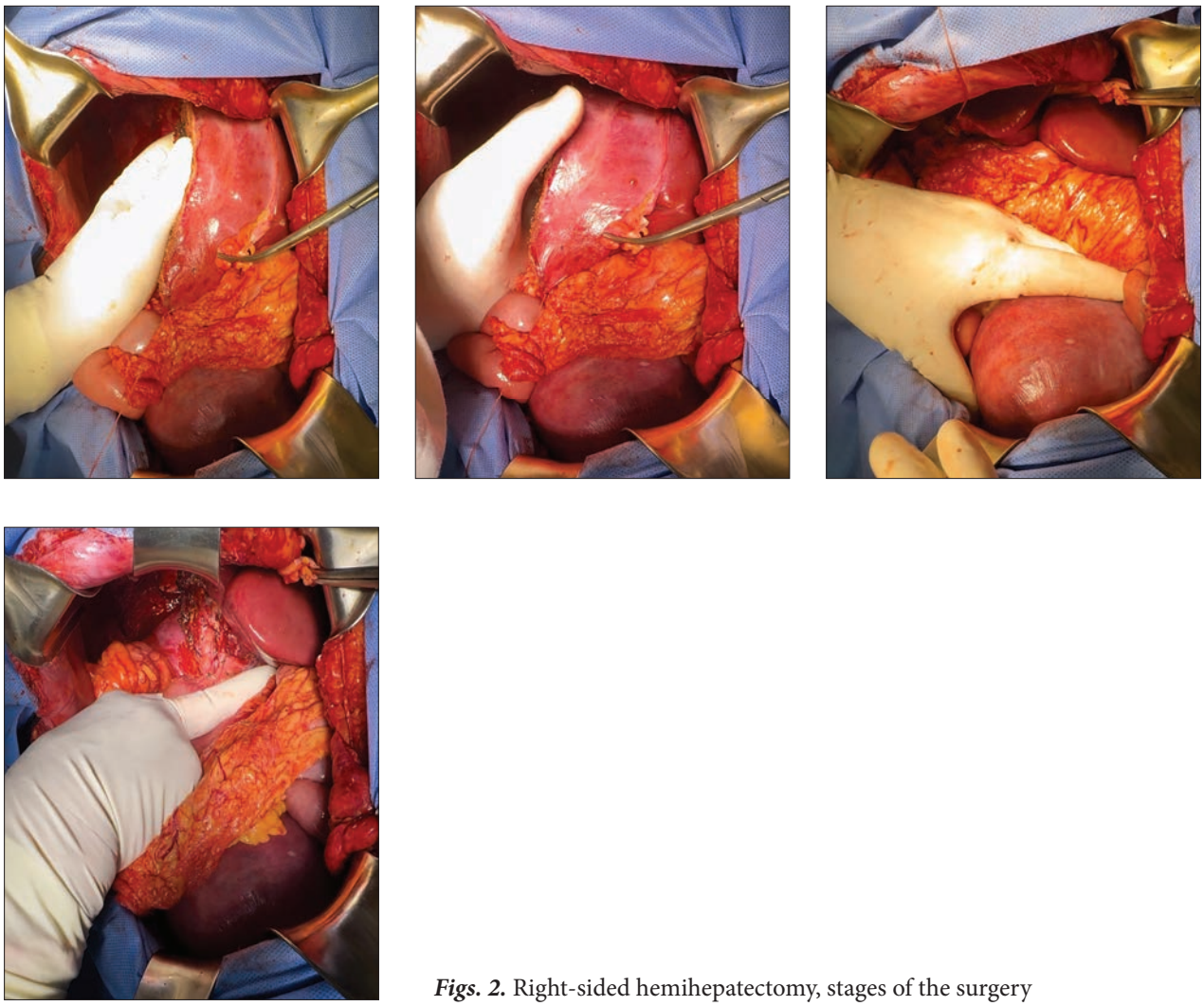
Based on the above data, the clinical diagnosis was established as primary liver carcinoma (cholangiocarcinoma?) cT3N1M0, stage III. First pregnancy, 24—25 weeks. Twins: dichorionic diamniotic.

The decision of the multidisciplinary team: Considering the presence of a histologically verified malignant liver tumor, first detected during this pregnancy at 16—17 weeks, in a patient with a dichorionic diamniotic twin pregnancy, and the woman's strong desire to preserve it, it was decided to proceed with surgical treatment during the pregnancy while maintaining it. Prophylaxis for fetal respiratory distress syndrome was performed, and a "progesterone block" was established.

Surgical intervention: Right-sided laparotomy according to Rio-Branco. Right hemihepatectomy. Lymph node dissection (D3). Diaphragmatic peritonectomy on the right. Abdominal cavity drainage.

Intraoperative findings:

- Tumor in Sg6 extending along Glisson's capsule into Sg5, measuring 5 × 6 cm, reaching the bifurcation of the portal vein.



Figs. 2. Right-sided hemihepatectomy, stages of the surgery

• Enlarged dense lymph node of group 12, measuring 1.5 × 1.5 cm.

• Small lesions (carcinomatosis) on the diaphragmatic peritoneum on the right.

Lymphadenectomy (D3) was performed from the left gastric artery region, including lymph nodes of groups 8, 9, 12, and 13.

Considering the extent of the tumor process involving segments Sg5—6, the decision was made to perform a right-sided anatomical hemihepatectomy. This included transection and suturing of two branches of the right portal vein, closure of the right lobar bile duct, and ligation of the right hepatic artery (Figs. 2 and 3). Total blood loss was 1600 mL. The duration of surgery was 7 h 30 min. The duration of anesthesia was 8 h 45 min. On the following day after surgery, an ultrasound of the fetuses was performed: pregnancy at 24 weeks + 3 days, progressing. Dichorionic diamniotic twins.

Postoperatively, the following was registered: hypokalemia, hyperchloremia, hypoglycemia, hypoalbuminemia, and the gradual increase in bilirubin levels, predominantly due to the direct fraction, and cytolytic syndrome (elevated ALT and AST levels). Iron deficiency anemia was\ confirmed by a low ferritin level of 46.1 ng/mL (reference range: 10—291 ng/mL), which was considered low for a pregnant woman with twins, particularly in the context of cancer liver pathology after right hemihepatectomy.

According to the results of the pathological examination of the postoperative specimen, the diagnosis was intrahepatic cholangiocarcinoma, large-duct variant: pT2 pN1 (1/8) pM1 L1 V0 Pn1 R0.

Timely and adequate correction and treatment of the associated conditions were carried out, including antibacterial therapy; gastroprotective therapy; glucocorticoid therapy (Solu-Cortef at a dose of 250 mg/day with gradual dose reduc-

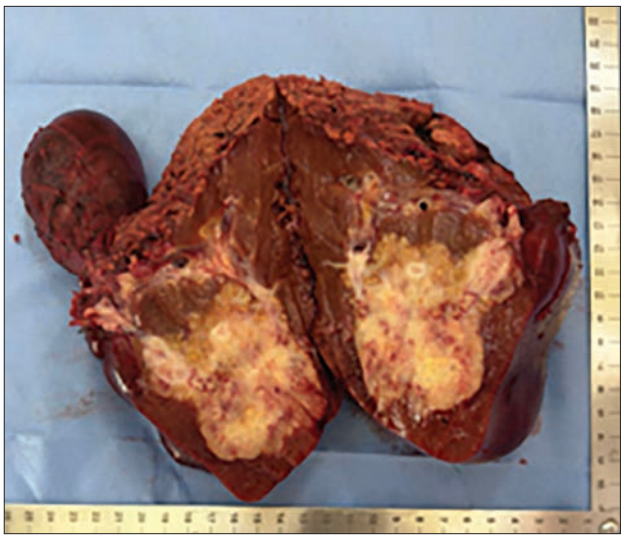


Fig. 3. Macroscopic specimen of the right lobe of the liver

tion); anticoagulant therapy; hormonal therapy; daily correction of potassium, chloride, glucose, and protein levels in the blood; and close monitoring of the fetuses' condition.

During the treatment, 2 pleural punctures due to pleural effusion, which is characteristic after large liver resections, were performed. Ultrasound monitoring of the fetuses was performed weekly.

Postoperatively, an increase in bilirubin levels to 83 μmol/L with normal transaminase levels and hypokalemia were observed. Gilbert's syndrome was excluded through molecular-genetic testing. An MRI cholangiopancreatography was performed without intravenous contrast: status post right-sided hemihepatectomy. The bile ducts are not dilated. No signs of disease progression were found. Postoperative fluid accumulation along the umbilical fissure and under the liver.

During the stay in the surgical ward, daily monitoring of the pregnancy was conducted. The uterus remained in normal tone; blood pressure did not increase; peripheral edema was absent. No proteinuria was detected throughout the entire observation period. The patient experienced a mild form of COVID-19 for 10 days and received symptomatic treatment.

Two months after the surgery, the patient returned to the Department of Operative Gynecology. On the same day, an ultrasound of the fetuses confirmed the antenatal death of one of them. The pregnancy was at 33 weeks + 1 day. One fetus was in breech presentation and the other — in transverse lie. The condition of the latter was not disturbed. Left-sided hydronephrosis of stage I. Respiratory distress syndrome (RDS) prevention for the fetus was carried out using dexamethasone. During the RDS prevention procedure, both ultrasound and cardiotocography (CTG) monitoring of the fetus were performed.

At 33 weeks + 3 days, through a cesarean section in the lower uterine segment, the dead preterm girl was delivered. She had a double nuchal cord around her neck with a true knot at the first twist and around her body "like a shoulder belt," weighing 1560.0 g and measuring 44 cm in length. The live preterm girl was delivered, weighing 2120.0 g and measuring 44 cm, with an Apgar score of 4—5 points. The total blood loss was 450 mL. Lactation was immediately suppressed with cabergoline. The postoperative postpartum period proceeded without complications.

One week after delivery, a CT scan of the chest organs with intravenous contrast was performed: no signs of inflammatory or neoplastic changes in the lung parenchyma were detected. According to the results of an MRI of the abdominal organs with intravenous contrast: status post right-sided hemihepatectomy. In the postoperative period, fluid accumulation along the umbilical fissure and under the liver at the site of lymphodissection decreased.

Three weeks after delivery, a session of plasmapheresis was performed, after which the bilirubin levels returned to normal. The plasmapheresis session allowed the initiation of chemotherapy according to the protocol: gemcitabine 1000 mg/m^2 and cisplatin 25 mg/m^2 on days 1 and 8, a 21-day cycle. The infant was in the neonatal intensive-care unit and post-intensive-care unit for 58 days. She was discharged home in good health.

Currently, the patient has completed the 3rd cycle of chemotherapy. Follow-up radiological examinations were performed: CT scan of the chest organs with intravenous contrast and MRI of the abdominal organs with intravenous hepatotropic contrast — no signs of disease progression were found.

Discussion

This case report is, to our knowledge, the first case of cholangiocarcinoma in a patient with twin pregnancy. At present, only 12 cases of cholangio-

carcinoma occurring during pregnancy (one fetus) and postpartum have been reported (based on PubMed database search). Out of them, in 4 patients, the diagnosis was established only after delivery [8]. Of those 12 cases, 3 patients died within 2 mont hs after diagnosis without starting specialized treatment, the outcome for another 4 is unknown, 4 patients received surgical or chemotherapy treatment, and only 1 patient received combined treatment during pregnancy [8]. The obstetric situation for the majority of these patients was unknown. Therefore, the case of cholangiocarcinoma during a twin pregnancy described by us seems to be unique.

In a pregnant patient, cholangiocarcinoma is a significant management challenge given the rarity and poor prognosis of this disease.

In our case, the diagnosis in the pregnant patient was histologically confirmed at 16 weeks of gestation at her place of residence. However, the referral for further oncological examination to specialized medical institutions was not made by her doctors. At 21—22 weeks of pregnancy, the patient went to our Center. There was a delay of 5—6 weeks before the patient was admitted to the Department of Operative Gynecology. This is important because performing surgery at 17—18 weeks and 24—25 weeks (in our case) differs because of significant implications, primarily due to the twin pregnancy and the progression of the malignant disease.

Surgical resection is the only potentially curative treatment, so the patient was operated at 25 weeks of pregnancy. The surgical treatment was performed without significant complications.

At 33 weeks of gestation, the antenatal death of one fetus was diagnosed due to double nuchal cord entanglement. At 33 weeks + 3 days, a cesarean section was performed, resulting in the delivery of the dead preterm girl and the live preterm girl. The postoperative postpartum period proceeded without complications.

In the first-line setting, systemic treatment includes chemotherapy with gemcitabine, cisplatin, and anti-PD-L1 antibody durvalumab [9], which is unavailable in Ukraine, so the patient received only chemotherapy.

Currently, six months after the surgical intervention, the patient is free from malignant disease and has a healthy child!

REFERENCES

1. Silverstein J, Annalisa L, Chien A, et al. Multidisciplinary management of cancer during pregnanacy. *JCO Oncol Pract*. 2020;16(9):545-557. https://doi.org/10.1200/OP.20.00077
2. Wolters V, Heimovaara J, Maggen C, et al. Management of pregnancy in women with cancer. *Int J Gynecol Cancer*. 2021;31(3):314-322. https://doi.org/10.1136/ijgc-2020-001776
3. de Haan J, Verheecke M, Van Calsteren K, et al.Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol.* 2018;19:337-346. https://doi.org/10.1016/S1470-2045(18)30059-7
4. Masturzo B, Parpinel G, Macchi C, et al. Impact of cancer in the management of delivery: 10 years of variations. *J Matern Fetal Neonatal Med*. 2020;33:2006-2011. https://doi.org/10.1080/14767058.2018.1536117
5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019;69:7-34. https://doi.org/10.3322/caac.21551
6. Doherty B, Nambudiri VE, Palmer WC. Update on the diagnosis and treatment of cholangiocarcinoma. *Curr Gastroenterol Rep*. 2017;19(01):2. https://doi.org/10.1007/s11894-017-0542-4
7. Francis AP, Chang M, Dolin CD, et al. Recurrent cholangiocarcinoma in pregnancy: a case report. *AJP Rep*. 2018;8(4):e261-e263. https://doi.org/10.1055/s-0038-1675376
8. Washburn L, Mahipal A, Jatoi A, et al. Postpartum related intrahepatic cholangiocarcinoma with *FGFR2* fusion and severe hyperbilirubinemia with response to FGFR inhibitor pemigatinib: case report and review. *J Gastrointest Oncol*. 2023;14(6):2627-2636. https://doi.org/10.21037/jgo-23-693
9. Oh DY, Ruth He A, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. *NEJM Evidence* 2022;1:EVIDoa2200015 https://doi.org/10.1056/EVIDoa2200015

Submitted: January 10, 2025

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ХОЛАНГІОКАРЦИНОМА ПРИ ВАГІТНОСТІ
ДВІЙНЕЮ: КЛІНІЧНИЙ ВИПАДОК

Холангіокарцинома під час вагітності є дуже рідкісним захворюванням. Ми представляємо випадок 35-річної вагітної жінки з внутрішньопечінковою холангіокарциномою. Це перший випадок холангіокарциноми у пацієнта з вагітністю двійнею. У терміні вагітності 25 тижнів виконано оперативне втручання: правобічна гемігепатектомія, лімфодисекція D 3 і перітонеумектомія діафрагми справа. У терміні 33 тижні виконано кесарів розтин. На даний час пацієнтка отримує хіміотерапію. Мультидисциплінарний підхід є ключовим в ухваленні рішення щодо тактики лікування вагітної з онкологічним діагнозом.

Ключові слова: холангіокарцинома, вагітність, клінічний випадок.