

Atypical presentation of intrahepatic cholangiocarcinoma---Fever and ascites in a postpartum lady

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ABSTRACT

Intrahepatic cholangiocarcinoma is an uncommon malignancy which usually occurs in the 7th decade. Here we present a postpartum patient with fever, hepatomegaly, and ascites, who was diagnosed to have metastatic intrahepatic cholangiocarcinoma.

Keywords: Cholangiocarcinoma, jaundice in pregnancy, pregnancy associated cancer

Introduction

Cholangiocarcinoma accounts for 3% of gastrointestinal malignancies.^[1,2] Median age of presentation is the 7th decade.^[2] Occurrence of cholangiocarcinoma in a pregnant patient is uncommon, with few reported cases.^[3-7] Here we present a postpartum patient with cholangiocarcinoma.

Case Presentation

A 28-year-old lady presented with 1 week of high-grade fever on postpartum day 10. She had right upper abdominal pain and jaundice from week 20 of gestation. She had postprandial vomiting throughout pregnancy. She underwent regular antenatal checkups and fetal ultrasound scans during this pregnancy. Provisional diagnosis of acute fatty liver of pregnancy (AFLP) was made by her treating physician. She delivered via normal vaginal delivery at week 33. Abdominal distention, initially attributed to pregnancy, worsened after delivery. There was no

loss of weight, melena, pruritus, or pale stools. She denied history of smoking, diabetes mellitus, hypertension, and malignancy in family members. Due to worsening symptoms she was referred to our hospital for evaluation.

On examination, her pulse rate was 122/min and temperature 101F. Systemic examination revealed a hard liver palpable 12 cm below the right costal margin. Shifting dullness was present. Pelvic examination was normal.

Differential diagnoses considered were infectious causes (liver abscess, malaria, endometritis) and non-infectious etiologies (Budd Chiari syndrome, AFLP). Neoplastic etiology was also considered due to chronic history of jaundice and abdominal pain. Blood investigations have been mentioned in Table 1. Ascitic fluid analysis revealed 240 cells/ml (neutrophils-24%, lymphocytes-76%), albumin and protein of 1.4 g/dl and 3.1 g/dl, respectively. Blood, urine, and ascitic fluid cultures did not reveal growth. Computed tomography (CT) scan showed hepatomegaly with multiple liver lesions, largest being 13 × 10 × 8 cm. Multiple lung nodules, enlarged lesser omental, para-aortic, aortocaval lymph nodes, and lytic lesion in the first lumbar vertebra were noted.

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Ultrasound-guided biopsy of the largest liver lesion was done. This was reported as cholangiocarcinoma [Figure 1]. Our final

diagnosis was metastatic intrahepatic cholangiocarcinoma. Our patient was initiated on palliative chemotherapy with capecitabine and opted for follow-up at another center.

Table 1: Relevant laboratory investigations

Test	Patient's Values	Reference Range
Hemoglobin (gram/dl)	8.5	11-15
Total Leucocyte Count (mm ³)	13,400	4,400-11,000/ μ L
Neutrophils	84	40-70%
Lymphocytes	8	20-40%
Monocytes	8	2-6%
Platelets	3,42,000	1.5-4.5 lacs/ μ L
Creatinine (mg/dL)	0.52	0.5-1.4
Total bilirubin (mg/dl)	0.50	0.5-1
Direct bilirubin	0.35	0.5-1
SGOT (U/L)	48	8-40
SGPT (U/L)	31	5-35
Alkaline phosphatase (U/L)	302	40-125
Total protein (gram/dl)	5.9	6-8.5
Albumin (gram/dl)	2.1	3.5-5
Gamma-glutamyl transferase (U/L)	106	<55
Beta-HCG (mIU/ml)	11	<5
Carcinoembryonic Antigen	11.5	<5
Alpha-fetoprotein (IU/ml)	29.6	<5
HIV 1 and 2 antibodies	Non-reactive	
Hepatitis B surface antigen	Negative	
Hepatitis C antibody	Negative	

Discussion

Common causes of postpartum fever include endometritis, urinary tract infection, mastitis, and perineal/episiotomy site infections.^[8,9] Cholangiocarcinoma presenting as postpartum fever is rare.^[10]

Risk factors for cholangiocarcinoma include primary sclerosing cholangitis, hepatobiliary flukes, bile duct cystic disorders, cirrhosis, diabetes mellitus, and obesity.^[11-16] Our patient was a 28-year-old female without any risk factors for cholangiocarcinoma.

In our patient, ascitic fluid analysis was consistent with malignant ascites (low-serum ascites albumin gradient, high-ascitic fluid protein). Fever, though uncommon, has been reported in other cases of cholangiocarcinoma.^[17,18]

Abdominal pain and jaundice are common symptoms of cholangiocarcinoma.^[19] Clinical presentation of cholangiocarcinoma can mimic that of AFLP and HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) [Table 2].^[4,6]

Table 2: Cholangiocarcinoma diagnosed in pregnancy/postpartum period

Clinical Features	Case 1 (Qasrawi <i>et al.</i> ^[4])	Case 2 (Balderston <i>et al.</i> ^[6])	Case 3 (Goswami <i>et al.</i> ^[7])
Age	38	23	22
Obstetric history	4 th pregnancy	Primigravida	NA
Symptoms and duration	RUQ pain, dark urine - one week	Vomiting, abdominal pain*	Abdominal pain, weight loss, fever-three weeks
Gestation in weeks at symptom onset	36	26	2 weeks post-partum
Abnormal examination findings	Palpable liver, jaundice	RUQ mass, jaundice, new onset high blood pressure	RUQ mass, jaundice
Onset of jaundice	36 weeks of gestation	26 weeks of gestation	2 weeks postpartum
Laboratory investigations (Reference range):			
Total bilirubin in mg/dL (0.5-1)	6.4	3.6→5.1	17.3
Direct bilirubin in mg/dL	5	NA	10.5
Aspartate Aminotransferase in Units/L (8-40)	83	70	95
Alanine Aminotransferase in Units/L (5-35)	87	31	70
Alkaline Phosphatase in Units/L (40-125)	319	NA	680
Prothrombin Time with International Normalized ratio in seconds (11-13.5)	17 and 1.4	NA and 1.8	NA
Imaging:			
Ultrasound	Hepatomegaly with liver mass	Liver mass lesion	Dilated CBD with filling defect
Computed Tomography	NA	NA	Intramural lesions in CBD, cystic duct, gall bladder; dilated gallbladder and CBD
Magnetic Resonance Imaging	Mass lesions in the liver; intrahepatic biliary dilation	NA	NA
Endoscopic Retrograde Cholangio-Pancreatography	Not done	Right sided hepatic tumor; constriction of right biliary system and CBD	Dilated CBD with obstruction
Final Diagnosis	Intrahepatic cholangiocarcinoma	Intrahepatic cholangiocarcinoma	Biliary intraductal neoplasm
Outcome	Died 6 months after diagnosis	Died 3 weeks after diagnosis	NA

*Symptom duration not available; NA-Details not available; CBD-Common Bile Duct; RUQ-right upper quadrant

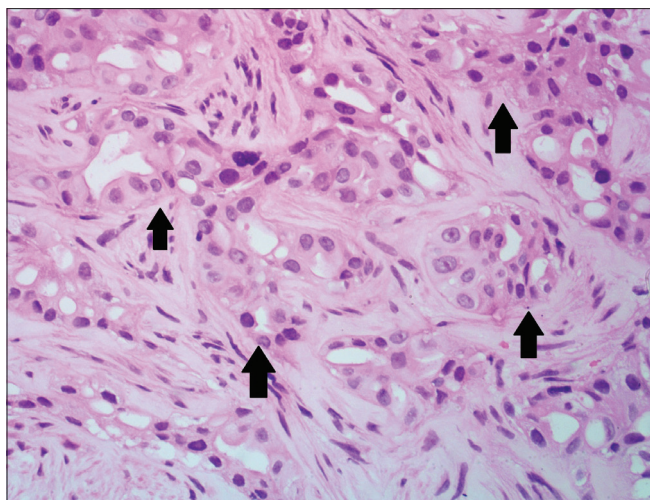


Figure 1: Photomicrograph depicting infiltrating malignant tumor glands (black arrow) of cholangiocarcinoma (400x, H and E)

In our patient, pregnancy could have masked hepatomegaly and ascites and led to delay in establishing diagnosis.

Antenatal ultrasound scans focus on fetal parameters and may not detect maternal visceral abnormalities. CT scans are contraindicated in pregnancy. Tumor markers like alpha-fetoprotein and alkaline phosphatase are elevated in normal pregnancies. Weight loss due to malignancy may not occur in a pregnant patient. Vomiting due to other causes may be attributed to pregnancy. The above factors lead to difficulty in diagnosis of malignancy in a pregnant patient.

A significant proportion of antenatal checkups are conducted by primary care and family medicine physicians. Jaundice in pregnancy is associated with maternal complications and high maternal and perinatal mortality rates.^[20] At primary care level, pregnant patients with jaundice should be referred to higher centers as they require multidisciplinary approach.^[21]

Conclusion

Though rare, cholangiocarcinoma can occur in pregnancy and postpartum state.

Symptoms and signs of a neoplastic process maybe masked during pregnancy.

Low index of suspicion and limited diagnostic modalities may prevent early diagnosis of malignancy in pregnant women.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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