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Case Report

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Rare Case of Gallbladder Carcinoma Misdiagnosed as Pancreatic Adenocarcinoma in a 5 Week Pregnant Female Patient: A Case Report

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Abstract

Background: Gallbladder carcinoma is the fifth most common gastrointestinal malignant neoplasm and the most frequent malignant tumor of the biliary tract. It has a poor prognosis, with a 50% 1-year survival rate for patients with stage 1 disease. Unfortunately, this rare disease usually presents at a more advanced stage, with a 5-year survival rate of only 5%.

Case Presentation: The present study describes a case of gallbladder adenocarcinoma presenting in a 34 years old female patient of 5 weeks gestational age in the form of a right upper quadrant pain radiating to the back. The patient had no known history of gallstones, cholecystitis, chronic H. pylori infection or other risk factors. Being 5 weeks pregnant, imaging was first restricted to an abdomino-pelvic ultrasound and MRI without contrast, which revealed a peri-duodenal-pancreatic mass. There was a high suspicion of pancreatic tumor after an endoscopic ultrasound FNA had revealed an adenocarcinoma, on pathology. It was only after opting for a Whipple procedure that pathology revealed that the primary tumor was a gallbladder adenocarcinoma with an 8 cm peri-pancreatic mass, represented by a poorly-differentiated adenocarcinoma, that probably developed within a lymph node. Fortunately, the patient presented early and resection was successfully performed. She is following-up with oncology for chemotherapy.

Conclusions: The purpose of this report is to highlight a rare disease occurring in a young pregnant patient, and how it was misdiagnosed as a pancreatic adenocarcinoma due to the involvement of the peri-pancreatic lymph node, the results of the EUS guided FNA, and of the preoperative imaging studies.

Keywords: Gallbladder carcinoma, rare case, misdiagnosis, pregnant patient, case report

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Background

Gallbladder carcinoma (GBC) is exceedingly rare, particularly in the United States, as well as most European and Mediterranean countries including Lebanon [1]. In Lebanon, GBC was reported to occur at a rate of 1.2 per 100,000 for males and 1.7 per 100,000 for females [2]. On the other hand, Mapuche Indians from Chile, South America, are known to have much higher incidences, reaching 12.3 per 100,000 for males and 27.3 per 100,000 for females [1]. This variability has been attributed to genetic factors and environmental exposures.

One genetic factor is gallstone disease, which by itself, increases the risk of gallbladder cancer. A family history of gallstone disease accounts for around 25% risk of developing cholelithiasis, a well-established risk factor of GBC, with gallstones found in about 85% of GBC cases [3]. Evidence regarding genetic factors that may also contribute to the development of GBC includes variants of genes related to lipid metabolism such as the rs693 polymorphism of the Apolipoprotein B as well as certain gene variants involved in arsenic metabolism (haplotypes of the Arsenic Methyl Transferase gene AS3MT) [4].

Of the environmental factors, infections with Salmonella and Helicobacter species may lead to chronic cholecystitis, and in turn, to GBC via alteration of proto-oncogenes as well as tumor suppressor genes [1]. Porcelain gallbladder due to chronic inflammation is frequently (~25%) associated with GBC [5]. Environmental exposure to heavy metals, certain medications (including OCPs) and smoking also play a role [3]. Besides cholelithiasis and cholecystitis, gallbladder pathologies such as primary sclerosing cholangitis, polyps, congenital cysts, and pancreaticobiliary mal-junction anomalies are also considered risk factors for developing GBC [6].

Additional risk factors include demographic factors such as advanced age, female gender, genetic predisposition, certain ethnicities and residency in specific geographical areas [7]. Hormonal factors may play a role, as a significant association was found between gallbladder carcinoma and increased exposure to estrogen and progesterone through factors like young age at menarche, multiple pregnancies, late menopause, etc..., also explaining the higher rate of the disease in women [8].

Early diagnosis is important for this potentially lethal cancer. The fact that it has an occult presentation does not help. The most common presenting symptom is right upper quadrant or epigastric pain, followed by jaundice, nausea and vomiting, anorexia and weight loss [3]. The ambiguity of its presentation, its aggressive nature, and its anatomical location contribute to diagnosis at an advanced stage [9]. The initial imaging modality used when suspecting GBC is ultrasonography (USG). However, in early disease, USG may fail to show any abnormality [3]. Hence, the most commonly used evaluative imaging technique is the CT scan, which may show a polypoid mass, focal or diffuse wall thickening, and, possibly, a mass replacing the gallbladder. A Multidetector row CT (MDCT) may be used to distinguish between malignant and benign wall thickening, with a specificity of 75.9% and a sensitivity of 82.5% [10]. Other imaging modalities may also be used. Cytopathology may help with the diagnosis and staging of GBC, which has various histologic subtypes, the most common being adenocarcinoma (98% of GBC) [3].

Complete tumor resection is the only curative modality for GBC. Adjuvant therapy consisting of gemcitabine or 5-FU based in combination with cisplatin may be used as first-line therapy [3]. Though there is no standard second-line therapy, 5-FU/capecitabine, oxaliplatin-based regimen, irinotecan or taxanes, based therapy may be considered, and targeted therapy in combination with chemotherapy has shown some benefit particularly with cetuximab, bevacizumab, sunitinib, selumetinib and others [11].

In this report, we present the case of a 34-year-old pregnant female patient who presented to the ER with a right upper quadrant pain radiating to the back. Imaging was suggestive of a pancreatic tumor and the patient underwent a Whipple procedure during which she was found to have gallbladder adenocarcinoma.

Case Report

A 34-year-old female patient presented to the emergency department complaining of right upper quadrant pain. The patient was 5 weeks pregnant with an obstetric resumé of G3P2, and a history of two uncomplicated normal vaginal deliveries. She described the abdominal pain as sharp, colicky, located in the RUQ, and radiating to the back. The pain was reported to be mainly post-prandial and associated with nausea, decreased PO intake and weight loss.

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The patient denied abnormal bowel movements but did report dark urine with no other symptoms.

The patient had no history of gallstones or any biliary tract diseases; she is previously healthy, had no previous surgeries, was a nonsmoker and did not consume any alcohol. Her family history was clear of malignancy of any type.

On presentation, complete blood count and differential were normal. Direct and total bilirubin were within the normal range. Her biochemistry tests (sodium, potassium, chloride, CO2, urea, creatinine, GGT, ALP, SGPT, lipase, amylase) were also within normal except for GGT, ALP, and SGPT which were found to be slightly elevated.

An abdominopelvic ultrasound was done and showed a mixed solid mass within the sub-hepatic area, in contact with the pancreatic head and gallbladder bed, showing a mass effect on the common bile duct, with no biliary tree or pancreatic duct dilatation. An MRI was recommended for better analysis. An abdominal MRI without IV contrast was performed and showed a 4.9 x 4.6 cm (TV x AP) well defined ampullary mass with cystic and solid components; the latter showed a restricted diffusion necessitating histopathological correlation (Fig. 1, Fig 2). The mass was seen pushing cranially the head of the pancreas, and anteriorly the cystic bile duct, with no evidence of biliary tree or main pancreatic duct dilatation.

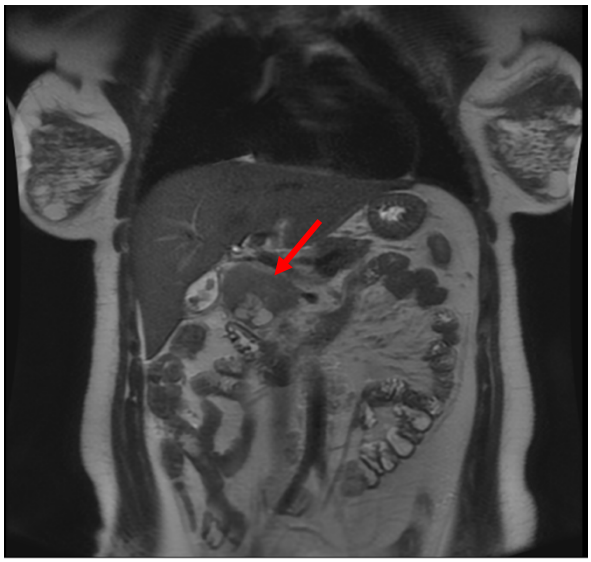

Figure 1: Coronal section of MRI done at 5 weeks gestation showing the 4.9 x 4.6 cm (TV x AP) well defined ampullary mass appearing as mixed with cystic and solid components

An endoscopic ultrasound fine-needle aspiration was performed and showed a 51 mm x 37 mm hypoechoic mass in the retroperitoneal space. Cytology and flow cytometry revealed an adenocarcinoma.
At 7 weeks of gestational age, the patient had a missed abortion and required suction dilation and curettage.

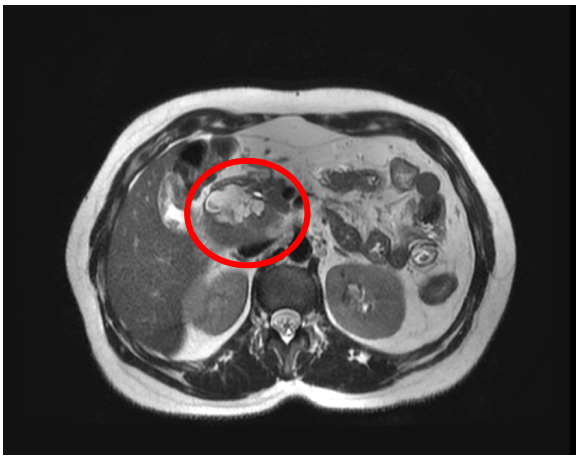

Figure 2: Transverse section of MRI done at 5 weeks gestation showing the 4.9 x 4.6 cm (TV x AP) well defined ampullary mass appearing as mixed with cystic and solid components

In quest of the primary tumor, the patient underwent a colonoscopy. No polyps or lesions were noted. An abdominopelvic CT scan with injection further characterized the lesion as a 6.3 x 5 x 5 cm enhancing soft tissue mass that is partially necrotic, and that has a moderate effect over the duodenum and head of the pancreas, displacing them anteriorly and toward the midline, without a clear connection to these structures (Fig. 3). The origin of the tumor remained uncertain. Multiple sub-centimetric retroperitoneal lymph nodes were noted but the portal vein, celiac artery and superior mesenteric artery were well opacified and patent. A chest CT with injection was also done and was found to be unremarkable.

The patient was therefore scheduled for a Whipple procedure for removal of the peri-duodenal-pancreatic mass. The abdominal cavity was opened and inspected. The large mass was seen at the level of the duodenum; it was hard to palpation and adherent to the inferior vena cava. It was carefully dissected and the tumor was separated from the duodenum. A retrograde cholecystectomy was performed with ligation of the CBD and cystic artery. Frozen sections of the

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gallbladder revealed adenocarcinoma of the gallbladder. The Whipple procedure was continued. The distal stomach with the whole duodenum, the head of the pancreas and the distal CBD were transected and sent to pathology (Fig.4). An end-to-end pancreato-jejunal anastomosis was done. The patient was extubated and transferred in stable condition.

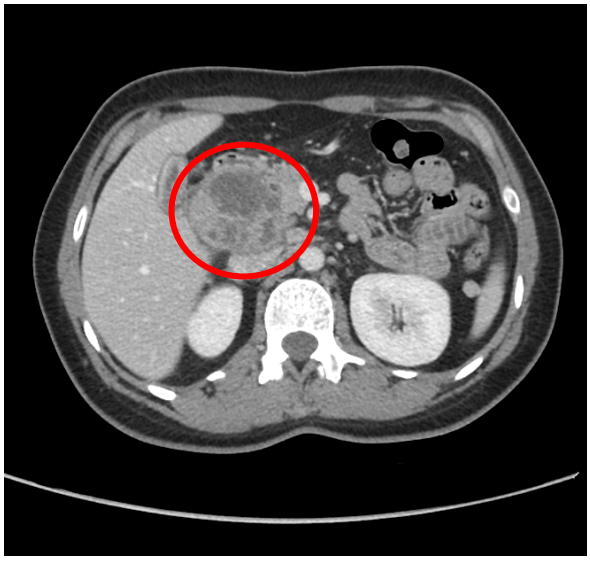

Figure 3: Transverse section of CT scan showing a lesion of 6.3 x 5 x 5 cm enhancing soft tissue mass that is partially necrotic and that has a moderate effect over the duodenum and head of the pancreas displacing them anteriorly and toward the midline without h

Pathology of the specimens showed well-differentiated adenocarcinoma of biliary-type infiltrating the entire wall of the gallbladder and sparing the deep fat and liver bed. Lymph nodes, including aortocaval and celiac nodes, were all negative for a metastatic lesion. The resected pancreatic segment was normal. An 8 cm peri-pancreatic mass, showed a poorly-differentiated adenocarcinoma that probably developed within a lymph node, with hepatoid features, and a minor component of well-differentiated adenocarcinoma and mucinous areas.

The patient was started on a chemotherapy regimen consisting of Cisplatin 75 mg IV in 1L NSS in 1 hour and Gemzar (gemcitabine) given intravenously in a dose of 1600 mg in 250 cc NSS in 1 hour.

Discussion

Gallbladder carcinoma is very rare and has a very high mortality rate. Its high prevalence in areas such as South America is attributed especially to the non-modifiable risk factors, in particular, the genetic background [4]. Yet, the most common risk factor worldwide remains chronic cholecystitis due to gallstones. Our patient had no history of gallbladder disease of any kind, or of environmental exposures that may increase the risk of GBC. She had no family history of GBC or malignancy of any type and had no known modifiable risk factors. The only identified risk factor in her case was the female gender.

Early diagnosis of GBC has been difficult and usually delayed because of the vague symptoms that may mimic other conditions. In this case, the results of the EUS guided FNA and the pre-operative imaging studies which showed a poorly differentiated peri-pancreatic adenocarcinoma that seemed to have developed within a lymph node, mislead the diagnosis towards a pancreatic adenocarcinoma. However, consideration of GBC whenever someone presents with RUQ pain as a differential diagnosis may help improve the detection of this disease, especially with other associated symptoms that our patient did not have but include vomiting, jaundice, and pruritus [12].

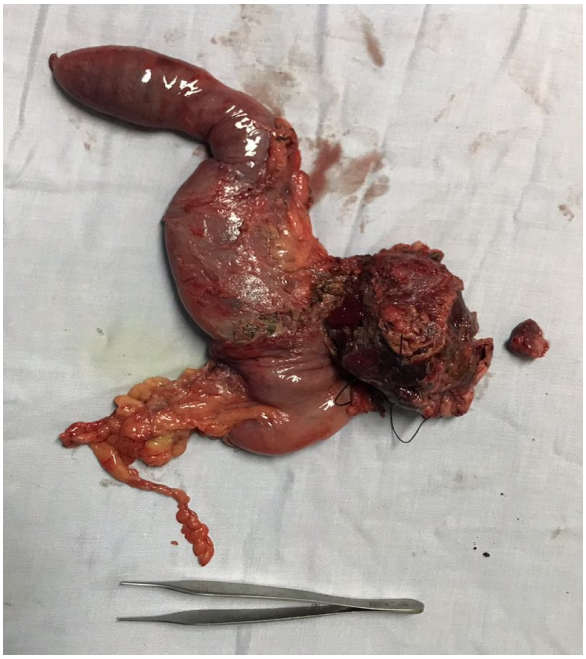

Figure 4: Transected specimen of the peri-duodeno-pancreatic mass with distal stomach, duodenum, head of the pancreas and the distal CBD

Imaging modalities have facilitated the diagnosis of GBC. Ultrasound findings may be subtle in the early stage of the disease. The most useful imaging studies in diagnosis are CT and MRI, which are also important in determining the extent

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and resectability of the disease. Yet, only about 50% of cases are diagnosed preoperatively, with the rest diagnosed during surgery, as was the case with our patient [13]. Also, our case presented at 5 weeks gestational age, further complicating the diagnosis and limiting the imaging modalities initially. After the missed abortion the use of better modalities became possible. However, despite the advancement of imaging, the diagnosis was made intraoperatively.

Fortunately, the diagnosis of GBC was made in an early stage of the disease and the primary tumor and lymph nodes involved were resected, and the patient is responded well to the first-line therapy consisting of gemcitabine in combination with cisplatin. She is also following up with a psychologist to cope with the distress that this disease has caused.

Conclusion

The case described in the following report is a young previously healthy pregnant female, presenting at 5 weeks GA for RUQ pain, thought to have pancreatic adenocarcinoma on workup but found to have GBC with lymph node involvement after opting for Whipple procedure.

The patient underwent an extensive workup and a Whipple surgery before reaching the diagnosis. Consideration of the diagnosis and collaboration between surgeons, radiologists, obstetricians, and any specialist whenever the presentation is suspicious may maximize the discovery of the disease before surgery, and follow up with an oncologist and a mental health specialist is essential in the care of a rare occurrence as with the case presented.

References

1. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. Clin Epidemiol. 2014;6:99-109. Published 2014 Mar 7. https://doi.org/10.2147/CLEP.S37357 PMid:24634588 PMCid:PMC3952897

2. Shamseddine A, Saleh A, Charafeddine M, Seoud M, Mukherji D, Temraz S, Sibai AM. Cancer trends in Lebanon: a review of incidence rates for the period of 2003-2008 and projections until 2018. Popul Health Metr. 2014 Mar 4;12(1):4. https://doi.org/10.1186/1478-7954-12-4 PMid:24593777 PMCid:PMC3996020

3. Kanthan R, Senger JL, Ahmed S, Kanthan SC. Gallbladder Cancer in the 21st Century. J Oncol. 2015;2015:967472. https://doi.org/10.1155/2015/967472. Epub 2015 Sep 1. PMid:26421012 PMCid:PMC4569807

4. Arroyo GF, Gentile A, Parada LA. Gallbladder cancer: South American experience. Chin Clin Oncol. 2016 Oct;5(5):67. https://doi.org/10.21037/cco.2016.10.01 PMid:27829280

5. Shaffer EA. Gallbladder cancer: the basics. Gastroenterol Hepatol (N Y). 2008 Oct;4(10):737-41. PMid: 21960896; PMCid: PMC3104187.

6. Maharaj R, Cave C, Sarran K, Bascombe N, Dan D, Greaves W, Warner WA. A case report of the clear cell variant of gallbladder carcinoma. Int J Surg Case Rep. 2017;32:36-39. https://doi.org/10.1016/j.ijscr.2017.01.020. Epub 2017 Jan 12. PMid:28222323 PMCid:PMC5318351.

7. Gourgiotis S, Kocher HM, Solaini L, Yarollahi A, Tsiambas E, Salemis NS. Gallbladder cancer. Am J Surg. 2008 Aug;196(2):252-64. https://doi.org/10.1016/j.amjsurg.2007.11.011 PMid:18466866

8. Khan I, Panda N, Banerjee M, Das R. Epidemiological factors in gall bladder cancer in eastern India-a single centre study. Indian J Surg Oncol. 2013 Mar;4(1):67-72. https://doi.org/10.1007/s13193-012-0203-x. Epub 2012 Dec 22. PMid:24426702 PMCid:PMC3578539

9. Zou ZY, Yan J, Zhuge YZ, Chen J, Qian XP, Liu BR. Multidisciplinary collaboration in gallbladder carcinoma treatment: A case report and literature review. Oncol Lett. 2016 Oct;12(4):2696-2701. https://doi.org/10.3892/ol.2016.5020. Epub 2016 Aug 16. PMid:27698845 PMCid:PMC5038553

10. Vijayakumar A, Vijayakumar A, Patil V, Mallikarjuna MN, Shivaswamy BS. Early diagnosis of gallbladder carcinoma: an algorithm approach. ISRN Radiol. 2012 Oct 18;2013:239424. https://doi.org/10.5402/2013/239424 PMid:24959553 PMCid:PMC4045520

11. Malka D, Fartoux L, Rousseau V, Trarbach T, Boucher E, Fouchardiere CDL, Faivre SJ, Viret F, Blanc J-F, Assenat E, Hammel P, Louvet C, Wichert GV, Ducreux M, Rosmorduc O, Pignon J-P, Greten TF. Gemcitabine and oxaliplatin (GEMOX) alone or in combination with cetuximab as first-line treatment for advanced biliary cancer: Final analysis of a randomized phase II trial (BINGO). Journal of Clinical Oncology. 2012;30:4032-4032. https://doi.org/10.1200/jco.2012.30.15_suppl.4032

12. Tairo-Cerron T, Paredes-Orue R, Moreno-Loaiza O. Frequency and characteristics of gallbladder cancer at a referral hospital in southern Peru, 2009-2014: a descriptive study. Medwave. 2018 Mar 26;18(2):e7184. Spanish, English. https://doi.org/10.5867/medwave.2018.02.7184 PMid:29624571

13. Löhe F, Meimarakis G, Schauer C, Angele M, Jauch KW, Schauer RJ. The time of diagnosis impacts surgical management but not the outcome of patients with gallbladder carcinoma. Eur J Med Res. 2009 Aug 12;14(8):345-51. doi: 10.1186/2047-783x-14-8-345. PMID: 19666394; PMCID: PMC3352165. https://doi.org/10.1186/2047-783X-14-8-345 PMid:19666394 PMCid:PMC3352165

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