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Case Report

# Gall Bladder Perforation: An Unusual Cause of Elevated CA19-9 Levels

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**Abstract**

Elevated levels of Carbohydrate Antigen 19-9 (CA19-9) often raise suspicions of malignant disease, particularly in patients presenting with symptoms suggestive of biliary obstruction. However, interpreting CA19-9 elevation can be challenging, as it can also occur in benign conditions such as gallbladder perforation and empyema. We present a case of a 48-year-old male with jaundice, intermittent fever, and right upper quadrant pain, initially suspected to have malignancy based on markedly elevated CA19-9 levels. Subsequent workup revealed perforated gallbladder. The diagnostic journey underscores the complexity of interpreting CA19-9 levels in gallbladder pathology and highlights the importance of a comprehensive approach integrating clinical evaluation, imaging studies, and serial CA19-9 measurements. Clinicians should be aware of the potential for benign etiologies of CA19-9 elevation, particularly in the context of inflammatory biliary diseases, to avoid unnecessary invasive procedures and optimize patient management. Further research elucidating the mechanisms underlying CA19-9 elevation in benign gallbladder diseases is needed to refine diagnostic strategies and improve patient outcomes.

**Keywords:** Carbohydrate Antigen 19-9; Carcinoembryonic Antigen; Benign and Inflammatory Conditions of Gall bladder; Liver Function Test.

## Patient Presentation

A 48-year-old Pakistani male, known case of Diabetes Mellitus Type II, presented to the surgical outpatient department with complaints of yellowish discoloration of the skin and sclera, intermittent fever ranging from 100-101°F, occasional right upper quadrant pain for the past month (relieved with medication but exacerbated by food intake), and 10 Kg weight loss which is described by loosening of clothes. The patient also reported vomiting, loss of appetite, but no other associated symptoms of upper gastrointestinal bleeding. A working diagnosis of obstructive jaundice was made and the he was advised a triphasic CT abdomen and pelvis with a pancreatic protocol, along with CA 19-9 levels to rule out malignancy alongwith baseline investigations.

| ***Liver Function Test (LFT's)*** | **Ref range** | **Unit** | **At presentation** | **After Antibiotics** | **Postop** |
|---|---|---|---|---|---|
| Bilirubin Total | 0.10 - 1.10 | mg/dL | 2 | 1.3 | 1.1 |
| Bilirubin Direct | 0.10 - 0.40 | mg/dl | 1.7 | 1 | 1 |
| Bilirubin Indirect | 0.10 - 0.70 | mg/dL | 0.1 | 0.3 | 0.1 |
| Alkaline Phosphatase | 40.00-135.00 | U/L | 361 | 246 | 308 |
| SGPT (ALT) | 5.00 - 40.00 | U/L | 31 | 17 | 22 |
| SGOT (AST) | 5.00 - 40.00 | U/L | 31 | 22 | 37 |
| Albumin | 3.50 - 5.00 | g/dL. | 2.4 | 2.7 | 3 |
| Proteins Total | 6.30 - 8.30 | g/dL | 7.3 | 7.2 | 8.6 |
| Gamma G.T | 5.00 - 50.00 | U/L | 279 | 271 | 368 |
| ***CBC*** | | | | | |
| Hb | 14-18 | G/dl | 8.1 | 8.7 | 11.1 |
| TLC | 04-Nov | X10e3/uL | 16.46 | 10.5 | 11.8 |
| PLT | 150-450 | X10e3/uL | 640 | 438 | 515 |
| ESR | Oct-20 | mm/1sthour | 79 | 77 | 95 |

**Table 1:** Liver Function Test (LFT's).

| **Serum Electrolytes** | **Reference Range** | **Unit** | **At Presentation** | **After Antibiotics** |
|---|---|---|---|---|
| Sodium (Na+) | 135.00 - 145.00 | mmol | 132 | 133 |
| Potassium (K+) | 3.50 - 5.10 | mmol | 4.4 | 4.2 |
| Chloride | 96.00 - 108.00 | mmol | 102 | 104 |

**Table 2:** Serum Electrolytes.

| **Renal Profile** | **Reference Range** | **Unit** | **At Presentation** | **After Antibiotics** |
|---|---|---|---|---|
| Creatinine | 0.50 - 1.30 | mg/dL | 0.5 | 0.5 |
| eGFR | >90 | mL/min | 215 | 215 |

**Table 3:** Renal Profile.

| **Coagulation profile** | **Ref range** | **Unit** | **At presentation** |
|---|---|---|---|
| PT TEST | Oct-14 | Seconds | 15 |
| PTT TEST | | Seconds | 12 |
| INR | | | 1.2 |

**Table 4:** Coagulation profile.

Examination showed, scleral icterus along with yellowish discoloration of skin i.e. jaundice. A globular distended mass was palpated in the right upper quadrant.

CT scans confirmed a distended gallbladder with wall thickening (15.7 mm) infiltrating liver segments IV and V (70 x 22 mm), inseparable from the duodenum and gastric pylorus, with small gallbladder calcifications suggesting cholelithiasis. Enlarged lymph nodes were noted in the porta hepatis, peripancreatic, retroperitoneal, and para-aortic areas, the largest being 26 x 21 mm. Other abdominal organs appeared normal. The findings suggested gallbladder carcinoma, supported by elevated CA19-9 levels.

An ultrasound-guided Tru-Cut liver biopsy of segment IV was done. Distorted liver parenchyma with moderate chronic inflammation, bile ductular proliferation, periportal fibrosis, and moderate intrahepatic cholestasis seen. Subsequent MRCP showed an infiltrating gallbladder mass but no biliary dilatation. The common bile duct measured 5 mm, with the gallbladder wall thickness of 5.5 mm. The spleen and pancreas show normal parenchyma, with no pancreatic duct dilation. No malignancy or microorganism growth was detected in any investigation.

Even though sufficient evidence was present to proceed with the diagnosis of gallbladder carcinoma there have been incidences of increased CA19-9 levels in various benign conditions such as acute on chronic cholecystitis, Mirrizzi syndrome, empyema gall bladder and so on [1-8]. An initial antibiotic trial with Intra venous cefixime was administered for 10 days, during which the CA19-9 levels showed a downward trend. The possibility of a benign biliary condition was thus considered. The antibiotic trial was completed and surgery was planned.

The patient was admitted for laparoscopic cholecystectomy, and was found to have gallbladder perforation with multiple adhesions involving the liver along with the duodenum and pylorus of the stomach, and transverse colon and omentum laterally, along with the presence of 30ml of pus and flakes. Postoperatively, the patient was managed with a transamine protocol and injections of vitamin K for three days (INR 1.2). He was discharged on the third postoperative day with antibiotics; piperacillin + tazobactam and cefixime.

Follow-up showed jaundice to be resolved, and the patient reported a significant improvement in appetite.

This case highlights the diagnostic challenges and evolving clinical course encountered in managing a patient presenting with symptoms suggestive of bile duct obstruction. The multidisciplinary approach led to successful management and improved patient outcomes [6].

## Introduction

Carbohydrate Antigen 19-9 (CA19-9) is a valuable biomarker commonly associated with diagnosis, prognosis, and monitoring gastrointestinal malignancies, particularly pancreatic adenocarcinoma, cholangiocarcinoma, gallbladder carcinoma and so on. However, the interpretation of CA19-9 levels can be intricate, as its elevation is not exclusive to malignant conditions. Benign diseases, especially those involving the biliary system, can also lead to heightened CA19-9 levels, posing a diagnostic challenge and necessitating a nuanced approach to patient management [6,9].

Gallbladder pathology, encompassing conditions like perforation, represents a fascinating aspect of this diagnostic conundrum. These complications can present with markedly elevated CA19-9 levels, mimicking the signature elevation seen in pancreatic and biliary malignancies. This discussion explores the complex interplay between CA19-9 levels and benign gallbladder diseases, shedding light on the mechanisms underlying their elevation and the implications for clinical practice.

## Discussion

Gallbladder perforation is a rare, yet potentially life-threatening complication of chronic gallbladder disease. These conditions arise from prolonged inflammation and gallstone impaction, leading to a cascade of inflammatory responses culminating in gallbladder wall compromise and the accumulation of infected bile.

A study aimed to evaluate the effectiveness of serum carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 levels in screening for multiple-organ cancers [6]. It analyzed data from asymptomatic individuals undergoing opportunistic cancer screening. Results showed low sensitivity and positive predictive values for both markers, indicating their limited utility in multiple-organ cancer screening [10,11].

Case reports detailing patients with acute cholecystitis and markedly elevated CA19-9 levels underscore the diagnostic challenge posed by benign gallbladder diseases. In these cases, initial suspicions of pancreatic or biliary malignancy based on CA19-9 elevation necessitate thorough clinical evaluation and imaging studies to differentiate between benign and malignant etiologies [3, 4].

Furthermore, studies investigating the dynamics of CA19-9 levels following therapeutic interventions, provide valuable insights into the reversible nature of CA19-9 elevation in benign biliary diseases. According to some studies, baseline CA19-9 levels were higher in malignant than benign patients. After drainage, malignant patients experienced a 39.2% reduction, while benign patients saw

a larger reduction of 75.7%. Biliary obstruction and inflammation contribute to CA19-9 elevation. New correction formulas improve diagnostic accuracy, aiding in distinguishing between benign and malignant conditions [12].

The elevation of CA19-9 levels in gallbladder perforation can be attributed to several factors. Firstly, the inflammatory milieu within the gallbladder and biliary tract triggers the release of various cytokines, growth factors, and other inflammatory mediators [13, 14]. These molecules stimulate the production and shedding of CA19-9 from epithelial cells lining the biliary tree, resulting in its systemic elevation. Additionally, the disruption of biliary flow and the accumulation of infected bile in the gallbladder lumen further exacerbate the inflammatory response, amplifying CA19-9 release and its elevated serum levels [15].

Serum CA 19-9 levels below 100 U/mL generally indicate a likelihood of resectable disease, while levels surpassing 100 U/mL suggest potential unresectability or the presence of metastatic disease [16, 17]. Although, the definitive treatment for such conditions remains laparoscopic removal of gall bladder and inflammatory debris, which was done in this case. This reversibility underscores the transient nature of CA19-9 elevation in response to inflammatory stimuli, highlighting the importance of considering clinical context and serial measurements in interpreting CA19-9 levels [18].

## Conclusion

In conclusion, the interplay between CA19-9 levels and benign gallbladder diseases, including perforation, underscores the complexity of tumor marker interpretation in clinical practice. While traditionally associated with malignancies, CA19-9 elevation can also occur in benign conditions, particularly those involving inflammatory processes within the biliary system.

As clinicians navigate the diagnostic challenges posed by elevated CA19-9 levels in gallbladder pathology, a comprehensive approach encompassing clinical evaluation, imaging studies, and serial measurements of CA19-9 is essential. By recognizing the benign etiologies of elevated CA19-9 levels and integrating this understanding into clinical decision-making, clinicians can optimize patient management and avoid unnecessary invasive procedures.

Further research elucidating the specific mechanisms underlying CA19-9 elevation in benign gallbladder diseases is warranted. By deepening our understanding of the factors influencing CA19-9 levels in these contexts, clinicians can refine their diagnostic strategies, enhance patient care, and ultimately improve clinical outcomes.

## List of Abbreviations

CA 19-9: Carbohydrate antigen 19-9

CEA: Carcinoembryonic antigen

LFT: Liver function test

APTT: Activated partial thromboplastin time

PT: Prothrombin Time

CBC: Complete Blood Count

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**Authors' Contributions:**

AS: Conception and design of study, drafting of manuscript with critical intellectual input. AP; HI; FM: Acquisition and analysis of data, drafting of the manuscript HA: Acquisition and analysis of data SA: Drafting of the manuscript with critical intellectual input.

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