

Case Report

A case of elevated carbohydrate antigen 19-9 with a benign cause

Jayesh V. Parikh, Parth R. Dalal, Piyush N. Baraiya*, Sachin R. Vishwakarma

Department of General Surgery, B J Medical college and Civil hospital, Ahmedabad, Gujarat, India

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*Correspondence:

Dr. Piyush N Baraiya,

E-mail: piyush5121994@gmail.com

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ABSTRACT

Serum carbohydrate antigen 19-9 (CA 19-9), a marker of malignant tumors, is generally slightly elevated in benign conditions. We report a case of cholecystitis with perforated gall bladder with significantly elevated level of serum CA 19-9 based on abdomen computed tomography and intra operative findings. A 70 years diabetic and hypertensive female presented with right hypochondriac pain associated with occasional itching and nausea without vomiting with markedly raised CA 19-9 (1554 U/ml) with CECT abdomen suggestive of perforated gall bladder with cholecystitis. Patient electively operated for open cholecystectomy and per operative findings were distended gall bladder with multiple calculi within with edematous gall bladder wall and adhesions between gall bladder and omentum and colon. Gall bladder removed and biopsy suggestive of chronic calculus cholecystitis. On post-operative day 5th and 7th CA 19-9 was repeated twice and drastic fall to 5 U/ml and 12 U/ml respectively. Chronic calculus cholecystitis with high elevation of CA 19-9 is rare.

Keywords: Carbohydrate antigen 19-9, Hepatobiliary malignancy, Cholecystitis, Gall bladder perforation, Cholangitis

INTRODUCTION

Carbohydrate antigen 19-9 (CA19-9) is a glycoprotein antigen which is expressed on cells of hepatobiliary epithelium. CA19-9 has been considered a tumor marker for biliary, pancreatic and gastric malignancies.¹ The upper normal limit of CA19-9 is 37 U/ml. Elevated levels of CA 19-9 are also associated with certain benign conditions. With levels more than 1000 U/ml, the specificity for malignancy approximately 100 percent. Because of this CA19-9 is currently considered the gold standard tumor marker assessment in diagnosis and prognosis of upper gastrointestinal, pancreatic, and biliary cancer. However, multiple case reports and studies have shown that elevated CA19-9 levels beyond 1000 U/L occur in non-neoplastic/benign conditions as well.² This has led to doubt its specificity. CA19-9 levels are three times higher than the upper normal limit, which raises concerns for malignant disease.² CA 19-9 serum

levels have a sensitivity and specificity of 79-81% and 82-90% respectively for the diagnosis of pancreatic cancer in symptomatic patients; but are not useful as a screening marker because of low positive predictive value.³

CASE REPORT

A 70 years hypertensive and diabetic female has right hypochondriac pain for one month. It was also associated with occasional itching and nausea but no vomiting. It was not associated with fever, diarrhea, constipation, weight loss, decreased appetite, and icterus. On physical examination approximately 8×10 cm non tender, well defined, irregular, granular, non-ballotable lump was found in the right hypochondrium. Laboratory investigations revealed an elevated total bilirubin (6.68 mg/dl), direct bilirubin (2.84 mg/dl), serum alanine transaminase (135I U/l) and alkaline phosphate (424 U/l).

CA 19-9 was markedly raised with 1554 U/ml, which is approximately 40 times higher than the upper limit of normal levels. 24hour urinary metanephrine was normal (0.2mg/24hr). Plain abdominal radiograph was normal. A contrast enhanced CT of abdomen revealed changes of cholecystitis with perforated gall bladder and a large but localized collection. Intra and extra hepatic biliary radicles, duodenum and pancreas were normal. Also, an incidental finding of right adrenal myelolipoma was made. Patient was electively operated for open cholecystectomy under general anesthesia and intra operative findings of localized sub hepatic collection with sealed off gall bladder perforation and distended gall bladder.

Cholecystectomy was performed and the collection drained. An abdominal drain was placed and abdomen closed in layers. On post op day 1 laboratory investigations revealed normal total bilirubin (1.06 mg/dL), direct bilirubin (0.65 mg/dL), alkaline phosphate (115 U/l), alanine transaminase (32 IU/l). The postoperative recovery was uneventful. The drain was removed on post-operative day 2. On post-operative day 5 and 7 CA 19-9 levels were repeated twice which showed a drastic fall to 5.08 U/ml and 12 U/ml respectively. Patient was discharged on post-operative day 7 with symptomatic improvement, vitally stable, well mobilized and taking full oral diet.

DISCUSSION

CA 19-9 is synthesized in the normal pancreatic parenchyma and biliary tract however mechanisms of elevation of CA 19-9 remain unclear. It is also produced from the epithelial cells of the gastric, colonic, and uterine mucosa, as well as the salivary glands.⁴ CA 19-9 is often elevated in benign pancreaticobiliary diseases such as cholangitis, obstructive jaundice and pancreatitis. Additionally, it has been reported that elevated CA 19-9 levels can be found in other non-malignant conditions such as pulmonary and thyroidal diseases, diabetes mellitus, and gynecologic diseases.

In patients with an elevated CA 19-9 level, sufficient examination including an abdominal computed tomography (CT) scan in search of malignant diseases is generally performed first. When no malignant disease is found, a short-term follow-up is usually recommended.⁴ It is unclear as to what causes the elevation in CA19-9 levels in the setting of hyperbilirubinemia. Biliary epithelial cells secrete CA19-9; thus, it is hypothesized that increased proliferation of biliary epithelial cells in the setting Case Reports in of obstructive jaundice caused by irritation, inflammation, and bile stasis leads to increased secretion and accumulation of CA19-9. Increased permeability between the bile and blood leads to an accumulation of CA19-9 in the serum. The resolution of the cholestasis or obstruction will reverse this process and a decrease in CA19-9 levels will be seen. CA19-9 is excreted in the bile; thus, intrahepatic

congestion or extra hepatic biliary obstruction can lead to rising levels of CA 19-9.

Table 1: Raised ca19-9 level in various benign states.⁶

Disease	Percentage of patients with raised CA19-9
Chronic HCV infection	84
Alcohol liver disease	73
Acute hepatitis B infection	70
Primary sclerosing cholangitis	61
Primary biliary cirrhosis	60

Table 2:⁵

Etiologic diseases	No. of subjects (percentage out of 192)
Hepatic diseases	63 (32.8%)
Pulmonary diseases	32 (16.7%)
Gynaecologic diseases	38 (19.8%)
Endocrine diseases	13 (6.8%)
Spleen cyst	1 (0.5%)
Unknown cause	45 (23.4%)

CONCLUSION

Elevated levels of CA19-9 beyond 1000u/L is fair indicator of pancreaticobiliary malignancy. However, marginally elevated levels can be seen in non-pancreaticobiliary and benign conditions like cholecystitis, cholangitis, Mirizzi syndrome, pulmonary and thyroidal diseases, diabetes mellitus and some gynecological diseases. Thus, elevated CA19-9 level should raise a suspicion of malignancy, particularly in the elderly. Also treating physician should keep in mind the various causes of elevated CA19-9.

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