

## Original Research Article

# Nonalcoholic Steatohepatitis with Significantly Elevated Levels of Carbohydrate Antigen 19-9

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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 58 year old male with jaundice and elevated CA 19-9 levels (8,474 IU/ml). Radiological imaging of the liver, pancreas and extrahepatic biliary tree revealed neither malignancy, nor obstruction. The only remarkable finding was biopsy-proven nonalcoholic steatohepatitis (NASH). This presentation indicates that significantly high CA 19-9 levels could be associated with NASH.

**Keywords:** CA 19-9, Nonalcoholic Steatohepatitis (NASH)

## INTRODUCTION

Carbohydrate antigen 19-9 (CA 19-9), which was first described by Koprowski et al in 1979, is produced in the biliary and pancreatic ductal cells [1]. A CA 19-9 level of <37 U/ml is considered normal. CA 19-9 can be detected in gastrointestinal and non-gastrointestinal cancers [1, 3], especially pancreatic and biliary cancers, it is a useful serum biomarker for these malignancies. Although many patients with primary pancreatobiliary cancers express elevated levels of tumor marker CA19-9, it is well known that there are some CA19-9 positive patients with benign diseases such as pancreatitis, cholecystitis, cholangitis, liver cirrhosis, viral and alcoholic hepatitis [2]. However, the elevation of CA 19-9 levels in these conditions is usually mild. We report a case of nonalcoholic steatohepatitis (NASH) presenting with significantly elevated serum CA19-9.

## CASE PRESENTATION

A 58 year old Caucasian male, previously healthy, was admitted to hospital with sudden onset right upper quadrant abdominal pain and jaundice for about 1 week. Neither fever, nor infectious symptoms were reported. Initial workup showed an AST of 79 U/L (normal 10-40 U/L), ALT, 73 (normal range 12-78 U/L), Gamma Glutamyl Transferase (GGT) > 1600 (normal range 15-85U/L), alkaline phosphatase (ALP) 178 U/L (normal range 50-136), Total bilirubin, 231 umol/L (normal range 3-17). Patient had normal complete blood counts (CBC). Pancreatitis, Viral hepatitis and metabolic causes for jaundice and elevated liver enzymes were ruled out. Septic work up was unremarkable. Abdominal ultrasound and CT abdomen

showed an enlarged severe fatty liver without any evidence of intrahepatic or extrahepatic biliary dilatation. Patient's abdominal pain resolved however his jaundice worsened, his liver enzymes and bilirubin continued to elevate. He was initially treated for a presumed autoimmune hepatitis (AIH) with intravenous steroids, despite negative work up for AIH. Prior to that, he was also treated empirically for a possible biliary tract infection with Piperacillin-Tazobactam for few days. Patient received all mentioned treatments at his local hospital without any clinical improvement. Patient was transferred to a tertiary care hospital where he was evaluated by Hepatology team. Liver enzymes upon transfer were elevated, AST at 255, ALT at 434 U/L, ALP at 285 U/L, total bilirubin at 230.8 umol/L and direct bilirubin at 163.5 umol/L, INR, 1.2. A CA-19-9 was done as part of work up and was surprisingly elevated at 8474 U/mL (normal range < 37), other tumor markers including Alpha Fetoprotein (AFP) and Carcinoembryonic Antigen (CEA) were normal. CT scans of the thorax, abdomen and pelvis were repeated and showed fatty liver disease only with no evidence for biliary obstruction or malignancy. Magnetic resonance cholangiopancreatogram (MRCP) was unremarkable. Endoscopic Retrograde Cholangio Pancreatography (ERCP) was done as well and revealed no abnormalities. Liver biopsy was done, pathology revealed Steatohepatitis grade 2/3, stage ¾. He eventually experienced a clinical improvement as an inpatient four weeks after the onset of the event. His CA19-9 fluctuated at high levels and decreased to 2519 U/mL on discharge from hospital. CT Scan of the abdomen done one month after discharge was remarkable for inflammatory changes around the

pancreas without clear evidence for pancreatobiliary malignancy. CA19-9 decreased to 1452 U/mL. ALT decreased to 46U/L, AST decreased to 68U/L, GGT decreased to 201. His bilirubin also decreased to 86.1umol/L and direct bilirubin noted to be 55.9 umol/L.

## DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is seen worldwide and is the most common liver disorder in Western countries, where the major risk factors for NAFLD, central obesity, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome are common. In the United States, studies report a prevalence of NAFLD of 10 to 46 percent, with most biopsy-based studies reporting a prevalence of NASH of 3 to 5 percent [4].

Serum carbohydrate antigen 19-9 (cancer antigen 19-9; CA-19-9) was first discovered in the late 1970s. It is a type of carbohydrate secreted by exocrine epithelial cells and, more specifically, a derivative of the Lewis antigen [5]. Studies from the 1980s demonstrated that the antigen is increased in the sera of patients with digestive cancers. Between 5% and 10% of the general population are unable to express CA-19-9 which is produced in normal human pancreatic and biliary ductal cells.

Since the exact pathway between tissue and blood is still not well known, the real mechanism of the elevated serum CA19-9 remains not well understood. This might be attributed to an imbalance between the production and metabolism of CA19-9. The presence of a digestive cancer may enhance the production of CA19-9 and altered liver function may contribute to the decrease of metabolism.

A CA19-9 value of more than 1,000 U/mL usually indicates a pancreatobiliary cancer and has been reported to have a specificity greater than 99% for pancreatic cancer [7], nevertheless, false-positive results owing to benign diseases such as pancreatitis, cholecystitis, cholangitis, hepatitis and liver cirrhosis have been noted.

In this case, the usual causes of CA19-9 elevation were ruled out before linking it to the possibility of it being NASH-related.

To our knowledge, High CA19-9 levels associated with NASH is extremely rare and we didn't come across any reported cases in the literature. The mechanism of this relation remains unclear. In addition, the epithelial tissue target involved in CA19-9 secretion by NASH is unknown.

## CONCLUSION

Although high CA 19-9 level (> 1000 IU/ mL) is highly suggestive of malignancy, extremely high levels could be associated with benign conditions like NASH.

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