Unusually Elevated CA 19-9 in Choledocholithiasis

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INTRODUCTION
Serum CA 19-9 (carbohydrate antigen 19-9) is a glycosphingolipid that was first isolated in 1979 by Koprowski as a monoclonal antibody to cultured cell from human colonic cancer. Since then, it has been used as a tumor marker for most pancreatic and biliary cancers, as well as several gastrointestinal cancers (liver, gastric, colorectal). However, high levels of CA 19-9 are occasionally found in benign diseases of the liver and biliary tract with a value usually < 5000 U/ml. We present a patient with choledocholithiasis with a significantly elevated CA 19-9 level that decreased rapidly without definitive treatment.

CASE
A morbidly obese 69 year-old male presented with a two day history of painless jaundice. He had no history of viral hepatitis or liver disease however his family history was significant for pancreatic carcinoma. Physical examination revealed an obese male with scleral icterus and jaundice. Laboratory studies showed aspartate aminotransferase (AST) 196 U/L, alanine aminotransferase (ALT) 151 U/L, alkaline phosphatase (ALP) 1045 U/L, total bilirubin 12 mg/dl, Carcinoembryonic antigen (CEA) 3.2 ng/ml and a CA 19-9 of 38310 U/ml. Ultrasonographic examination and computed tomography of the abdomen were of poor quality due to body habitus. Magnetic resonance imaging (MRI) of the abdomen showed intrahepatic biliary dilatation, a dilated common bile duct of 11mm and no pancreatic mass. Endoscopic ultrasound revealed cholelithiasis as well as an impacted stone in the ampulla. The pancreatic head appeared normal (Figures 1 and 2). He underwent two attempts of endoscopic retrograde cholangiopancreatography done by two endoscopists; however his bile duct could not be cannulated due to anatomic distortion from his body habitus. After two days, his symptoms started to improve. A repeat CA 19-9 level obtained one week later was 36 U/ml (within the normal range).

DISCUSSION
CA 19-9 is produced in normal pancreatic and biliary ductal cells. The exact pathway between the tissue and the blood is still not known, so the real mechanism behind the elevation of this marker remains unclear. The upper limit of normal for CA 19-9 is 37-40 U/ml, with elevations being 90% specific and significant elevations above 1000 U/ml being 99% specific for the diagnosis of pancreatic cancer. Positive results can also be found in benign diseases such as pancreatitis and cirrhosis, as well as benign biliary tract diseases.

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A CASE REPORT

Surprisingly, extreme elevations of serum CA 19-9 levels with benign biliary tract diseases have been reported in the literature. Murohisa et al. presented a case of common bile duct stone and acute cholangitis with a CA 19-9 level of 60,000 U/ml that returned to normal after PTC drainage. Marcouizos et al. presented a similar case of acute cholangitis with a CA 19-9 level of 99,070 U/ml that also returned to normal one month after cholecystectomy. However, there is only one case of extreme elevation of CA 19-9 reported in choledocholithiasis by Katsanos et al., in which the patient with a history of Billroth type II surgery presented with painless jaundice and a CA 19-9 of 98,628 U/ml, that returned to normal 3 months after cholecystectomy. In our case, the level returned to normal after one month without intervention.

Although the exact mechanism is not clear, several explanations and hypotheses have been postulated to explain the degree of elevation of CA 19-9 in benign biliary tract disease: (1) Inflammation resulting in increased proliferation of the epithelial cells leading to increased production of CA 19-9, (2) biliary tract obstruction leading to accumulation of CA 19-9 in the biliary lumen, (3) increased biliary pressure leading to irritation of bile duct cells and therefore increased production of CA 19-9, and (4) reflux of CA 19-9 into the circulation induced by obstruction.

Although the marked elevation of CA 19-9 is usually highly suggestive of the presence of digestive or biliary cancers, such elevations can also occur in benign diseases such as choledocholithiasis and cholangitis. Therefore, clinicians should never use tumor markers alone to establish the diagnosis of malignancy and should be prompted on other causes that could be optimally treated.

References