Painless Jaundice With a Significantly Elevated CA 19-9; It Is Not Always Pancreaticobiliary Cancer

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Introduction

- Carbohydrate antigen 19-9 (CA 19-9) is often very high in pancreaticobiliary cancers.
- However, CA 19-9 can be substantially elevated in benign diseases also.
- Vanishing bile duct syndrome (VBDS) is a rare complication of drug induced liver injury (DILI) which may present similarly to pancreatic cancer but has rarely been associated with an elevated CA 19-9.
- We present a case of painless jaundice with a significantly elevated CA 19-9 from vanishing bile duct syndrome.

Case Description

- A 65-year-old male with obesity, hypertension, hyperlipidemia and prior cholecystectomy presented with two weeks of painless jaundice and 10 pounds unintentional weight loss.
- Physical exam noted scleral icterus and jaundice and lab results revealed a T.Bili of 23 mg/dL and CA 19-9 of 1,480 U/mL concerning for malignancy for which he was admitted (Table 1).
- A CT scan found intrahepatic bile duct dilation and a 10 mm CBD without a discrete mass. ERCP demonstrated a low-grade main bile duct stricture which was stented. Bile duct brushings and fine needle aspiration of the pancreas were negative for malignancy.
- On follow-up MRCP, biliary dilation had resolved but the bilirubin level remained high.
- Infectious and autoimmune workup was unremarkable and repeat cholangiography with brushings reconfirmed no obstruction or malignancy (Fig.1A).
- EUS-guided liver biopsies revealed cholestasis with dilated bile canaliculi, hepatocytes with ballooning degeneration and a paucity of bile ductules. IHC staining demonstrated > 50% ductopenia, confirming VBDS (Fig.1B,C).
- Follow up at hepatology clinic determined triamterene-HCTZ, atorvastatin or omeprazole stopped during prior hospitalization to be the likely culprit. His CA 19-9, LFTs and symptoms improved over the following weeks (Table 1).

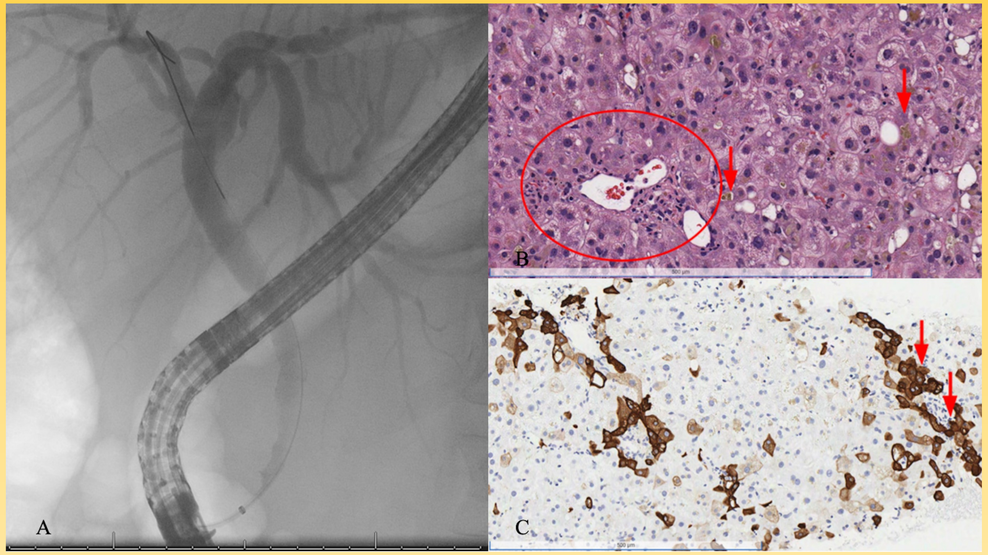

Figure 1. A) ERCP with cholangiogram showing a low-grade distal biliary stricture without significant upstream dilation. B) Liver biopsy with H&E stain, 500µm magnification showing small portal tracts with no bile ducts (red circle); note marked cholestasis (arrows) in dilated canaliculi and lack of ductular reaction. Also visible at this magnification is the ballooning degeneration of hepatocytes. C) Liver biopsy with cytokeratin 7 immunostain, 500µm magnification. Small portal tracts with no terminal/small bile ducts. Early signs of ductular reaction seen by hepatocytes taking up CK7 stain (arrows).

	Normal Range	Hospital Admission*	2 Weeks	3 Weeks **	4 Weeks ***	7 Weeks	13 Weeks
Total Bilirubin	0.2-1.3 mg/dL	23	22.7	22	19.7	4.7	1.3
Direct Bilirubin	0.0-0.2 mg/dL	>13	n/a	14.9	14.6	4.2	0.6
AST	0-45 U/L	107	134	172	200	121	27
ALT	0-50 U/L	190	130	163	182	120	35
ALP	40-150 U/L	267	179	187	168	132	109
CA 19-9	0-35 U/mL	1480	n/a	n/a	85	49	n/a

Table 1. LFT trends during the course of presentation. AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; CA19-9, carbohydrate antigen 19-9; n/a, not available. * ANA, anti-AMA, anti-SMA, anti-TTG, anti-LKM 1/2 IgG, and EBV IgG antibodies were negative. Serum IgA, A1AT, ceruloplasmin, TSH, iron levels, hepatitis panel, serum protein electrophoresis and acetaminophen levels were normal. Acetaminophen, multivitamin, iron, triamterene- HCTZ, omeprazole and atorvastatin were stopped on discharge. ** Three weeks post hospitalization. Repeat EUS/ERCP showed biliary decompression. VBDS diagnosed on liver biopsies. *** Seen in liver clinic. Started ursodiol 2000mg daily.

Discussion

- VBDS is an acquired cholestatic liver disease that may mimic the presentation of pancreatic cancer.
- CA 19-9 can be substantially elevated through T-cell mediated destruction of small bile ducts causing impaired excretion, inflammatory production, and decreased clearance.
- Severity of liver damage depends on the duration of injury and degree of bile duct loss at the time of diagnosis. Early diagnosis is important to prevent cirrhotic progression, improve outcomes, and avoid unnecessary treatments.
- Recognizing its association with an elevated CA 19-9 may help with early diagnosis but is scarcely reported in the literature.

Conclusions

- **A very high CA 19-9 in the setting of painless jaundice is often related to malignancy, but benign conditions should also be considered.**
- **We report on a significantly elevated CA 19-9 from drug-induced VBDS.**
- **CA 19-9 is not typically checked in cases of VBDS. We suspect it may be commonly elevated in this disease.**
- **Providers should be aware of this association when faced with a patient with painless jaundice and a significantly elevated CA 19-9 but no obvious malignancy.**