

Evaluation of Painless Jaundice - How Aggressive Should One be?

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Story from the front lines

An woman in her 90s with recent recently diagnosed lower extremity pressure ulcers complicated by cellulitis and ongoing treatment with oral clindamycin was transferred from an outside hospital to further evaluate new onset painless jaundice. Jaundice was noticed by nursing staff in her usual place of residence. Of note, she had no complaints such as abdominal pain, pruritus, or fever. She was found to have cholestatic hepatitis with total bilirubin 11.6 mg/dL, direct bilirubin 6.4 mg/dL, AST 271 U/L, ALT 145 U/L, and alkaline phosphatase 739 U/L. Other blood work included white blood cell count $13 \times 10^9/L$, lipase 28 U/L, and undetectable acetaminophen level. Infectious workup was negative for HIV and hepatitis A, B, C. Carbohydrate antigen 19-9 (CA 19-9) was 243.1 (0.0 - 35.0 U/mL) and carcinoembryonic antigen (CEA) was 4.2 (0.0 - 3.0 ng/mL). She underwent abdominal ultrasound, CT abdomen/pelvis, and MRCP which were all normal. ERCP was performed but incomplete due to technical issues with accessing the common bile duct. No further invasive testing was performed after discussing with patient who expressed disinterest in knowing if an underlying malignancy was present. Medication review revealed ongoing treatment with oral clindamycin for lower extremity cellulitis over the prior 2 weeks. This medication was stopped in the event it was causing drug-induced liver injury (DILI), a known adverse effect of this drug. Her liver enzymes improved gradually and she was discharged back to her nursing facility.

Teachable moment

Painless jaundice is a worrisome finding and is often caused by hepatocellular disease (e.g. toxin, medication, ischemia, or infection) or biliary obstruction (e.g. gallstones and pancreatic or biliary malignancy). Medication review is crucial as DILI accounts for approximately 10% of acute hepatitis cases [1]. DILI is often a diagnosis of exclusion given appropriate concerns for excluding an underlying malignant etiology. Clindamycin was eventually determined as the likely cause of cholestatic hepatitis in this patient but only after extensive testing was performed. Clindamycin is metabolized and excreted by the liver. Hepatotoxicity from clindamycin is uncommon but has been described in case reports [2, 3]. In this case, medication review was difficult and incomplete as patient could not provide details, there was a lack of access to electronic and paper medical records, and she received care and prescriptions from various providers recently.

It is important to consider pancreaticobiliary malignancy in painless jaundice. In one prospective study, 79% of patients with extrahepatic cholangiocarcinoma presented with painless obstructive jaundice [4]. This patient had ultrasound, CT scan, MRCP, and ERCP (incomplete) without findings to suggest malignancy. ERCP may provide diagnostic data in the form of brush cytology and biopsy specimens. However, ERCP is associated with adverse effects such as pancreatitis, bleeding, cholangitis, cholecystitis, perforation, and anesthesia associated

cardiopulmonary adverse events [5]. Physicians should always weigh risks and benefits and provide patient-centered guidance to help patients to make decisions. In this case, one might have reasonably deferred ERCP based on her advanced age, comorbidities, stated preferences, and reassuring imaging results. It was initially unclear how much understanding this patient and her family had about the various tests she received, as this patient later clarified that she would not want to know if she had active malignancy. Further invasive testing such as repeat ERCP and EUS were deferred given patient preference and probable DILI diagnosis.

References

1. Zimmerman HJ. Drug-induced liver disease. *Clin Liver Dis.* 2000 Feb;4(1):73-96, vi.
2. Aygun C, Kocaman O, Gurbuz Y, et al. Clindamycin-induced acute cholestatic hepatitis. *World J Gastroenterol.* 2007 Oct 28;13(40):5408-10.
3. Sahagún Flores JE, Soto Ortiz JA, Tovar Méndez CE, et al, Stevens-Johnson syndrome plus intrahepatic cholestasis caused by clindamycin or chlorpheniramine. *Dermatol Online J.* 2009;15(5):12.
4. Vasilieva L, Papadhimitriou SI, Alexopoulou A, et al. Clinical presentation, diagnosis, and survival in cholangiocarcinoma: A prospective study. *Arab J Gastroenterol.* 2016 Dec;17(4):181-184.
5. Chandrasekhara V, Khashab MA, Muthusamy VR, et al. Adverse events associated with ERCP. *Gastrointestinal Endoscopy.* 2017;85(1):32-47.