

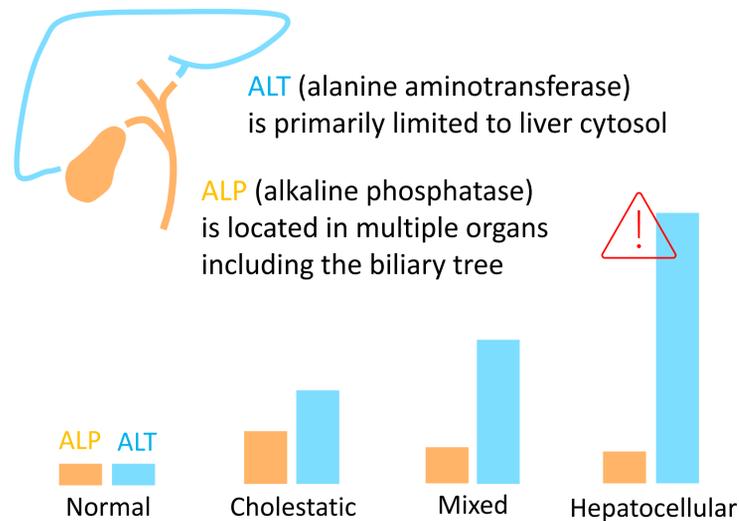
Identifying Olanzapine Induced Liver Injury in the Setting of Acute Hepatitis C

Andrea Brelje, MDⁱ, Bailey Fay, MDⁱ, Scott Mariouw, MDⁱ, and Amy VandenBerg, PharmDⁱⁱ

ⁱUniversity of Michigan Department of Psychiatry and ⁱⁱUniversity of Michigan College of Pharmacy

Drug induced liver injury (DILI):

the most common cause of acute liver failure in the developed world.¹ DILI subtypes are characterized by patterns of elevated liver enzymes outlined below.²



Severe (hepatocellular) DILI:

- Defined by ALT > 5x upper limit of normal (ULN)³
- Olanzapine is the most common antipsychotic culprit³
- Occurs in about 0.2% of patients on olanzapine— about ten times more often than with haloperidol.³
- Olanzapine DILI is dose independent and can occur anywhere from a few days to 8 years after initiation. If you don't consider it, you could miss it.^{4,5}

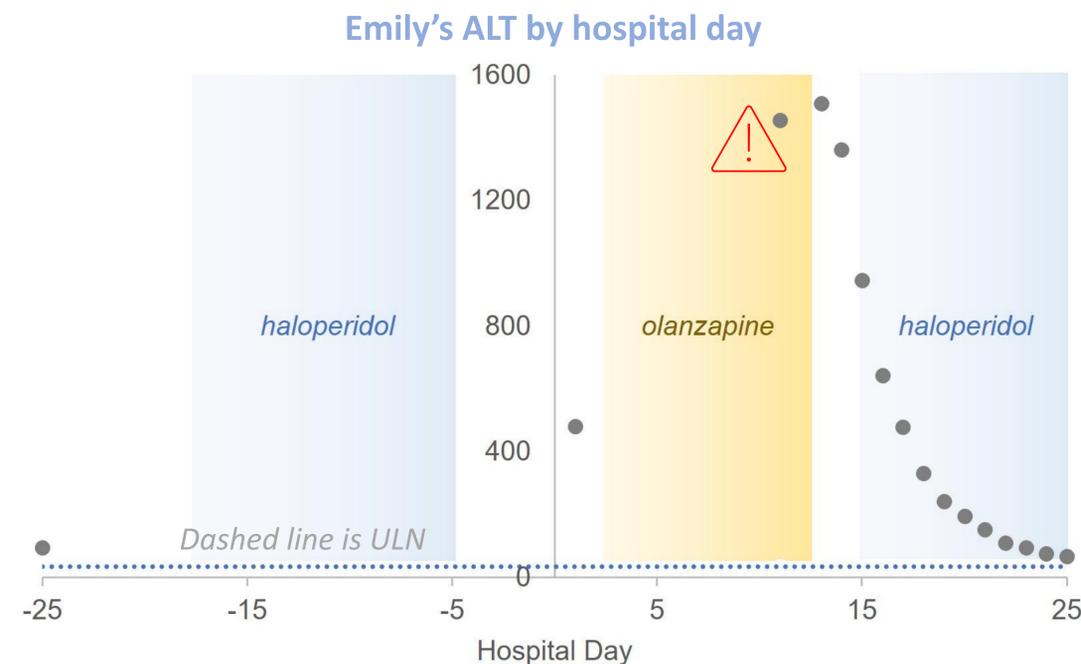
Acute hepatitis C: a DILI doppelgänger

- Acute hepatitis C should be high on differential for any patient with ALT > 5x ULN and IV drug history.⁶
- *Why should we care?* Hepatitis C is treatable, and chronic hepatitis C can cause cirrhosis and hepatocellular carcinoma (which can be lethal).⁷

Meet Emily

a 27 year old female with anxiety, IV drug use, and two recent hospitalizations for psychosis.

- Symptoms improved on haloperidol but she quickly decompensated after inpatient discharge when she self-discontinued it because of akathisia.
- Tried olanzapine, and she slowly started to feel much better.
- Meanwhile, ALT was 13x > ULN on admission, only 3x > ULN one month prior. Workup was positive for acute hepatitis C. Hepatology consult recommended inpatient monitoring of liver enzymes and outpatient hepatitis C treatment. One week later, ALT was 40x > ULN. Hepatology acknowledged another liver injury may be going on but also felt this could be entirely explained by acute hepatitis C. They deferred to Emily and Psychiatry's risk / benefit analysis to determine if it would be worth holding olanzapine.



- ALT began to fall precipitously after olanzapine was held. Emily agreed to re-try haloperidol, which had lower risk of DILI⁴, with propranolol. She had some breakthrough psychotic symptoms during the cross-titration but ultimately was discharged home with normal liver enzymes and no psychotic symptoms.

RUCAM: Roussel Uclaf Causality Assessment Method⁸

Helps link elevated liver enzymes to a causative drug.

- + 2 for timing of injury corresponding to initiation of olanzapine
- + 3 for injury resolving after cessation of olanzapine
- + 0 for risk factors
- + 0 for other drugs potentially causing DILI
- 0 for ruling out hepatitis A/B, biliary obstruction, alcohol, & shock
- + 2 for olanzapine being a published cause of DILI
- + 0 for no repeat challenge conducted

7 = "probable" cause of DILI

Key points

- DILI and acute hepatitis C can co-occur-- Don't stop looking when you find one diagnosis for elevated ALT.
- Pretest probability of detecting DILI in all patients on olanzapine is low, so we do not recommend regular asymptomatic screening of liver enzymes.
- Patients taking olanzapine with known liver disease may be at higher risk of quickly developing DILI.
- Patients should be educated about DILI as a potential rare side effect so they can alert their providers if they have any new symptoms suggestive of liver injury.
- If DILI is suspected, stopping the offending agent typically results in a rapid improvement of ALT.

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