Acute on Chronic Liver Failure from Wilson's Disease after initial therapy with Ammonium tetrathiomolybdate followed by zinc monotherapy for 35 years: A Case Report

Shuji Mitsuhashi MD[1], Ritu Nahar MD[2], Akash Patel DO[1], Katherine Keck BS[3], Nicholas Zirn MD[1], Dina Haleguoua-Demarzio MD[2]

[1]Department of Medicine, Thomas Jefferson University Hospital, Philadelphia, PA
[2]Department of Medicine, Division of Gastroenterology and Hepatology, Thomas Jefferson University Hospital, Philadelphia, PA
[3]Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia PA

INTRODUCTION

Wilson's disease (WD) is an inherited disease of toxic accumulation of Copper (Cu) mainly affecting the brain and liver[1,2]. We describe a case of acute on chronic liver failure caused by WD while being stable on Zinc (Zn) maintenance therapy for 35 years after initial treatment with ammonium (NH4) tetrathiomolybdate.

CASE PRESENTATION

- 58-year-old Caucasian male with WD presented to a local hospital with acute onset of jaundice and dark urine.
- He is a minimal alcohol drinker. He had no exposures to hepatotoxic agents and no prior evidence of liver fibrosis or decompensation.
- Diagnosed WD at age 18 with neurologic symptoms and was treated in a clinical trial with NH4 tetrathiomolybdate at the time of diagnosis followed by Zn monotherapy.
- His Zn dosage was adjusted by his PCP based on blood level.

On admission:

- Vitals were stable
- Exam revealed jaundice, scleral icterus, and abdominal distension. No encephalopathy or asterixis was present
- Labs were notable for INR 2.4, ALP/AST/ALT 86/148/47 IU/L, Tbili 12.6 mg/dL, Cr 0.9 mg/dL, mildly elevated Cu, and normal ceruloplasmin.
- CT abdomen noted cirrhotic liver morphology

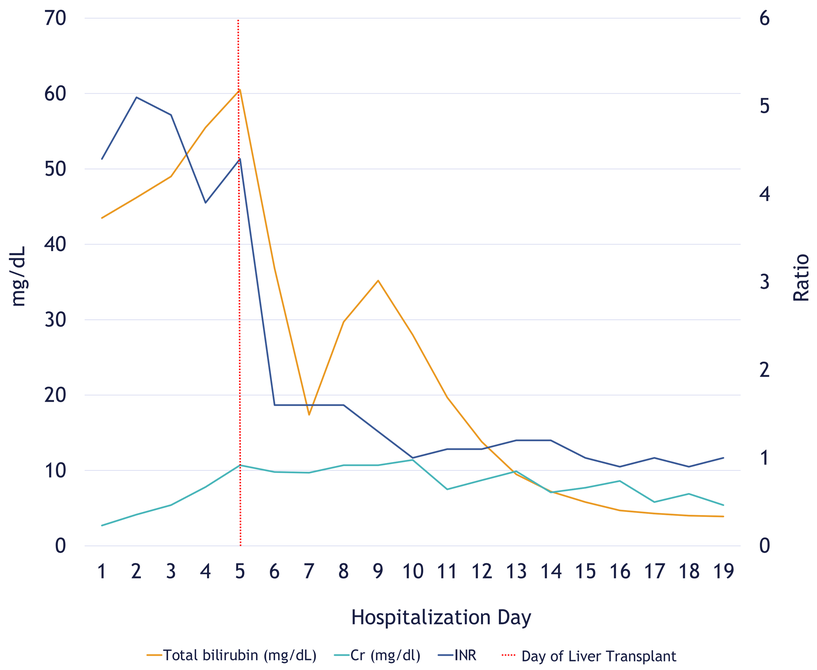

Figure 1. Trend of patient's total bilirubin, creatinine, and INR during hospitalization

HOSPITAL COURSE

- **DAY 1** – he was transferred to our hospital for an urgent liver transplant (LT) evaluation
- An extensive liver workup demonstrated negative for viral and autoimmune hepatitis, ethanol, acetaminophen, and salicylate overdose.
- His hospital course was complicated by rapidly progressive with active hemolysis and elevated total bilirubin (peaked at 60.1) and creatinine
- **DAY 2** – he was sent to ICU for dialysis and was listed for transplant as Status 1A
- **DAY 5** – he successfully underwent deceased donor LT
- Liver explant showed cholestatic hepatitis on chronic hepatitis with cirrhosis consistent with WD
- **DAY 19** – he was discharged with recovery of renal function

DISCUSSION

- NH4 tetrathiomolybdate is an efficacious treatment option for neurologic predominant WD but not yet commercially available[3].
- Zn monotherapy is as effective as penicillamine in preventing neurologic and hepatic decompensation by inhibiting Cu uptake by intestinal mucosa[4].
- Current AASLD and EASL recommend monitoring liver function test, serum Cu, ceruloplasmin and physical exam twice yearly, and urine Cu yearly[5].
- However, parameters for treatment failure of Zn need to be clearly defined to consider alternative treatment before disease progression occurs.
- LT is the only effective option for WD patients with decompensated liver disease unresponsive to medical therapy. One-year survival following LT ranges from 79-87%[5].

CONCLUSION

- Despite being on treatment, liver failure can still occur suddenly in patients with WD

REFERENCE

1. Kathawala M, Hirschfield GM. Insights into the management of Wilson's disease. Therap Adv Gastroenterol 2017;10:889-905.
2. Rodriguez-Castro KI, Hevia-Urrutia FJ, Sturniolo GC. Wilson's disease: A review of what we have learned. World J Hepatol 2015;7:2859-70.
3. Lee VD, Northup PG, Berg CL. Resolution of decompensated cirrhosis from Wilson's disease with zinc monotherapy: a potential therapeutic option? Clin Gastroenterol Hepatol 2006;4:1069-71.
4. Saroli Palumbo C, Schilsky ML. Clinical practice guidelines in Wilson disease. Ann Transl Med 2019;7:S65.
5. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology 2008;47:2089-111.