

## Learning Objectives

- 1) Present a unique case of Herbal Supplement implicated Drug Induced Liver Injury.
- 2) To increase awareness into potential hepatotoxicity of supplements unregulated by the FDA.
- 3) To reinforce the importance of complete and thorough history-taking.

## Patient Presentation

A 56 year-old female with no reported medical history presented to the hospital with a chief complaint of dyspnea. On presentation, vital signs were significant for tachycardia and mild tachypnea however she maintained normal O<sub>2</sub> saturation on room air. Review of systems questioning was negative except for increased anxiety x 1 week.

### Physical Exam:

Vitals: Temp 98.2, HR 129, BP 135/97, RR 22, SpO<sub>2</sub> 98% on room air

General: No acute distress

Eyes: Conjunctiva clear, PERRLA, no scleral icterus.

Cardio: Tachycardia, regular rhythm, reduced heart sounds, +2 pitting edema up to the knees bilaterally. Pulses equal and intact.

Respiratory: Poor inspiratory effort, decreased breath sounds bilaterally.

GI: Soft, non-tender, non-distended, bowel sounds appreciated.

MSK: Normal range of motion, all compartments compressible.

## Lab Values

138	99	25
3.3	18	1.05
16.5	270	43.6

**ALT/AST: 1979/2907**

**DBili: 0.9 TBili 2.5**

**ALP: 166**

Salicylate: < 0.3

Acetaminophen: < 5.0

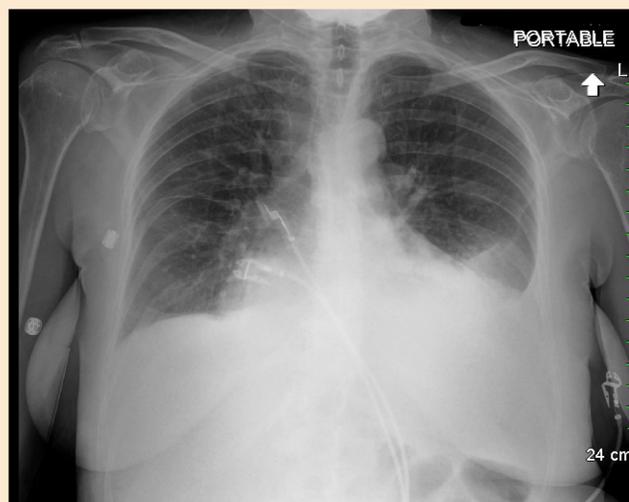
Hepatitis panel negative

**NT-pro BNP: 8769**

## Chest X-Ray Findings

- Left pleural effusion with probable left basilar subsegmental atelectasis. Mild bilateral parahilar interstitial prominence. Mild cardiomegaly.

## CXR



## Hospital Course

- After repeated questioning days into admission, she ultimately endorsed recent supplement use to promote kidney health following an elevated creatinine on outpatient labs.
- These supplements included astragalus root, Rhodiola extract, alpha lipoic acid, bromelain, and Coenzyme Q-10.



- The patient was found to have an elevated **Copper** level of **216** with normal ceruloplasmin.
- The case was discussed with poison control, who recommended N-acetylcysteine (NAC) therapy for non-Tylenol induced acute liver injury.
- Complicating the patient's hospitalization was a new diagnosis of CHF, with TTE report indicating: Moderate to severely dilated LV cavity size with normal wall thickness and severely reduced EF, estimated 25-30%. Global hypokinesis, more severe in the septal and apical regions. Small mobile 1.8 x 0.8 cm mass along the anteroseptal wall, most likely a thrombus.

## Hospital Course (continued)

- Incidental finding of LV thrombus further complicated hospitalization as patient required initiation of anticoagulation.
- Subsequent cardiac catheterization showed patent coronary arteries.
- The patient also developed recurrent pleural effusions requiring serial thoracenteses.
- The patient's liver enzymes improved after NAC therapy, with normalization prior to discharge. A RUQ ultrasound showed mild fatty liver but no cirrhotic changes.
- Per poison control, no definitive link exists between the individual supplements and new onset hepatic or heart failure, however the combination used concurrently has not been studied.
- Other pertinent negative tests included: ANA, ASMA, complement, ethylene glycol, methanol, proteinase-3-antibody, myeloperoxidase antibody, COVID-19, pleural fluid acid-fast bacilli and fungal culture, urine culture.

## Drug-Induced Liver Injury (DILI)

- Drug induced liver injury (DILI) can be categorized as non-idiosyncratic (predictable) or idiosyncratic (unpredictable) based on the culprit agent.
- Idiosyncratic DILI accounts for approximately 11% of acute liver failure in the United States, and the incidence of idiosyncratic DILI is estimated to be 19.1 cases per 100,000 people per year.
- While antibiotics remain the most common cause of idiosyncratic DILI, herbal and dietary supplements are becoming more recognized as potential culprits due to unregulated nature and ease of procurement.
- Furthermore, patients often refrain from reporting supplement use to healthcare professionals due to their seemingly "all-natural" composition.

## Take Home Points

- This case raises an important question about the potential for acute hepatotoxicity behind poly-supplement use.
- Supplements are not regulated by the FDA and the manufacturing of these substances is not routinely monitored.
- Little is known about the supplement packaging processes and possible contamination with hepatotoxic heavy metals such as Copper.
- Although research shows that the above-mentioned supplements are not inherently hepatotoxic on an individual basis, they may potentiate DILI when used concurrently.
- This case cements the fundamental tenet of medicine: obtaining a complete and thorough history. When discussing a patient's medication history, it is crucial to explore non-pharmaceutical substances such as supplements and herbal remedies.

## References

- 1) Katarey, D., Verma, S., "Drug-Induced Liver Injury." *Clin Med(Lond)*. 2016 Dec; (Suppl 6): s104-s109.
- 2) Leise, M., Poterucha, J., Talwalkar, J., "Drug-Induced Liver Injury." *Mayo Clinic Proceedings*. 2014 January; 89, 1: 95-106.