Drug-Induced Autoimmune Hepatitis Post Acute Liver Injury From Skullcap Supplements: An Unfortunate Case of Herbal Toxicity

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BACKGROUND

The use of herbal medicinal products (HMP) has exponentially increased over the last three decades with approximately 25% Americans reporting HMP use at some point in their life.

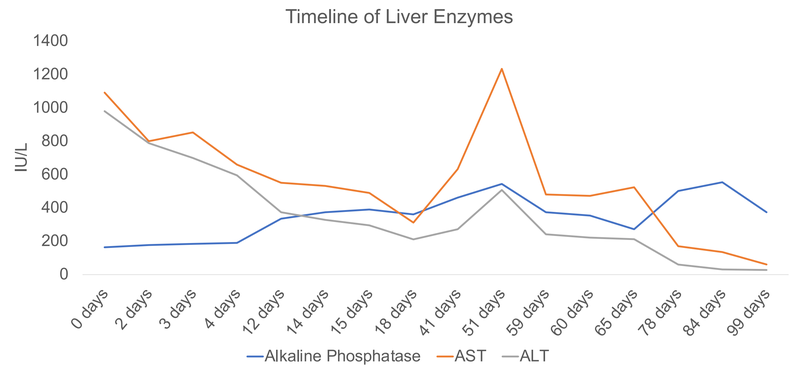
Skullcap (*Scutellaria lateriflora)* is a flowering plant native to North America that has been implicated in rare cases of liver injury.

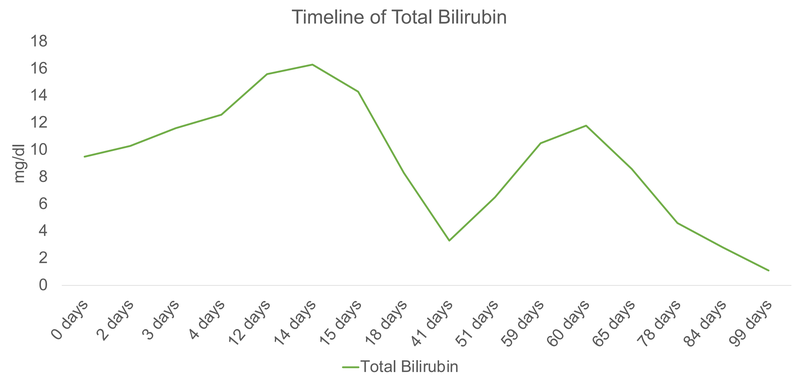
We describe a rare case of severe drug induced liver injury (DILI) and de-novo autoimmune hepatitis resulting from the use of skullcap supplements.

CASE PRESENTATION

62-year-old Caucasian woman with a h/o of Sjogren's disease presenting with new onset jaundice.

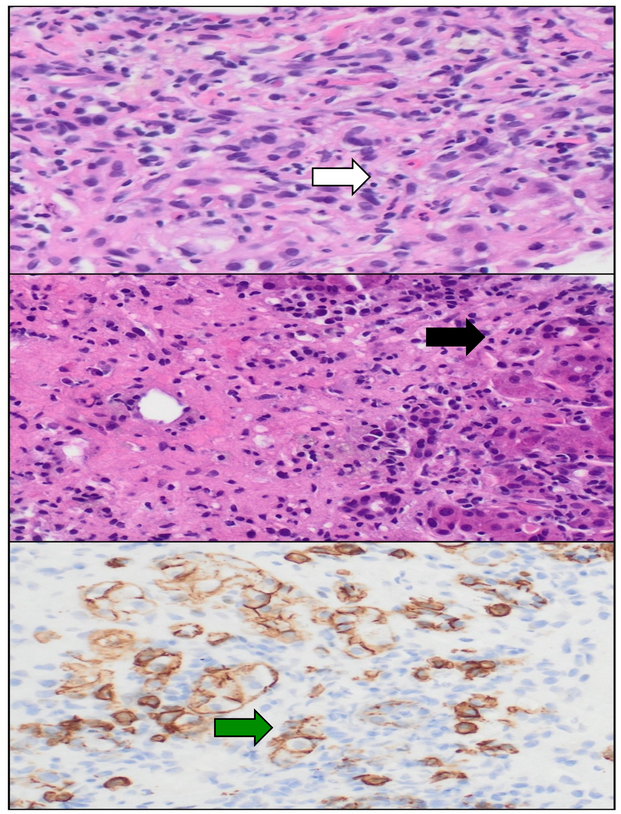
- **Labs on presentation:** Alkaline Phosphatase (Alk Phos) 164 IU/L, AST 1091 IU/L, ALT 980 IU/L, Total Bilirubin (T bili) 9.5, INR 2.4. (Normal 4 months prior to presentation)
- **MRI/MRCP:** Unremarkable
- Patient denied any history of liver disease but admitted to using Skullcap supplements over the last month for insomnia
- **Workup for chronic liver disease – negative.** ANA was chronically positive - 1:1280. **IgG elevated at 2573 mg/dl.**
  Initial Liver biopsy: Resolving centrilobular necrosis with predominant eosinophilic inflammation.
- LFT's downtrended over the next 72 hours. Patient was discharged with outpatient follow up. Re-admitted 1 month later due to worsening jaundice and acute kidney injury
- **Labs on readmission:** Alk Phos 619 IU/L, AST 1222 IU/L, ALT 540 IU/L, T bili 6.6 mg/dl. **ANA 1:160, IgG 2023**
  Repeat liver biopsy: Extensive plasma cells consistent with drug induced autoimmune hepatitis
- **Outcome:** Listed for simultaneous liver-kidney transplantation but patient recovered without requiring a transplant.





DISCUSSION

- Drug induced liver injury (DILI) is defined as hepatic synthetic dysfunction which results from the use of prescription drugs, over the counter medication and HMP
- DILI is essentially a diagnosis of exclusion.
- Diagnostic algorithms such as Naranjo algorithm, Roussel Uclaf Causality Assessment Model (RUCAM) and Drug-Induced Liver Injury Network (DIILIN) expert consensus opinion can help in establishing diagnosis.
- In our case the the initial biopsy showed centrilobular necrosis with eosinophilic infiltration, highly concerning for DILI. The RUCAM score was 5 and the DIILIN severity index was 4.
- The subsequent biopsy however showed significant plasma cell infiltration with an elevated IgG indicative of de-novo Autoimmune Hepatitis.
- The hepatotoxic effects of Skullcap is likely mediated by flavonoids such as *scutellarin* and *baicalin.*



Histology: **Top**: Initial biopsy showing confluent centrilobular necrosis with interspersed eosinophils (White arrow).
Middle: Resolving centrilobular necrosis with plasma cells (Black arrow).
Bottom: Immunohistochemical staining of plasma cells with CD 138 (Green arrow).

CONCLUSION

- HMP'S continue to be a major contributor to the annual incidence of DILI.
- Given the lack of FDA regulation on dietary supplements and HMP's the incidence continues to rise.
- Implementation of a centralized resource for documentation and reporting can help in reducing under-reporting of DILI.

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