An Interesting Case of Meloxicam-Induced Autoimmune Hepatitis

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Learning Objectives

1. Autoimmune hepatitis (AIH) is an immune-mediated inflammatory liver disease with a highly variable clinical presentation ranging from mildly abnormal liver tests to hyperacute, fulminant liver failure.
2. To discuss a rare presentation of drug-induced AIH (DI-AIH) from the NSAID meloxicam.
3. DI-AIH from meloxicam and other NSAIDS is an underappreciated entity. Early identification and management may prevent chronic liver injury progression and the need for liver transplantation.

Initial Presentation

A 33-year-old female with history of obesity and rheumatoid arthritis (RA) presented with symptoms of abdominal pain, fatigue, nausea, and non-bloody emesis for one month. She denied alcohol or drug abuse, liver disease, and recent herbal supplements.

Past Medical History:
Obesity
Rheumatoid Arthritis

Medications:
Advil 1600mg daily
Dicyclomine 10mg daily
Gabapentin 300 TID
Hydrocodone
Ibuprofen
Meloxicam 15mg daily
Tizanidine
Tylenol

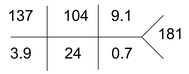
Family History:
No pertinent family hx

Social History:
Denies tobacco use
Denies alcohol use
No illicit drug use

Review of systems:
- Positive for constipation, abdominal pain, fatigue, nausea, and non-bloody emesis.
- Negative for fevers, weight loss, melena, hematemesis, hematochezia

Pertinent Physical Exam:
Vital signs: HR 60, RR 17, Temp 98.3, BP 120/74, BMI 69
Gen: obese, no acute distress
CV: tachycardia; S1S2; no m/r/g
Abd: non-tender, non-distended, nml BS
Skin: no jaundice, no spider angioma

Initial Labs:
- Immunoglobulin G (IgG) of 1680 mg/dL
- ANA of 1:320
- Positive mitochondrial IgG Ab 22.6 ZZ
- Negative for HBV, HCV, HAV, anti-smooth muscle antibody, and human simplex virus (HSV) 1-2 PCR



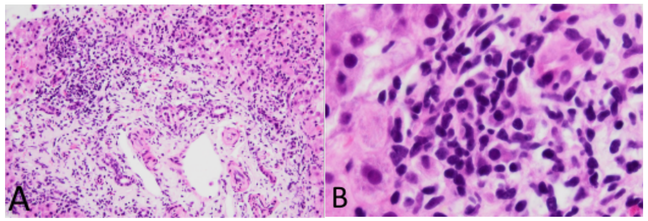
Hospital Course

Hospitalization:
- The patient presented with initial symptoms and was admitted for expedited workup of elevated liver function tests (LFT). She had two prior visits to the ER and her work up was only remarkable for mild LFT elevations that was attributed to non-alcoholic steatohepatitis (Table 1). She was taking meloxicam for the last year for sero-negative RA. She was taking tizanidine as needed for the last 3 years.
- The patient discontinued meloxicam 2 weeks prior to her admission and tizanidine was held on admission.
- The patient received IV N-acetylcysteine 150mg/Kg and IV vitamin K on admission.
- Hepatic Ultrasound was normal. Liver biopsy was obtained.

Table 1: Trend of Liver Chemistry Tests

Date/Event	Length of Meloxicam	AST	ALT	INR	T.Bili	ALP
03/2/2020	4 months prior to initiation	11	15	n/a	0.3	47
05/11/2021 Onset of symptoms	10 months after initiation	44	83	n/a	0.6	37
06/29/2021 Hospital Admission	2 weeks after discontinuation	772	962	1.63	2.9	68
07/04/2021 Hospital Discharge	3 weeks after discontinuation	29	234	1.48	1.6	53
08/06/2021 Clinic Follow-up	8 weeks after discontinuation	21	49	n/a	0.3	47
10/08/2021 Clinic Follow-up	17 weeks after discontinuation	41	79	n/a	0.6	34

Diagnostic Findings:
- Liver biopsy revealed moderate periportal and pericentral lymphoplasmacytic inflammatory infiltrate associated with interface hepatitis and marked zone three hepatocyte dropout (Figure 1A, Figure 1B).
- Liver biopsy also showed interlobular bile ducts are present in most portal tracts with no active inflammatory injury.



A) Periportal inflammation B) Lymphoplasmacytic interface hepatitis

Follow-up:
- She was started on 60mg/day oral prednisone with chronic taper with clinic follow up.
- Follow up in clinic showed significant improvement of patient's liver chemistry tests and symptoms (table 1).
- Serology showed resolution of her IgG autoantibody to 1004 mg/dL after discontinuation of meloxicam.
- Tizanidine was resumed and liver function testing remained stable at further follow up.

Discussion

- Drug induced autoimmune hepatitis is an idiosyncratic hepatotoxicity which can present as acute or chronic liver injury.
- DI-AIH can present like other forms of acute liver injury, such as drug-induced liver injury and classic autoimmune hepatitis. It is important to differentiate these ailments as management plans vary based on the correct diagnosis.
- Early diagnosis of DI-AIH is important because DI-AIH is responsive to immunosuppressive therapy, and early initiation of treatment can obviate the need for liver transplantation.
- Some distinguishing factors of DI-AIH include resolution of transaminitis after discontinuation of the offending agent, and lower duration of treatment required without relapse.
- To our knowledge, there are very few case reports describing meloxicam induced-AIH. However, a retrospective cohort did report that most DI-AIH cases were due to nitrofurantoin (67%), followed by NSAIDS (17%).
- NSAIDs are more frequently associated with this disease process than previously considered and should be on the differential when posed with acute liver injury. This would allow early identification and management of affected patients, and may prevent chronic liver injury progression and the need for liver transplantation.

References

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