Interesting Presentation of Autoimmune Hepatitis Superimposed With Acetaminophen Toxicity

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Background

- Idiopathic Autoimmune Hepatitis (IAH) is a rare form of chronic hepatitis with a strong predominance in females in bimodal age distribution between 10-20 years or 40-60 years[1].
- The etiology of IAH is unclear, but it's believed to be autoimmune process as it concurrently presents with other autoimmune diseases such as Type 1 Diabetes or Rheumatoid Arthritis[2].
- Minocycline, nitrofurantoin, hydralazine, statins, infliximab, and etanercept have been found to be implicated in causing Drug-Induced Autoimmune Like Hepatitis(DI-ALH)[3].
- Distinguishing DI-ALH from IAH is quite challenging because its presentation, diagnostic test results(with positive autoimmune serology), and liver biopsy features can closely resemble IAH[3].
- Acetaminophen hepatotoxicity typically presents with fulminant liver failure with elevation of INR(coagulopathy), liver enzyme levels greater than 1000 U/L, and encephalopathy[6].

Case Presentation

HPI

- A 75 y/o F with lumbar retinopathy, HTN, and Type II DM presents to her PCP for routine lab tests.
- Her AST and ALT are elevated at 231 and 221, respectively.
- Upon questioning, patient admits to taking Tylenol up to 3900 mg daily for the past two years. She was asymptomatic
- At the ED, her acetaminophen was elevated at 7.6, and she was treated with 20-hour IV N-Acetylcysteine (NAC). Her liver enzymes normalized upon discharge.
- A week later, patient returns with new onset profound fatigue and generalized pruritis.

Lab Results, Imaging, and Biopsy

- Her lab findings now show AST and ALT elevated at 143 and 171, respectively, INR 1.3, positive Antinuclear Antibody(ANA 1:5120), positive p-ANCA antibody, positive Smooth Muscle Antibody(AMA), upper limit of normal serum IgG
- Other labs including GGT, Anti-Mitochondrial Antibody, Alkaline phosphatase, Bilirubin, and Hepatitis Panel were all negative.
- Abdominal US shows hepatomegaly
- US guided Biopsy of the liver shows inflammatory infiltrate predominantly consisted of small lymphocytes and plasma cells (Figure 1) as well as interface hepatitis with bridging fibrosis (Figure 2)

Histopathology Findings

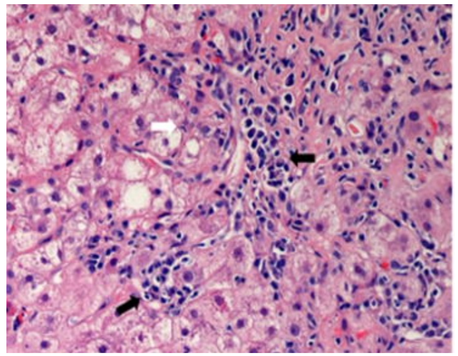

Figure 1. Marked Interface activity with inflammation dominated by plasma cells (black arrows)[4]

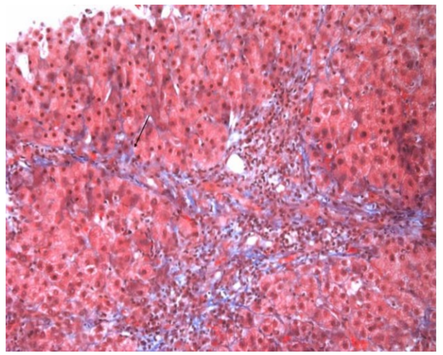

Figure 2. Fibrosis with early bringing formation[5]

Discussion

- Our case was interesting in that our patient was beyond the typical bimodal age associated with IAH. In addition, she did not have any other autoimmune conditions.
- Acetaminophen hepatotoxicity is associated with fulminant liver failure but has not been yet found to be implicated in causing DI-ALH. However, one can theorize that chronic use of acetaminophen may cause chronic inflammation therefore DI-ALH.
- In our case, it is unclear if her chronic acetaminophen use caused DI-ALH or served as a trigger for IAH.
- DI-ALH is typically treated with discontinuation of the drug with complete resolution of the condition, although the recovery can be delayed and may prompt the use of corticosteroids[6].

Conclusion

- IAH and DI-ALH have overlapping features in clinical presentation, immunological, and histologic findings. Currently, the only way to distinguish DI-ALH from IAH is the presence of relapse after discontinuation of offending drug or corticosteroids[7].
- In conclusion, there should be a better diagnostic criteria that may help distinguish the phenotype of DI-ALH from IAH.