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Rare Case of Acute Hepatitis of Unknown Etiology in an Adult Female: A Case Report

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dass and co-others in this article report on a ‘Rare Case of Acute Hepatitis of Unknown Etiology in an Adult Female’’. The manuscript is of clinical interest although the authors need to address some points as follows: - To help ruling out AIH; what is the patient’s total IgG? Is there an evidence of piecemeal necrosis in the liver biopsy? As there is a term called ‘’autoantibody negative AIH’’. - Did you investigated for Wilson’s disease? - When was the date of discharge? - What were the results of her liver functions after discharge? Did she resolve or worsened? Thanks

Authors’ response: The patient’s total IgG was 2255 on 7/25/22. According to the biopsy report, there was no evidence of piecemeal necrosis. We did indeed investigate for Wilson’s disease, which came back negative. Her ceruloplasmin level was 62, a bit higher than normal, and we attributed this to her current inflammatory state. She was discharged on 7/29/22, five days after admission. Unfortunately, the patient was lost to follow up, so we could not retest her LFTs. We mentioned this in the “outcome and follow-up” section.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: Acute hepatitis of unknown origin (AHUO) is unusual in adults and remains a diagnostic and treatment challenge. In this manuscript, the authors presented a case of 58-year-old female who was diagnosed as acute hepatitis with AST 3159 Unit/L, ALT 2500 U/L, and Bilirubin (Total/Direct) 6.4/4.4 mg/dL. Serological markers for hepatotropic viruses, e.g. A, B, C, and E were all negative. Further infective work-up revealed negative serology for CMV, EBV, herpes virus 1 & 2, and HIV. All the tested autoantibodies, including antinuclear antibody, anti-smooth muscle antibody, anti-mitochondrial antibody, liver soluble antibody, and anti–liver-kidney microsomal 1 antibody were also negative. Liver biopsy showed moderate to severe active hepatitis with focal confluent necrosis, consisting mostly of lymphocytes. This is an interesting

case of acute hepatitis of unknown origin. The preparation of manuscript and data presentation were not so appropriate. Nonetheless, this manuscript could provide useful information for clinicians to manage patients with acute hepatitis. Comments 1. The authors should present the results of serological examinations in a Table. 2. The authors should present the Figures of image studies. 3. The authors should present the histological figures of liver biopsy. 4. The English needs polishing.

Authors' response: Thank you for your thoughtful comments. We have added a table with results of serological examinations as you suggested (see table 2). We have also presented the images of several imaging studies we carried out (see figures 1 and 2). The histology images were added as figure 3. We have all reviewed the manuscript for language and hopefully it reads a bit more polished this time!