February 2024 (symptomatic clinical pattern with jaundice), corroborated by serology (IgM + antibodies) remission with supportive treatment in April. In May, she presented a new jaundice event, general malaise, and asthenia, so she underwent evaluation. On examination, jaundice and hepatomegaly were observed. Laboratory studies: BT 23.5mg/dL, BD 19.9mg/dL, ALT 534U/L, AST 827U/L, FA 128U/L; suggestive of acute hepatocellular injury (R factor=14). Hepatobiliary ultrasound rules out the obstruction and reports a diffuse increase in echogenicity; Serology: IgM HAV non-reactive, IgG HAV+ (ruling out a prolonged course of hepatitis A). Consumption of drugs, alcohol, and infections by other viruses (B, C, E, Epstein Barr, and HIV) are ruled out. The measurement of serum globulins reports hypergammaglobulinemia (IgG x 1.6 ULN); in addition, increased levels of antinuclear antibodies (ANAs, dilution 1:80) are detected by Immunofluorescence (IF); histopathological report of liver biopsy: chronic interface hepatitis, portal lymphoplasmacytic infiltrate and lobular damage, (fibrosis: F2); meeting all suggested criteria for the diagnosis of autoimmune hepatitis defined by the International Autoimmune Hepatitis Group Criteria.[5] Due to all of the above, it was decided to start treatment with parenteral steroid at a dose of 1 mg/kg/day (prednisone equivalent), with a good response to medical management, observing a gradual reduction in the levels of bilirubin, liver enzymes, and immunoglobulin G levels after the first 72 hours of medical treatment.

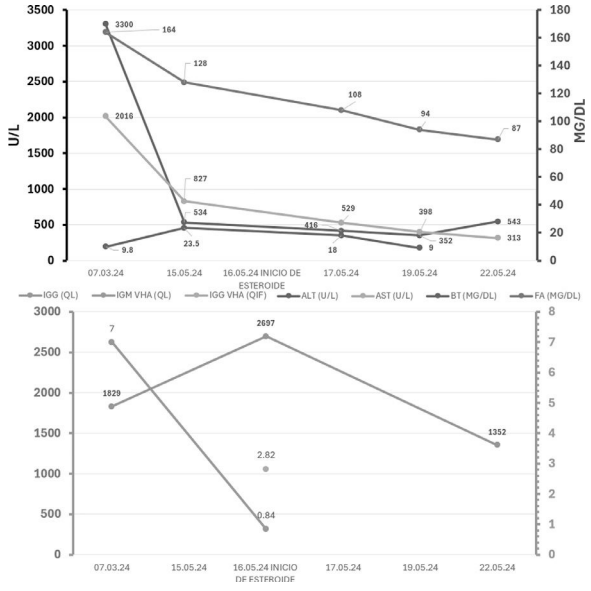
Results: Several triggers have been identified for the appearance of outbreaks of autoimmune hepatitis among them viral infections, which are reported in the literature. In rare cases, the hepatitis A virus can precede an outbreak of autoimmune hepatitis type 1. The treatment to induce immune remission is based on the administration of steroids, which usually guarantees a good response, as in the reported clinical case.

Conclusions: Hepatitis A virus infection is associated with altered immunotolerance with subsequent activation of lymphocytes and the production of specific antibodies that trigger molecular mimicry, which is directly involved in the pathophysiology of autoimmune hepatitis. Exposure to external factors is considered necessary to trigger the autoimmune reaction against hepatic structures.

Ethics statement: The procedures indicated above are under the General Health Law on Research in Human Beings regulations, as as well as the Declaration of Helsinki and subsequent amendments.

Conflict of interest statement: None.

Financing: Regional Hospital Lic. Adolfo López Mateos ISSSTE.



https://doi.org/10.1016/j.aohep.2025.101827

Cholestatic Injury Induced by Naproxen: A Rare Cause of NSAID-Induced Hepatotoxicity. Case Report.

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Introduction and Objectives: Naproxen-induced liver injury is very rare (1-3 cases per 100,000 exposed individuals), typically occurring 1-6 weeks after ingestion[1]. The damage can manifest with or without immunoallergic features and varying degrees of hepatocellular injury and cholestasis[2]. We illustrate a case of a patient who developed cholestatic injury.

Materials and Patients: A 51-year-old man, with the only relevant history being self-prescribed ingestion of 220 mg gel capsules of naproxen sodium two weeks prior for post-exercise muscle pain, presented on 04/05/24 with asthenia, vague abdominal pain in the right hypochondrium, jaundice, acholia, and dark urine. He sought medical emergency services two days later, where pronounced mucocutaneous jaundice, hepatomegaly, and hepatodynia were observed. Paraclinical tests showed hyperbilirubinemia: total bilirubin (TB) elevated due to direct bilirubin (DB), marked elevation of alkaline phosphatase (AP) and gamma-glutamyl transferase (GGT), and slight elevation of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (R factor = 2 mixed). Hepatic and biliary tract ultrasound reported diffuse increased hepatic echogenicity, ruling out biliary tract obstruction. Serological testing for hepatotropic viruses and TORCH screen were negative, as was the serological profile for autoantibodies. A percutaneous ultrasound-guided liver biopsy was performed; biopsies demonstrated intrahepatic cholestasis, minimal and focal lobular and portal interface hepatitis, macrovesicular steatosis; special stains negative for hemosiderin and glycogen deposits, fibrosis and copper-bound proteins; suggested of drug induced liver damage **(Figure 1)**.

Results: Drug-induced liver injury is a diagnosis of exclusion, only to be suspected when major causes of liver damage have been ruled out. Naproxen, a non-steroidal anti-inflammatory drug (NSAID) derived from propionic acid, has been reported to cause hepatotoxicity phenotypes of hepatocellular injury (acute hepatitis) and cholestasis through metabolic, immunoallergic and idiosyncratic mechanisms[3]. In this patient, the toxicity was non-dose-dependent, with an acute presentation characterized by a predominant elevation of cholestatic markers. Only supportive measures were provided, with close clinical and biochemical monitoring to identify early signs of liver dysfunction. The patient showed favorable evolution towards remission, characterized by symptomatic improvement and a progressive decrease in cholestatic markers within the first few days **(Figure 2)**. After nine days of hospitalization, discharge was decided due to improvement, with a follow-up appointment for continued monitoring.

Conclusions: In suspected naproxen-induced cholestatic injury, a liver biopsy is not required for diagnosis[4] but is useful for understanding etiology, severity, extent, and prognosis. Discontinuing the causative agent is the first measure, and medical treatment should be directed solely by the clinical and biochemical evolution of the patient.

Ethical statement: The procedures performed comply with the regulations of the General Health Law on Research in Humans and the Declaration of Helsinki of 1975 and subsequent amendments. According to Article 5 of the General Health Law, this research

contributes to the prevention and control of health problems of interest. The research was conducted by health professionals under the supervision of competent health authorities.

Declaration of interests: None.

Funding: Hospital Regional Lic. Adolfo López Mateos ISSSTE.

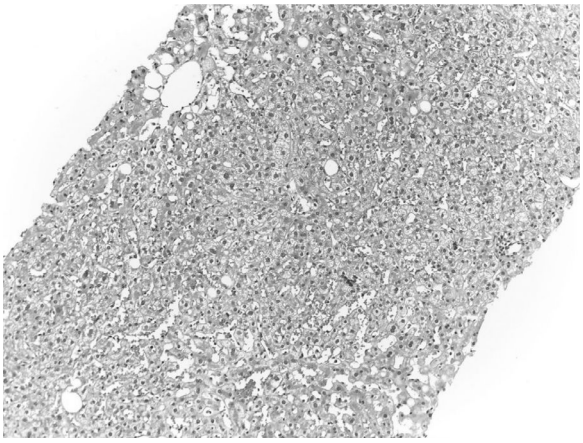

Figure 1.

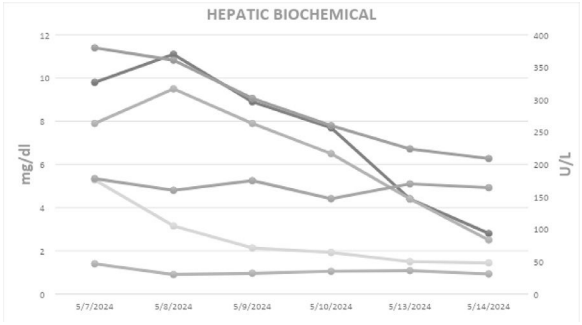

Figure 2.

https://doi.org/10.1016/j.aohep.2025.101828

Oxidative damage to lipids improves with Omega-5 fatty acid supplementation treatment in patients with severe alcoholic hepatitis

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Introduction and Objectives: Chronic and excessive alcohol consumption causes alcoholic liver disease (ALD). Alcoholic hepatitis (AH) is a severe clinical event that develops in patients with ALD and active alcohol consumption, and it has a high mortality rate within 30 days. Inflammation and redox imbalance play a crucial role in promoting the dysfunction of hepatocytes and reducing patient survival. Glucocorticoids have a transient beneficial effect in AH; however, it is necessary to understand the effect of antioxidant therapy in this pathology. To evaluate oxidative stress of lipids in patients with alcoholic hepatitis whose treatment included Omega-5

Materials and Patients: The randomized, double-blind clinical study included two groups of patients (men and women) with severe alcoholic hepatitis: 1) Patients treated with Prednisone (40 mg/day) + oral administration of Omega-5 (0.64 g/day) (n=20; 10% women and 90% men), and 2) Prednisone + Placebo group (n=20; 15% women, 85% men). Both groups received treatment for 28 days. Alcohol consumption was calculated in g/day. Biochemical and hematological laboratory test were performed. The MELD, Glasgow, ABIC, and Lille scales were evaluated, as well as serum levels of lipid oxidation through malondialdehyde (MDA) at 7, 14, and 28 days. The data was analyzed by Kruskal-Wallis, Mann-Whitney U and ANOVA statistical tests by SPSS v.22, significance of $p<0.05$.

Results: Both groups had similar characteristics; there was no difference in severity and alcohol consumption. After 7 days of treatment, both groups of patients showed similar levels of MDA, with the highest determination of MDA observed at this point. However, a reduction in serum MDA levels was observed at 14 days (5%) in the Omega-5 group; similarly, a 22% reduction in MDA was observed at 28 days. In contrast, the placebo group showed a continuous increase in MDA levels: 19.6% and 35% at 14 and 28 days, respectively. However, there were no statistical differences, indicating the need for further studies to evaluate changes in MDA levels over six months, as well as the effects of different doses and Omega-5supplementation time.

Conclusions: The oral administration of Omega-5 fatty acid in combination with prednisone can reduce oxidative stress of lipids at the systemic level. The use of antioxidant therapy as an adjuvant may improve the redox state and inflammation, which could decrease infectious events and, consequently, mortality in alcoholic hepatitis.

Ethical statement: Clinical trial registration at NIH (ClinicalTrials.gov Identifier: NCT03732586). The protocol was approved by the Ethics and Research Committees of the General Hospital Dr. Manuel Gea González and the Faculty of Medicine at UNAM. All participants provided written informed consent, and the study was conducted in accordance with the provisions of the Declaration of Helsinki

Declaration of interests: None.

Funding: Partial support from Distribuidora Biolife S.A. de C.V.

https://doi.org/10.1016/j.aohep.2025.101829

Differences in the progression of liver disease in male and female rats induced by TAA: considerations in the development of pharmacological therapies

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Introduction and Objectives: Thioacetamide (TAA) is a hepatotoxic agent that causes fibrosis, cirrhosis, and cancer. Various doses and regimens of TAA have been tested in different murine models to validate hepatoprotective compounds. To date, only two studies have reported differences in TAA susceptibility according to sex in murine models. To compare the progression of liver disease in male and female Wistar rats induced by TAA.