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Mesalamine induced hepatotoxicity. Is mesalamine safe?

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Dear Editor,

Mesalamine is widely used in the treatment of patients with ulcerative colitis (UC). Although this drug is considered to be safe, it is not without adverse effects. Hepatotoxicity has been reported with an incidence of 0-4 %. The present clinical case includes laboratory, imaging, and histological findings in a patient with hepatotoxicity due to mesalamine.

Case report

A 79-year-old female presented with a history of total thyroidectomy for thyroid cancer. In the context of chronic diarrhea, a left-sided UC was suspected, and oral mesalamine 4 g

per day, and mesalamine suppositories were initiated. Before starting treatment, she had normal liver test results. After a period of three months, she presented with a headache, fatigue, and intermittent low fever. Laboratory tests showed a normal blood count, a liver profile with a cholestatic pattern (Fig. 1A), and elevation of inflammatory parameters. Mesalamine was suspended, and an extensive study was performed with serology for hepatitis A, B, C, and E, cytomegalovirus, and Epstein-Barr viruses. Antinuclear, antimitochondrial, and anti-smooth muscle antibody test results were all negative, with normal immunoglobulin counts and subclasses. Magnetic resonance imaging (MRI) reported intra and extrahepatic bile duct dilation without obstruction, and thickening of the intrahepatic bile duct (Fig. 1B and C). The disease progressed with worsening of the liver profile without signs of liver failure. A liver biopsy was performed (Fig. 1D-F), which showed non-suppurative cholangitis with granulomas and focal concentric fibrosis related to medium-caliber bile ducts, and IgG4 staining was negative. QuantiFERON®-TB-Gold was negative, and angiotensin-converting enzyme activity was in the normal range. Ursodeoxycholic acid was initiated with a good initial response, but after 13-weeks, the patient presented again with a slight elevation of liver enzymes, so a short course of prednisone was administered. MRI changes disappeared, systemic symptoms subsided, but cholestasis regression was slow, so bezafibrate was added to the therapy. During follow-up, there was no diarrhea, fecal calprotectin was normal, and colonoscopy ruled out UC. The patient presented improvement of the liver profile to a near-normal degree at 50 weeks after drug withdrawal.

Discussion

Although mesalamine induced hepatotoxicity has a low incidence, it should be suspected in a patient receiving this drug with sudden liver profile alteration. Since the patient had normal liver tests prior to starting mesalamine, a negative autoimmune serology and non-compatible MRI and liver biopsy findings, primary sclerosing cholangitis was ruled out. Among histopathological findings reported in the literature, the presence of non-caseating granulomas is a frequent finding.

References

1. Barnhill MS, Steinberg JM, Jennings JJ, et al. Hepatotoxicity of agents used in the management of inflammatory bowel disease: a 2020 update. *Curr Gastroenterol Rep* 2020;22(9):47. DOI: 10.1007/s11894-020-00781-3
2. Feagan BG, Chande N, MacDonald JK. Are there any differences in the efficacy and safety of different formulations of oral 5-ASA used for induction and maintenance of remission in ulcerative colitis? Evidence from Cochrane Reviews. *Inflamm Bowel Dis* 2013;19(9):1. DOI: 10.1097/MIB.0b013e3182920108
3. Bessone F, Hernández N, Mendizábal M, et al. Cuando la creación de un consorcio proporciona respuestas útiles: experiencia de la Latin American DILI network (LATINDILIN). *Clin Liver Dis* 2019;13(S1):S17-23. DOI: 10.1002/cld.840
4. Sehgal P, Colombel J-F, Aboubakr A, et al. Systematic review: safety of mesalazine in ulcerative colitis. *Aliment Pharmacol Ther* 2018;47(12):1597-609. DOI: 10.1111/apt.14688
5. Núñez FP, Castro F, Mezzano G, et al. Hepatobiliar manifestations in inflammatory bowel disease: a practical approach. *World J Hepatol* 2022;14(2):319-37. DOI: 10.4254/wjh.v14.i2.319

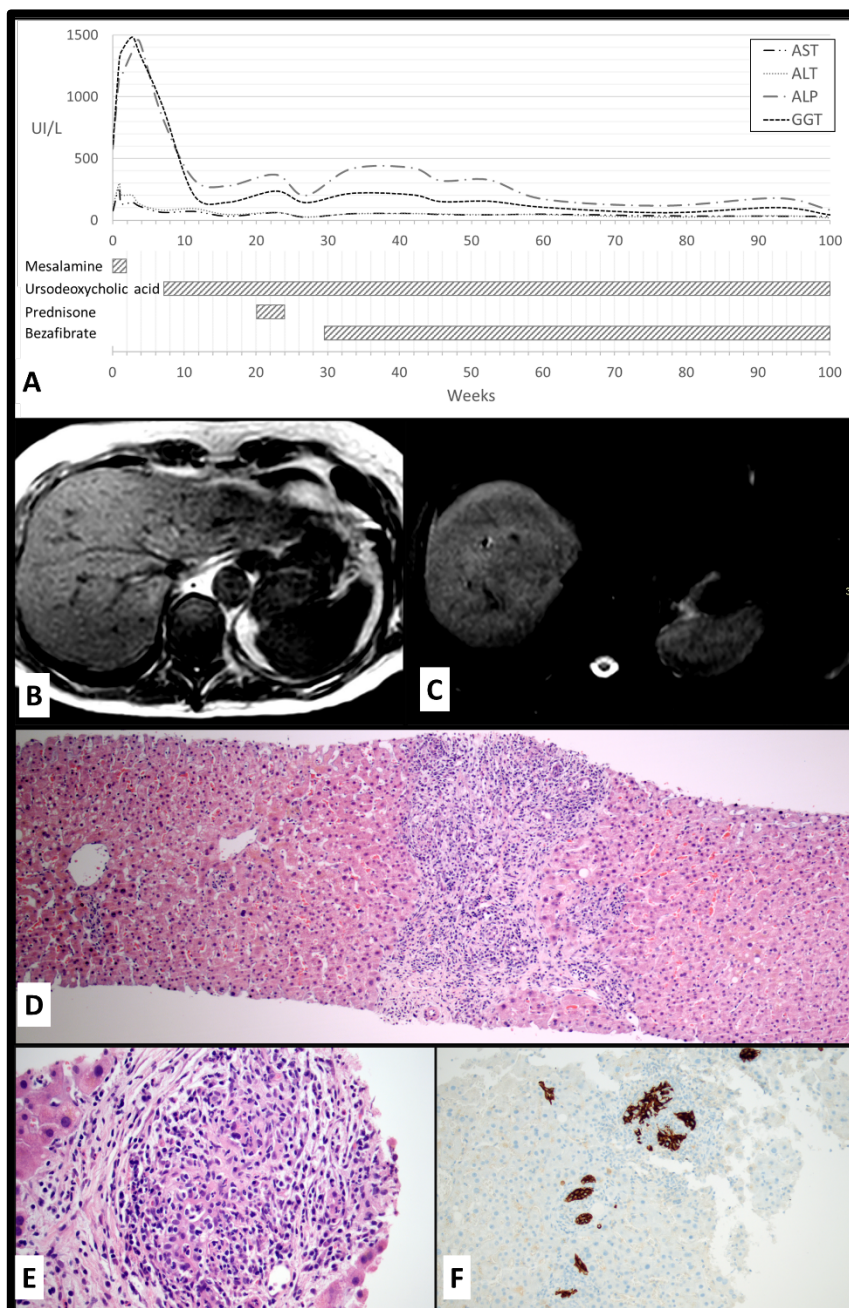


Fig. 1. A. Evolution of liver tests during follow-up. Top: it shows a predominantly cholestatic pattern; bottom: relevant medication received by the patient; bars show the time-period the patient received each medication. B. GRE axial T1-weighted MRI showing

intrahepatic bile duct dilation. C. Axial T2-weighted MRI showing intrahepatic bile duct diffuse hyperintensity and dilation. D. Wide portal spaces secondary to predominantly mononuclear infiltrate. E. Portal space with mononuclear infiltrate with granulomatous reaction in relation to the bile duct. F. Portal spaces with evident ductal damage. AST: aspartate aminotransferase; ALT: alanine transaminase; ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; GRE: Gradient Recalled Echo; MRI: magnetic resonance imaging.

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