Drug-induced autoimmune hepatitis triggered by infliximab

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BACKGROUND

Infliximab, a tumor necrosis factor α (TNF-α) inhibitor, is frequently used in the treatment of inflammatory bowel disease (IBD). A rare but important adverse effect of infliximab therapy is drug-induced liver injury (DILI), including drug-induced autoimmune hepatitis (DIAIH). Although more than 40 drugs are know to cause DIAIH, infliximab appears to carry a particularly high risk, with an estimated incidence of approximately 1 in 120 to 1 in 160 patients. DIAIH typically develops after multiple infusions, with an average time of onset of 14 to 18 weeks after initiation of infliximab treatment. Diagnosing DIAIH is challenging as patients are often asymptomatic. The condition mimics idiopathic autoimmune hepatitis (AIH) in its biochemical features (elevated transaminases), serological features (positive antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and elevated immunoglobulin (Ig) G levels) and histological features (infiltration with lymphocytes and plasma cells, interface hepatitis, rosette formation). Liver biopsy is required to exclude other potential causes of hepatopathy in IBD (e.g., primary sclerosing cholangitis). Furthermore, beside DIAIH, infliximab has been associated with three additional forms of hepatic injury: (1) transient, asymptomatic elevations of aminotransferase levels that usually resolve with drug cessation; (2) a cholestatic form of liver injury that is usually self-limiting; and (3) a reactivation of chronic hepatitis B in HBsAg carriers, which can be severe or even deadly but preventable with antivirals. Each type of liver injury has different timing and clinical features. The prognosis of DIAIH is generally favourable. It most often resolves spontaneously within six months after discontinuating infliximab. Some patients may benefit from a short course (1 to 2 months) of corticosteroids, but generally do not require long-term immunosuppression, unlike in idiopathic AIH. Nevertheless, long-term follow-up is recommended as DIAIH can progress to chronic liver injury. We present a case of a female patient with ulcerative colitis who developed DIAIH after the initiation of infliximab.

CASE REPORT

A 26-year-old female presented to our outpatient clinic with a relapse of ulcerative colitis, experiencing frequent bloody stools over the past two weeks. She was diagnosed with left-sided ulcerative colitis four years ago and had been receiving vedolizumab for the past 3.5 years. Her most recent colonoscopy, performed 8 months ago, showed endoscopic and histologic remission.

At the time of examination, no significant discrepancies were found in the clinical status. However, her blood work revealed elevated CRP levels (24 mg/L).

With negative stool cultures an infectious cause was excluded. A rectoscopy was performed and showed active disease with a Mayo score of 2. Mesalazine enemas were initiated, and after a multidisciplinary board review, vedolizumab was discontinued and replaced with an infliximab regimen. At the five-month follow-up, the patient initially experienced a positive clinical response, but this gradually diminished towards the end of the dosing interval, with persistent bloody stools. As a result, the dosing interval of infliximab was shortened from 8 to 4 weeks, but this adjustment did not lead to any improvement. Further evaluation revealed elevated liver enzymes (aspartate transferase (AST) 4.06 μkat/L; alanine transaminase (ALT) 7.88 μkat/L). To identify the cause of hepatopathy, serological tests for viral hepatitis, a proteinogram review and liver autoantibodies were conducted. These tests revealed latent EBV and CMV infections, elevated IgG levels, antinuclear antibodies (ANA) and antibodies to liver cytosol (anti-LC1). It was concluded that the liver dysfunction was most likely drug-induced autoimmune hepatitis (DILI-AIH) triggered by infliximab – no liver biopsy was performed as it was unlikely to change management. Treatment with infliximab was consequently discontinued and bridging therapy with mesalazine and locally-acting corticosteroids was introduced. Within two months of discontinuing infliximab, the liver enzymes decreased substantially and remained within normal limits at subsequent follow-up visits as the patient was treated with ustekinumab.

References:

1. Andrade RJ, Aithal GP, Boer YS de, et al. Nomenclature, diagnosis and management of drug-induced autoimmune-like hepatitis (DI-ALH): An expert opinion meeting report. J Hepatol. 2023 Sept 1;79(3):853–66.
2. Worland T, Chin KL, van Langenberg D, et al. Retrospective study of idiosyncratic drug-induced liver injury from infliximab in an inflammatory bowel disease cohort: the IDLE study. Ann Gastroenterol. 2020;33(2):162–9.
3. Ghabril M, Bonkovsky HL, Kum C, et al. Liver Injury From Tumor Necrosis Factor-α Antagonists: Analysis of Thirty-four Cases. Clin Gastroenterol Hepatol. 2013 May 1;11(5):558-564.e3.
4. Björnsson ES, Gunnarsson BI, Gröndal G, et al. Risk of drug-induced liver injury from tumor necrosis factor antagonists. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2015 Mar;13(3):602–8.
5. Björnsson HK, Björnsson ES. Hepatotoxicity in inflammatory bowel disease: Immunomodulators, biologics, and beyond. Clin Liver Dis. 2024 June;23(1):e0199.