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CASE REPORT

Infliximab and the Liver: A Hidden Autoimmune Mimic - Case Report and Literature Review

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Abstract

Infliximab is a tumour necrosis factor (TNF) - α inhibitor used in Crohn's disease management. While generally safe, it has been implicated in rare cases of drug induced autoimmune-like hepatitis (DI-ALH), a distinct and serious form of drug-induced liver injury. We present a case of a 46-year-old woman with ileo-colonic Crohn's disease presented with abnormal liver function tests three months after initiating infliximab therapy. Work-up excluded viral, metabolic, biliary, and vascular causes of liver injury. Autoimmune screen showed newly elevated titres for ANA, elevated IgG, and liver biopsy demonstrated interface hepatitis with plasma cells, lobular inflammation, and confluent necrosis; consistent with AIH. Infliximab was discontinued, and corticosteroids initiated, resulting in complete biochemical resolution. Maintenance for Crohn's disease was switched to Vedolizumab and remained in clinical remission. Early diagnosis, drug cessation, and immunosuppressive therapy are crucial for recovery.

1. Learning Points

- Infliximab, though effective for inflammatory bowel disease (IBD), can rarely cause autoimmune-like hepatitis, a potentially serious form of drug-induced liver injury (DI-ALH).
- DI-ALH may be asymptomatic and detected only via routine liver function monitoring, highlighting the importance of regular monitoring during biologic therapy.
- Liver biopsy is essential to distinguish DI-ALH from other hepatic conditions and supports timely diagnosis.
- Early discontinuation of infliximab and initiation of corticosteroid therapy can result in full biochemical and clinical recovery.
- Switching to a non–TNF-α biologic, is a safe and effective strategy for ongoing IBD treatment in patients with DI-ALH.

2. Case History

A 46 years old woman presented to the clinic with frequent loose bowel motions, right sided abdominal pain, abdominal cramps and nausea. Her symptoms have progressively worsened over a month with a past medical history of Crohn's disease involving terminal ileum and right colon on maintenance therapy with Azathioprine and Asacolon. She gave a history of frequent exacerbations necessitating intermittent intake of steroids. She is a non-smoker. Abdominal examination was unremarkable.

The results of her bio-profile were remarkable for a weakly positive ANA while the viral screening, autoimmune liver antibodies, coeliac screening, metabolic markers, Quantiferon test, and the chest X-ray were completely normal. An ileocolonoscopy showed active moderate colitis mainly in the right side and terminal ileum (**Fig. 1**) with evidence of non-caseating granuloma on histopathology. Furthermore,

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MRI enterography showed distal terminal ileum involvement. She was started on induction and maintenance therapy with Infliximab infusion in August 2024 with a good response.

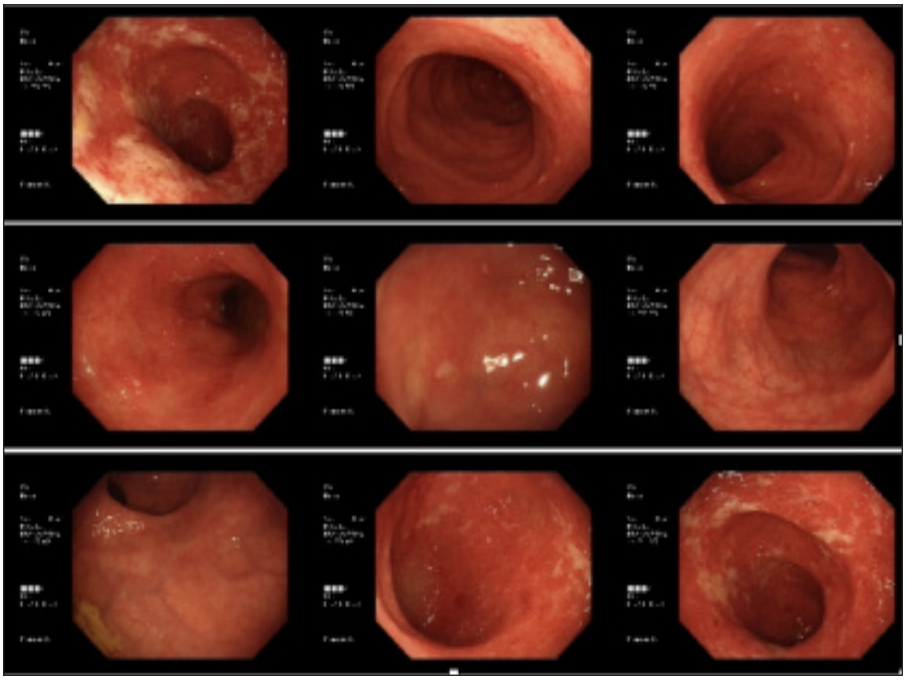


Figure 1. *Images from colonoscopy demonstrating active colitis involving the right side of the colon*

Four months later, she presented with a right upper abdominal and epigastric postprandial pain with noticeable elevation of alanine aminotransferase (ALT) (**Tab. 1**). She had no risk factors of hepatitis, including herbal or complementary medicine intake. Abdominal examination was unremarkable. Work-up excluded viral, metabolic, biliary, and vascular causes of liver injury. The autoimmune screen showed newly elevated titres for ANA and elevated IgG.

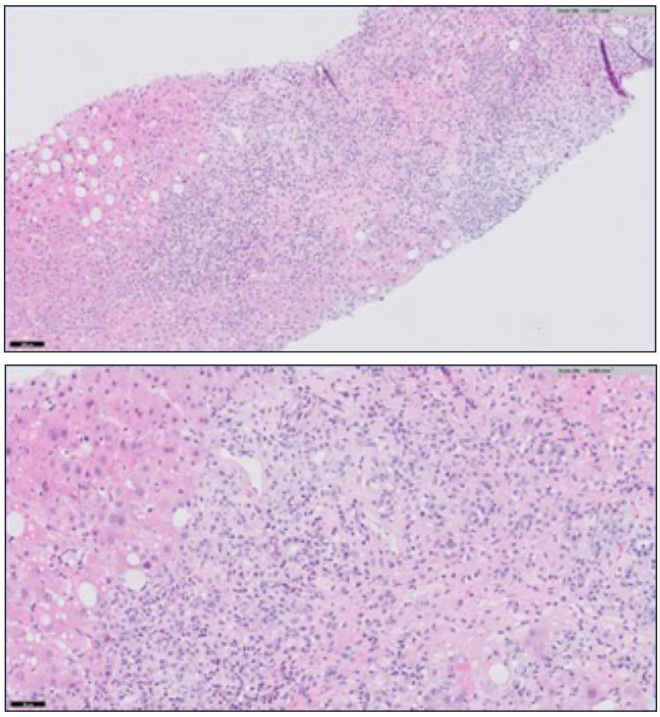
Table 1. *Main Laboratory data (biochemical evolution) from the case report*

Time	ALT	AST	AP	Bilirubin	GGTP	IgG	ANA	ASMA	INR
Baseline	22	28	61	6.2	20		+ve (very week)		
3 month	254		71	7.6					
4 months	487		126	12.9	165				
5 months	375	318	174	21	173	26.41	+ve(4)	-ve	1.2
6 months	277		180	17.9					1.2
7 months	39		62	6.2	24	12.57			

ALT (5-34UL)- alanine aminotransferase; AST (5-31UL) aspartate aminotransferase; AP (30-130IU/L) alkaline phosphatase; GGTP (6-42UL) gamma glutamyl-transferase; Bilirubin (2-21umol/L); IgG (7-16g/L) immunoglobulin G; ANA anti-nuclear antibody; ASMA: anti -smooth muscle antibody; INR: international normalization ratio.

CT abdomen and pelvis with contrast showed normal appearance of liver and biliary tree and normal gallbladder, pancreas and spleen with no evidence of active Crohn's disease. There was no evidence of vascular liver injury on CT or doppler studies. A working diagnosis of drug induced liver injury (DILI) was considered and an US guided liver biopsy (**Fig. 2.**) was performed. Histopathology reported inflammatory infiltrate of plasma cells and eosinophils, multifocal interface hepatitis, brisk lobular inflammation, confluent necrosis is present and moderate steatosis. The findings were supportive of a clinical impression of drug induced autoimmune like hepatitis (DI-ALH).

Further Infliximab infusions were ceased and she commenced on a tapering dose of Prednisolone 40mg resulting in steady improvement of LFT to a complete normalization as well as normal IgG level at 3 months after stopping Infliximab. The biological therapy for Crohn's disease maintenance of remission was switched to anti-integrin (Vedolizumab). She remained well thereafter with no symptoms and normalised LFT.



Top image: The patient's liver core biopsy contained multifocal portal inflammation with focal bile duct proliferation, multifocal interface hepatitis and brisk lobular inflammation with confluent necrosis. There was moderate steatosis of the background liver parenchyma. There was a lack of elastin staining, consistent with parenchymal collapse.

Bottom image: The portal inflammatory infiltrate was composed of occasional single and clustered plasma cells as well as numerous eosinophils.

Figure 2. *Liver Biopsy*

3. Discussion

Drug-induced liver injury (DILI) represents a significant diagnostic challenge, particularly when it mimics autoimmune hepatitis (AIH). Infliximab, a monoclonal antibody against tumour necrosis factor-alpha (TNF-α), is widely used in treating inflammatory bowel disease (IBD). While generally well tolerated, infliximab has been increasingly associated with adverse effects, including infections, allergic reactions, cytopenias, heart failure exacerbation, seizures, lymphomas, and liver injury. One notable phenotype of liver injury linked to infliximab is drug-induced autoimmune-like hepatitis (DI-ALH).

Our patient developed a hepatocellular pattern of liver injury, with markedly elevated transaminases and serum IgG, approximately three months after initiating infliximab therapy. This occurred in the absence of other hepatotoxic exposures or alternative causes of liver disease. Liver histology revealed features typical of autoimmune hepatitis: interface hepatitis, portal and lobular inflammation, plasma cell and eosinophil infiltrates, and confluent necrosis.

Infliximab-induced hepatotoxicity can present in two patterns: asymptomatic rise in liver enzymes, or an immune-mediated hepatitis that mimics idiopathic AIH. The latter may be indistinguishable from classical AIH without careful attention to drug history and temporal correlation.

The pathogenesis of DI-ALH is incompletely understood. It is believed to involve a loss of immune tolerance induced by TNF-α blockade, triggering autoreactive immune responses against hepatocytes. Genetic predisposition and individual immune variability are likely contributors.

Autoimmune hepatitis (AIH) itself is characterized by elevated transaminases, detectable autoantibodies, raised IgG, and classic histological features. DI-ALH shares nearly all of these features, making the differentiation extremely difficult. A number of drugs have been implicated in DI-ALH, including infliximab, adalimumab, nitrofurantoin, minocycline, methyldopa, and herbal or dietary supplements. Histologically, DI-ALH often lacks advanced fibrosis seen in idiopathic AIH. Moreover, the absence of relapse after drug cessation—often without long-term immunosuppression—supports a drug-induced aetiology.

To support diagnosis, structured causality assessment tools such as RUCAM may be used. It helps clinicians differentiate DILI and DI-ALH from classical AIH, particularly when liver biopsy shows overlapping features. The calculated score in our case was 6 which indicates the causality assessment of the possible offender drug causing the liver injury is probable.

A clinical classification has been proposed to categorize these patients into 3 categories: De novo AIH, DI-ALH (direct immune-mediated injury) and DILI-ALH (DILI initially, followed by AIH progression after drug withdrawal). In our case, the temporal link with infliximab, histological findings, and favourable response to drug withdrawal and

corticosteroids support a diagnosis of DI-ALH. While some cases of DI-ALH may resolve spontaneously after stopping the offending drug; corticosteroids may be considered in more severe cases, particularly those that don't improve or worsen after drug withdrawal. In our case, corticosteroids use was considered due to severe histologic findings.

Management of DI-ALH includes immediate withdrawal of the offending drug and, where necessary, a short course of corticosteroids. Most cases show full biochemical and immunological resolution. Rechallenge with the same agent is discouraged due to the risk of recurrence or worsening injury. Vedolizumab, an anti-integrin agent, was used in our patient with successful maintenance of IBD remission and no liver injury recurrence.

The latency period for DI-ALH typically ranges from a few weeks to several months. Most cases follow a hepatocellular pattern, although cholestatic injury has also been reported. Unlike classical DILI, features of hypersensitivity (e.g., rash, fever, eosinophilia) are often absent. Notably, long-term follow-up may be necessary in rare cases of DI-ALH that progress to chronicity.

A modified diagnostic and management algorithm has been proposed by international experts to help clinicians approach cases of DILI with autoimmune features (**Fig. 3).**

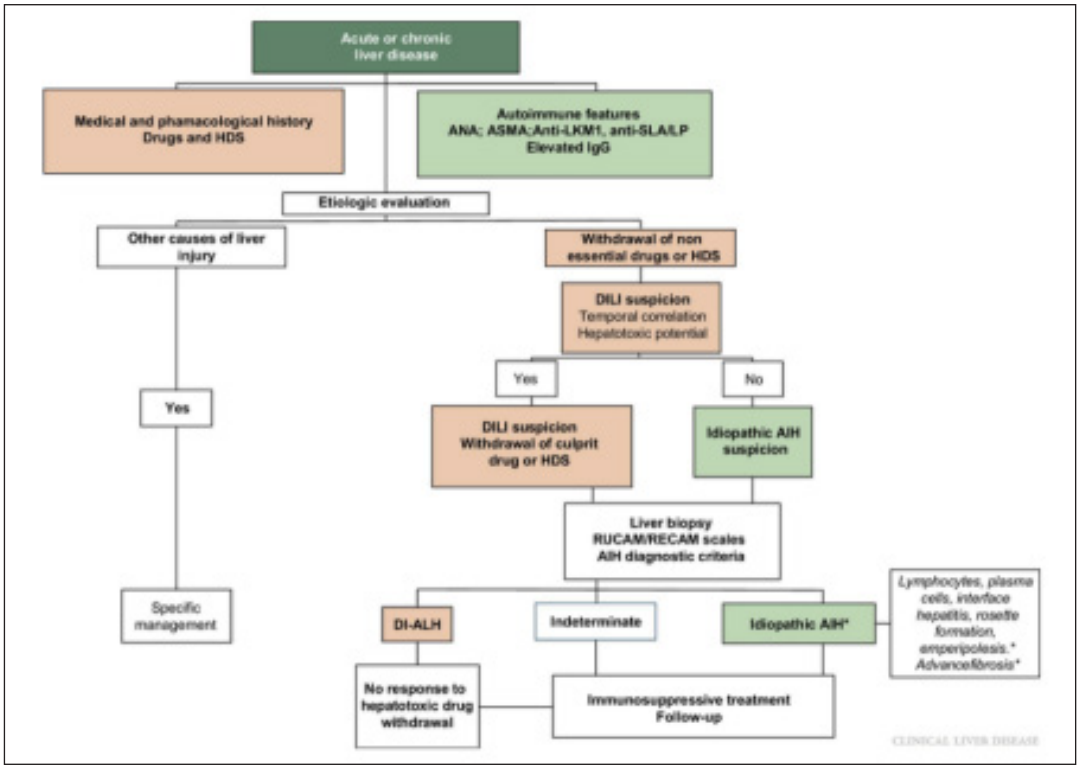


Figure 3. *Management algorithm of liver disease with DILI suspicion and autoimmune features. Abbreviations: AIH, autoimmune hepatitis; ANA, antinuclear antibody; anti-LKM1, anti-liver-kidney microsomal type 1 antibody; anti-SLA/LP, anti-soluble liver antigen/liver pancreas antigen; ASMA, anti-smooth muscle; DI-ALH, drug-induced autoimmune-like hepatitis; HDS, herbal and dietary supplements.*

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