

Chronic drug-induced liver injury with autoimmune-like features after multiple drug exposures: a case report with serial liver biopsies

Zixuan Gao

Department of Hepatology Division 2, Beijing Ditan Hospital, Capital Medical University

Shuojie Wang

Department of Hepatology Division 2, Beijing Ditan Hospital, Capital Medical University

Dianya Qiu

Department of Hepatology Division 2, Beijing Ditan Hospital, Capital Medical University

Hongxiao Hao

Department of Hepatology Division 2, Beijing Ditan Hospital, Capital Medical University

Minghui Li

wuhm2000@sina.com

Department of Hepatology Division 2, Beijing Ditan Hospital, Capital Medical University

Case Report

Keywords: drug-induced liver injury, autoimmune-like features, chronic drug-induced liver injury, liver biopsy, liver fibrosis, drug-induced autoimmune-like hepatitis

Posted Date: October 19th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11115811/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

We report a case of chronic drug-induced liver injury (DILI) following exposure to multiple agents. The patient was a 41-year-old female who developed fatigue, poor appetite and jaundice after self-administration of a weight-loss agent and a traditional Chinese medicine preparation. Laboratory tests at an outside hospital revealed ALT 564 U/L, AST 431 U/L and TBIL 113.6 $\mu\text{mol/L}$. Further evaluation revealed high-titer antinuclear antibody (ANA) positivity and elevated IgG, indicating prominent autoimmune-like serological features. After discontinuation of suspected drugs, liver biochemistry and IgG gradually returned to normal with glucocorticoid and supportive therapy, and the condition remained stable after glucocorticoid withdrawal in January 2024. On October 31, 2024, despite normal liver biochemistry and IgG, the initial liver biopsy still showed chronic hepatitis with G2S3–4. A repeat liver biopsy performed on January 13, 2026 was graded as G1S2, compared with G2S3–4 on the initial biopsy. Combined with the history of drug exposure, autoimmune-like serological and histological features, as well as the long-term non-relapsing course after cessation of immunosuppressive therapy, this case meets the probable diagnostic framework for drug-induced autoimmune-like hepatitis (DI-ALH). DI-ALH is currently favored, whereas classical autoimmune hepatitis (AIH) requires long-term follow-up for differential diagnosis. This case indicates that histological liver injury may persist in DILI patients even when liver biochemistry and IgG have normalized. Long-term follow-up and selective repeat liver biopsy help assess histological outcomes in patients with prior severe histological injury.

1. Introduction

Drug-induced liver injury (DILI) is markedly heterogeneous, and herbal and dietary supplements represent an important exposure associated with DILI in China^[1–4]. Most patients recover gradually after discontinuation of the suspected drugs, although some may follow a protracted course or progress to chronicity^[5–7]. The definition of chronic DILI has not yet been fully standardized; it generally emphasizes persistent abnormalities in liver biochemistry 6 to 12 months after onset, or evidence of ongoing liver injury on imaging or histology^[2,3,5,8]. Therefore, normalization of liver biochemistry does not necessarily indicate complete histological recovery.

Autoimmune-like features can complicate the interpretation of DILI, particularly when biochemical improvement does not parallel changes within the liver. Serial histological data in this setting remain scarce. Evidence from autoimmune hepatitis (AIH) suggests that ongoing histological activity may persist despite sustained biochemical remission^[9]. We therefore present a patient with DILI following exposure to a weight-loss agent and a traditional Chinese medicine preparation, focusing on the longitudinal distinction between DI-ALH and classical AIH and on the added information provided by repeat liver biopsy.

2. Case Presentation

The patient was a 41-year-old female with a BMI of 24.77 kg/m². She denied histories of smoking and alcohol consumption, had no metabolic disorders such as hypertension or diabetes, and her past and family histories were unremarkable. Starting from July 2023, she self-administered two separate

preparations, including a weight-loss agent and a traditional Chinese medicine, whose specific names, ingredients and doses were unavailable. Approximately one month later, she developed fatigue, poor appetite, abdominal distension, dark urine and scleral jaundice. She then discontinued the implicated preparations and sought medical care at an outside hospital on August 6, 2023. Laboratory tests at the outside hospital showed ALT 564 U/L, AST 431 U/L, and TBIL 113.6 $\mu\text{mol/L}$. Given the recent exposure to a weight-loss agent and a traditional Chinese medicine preparation, drug-induced liver injury was initially suspected. Concurrently positive ANA raised the possibility of autoimmune hepatitis (AIH). After discontinuation of the suspected agents and administration of supportive therapy for liver injury and cholestasis, liver function improved but did not fully normalize. At discharge, her ALT was 70 U/L, AST 54 U/L, TBIL 50 $\mu\text{mol/L}$, and DBIL 29 $\mu\text{mol/L}$. She continued oral glycyrrhizin compound after discharge.

On October 1, 2023, she presented to our emergency department with persistent fatigue, dark urine, and scleral icterus. Tests revealed liver injury accompanied by coagulation abnormalities, with an INR peaking at 1.75. She was admitted to our ward on October 2. On admission, her vital signs were stable; she was alert with no signs of hepatic encephalopathy or ascites. Laboratory results on October 4, 2023 were as follows: ALT 89.3 U/L, AST 400.7 U/L, TBIL 178.8 $\mu\text{mol/L}$, DBIL 145.9 $\mu\text{mol/L}$, ALB 30.6 g/L, GGT 159.6 U/L, ALP 117.4 U/L, TBA 136.8 $\mu\text{mol/L}$, INR 1.64, and PLT $142 \times 10^9/\text{L}$. The reference ranges for ALT and ALP were 7–40 U/L and 35–100 U/L, respectively. The R value calculated using paired ALT and ALP measurements on October 4, 2023 was approximately 1.90, with markedly elevated DBIL and TBA, indicating cholestatic features at this stage. Since these values were obtained after prior treatment, they could not be used to determine the biochemical phenotype of DILI at the initial presentation ^[2,8].

Etiological workup excluded active infection with hepatitis A, B, C, D and E viruses. She was HBsAg-negative, anti-HBc-positive and anti-HBs-positive, with persistently HBV DNA < 20 IU/mL, consistent with past HBV infection. Emergency abdominal CT demonstrated diffuse hepatic parenchymal changes and splenomegaly without definite biliary obstruction. An ultrasound obtained during the acute phase reported portal hypertension and development of collateral circulation, whereas subsequent follow-up scans showed no remarkable abnormalities.

Immunological tests on October 4, 2023 showed IgG 24.70 g/L (reference range, 7.51–15.6 g/L, ~ 1.58-fold the upper limit of normal), high-titer positive ANA (homogeneous nuclear pattern, 1:320), and weakly positive Ro-52. SMA, LKM and other autoantibodies associated with autoimmune liver diseases were all negative.

Despite discontinuation of suspected drugs and prior treatment, the patient's liver injury had not fully resolved on admission. She had prominent jaundice, coagulopathy, elevated IgG and high-titer ANA. Combining the timeline of drug exposure, etiological exclusion and autoimmune manifestations, DILI with autoimmune-like features was initially considered, while classical AIH remained an important differential diagnosis. Given the persistent liver injury together with marked autoimmune-like features, an immune-mediated component was considered likely. Dexamethasone 10 mg/d was initiated on October 12, 2023 for 5 days, followed by oral prednisone 30 mg/d. The glucocorticoid dose was tapered gradually according to changes in liver biochemistry and IgG, and glucocorticoids were discontinued in January 2024. Entecavir

was administered during treatment to prevent HBV reactivation. During follow-up, HBsAg and HBV DNA remained negative. No other immunosuppressants were used after glucocorticoid withdrawal, and liver biochemistry and IgG stayed within normal limits.

CHI3L1 was 218.8 ng/mL on July 30, 2024 (reference range, 0–79 ng/mL). In view of the prior severe liver injury, the first liver biopsy was performed on October 31, 2024 to evaluate intrahepatic inflammation and fibrosis; CHI3L1 on that day was 115.6 ng/mL. Pathology showed prominent lymphocytic and plasma-cell infiltration in portal tracts with mild-to-moderate interface hepatitis. Some periportal hepatocytes exhibited rosette-like changes. Fibrous septa, focal bridging fibrosis and incomplete pseudolobule formation were observed, leading to a diagnosis of chronic hepatitis, G2S3–4. The pathological report noted: “in combination with clinical context, changes after glucocorticoid therapy could not be excluded”.

Together with prior high-titer ANA, elevated IgG, the above AIH-like histological findings, and the disease course without relapse approximately 9 months after glucocorticoid cessation, these findings further supported a diagnostic leaning toward drug-induced autoimmune-like hepatitis (DI-AIH). Nevertheless, long-term follow-up was still required to differentiate it from classical AIH.

Subsequent follow-up showed persistently normal liver biochemistry and IgG, but the outcome of previous histological injury remained unclear, with fluctuations in CHI3L1 and liver stiffness measurement (LSM). After detailed discussion with the patient and obtaining informed consent, a repeat liver biopsy was performed on January 13, 2026 to observe long-term changes in inflammation and fibrosis. Pathology revealed only sparse lymphocytic and plasmacytic infiltration in portal tracts, no obvious interface hepatitis, mild perisinusoidal fibrosis and delicate fibrous septa; the diagnosis was mild chronic hepatitis, G1S2. Pre-S1, HBsAg and HBcAg on immunohistochemistry of both liver specimens were negative. Repeat IgG in January 2026 was 9.0 g/L. Autoantibodies specific for autoimmune liver diseases remained negative. The high-titer nuclear-pattern ANA detected in the acute phase was no longer present, with only cytoplasmic-pattern ANA at 1:100.

Dynamic LSM and CHI3L1 values are summarized in Table 3. The timeline of major treatments and follow-up is shown in Table 1, key laboratory parameters in Table 2, and representative pathological images from the two liver biopsies in Fig. 1.

Table 1
Timeline of major clinical events, treatment, and histological follow-up

Date	Clinical events and treatment
2023-07	Self-administered a weight-loss medication and a traditional Chinese medicine preparation.
2023-08	Developed jaundice and other symptoms after approximately 1 month of use; ALT 564 U/L and TBIL 113.6 μ mol/L at an outside hospital; suspected agents were discontinued.
2023-10-01	Presented to our hospital with persistent fatigue, dark urine, and scleral icterus, accompanied by coagulation dysfunction.
2023-10-12	Glucocorticoid therapy was initiated for persistent liver injury with prominent autoimmune-like features; dexamethasone 10 mg/day for 5 days.
2023-10-17	Switched to prednisone 30 mg/day, followed by gradual tapering.
2024-01	Glucocorticoids were discontinued after improvement in liver biochemistry and IgG.
2024-07-30	CHI3L1, 218.8 ng/mL (reference range, 0–79 ng/mL).
2024-10-31	Normal liver biochemistry and IgG; CHI3L1, 115.6 ng/mL; LSM, 8.5 kPa; first liver biopsy, G2S3–4.
2026-01-13	Liver biochemistry and IgG remained normal; CHI3L1, 121.3 ng/mL; LSM, 8.8 kPa; repeat liver biopsy, G1S2.

Table 2
Longitudinal changes in major laboratory parameters

Date	ALT (U/L)	AST (U/L)	TBIL (μ mol/L)	DBIL (μ mol/L)	ALB (g/L)	GGT (U/L)	ALP (U/L)	TBA (μ mol/L)	INR	IgG (g/L)
2023-10-01	84.2	663.3	150.1	116.5	33.2	—	—	—	1.56	—
2023-10-04	89.3	400.7	178.8	145.9	30.6	159.6	117.4	136.8	1.64	24.70
2023-10-09	202.1	491.2	232.5	186.7	31.2	176.7	129.6	369.5	1.63	—
2023-12-06	45.0	22.0	23.5	11.7	39.3	25.2	85.5	75.0	1.14	12.2
2024-01-31	24.4	17.1	15.1	5.2	41.2	16.2	96.1	20.4	1.14	—
2024-05-27	19.1	17.2	12.8	4.5	43.3	10.2	106.3	15.6	1.09	10.0
2024-07-29	16.8	16.7	17.0	5.2	45.4	12.8	99.9	13.9	1.02	11.7
2024-10-31	19.8	17.3	16.4	5.5	47.4	12.8	88.6	6.3	1.05	9.87
2025-02-11	20.5	14.3	18.6	6.3	44.2	26.2	68.6	3.1	—	8.67
2025-08-12	12.0	11.8	26.6	8.8	46.5	9.3	72.0	5.8	—	9.3
2026-01-13	14.1	13.0	18.1	5.2	46.1	11.1	76.5	3.3	1.01	9.0
Note: “—” indicates that the parameter was not tested or not recorded because a complete panel of laboratory results was unavailable for some follow-up dates. Coagulation function remained generally stable during follow-up, and INR was not routinely measured at all visits. Reference ranges: ALT, 7–40 U/L; AST, 13–35 U/L; TBIL, 0–18.8 μ mol/L; DBIL, 0–6.8 μ mol/L; ALB, 40–55 g/L; GGT, 7–45 U/L; ALP, 35–100 U/L; TBA, 0–10 μ mol/L; IgG, 7.51–15.6 g/L.										

Table 3
Longitudinal changes in CHI3L1, LSM, and liver histology

Date	CHI3L1 (ng/mL)	LSM (kPa)	Liver histology
2024-07-30	218.8	—	—
2024-10-31	115.6	8.5	G2S3–4
2025-02-11	87.9	11.3	—
2025-08-13	130.2	9.4	—
2026-01-13	121.3	8.8	G1S2
Note: The reference range for CHI3L1 was 0–79 ng/mL.			

3. Discussion

This patient developed persistent liver injury accompanied by prominent autoimmune-like manifestations following exposure to a weight-loss agent and a traditional Chinese medicine preparation. Liver biochemistry and IgG normalized after glucocorticoid therapy; however, the initial liver biopsy performed approximately 9 months after drug withdrawal still demonstrated G2S3–4. The subsequent repeat biopsy was graded as G1S2. This case highlights two key issues: the need to differentiate DI-ALH from classical AIH, and the dissociation between serological remission and histological recovery.

3.1 Diagnosis and Differentiation of DILI with Autoimmune-Like Phenotype and DI-ALH

DILI remains a diagnosis of exclusion [2,8,10]. Prior to the onset of liver injury in this case, the patient was concomitantly exposed to two independent agents: a weight-loss agent and a traditional Chinese medicine. Liver injury developed approximately one month after initiation of these agents, and the patient had no re-exposure to the implicated preparations after discontinuation. Common etiologies including active viral hepatitis and biliary obstruction were ruled out. Since the patient was exposed to two preparations with unknown constituents and key baseline data such as ALP were unavailable at disease onset, rigorous individual RUCAM assessment for each agent could not be performed. RUCAM scoring should in principle be applied separately for each suspected drug. Accordingly, we use the term “DILI associated with multiple drug exposures” in this report without further attribution to any single preparation [11]. Recent reports of herb-associated autoimmune-like hepatitis have likewise emphasized formal causality assessment using RUCAM [12].

Early in the disease course, the patient had ANA 1:320 and IgG at 1.58 times the upper limit of normal, indicating prominent serological autoimmune-like features. The initial liver biopsy was performed approximately 9 months after glucocorticoid withdrawal, and still revealed abundant plasma cell infiltration, interface hepatitis and hepatocyte rosette-like changes, further demonstrating AIH-like histological features. DI-ALH and classical AIH substantially overlap with respect to autoantibodies, IgG elevation and

histological findings. No single serological or histological marker can reliably distinguish the two entities; thus diagnosis requires comprehensive integration of drug exposure history, recovery after drug discontinuation, response to immunosuppressive therapy and long-term disease course following treatment cessation^[13]. Björnsson et al. proposed five diagnostic criteria for DI-ALH, which were subsequently cited in the EASL clinical practice guidelines for AIH: ☐ Presence of a suspected drug trigger together with autoimmune markers such as ANA, SMA or elevated IgG, plus liver histology compatible with AIH; ☐ Incomplete recovery, absence of recovery, or progressive worsening of liver injury after withdrawal of the suspected drug; ☐ Requirement for glucocorticoid therapy or spontaneous recovery after a prolonged period; ☐ No relapse for at least 6 months after glucocorticoid discontinuation; ☐ The implicated drug has the potential to induce DI-ALH with a chronic course. Satisfying the first four criteria defines probable DI-ALH, whereas fulfillment of three criteria suggests possible DI-ALH. Nevertheless, this framework lacks prospective external validation^[14,15]. The present case met the first four criteria: liver injury developed after exposure to a weight-loss agent and a traditional Chinese medicine preparation, accompanied by ANA 1:320, elevated IgG and AIH-like histology; liver injury failed to resolve completely after discontinuation of suspected agents and initial supportive care; subsequent glucocorticoid therapy normalized liver biochemistry and IgG; nearly two years after glucocorticoid withdrawal in January 2024, the patient received no further immunosuppression and experienced no biochemical or immunological flare. Taken together, this case fulfills the first four criteria and fits the diagnostic framework for probable DI-ALH. However, criterion ☐ could not be evaluated because the exact constituents of the weight-loss agent and herbal medicine remained unknown. Given the lack of adequate prospective validation of this framework, long-term follow-up is still required to differentiate it from classical AIH^[14,15]. Notably, the first biopsy showed stage S3–4 fibrosis, and advanced fibrosis is relatively uncommon in DI-ALH compared with classical AIH. Without baseline pre-morbid liver histology, previously unrecognized chronic liver injury or classical AIH cannot be fully excluded, and we cannot confirm that all fibrosis observed on the initial biopsy arose exclusively from this episode of liver injury^[15].

Based on the available data, and conservatively assigning 1 point for histology considered compatible with AIH, the simplified AIH score was retrospectively calculated as approximately 7^[16]. It should be emphasized, however, that the autoantibody, IgG and histological data contributing to this score were not all obtained at the same pretreatment time point, and the initial liver biopsy was performed after glucocorticoid therapy. EASL guidelines also caution against applying AIH diagnostic scoring in special settings such as DI-ALH. Therefore, this score only indicates strong cross-sectional AIH-like features in this patient and cannot independently establish a diagnosis of classical AIH. The patient remained off immunosuppression long after glucocorticoid withdrawal with persistently normal liver biochemistry and IgG, the high-titer nuclear-pattern ANA became undetectable, and subsequent histology demonstrated improvement. The absence of relapse during prolonged immunosuppression-free follow-up further supports a diagnostic leaning toward DI-ALH. Hence, DI-ALH is currently favored, though classical AIH still requires long-term follow-up for differentiation^[13]. With regard to classical AIH, recent reviews have systematically summarized advances in immunosuppressive treatment, remission induction and long-term prognostic management^[17].

The diagnosis of chronic DILI is not restricted to persistent abnormal liver biochemistry; it may also be established based on sustained imaging or histological evidence of liver injury ^[2,3,5,8]. The initial liver biopsy was obtained more than one year after disease onset. At that time, ALT, AST, TBIL, INR and IgG had all normalized, yet histology still demonstrated G2S3–4. Persistent histological inflammation and fibrosis support the diagnosis of chronic DILI.

3.2 Dissociation Between Biochemical/Immunological Remission and Histological Recovery

At the time of the first liver biopsy, ALT, AST, TBIL, and IgG had all returned to normal, yet histology still showed G2S3–4. These findings suggest that normalization of circulating biomarkers may precede complete resolution of intrahepatic injury. Longitudinal liver biopsy data describing this phenomenon in patients with DILI are scarce. Nevertheless, studies in AIH have demonstrated that histological activity persists in some patients even after sustained biochemical remission, which is associated with inadequate fibrosis regression and unfavorable long-term outcomes ^[9]. These data were derived from patients with AIH and cannot be directly extrapolated to DILI, but they suggest that serological remission and resolution of intrahepatic inflammation may be asynchronous. The patient discontinued glucocorticoids in January 2024, with an interval of approximately 9 months before the first liver biopsy. In the absence of baseline liver biopsy specimens obtained prior to glucocorticoid initiation, the pre-treatment histological severity cannot be determined, nor can the magnitude of histological improvement attributable to glucocorticoids be precisely quantified.

CHI3L1 has been investigated as a fibrosis-related serum biomarker in chronic liver disease. Data from chronic hepatitis B indicate that its level correlates with significant fibrosis ^[18]. In the present case, CHI3L1 levels measured around the time of the first and second liver biopsies were 115.6 ng/mL and 121.3 ng/mL, respectively; corresponding LSM values were 8.5 kPa and 8.8 kPa. The two biopsies were graded and staged as G2S3–4 and G1S2, respectively. Changes in these two non-invasive markers were discordant with the shift in histological findings. Currently, data on CHI3L1 in DILI remain limited; therefore, this marker was only used as an adjunctive follow-up parameter in this case. Recent studies have explored diagnostic and prognostic biomarkers for DILI from the perspective of serum and fecal metabolomics^[19].

3.3 Subsequent Histological Improvement and Potential Influencing Factors

The second liver biopsy demonstrated reduced inflammatory cell infiltration, absence of overt interface hepatitis, mild perisinusoidal fibrosis and delicate fibrous septa compared with the first biopsy. The two biopsies were graded and staged as G2S3–4 and G1S2, respectively. The patient discontinued glucocorticoids in January 2024 and received no further immunosuppressive therapy thereafter. The second biopsy was performed nearly two years after glucocorticoid withdrawal; accordingly, the subsequent histological changes cannot be attributed solely to glucocorticoid effects. Spontaneous recovery after discontinuation of the offending agent, prior immunosuppressive therapy, and long-term supportive treatment may all contribute to this improvement.

Glucocorticoids may be considered on a case-by-case basis for immune-mediated DILI with prominent autoimmune features^[2,3]. Expert opinion on DI-ALH suggests that glucocorticoids may be considered according to disease severity in patients with persistent or progressive liver injury after withdrawal of suspected drugs, with tapering and discontinuation timed based on therapeutic response^[13]. In this case, liver injury failed to resolve fully after discontinuation of the suspected agents and supportive care. Given the concurrent presence of marked jaundice, coagulopathy, high-titer ANA and elevated IgG, glucocorticoid treatment was initiated. The glucocorticoid dose was gradually tapered as liver biochemistry and IgG improved, and treatment was discontinued after approximately three months. No additional immunosuppression was administered in the subsequent nearly two years, and no biochemical or immunological flare occurred.

Following glucocorticoid cessation, the patient mainly received supportive therapy with glycyrrhizin preparations. Chinese DILI guidelines list glycyrrhizin preparations as optional therapeutic agents for liver injury in selected DILI patients^[2,3]. Previous randomized controlled studies have shown that magnesium isoglycyrrhizinate increases the rate of ALT normalization in patients with acute DILI, providing some clinical evidence for the use of glycyrrhizin preparations in DILI^[20]. Wang et al. conducted a 48-week randomized open-label trial in patients with chronic DILI/HILI with paired pre- and post-treatment liver biopsies. Their results indicated that glucocorticoid combined with glycyrrhizin therapy improves the sustained biochemical response rate, with observed reductions in histological activity and fibrosis^[21]. It should be emphasized that the subsequent histological improvement in this case may be jointly influenced by spontaneous recovery after stopping the offending agent, prior glucocorticoid therapy, and long-term supportive treatment. Therefore, the histological amelioration cannot be ascribed to glycyrrhizin preparations alone.

3.4 Role and Limitations of Liver Biopsy

Chinese DILI guidelines recommend that liver biopsy and long-term follow-up may be considered for DILI patients with autoimmune features^[2,3]. The initial biopsy in this case was performed to assess whether histological injury persisted after serological recovery. After the initial pathology revealed G2S3–4, the patient's serum markers remained normal, yet the histological outcome remained uncertain. Therefore, a second biopsy was carried out after thorough discussion with the patient. This repeat biopsy represented individualized re-evaluation rather than a routine requirement for DILI follow-up.

This case has several limitations. The patient concurrently took two preparations, a weight-loss agent and a traditional Chinese medicine, but their exact constituents and doses were unavailable. Consequently, rigorous individual RUCAM assessment for each agent could not be performed. The patient received glucocorticoids together with multiple supportive therapies during the acute phase, so the subsequent histological improvement cannot be attributed to any single treatment modality. Without baseline liver biopsy specimens obtained prior to glucocorticoid initiation, direct comparison of histological changes before and after treatment is not feasible. In addition, in the absence of pre-morbid liver histology, it cannot be definitively confirmed that all fibrosis observed on the first biopsy resulted exclusively from this episode of liver injury. Both biopsy specimens were 1.5 cm in length, containing 17 and 9 portal tracts respectively.

Although multiple pathological changes showed consistent trends, sampling variability cannot be entirely excluded. Not all data used for the simplified AIH score were collected at the same pretreatment time point; the utility of CHI3L1 in DILI also lacks adequate validation.

4. Conclusion

This case describes DILI occurring after exposure to multiple agents, accompanied by prominent autoimmune-like features. Integrating the history of drug exposure, autoimmune-like serological and histological findings, and the long-term relapse-free course following glucocorticoid withdrawal, this case fits the diagnostic framework for probable DI-ALH, and DI-ALH is currently favored. Nevertheless, long-term follow-up remains necessary because the exact constituents of the causative agents are unknown and no specific biomarkers can reliably differentiate DI-ALH from classical AIH. The initial liver biopsy demonstrated G2S3–4 despite normalization of serological markers, whereas the repeat biopsy was graded as G1S2, suggesting that serological remission and histological recovery may not occur in parallel. For patients with prior severe histological injury in whom routine follow-up markers cannot adequately assess histological outcomes, repeat liver biopsy may be considered individually when necessary.

Declarations

Ethics Statement and Informed Consent

Written informed consent was obtained from the patient for this case report, and all identifiable information has been de-identified in the manuscript and figures.

Consent for publication

Written informed consent for publication of this case report and the accompanying clinical and histopathological information was obtained from the patient.

Availability of data and materials

The data supporting the findings of this case report are not publicly available because they contain information that could compromise patient privacy, but they are available from the corresponding author upon reasonable request and subject to appropriate confidentiality safeguards.

Competing interests

The authors declare no competing interests.

Funding

Beijing Municipal Health Commission high-level public health technical personnel construction project (discipline leader-03-26); Beijing Research Ward Excellence Program (BRWEP2024W102170101); Beijing Hospitals Authority "peak" talent training program (DFL20241803).

Author Contributions

Zixuan Gao: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing. Shuojie Wang: Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. Dianya Qiu: Data curation, Investigation, Literature review, Validation, Writing – original draft, Writing – review & editing. Hongxiao Hao: Conceptualization, Supervision, Funding acquisition, Writing – review & editing. Minghui Li: Conceptualization, Supervision, Validation, Writing – review & editing. Zixuan Gao, Shuojie Wang, and Dianya Qiu contributed equally to this work.

Acknowledgements

Not applicable.

Clinical trial number

Not applicable.

References

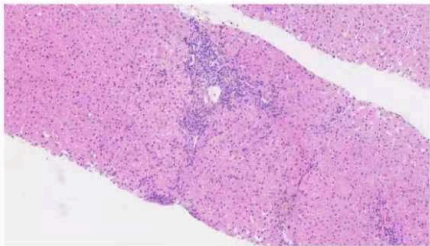
1. ANDRADE R J, CHALASANI N, BJÖRNSSON E S, et al. Drug-induced liver injury[J/OL]. Nature Reviews. Disease Primers, 2019, 5(1): 58. DOI:10.1038/s41572-019-0105-0.
2. Technology Committee on DILI Prevention and Management, Chinese Medical Biotechnology Association; Study Group of Drug-Induced Liver Disease, Chinese Medical Association for the Study of Liver Diseases. Chinese guideline for diagnosis and management of drug-induced liver injury (2023 version). Zhonghua Gan Zang Bing Za Zhi. 2023;31(4):355–384. doi:10.3760/cma.j.cn501113-20230419-00176.
3. MAO Y, MA S, LIU C, et al. Chinese guideline for the diagnosis and treatment of drug-induced liver injury: an update[J/OL]. Hepatology International, 2024, 18(2): 384-419. DOI:10.1007/s12072-023-10633-7.
4. CAO W H, JIANG T T, SHEN G, et al. Association of Cytokines with Clinical Indicators in Patients with Drug-Induced Liver Injury[J/OL]. Biomedical and environmental sciences: BES, 2024, 37(5): 494-502. DOI:10.3967/bes2024.054.
5. MEDINA-CALIZ I, ROBLES-DIAZ M, GARCIA-MUÑOZ B, et al. Definition and risk factors for chronicity following acute idiosyncratic drug-induced liver injury[J/OL]. Journal of Hepatology, 2016, 65(3): 532-542. DOI:10.1016/j.jhep.2016.05.003.
6. WANG C Y, DENG Y, LI P, et al. Prediction of biochemical nonresolution in patients with chronic drug-induced liver injury: A large multicenter study[J/OL]. Hepatology, 2022, 75(6): 1373-1385. DOI:10.1002/hep.32283.
7. ZHANG Y, REN Y L, SONG X R, et al. The incidence of chronic drug-induced liver injury: a systematic review and meta-analysis[J/OL]. Frontiers in Pharmacology, 2026, 17: 1710414. DOI:10.3389/fphar.2026.1710414.
8. EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER. EASL Clinical Practice Guidelines: Drug-induced liver injury[J/OL]. Journal of Hepatology, 2019, 70(6): 1222-1261.

DOI:10.1016/j.jhep.2019.02.014.

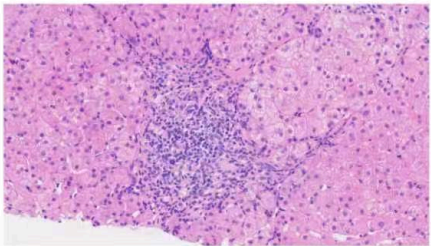
9. DHALI WAL H K, HOEROLDT B S, DUBE A K, et al. Long-Term Prognostic Significance of Persisting Histological Activity Despite Biochemical Remission in Autoimmune Hepatitis[J/OL]. *American Journal of Gastroenterology*, 2015, 110(7): 993-999. DOI:10.1038/ajg.2015.139.
10. YU Y C, MAO Y M, CHEN C W, et al. CSH guidelines for the diagnosis and treatment of drug-induced liver injury[J/OL]. *Hepatology International*, 2017, 11(3): 221-241. DOI:10.1007/s12072-017-9793-2.
11. DANAN G, TESCHKE R. RUCAM in Drug and Herb Induced Liver Injury: The Update[J/OL]. *International Journal of Molecular Sciences*, 2015, 17(1): 14. DOI:10.3390/ijms17010014.
12. HAGEN R, WU G Y. Khat-associated Autoimmune Hepatitis: A Review with RUCAM Analysis[J/OL]. *Journal of Clinical and Translational Hepatology*, 2025, 13(9): 754-765. DOI:10.14218/JCTH.2025.00180.
13. ANDRADE R J, AITHAL G P, DE BOER Y S, et al. Nomenclature, diagnosis and management of drug-induced autoimmune-like hepatitis (DI-ALH): An expert opinion meeting report[J/OL]. *Journal of Hepatology*, 2023, 79(3): 853-866. DOI:10.1016/j.jhep.2023.04.033.
14. BJÖRNSSON E S, MEDINA-CALIZ I, ANDRADE R J, et al. Setting up criteria for drug-induced autoimmune-like hepatitis through a systematic analysis of published reports[J/OL]. *Hepatology Communications*, 2022, 6(8): 1895-1909. DOI:10.1002/hep4.1959.
15. EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER. EASL Clinical Practice Guidelines on the management of autoimmune hepatitis[J/OL]. *Journal of Hepatology*, 2025, 83(2): 453-501. DOI:10.1016/j.jhep.2025.03.017.
16. HENNES E M, ZENIYA M, CZAJA A J, et al. Simplified criteria for the diagnosis of autoimmune hepatitis[J/OL]. *Hepatology*, 2008, 48(1): 169-176. DOI:10.1002/hep.22322.
17. MENG Z, YANG Y. Advances in the Treatment of Autoimmune Hepatitis[J/OL]. *Journal of Clinical and Translational Hepatology*, 2024, 12(10): 878-885. DOI:10.14218/JCTH.2024.00193.
18. JIN X, FU B, WU Z J, et al. Serum chitinase-3-like protein 1 is a biomarker of liver fibrosis in patients with chronic hepatitis B in China[J/OL]. *Hepatobiliary & pancreatic diseases international: HBPD INT*, 2020, 19(4): 384-389. DOI:10.1016/j.hbpd.2020.05.009.
19. YU S, WANG S, LI P, et al. Integrated Analysis of Serum and Fecal Metabolites Reveals the Role of Bile Acid Metabolism in Drug-induced Liver Injury: Implications for Diagnostic and Prognostic Biomarkers[J/OL]. *Journal of Clinical and Translational Hepatology*, 2025, 13(8): 619-629. DOI:10.14218/JCTH.2025.00073.
20. WANG Y, WANG Z, GAO M, et al. Efficacy and safety of magnesium isoglycyrrhizinate injection in patients with acute drug-induced liver injury: A phase II trial[J/OL]. *Liver International: Official Journal of the International Association for the Study of the Liver*, 2019, 39(11): 2102-2111. DOI:10.1111/liv.14204.
21. WANG J B, HUANG A, WANG Y, et al. Corticosteroid plus glycyrrhizin therapy for chronic drug- or herb-induced liver injury achieves biochemical and histological improvements: a randomised open-label trial[J/OL]. *Alimentary Pharmacology & Therapeutics*, 2022, 55(10): 1297-1310. DOI:10.1111/apt.16902.

Figures

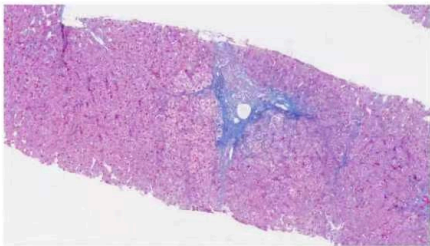
2024-10-31 (G2S3-4)



A: H&E×100

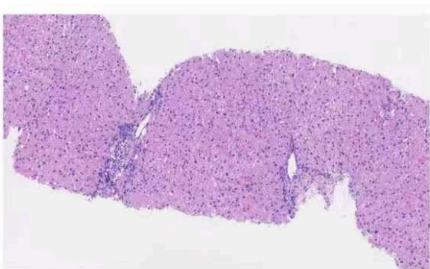


B: H&E×200

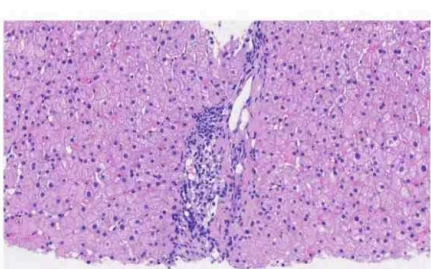


C: Masson's trichrome ×100

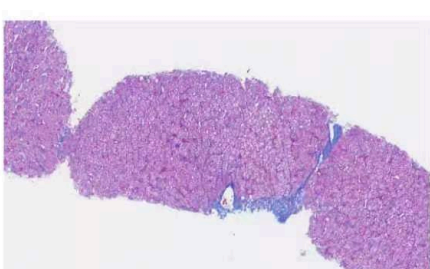
2026-01-13 (G1S2)



D: H&E×100



E: H&E×200



F: Masson's trichrome ×100

Figure 1

Representative histopathological findings from the two liver biopsies (H&E and Masson's trichrome staining). **A–C:** First liver biopsy performed on October 31, 2024, showing chronic hepatitis graded as G2S3–4. **D–F:** Repeat liver biopsy performed on January 13, 2026, showing mild chronic hepatitis graded as G1S2. **A, D:** H&E staining, ×100; **B, E:** H&E staining, ×200; **C, F:** Masson's trichrome staining, ×100. The first biopsy showed inflammatory cell infiltration in the portal areas, interface hepatitis, and fibrous septa. On repeat biopsy, inflammatory cell infiltration was reduced, no obvious interface hepatitis was observed, and the fibrous septa appeared thinner. The two biopsies were graded and staged as G2S3–4 and G1S2, respectively. Both biopsy specimens were independently evaluated by two pathologists experienced in liver pathology, with discrepancies reviewed by a third pathologist.