Case Report

HEPATOLOGY FORUM

Biliary complications from chronic HCV infection

doi: 10.14744/hf.2025.85914

Challenging biliary pain: An unusual extrahepatic manifestation of chronic hepatitis C

Tongluk Teerasarntipan[1,2], Tinh Khampaen[3]

[1]Division of Gastroenterology, Department of Medicine, School of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [2]Department of Gastroenterology and Hepatology, Thonburi Hospital, Bangkok, Thailand; [3]Division of Allergy, Immunology, and Rheumatology, Department of Medicine, Mahidol University School of Medicine, Ramathibodi Hospital, Bangkok, Thailand

Abstract

Hepatitis C virus (HCV) infection can cause various manifestations, including rare biliary complications. This case details a 44-year-old Thai woman with severe biliary pain but normal blood counts, liver function, and amylase levels. Abdominal MRI, MRCP, and endoscopic ultrasound ruled out mechanical obstruction but revealed diffuse thickening of the intrahepatic and common hepatic bile duct walls, and soft tissue thickening surrounding the left portal vein branch, suggestive of an inflammatory process. Further investigation confirmed positive HCV RNA. Serology revealed low complement levels, suggesting immune-mediated inflammation, though ANA, ANCA, and cryoglobulin were negative. Serum IgG4 levels were also normal. This led to a diagnosis of small vessel vasculitis of the biliary tract secondary to chronic HCV infection. Treatment with antiviral therapy and a short course of prednisolone resulted in significant symptom improvement. This case underscores the need for increased awareness of biliary complications associated with chronic HCV infection.

Keywords: Biliary pain; cholangitis; chronic hepatitis C; vasculitis.

Introduction

Hepatitis C virus (HCV) infection causes various extrahepatic manifestations (EHMs). This case highlights an unusual presentation of biliary pain related to HCV, contributing to the understanding of its extrahepatic effects.

Case Report

A 44-year-old Thai woman presented with severe dull, aching epigastric and right upper quadrant pain radiating to the back, worsened after meals, that had persisted for two days. The intensity was severe, ranging from 8 to 10 out of 10, and did not respond to proton pump inhibitors or antispasmodic medications. Partial relief was achieved with intravenous pethidine or morphine. No fever or jaundice was reported. One year prior, she had pruritic rashes on both legs, with a biopsy confirming small vessel vasculitis, but she was lost to follow-up. Six weeks ago, during a routine health check-up, a chest X-ray revealed a lung nodule; a computed tomography (CT) scan demonstrated consolidation in the right middle lung, and a bronchoscopy was scheduled.

Two days before this admission, the patient was admitted due to severe epigastric pain. Laboratory tests, including CBC and amylase, were unremarkable, as was the abdominal CT scan. An esophagogastroduodenoscopy found mild gastritis with Helicobacter pylori infection, treated with a quadruple regimen. However, her symptoms persisted.

On admission, the patient's vital signs were normal, and her abdomen was soft and non-tender, without hepatosplenomegaly. Blood samples collected during abdominal pain, including CBC, creatinine, liver function tests, and serum amylase, were within normal limits. Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) demonstrated long-segment circumferential wall thickening and enhancement of the intrahepatic and common hepatic ducts, without filling defects or stones (Fig. 1). No signs of pancreatitis or sphincter of Oddi dysfunction were observed. Endoscopic ultrasonography (EUS) revealed thickening of the left intrahepatic bile duct wall, but no definite lesion was identified (Fig. 2). A homogeneous hyperechoic lesion surrounding the left portal vein branch suggested thickened soft tissue. Other structures appeared normal.

The initial diagnosis included acute segmental cholangitis and active periportal inflammation. After multidisciplinary discussion, systemic inflammation was considered the most likely etiology. The patient was treated with intravenous dexamethasone 4 mg every 6 hours for one day, leading to dramatic improvement in symptoms. After the first dose of steroids, her abdominal pain completely resolved, prompting a switch to prednisolone at 0.5 mg/kg/day. The patient remained symptom-free thereafter.

Further investigation revealed positive anti-HCV and HCV RNA results (HCV RNA: log 6.46 IU/mL), but negative HBsAg. Serum autoantibodies, including ANA and cryoglobulin, were negative. P-ANCA was positive at a low titer of 1:10; however, anti-MPO and anti-PR3 results were both negative. Complement levels were low, with C3 measured at 0.52 g/L and C4 at <0.03 g/L. IgG4 levels were within the normal range at 19.40 mg/dL (reference range: 11–330 mg/dL). Bronchoscopy with biopsy of the lung consolidation revealed dense proliferation of small lymphoid cells, with immunohistochemical staining consistent with marginal zone lymphoma (MALT lymphoma).

How to cite this article: Teerasarntipan T, Khampaen T. Challenging biliary pain: An unusual extrahepatic manifestation of chronic hepatitis C. Hepatology Forum 2025; 6(4):170–172.

Received: November 26, 2024; **Accepted:** May 27, 2025; **Available online:** October 00, 2025

Corresponding author: Tongluk Teerasarntipan; Division of Gastroenterology, Department of Medicine, School of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand
Phone: +66 2 256 42 65; **e-mail:** kulgnotb@hotmail.com

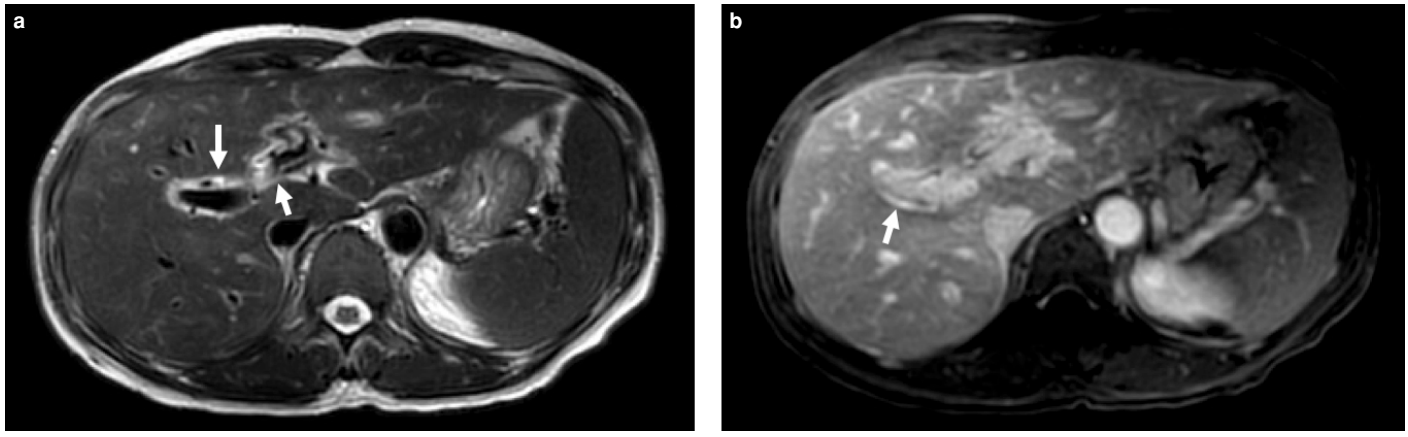

Figure 1. Abdominal MRI shows thickening and enhancement of the intrahepatic and common hepatic bile duct walls. **(a)** An axial T2-weighted image shows wall thickening of the intrahepatic bile duct (arrows). **(b)** An axial T2-weight image taken 5 minutes after Gadolinium injection shows enhancement of the wall thickening in the intrahepatic bile duct (arrow).

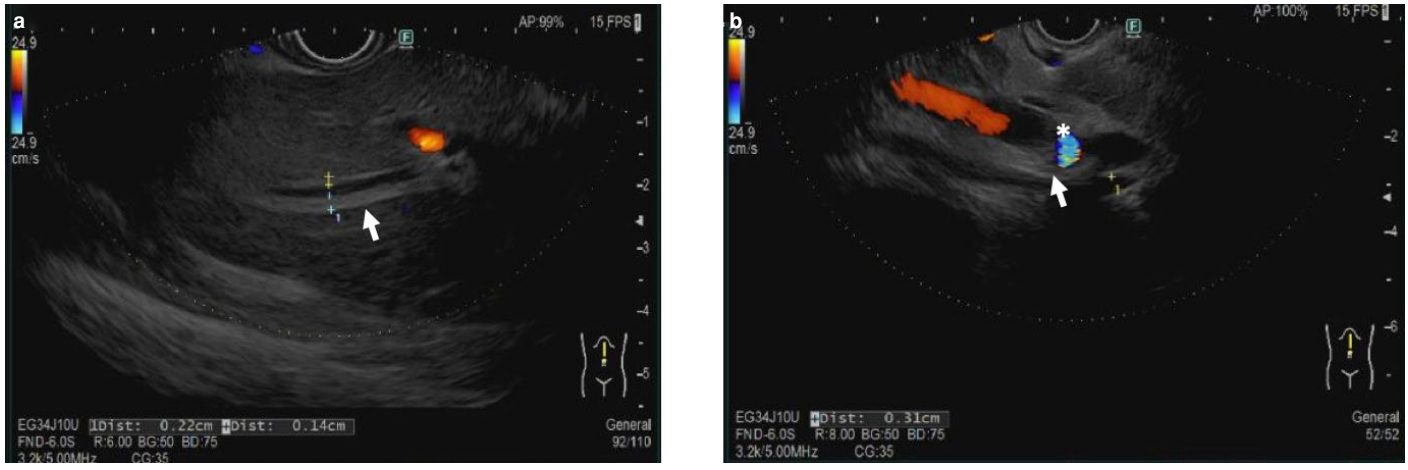

Figure 2. Linear endoscopic ultrasound shows thickening of the intrahepatic bile duct wall and periportal soft tissue. **(a)** Thickening of the intrahepatic bile duct wall (arrow). **(a)** Thickened whitish soft tissue (*) surrounding the left portal vein branch (arrow).

The final diagnosis was an extrahepatic manifestation (EHM) of chronic HCV infection, characterized by small vessel vasculitis (periportal inflammation and acute focal cholangitis and history of cutaneous vasculitis) and HCV-associated MALT lymphoma. The patient was treated with prednisolone 0.5 mg/kg/day for one week, with and tapering dose over the course of one month for small vessel vasculitis. HCV infection was managed with a 12-week course of Sofosbuvir/Velpatasvir (400/100 mg daily). One month after initiating steroid therapy, the patient reported significant improvement, with no abdominal pain. Continued monitoring and follow-up are planned to assess treatment response and address any residual issues.

Discussion

We present a challenging case of severe biliary pain attributed to an unusual complication of HCV infection. Initial tests (MRCP and EUS) ruled out mechanical obstruction and showed diffuse thickening of the intrahepatic bile duct wall and soft tissue surrounding the left portal vein, suggestive of an inflammatory or infiltrative process. Given the clinical presentation of sudden onset and intermittent pain, an inflammatory process seemed more plausible than an infiltrative or infectious process, which typically presents with a more gradual onset and persistent pain.

In considering the differential diagnosis, the patient's history of biopsy-confirmed small vessel vasculitis, coupled with low complement levels, indicates possible immune abnormalities and supports the diagnosis of immune complex-mediated vessel inflammation. With negative serology for primary autoimmune diseases, the most likely diagnosis is immune complex-mediated vasculitis, possibly secondary to chronic HCV infection or lymphoma. The significantly low C4 levels in this case suggest that the immune complexes may be influenced by both etiologies. Cryoglobulinemic vasculitis was also evaluated, as it can be associated with both malignancy and chronic HCV infection; however, this diagnosis was deemed less likely due to a negative cryoglobulin test in this case. The dramatic response to steroid treatment provides additional support for the diagnosis of vasculitis.

Previous studies have identified various pathophysiologic mechanisms linked to HCV complications. In terms of immune-related mechanisms, HCV-induced cryoglobulinemia and immune complex-mediated vasculitis are particularly relevant.[1] The chronic presence of the HCV antigen can drive polyclonal B-cell activation, leading to the formation of immune complexes that deposit in small- to medium-sized blood vessels. This deposition triggers an inflammatory response, activating complement pathways and recruiting immune cells, resulting in vascu-

lar damage and inflammation. Our patient exhibited low complement levels (C3 and C4), consistent with immune complex-mediated vasculitis described in the literature. Although cryoglobulinemia was negative, it is essential to note that only 40–60% of HCV-infected individuals test positive for cryoglobulinemia.[2] This highlights the variability of immune responses in chronic HCV infections.

The biliary complications observed in this case may be attributed to two potential mechanisms. First, HCV-induced immune complex vasculitis could lead to biliary damage through the formation of immune complexes and subsequent inflammatory responses affecting bile duct structures. Second, direct injury to bile duct cells by HCV cannot be ruled out. Previous studies indicate that intrahepatic bile duct cells are susceptible to HCV infection,[3,4] and the virus can be excreted into bile.[5] Chronic exposure to HCV may induce immune cross-reactivity with bile duct structures, possibly due to mimicry between epitopes on HCV viral polyproteins and human proteins, such as nitrogen oxide synthases, tyrosine kinase-Lck, and proto-oncogenes, leading to cross-reactivity to the bile duct[6] and further production of autoantibodies contributing to the observed complications. The association of HCV with other biliary conditions, such as primary biliary cholangitis, primary sclerosing cholangitis, and cholangiocarcinoma, remains inconclusive, with epidemiological studies suggesting links but lacking robust data elucidating the oncogenic mechanisms involved.[7,8] Further research is warranted to explore the underlying pathophysiological processes that might contribute to these associations.

In our case, EUS revealed a periportal soft tissue abnormality, raising the differential diagnosis of perivascular inflammation—potentially a complication of HCV—or infiltration by MALT lymphoma. Despite the lack of a confirmed pathological diagnosis, perivascular inflammation was deemed more likely due to the characteristic imaging patterns and absence of systemic evidence of malignancy. Perivascular inflammation typically exhibits a hyperechoic pattern in 91% of cases on ultrasound, with hematologic malignancies that commonly present as hypoechoic lesions.[9] While contrasting chronic inflammatory diseases causing perivascular soft tissue changes are sometimes observed in IgG4-related diseases, such phenomena have not been documented in other rheumatologic conditions. Histopathological features of perivascular inflammation, including vessel wall invasion, thrombosis, fibrinoid necrosis, and scar formation, have been noted in small- to medium-vessel vasculitides such as ANCA-associated vasculitis, cryoglobulinemic vasculitis, and drug-induced immune complex vasculitis.[10] In this case, periportal inflammation detected by EUS but not MRI is likely due to EUS's superior sensitivity for identifying abnormalities. This raises the possibility that perivascular inflammation in rheumatologic disease may be more common than the literature suggests, potentially under-recognized due to limitations in conventional imaging.

Treatment approaches for HCV-related vasculitis vary based on the severity of systemic involvement, ranging from antiviral therapy alone to combined regimens with immunosuppressive agents. In this case, given the patient's severe vasculitic symptoms but involvement of non-vital organs, a combination of antiviral therapy and a short course of prednisolone (0.5 mg/kg/day) was chosen, which effectively controlled symptoms. Due to the rarity of such cases and the lack of data on relapse rates, the decision was made to monitor the patient for clinical relapse without long-term immunosuppressive therapy. Should persistent HCV-associated MALT lymphoma arise, chemotherapy would be considered following viral eradication.

Conclusion

In conclusion, this case underscores the importance of awareness of biliary complications associated with chronic HCV infection. It contributes to the limited literature on this association and emphasizes the need for further research to elucidate the underlying pathophysiology that may contribute to these HCV complications.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from participants.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Use of AI for Writing Assistance: Authors used ChatGPT4.0 for assistance with grammar corrections and to make to text more concise. The AI played no role in the creation of the content itself.

Author Contributions: Concept – TT; Data Collection and/or Processing – TK; Literature Search – TT; Writing – TT, TK; Critical Reviews – TT, TK.

Peer-review: Externally peer-reviewed.

References

1. Méndez-Sánchez N, Coronel-Castillo CE, Ramírez-Mejía MM. Chronic hepatitis C virus infection, extrahepatic disease and the impact of new direct-acting antivirals. Pathogens 2024;13(4):339. [CrossRef]
2. Saadoun D, Landau DA, Calabrese LH, Cacoub PP. Hepatitis C-associated mixed cryoglobulinaemia: a crossroad between autoimmunity and lymphoproliferation. Rheumatology (Oxford) 2007;46(8):1234-1242. [CrossRef]
3. Delladetsima JK, Makris F, Psichogiou M, Kostakis A, Hatzakis A, Boletis JN. Cholestatic syndrome with bile duct damage and loss in renal transplant recipients with HCV infection. Liver 2001;21(2):81-88. [CrossRef]
4. Haruna Y, Kanda T, Honda M, Takao T, Hayashi N. Detection of hepatitis C virus in the bile and bile duct epithelial cells of hepatitis C virus-infected patients. Hepatology 2001;33(4):977-980. [CrossRef]
5. Monrroy H, Angulo J, Pino K, Labbé P, Miquel JF, López-Lastra M, et al. Detection of high biliary and fecal viral loads in patients with chronic hepatitis C virus infection. Gastroenterol Hepatol 2017;40(5):339-347. [CrossRef]
6. Tampaki M, Koskinas J. Extrahepatic immune related manifestations in chronic hepatitis C virus infection. World J Gastroenterol 2014;20(35):12372-12380. [CrossRef]
7. Navas MC, Glaser S, Dhruv H, Celinski S, Alpini G, Meng F. Hepatitis C virus infection and cholangiocarcinoma: An insight into epidemiologic evidences and hypothetical mechanisms of oncogenesis. Am J Pathol 2019;189(6):1122-1132. [CrossRef]
8. Pascale A, Rosmorduc O, Duclos-Vallée JC. New epidemiologic trends in cholangiocarcinoma. Clin Res Hepatol Gastroenterol 2023;47(9):102223. [CrossRef]
9. Fidan N, Mermi Yetis EU, Murat M, Yucesoy C, Turgal E, Metin M. Is the presence of echo-rich periportal cuffing in the liver indicator for abdominal inflammation in pediatric patients? Med Ultrason 2019;21(3):225-231. [CrossRef]
10. Conticini E, d'Alessandro M, Al Khayyat SG, D'Alessandro R, D'Ignazio E, Pata AP, et al. Inflammatory muscle involvement in systemic vasculitis: A systematic review. Autoimmun Rev 2022;21(3):103029. [CrossRef]