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EDITORIAL

Immunological crossroads: The intriguing dance between hepatitis C and autoimmune hepatitis

Jonathan Soldera

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Abstract

Delving into the immunological crossroads of liver diseases, this editorial explores the dynamic interplay between hepatitis C virus (HCV) and autoimmune hepatitis (AIH). While HCV primarily manifests as a viral infection impacting the liver, previous studies unveil a captivating connection between HCV and the emergence of AIH. The dance of the immune system in response to HCV appears to set the stage for an intriguing phenomenon—an aberrant autoimmune response leading to the onset of AIH. Evidence suggests a heightened presence of autoimmune markers in individuals with chronic HCV infection, hinting at a potential overlap between viral and autoimmune liver diseases. Navigating the intricate terrain of viral replication, immune response dynamics, and genetic predisposition, this editorial adds a layer of complexity to our understanding of the relationship between HCV and AIH. In this immunological crossroads, we aim to unearth insights into the complex interplay, using a compelling case where AIH and primary sclerosing cholangitis overlapped following HCV treatment with direct-acting antivirals as background.

Key Words: Liver diseases; Hepatitis C virus; Autoimmune hepatitis; Primary sclerosing cholangitis; Inflammatory bowel disease

Core Tip: This editorial delves into the dynamic interplay between hepatitis C virus (HCV) and autoimmune hepatitis (AIH), tracing the historical progression from the era of non-A non-B hepatitis to the discovery of HCV and the advent of direct-acting antiviralagents (DAAs). A recent case highlights the emergence of an overlap between AIH and primary sclerosing cholangitisfollowing successful DAA treatment for HCV. The case underscores the potential risks associated with rapid viral clearance and emphasizes the need for vigilance regarding the development of autoimmune liver diseases post-DAA treatment. This complex relationship warrants further exploration for refined treatment approaches.

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INTRODUCTION

The landscape of hepatitis posed a real challenge in the past, persisting into contemporary times, as cases of unexplained jaundice perplexed clinicians. The turning point occurred approximately five and a half decades ago when researchers such as Holland, Schmidt, Purcell, Walsh, and Alter delved into the study of "transfusion-associated hepatitis" in 1969[1]. It would take another two decades until the identification of the infectious agent, hepatitis C virus (HCV), in 1989[2]. Reflecting on the hepatology field during the era when non-A non-B hepatitis dominated discussions, instances of unexplained post-transfusion hepatitis were commonplace and intrigued physicians. Furthermore, numerous cases of "nosocomial" hepatitis[3] and cryptogenic hepatitis added complexity, compounded by a lack of specific diagnostic tests. Importantly, this period witnessed the misdiagnosis of many patients with acute and chronic hepatitis as having autoimmune hepatitis (AIH) prior to the identification of HCV[4,5]. The journey to unravel this intricate problem spanned 39-14 years from the identification of non-A non-B hepatitis to the discovery of HCV, and an additional 25 years from the discovery of HCV in 1989 to the approval of Sofosbuvir in 2013, one of the most prescribed and most efficacious direct-acting antiviral agents (DAAs) for HCV treatment[6]. In retrospect, these 39 years reveal a marvelous progress for the medical sciences, from the early clinical and epidemiologic studies by Alter and others to the present-day, marked by the creative pharmacological approach involving the design of DAAs inhibiting HCV infection through the blockade of viral assembly and replication[6], and a global initiative, led by the member countries of the World Health Organization, to eliminate HCV *via* treatment and prevention by the year 2030[7].

Intriguingly, the progress made from those early clinical and epidemiologic studies has now led us to a new chapter in the dance between HCV and AIH. I have read with great attention and interest a recent case reported by Morihisa *et al*[8], in which the authors present the case of a 74-year-old woman with chronic HCV infection who, after successful DAA treatment, developed an overlap of AIH and primary sclerosing cholangitis (PSC). This case stands out as the first reported instance of the overlap of AIH and PSC following DAA treatment for HCV, highlighting the intricate interplay between viral clearance and subsequent autoimmune liver diseases.

Moreover, this case underscores the potential risks associated with the restoration of host immunity following rapid viral clearance, emphasizing the need to consider the development of autoimmune liver diseases after DAA treatment[8]. While DAAs have become a mainstay in HCV treatment due to their high efficacy and minimal adverse events, cases such as this urge us to be vigilant about potential consequences. It is worth noting that this case is not isolated. Other reports describe instances of AIH occurring after HCV treatment with DAAs[9-12]. These cases collectively suggest a complex relationship between HCV, DAA treatment, and the subsequent development of autoimmune liver diseases.

The intricate interplay at the crossroads of HCV and AIH forms a complex and intriguing dance. Long-standing beliefs about a dynamic interconnection between these seemingly distinct entities raise questions about possible overlaps, therapeutic implications, and prognostic significance.

One compelling aspect focuses on the potential shared pathways in treating both HCV and AIH. Published data has highlighted that successful DAA treatment can bring about comprehensive improvement in patients concurrently dealing with HCV[13-16]. Furthermore, the presence of autoimmune markers in HCV infection has been extensively studied, with a prevalence above 10% of serological markers of autoimmunity in chronic hepatitis C patients[17-20], which could be a marker of more severe chronic hepatitis C[21]. This raises more questions about the accurate delineation between HCV-related and autoimmune-related liver pathology, since interface hepatitis is present in both HCV and AIH[22,23]. An intriguing discovery emerges from studies indicating a positive response to corticosteroid and ursodeoxycholic acid therapy in patients presenting both HCV and positive AIH markers. These findings challenge conventional expectations surrounding the role of these medications in the context of HCV infection[24,25]. There is more to the dynamic nature of HCV and its potential to trigger autoimmune responses, as other triggers for AIH after HCV treatment have been described[26,27].

As we navigate through the discussion the case published by Morihisa *et al*[8], it is crucial to reiterate the link between PSC and inflammatory bowel diseases (IBD), particularly emphasizing the connection with Ulcerative Colitis[28]. Even in overlap syndromes involving AIH and PSC, a systematic review has reported a prevalence of IBD to be 45.3%[29]. While PSC is a severe condition known for its poor response to treatment, there appears to be an association of the overlap syndrome with a comparatively low mortality rate and a favorable response to treatment[29]. While the reported case

discussed in this editorial does not explicitly mention the performance of a colonoscopy, it is crucial to emphasize to readers that, in accordance with the EASL guidelines for treating PSC, the undertaking of a colonoscopy with random biopsies is paramount. This recommendation holds especially true for patients without a known history of inflammatory bowel disease[30].

CONCLUSION

The intricate interplay between HCV and AIH unveils a multifaceted relationship that extends beyond conventional classifications. The presence of autoantibodies in chronic hepatitis C challenges our understanding of immune responses in viral infections and prompts a reevaluation of diagnostic and therapeutic paradigms. While studies offer glimpses into the complex web of interactions, numerous questions persist, beckoning researchers to unravel the mysteries that shroud this intriguing intersection of liver diseases. The nuances of the interactions between AIH and HCV necessitate continued research and clinical awareness to enhance our understanding and refine treatment approaches. Additionally, liver specialists could consider screening for autoantibodies and immunoglobulin G levels before and during DAA therapy to monitor for potential immune-related diseases and facilitate timely diagnosis and treatment.

FOOTNOTES

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REFERENCES

1 **Alter HJ**. The road not taken or how I learned to love the liver: a personal perspective on hepatitis history. *Hepatology* 2014; **59**: 4-12 [PMID: 24123147 DOI: 10.1002/hep.26787]
2 **Ward JW**. Hepatitis C virus: the 25-year journey from discovery to cure. *Hepatology* 2014; **60**: 1479-1482 [PMID: 25131647 DOI: 10.1002/hep.27377]
3 **Campollo O**, Valencia-Salinas JJ, Berumen-Arellano A, Pérez-Aranda MA, Panduro-Cerda A, Segura-Ortega J. [Epidemiological characteristics of liver cirrhosis at the Hospital Civil of Guadalajara]. *Salud Publica Mex* 1997; **39**: 195-200 [PMID: 9304222]
4 **Cassani F**, Muratori L, Manotti P, Lenzi M, Fusconi M, Ballardini G, Selleri L, Volta U, Zauli D, Miniero R. Serum autoantibodies and the diagnosis of type-1 autoimmune hepatitis in Italy: a reappraisal at the light of hepatitis C virus infection. *Gut* 1992; **33**: 1260-1263 [PMID: 1330845 DOI: 10.1136/gut.33.9.1260]
5 **Savage K**, Dhillon AP, Schmilovitz-Weiss H, el-Batanony M, Brown D, Dusheiko G, Scheuer PJ. Detection of HCV-RNA in paraffin-embedded liver biopsies from patients with autoimmune hepatitis. *J Hepatol* 1995; **22**: 27-34 [PMID: 7751584 DOI: 10.1016/0168-8278(95)80256-8]
6 **Zhao Q**, Xia N. The 2016 Lasker-DeBakey Clinical Medical Research Award: Innovative hepatitis C virus (HCV) replicons leading to drug development for hepatitis C cure. *Sci China Life Sci* 2016; **59**: 1198-1201 [PMID: 27785725 DOI: 10.1007/s11427-016-0313-9]
7 **Shahid I**, Jabeen Q. WHO Hepatitis C Elimination Goal by 2030: Feasible or not? In: Hepatitis C Virus-Host Interactions and Therapeutics: Current Insights and Future Perspectives.Ohwada: Bentham Science Publisher, 2023 [DOI: 10.2174/9789815123432123010015]
8 **Morihisa Y**, Chung H, Towatari S, Yamashita D, Inokuma T. Autoimmune hepatitis and primary sclerosing cholangitis after direct-acting antiviral treatment for hepatitis C virus: A case report. *World J Hepatol* 2024; **16**: 286-293 [PMID: 38495284 DOI: 10.4254/wjh.v16.i2.286]
9 **Gupta N**, Bodin R, Sule S. Autoimmune Hepatitis in Association With Sofosbuvir. *Am J Ther* 2015 [PMID: 26448334 DOI: 10.1097/MJT.0000000000000233]
10 **Dikopoulos N**, Zizer E. [Coincidence of a chronic Hepatitis C and an autoimmune Hepatitis Type 3 - successful therapy with the new direct-acting antiviral agents]. *Z Gastroenterol* 2016; **54**: 770-773 [PMID: 27529527 DOI: 10.1055/s-0042-109980]
11 **Covini G**, Bredi E, Badalamenti S, Roncalli M, Aghemo A, Colombo M. Autoimmune Hepatitis During Ledipasvir/Sofosbuvir Treatment of Hepatitis C: A Case Report. *Hepatol Commun* 2018; **2**: 1179-1183 [PMID: 30288473 DOI: 10.1002/hep4.1248]

12 **Montón C**, Escudero MªD, Pascual I. The development of type-1 autoimmune hepatitis after chronic hepatitis C (HCV) clearance by direct-acting antivirals (DAA). *Rev Esp Enferm Dig* 2020; **112**: 664-665 [PMID: 32686431 DOI: 10.17235/reed.2020.6785/2019]

13 **De Maria C**, Ghidotti I, Grillo F, Giannini EG. Successful DAA Treatment and Global Improvement in a Cirrhotic Patient with Concomitant HCV Infection and Autoimmune Hepatitis. *Dig Dis Sci* 2019; **64**: 591-593 [PMID: 30386944 DOI: 10.1007/s10620-018-5356-1]

14 **López Couceiro L**, Gómez Domínguez E, Muñoz Gómez R, Castellano Tortajada G, Ibarrola de Andrés C, Fernández Vázquez I. Healing of autoimmune hepatitis associated with hepatitis C virus infection treated with direct-acting antivirals. *Rev Esp Enferm Dig* 2019; **111**: 159-161 [PMID: 30449122 DOI: 10.17235/reed.2018.5528/2018]

15 **Soldera J**, Balbinot RS, Muscope ALF, Balbinot RA, Balbinot SS. Interferon-Free Therapy for Hepatits C in Brazil and Sustained Virological Response. *GMR* 2017; **1** [DOI: 10.31031/gmr.2017.01.000506]

16 **Cheinquer H**, Sette H Jr, Wolff FH, de Araujo A, Coelho-Borges S, Soares SRP, Barros MFA. Treatment of Chronic HCV Infection with the New Direct Acting Antivirals (DAA): First Report of a Real World Experience in Southern Brazil. *Ann Hepatol* 2017; **16**: 727-733 [PMID: 28809742 DOI: 10.5604/01.3001.0010.2717]

17 **Pavić S**, Simonović J, Boricić I, Svirtlih N. [Autoantibodies characteristic for autoimmune hepatitis found in chronic hepatitis C]. *Srp Arh Celok Lek* 2003; **131**: 437-442 [PMID: 15114784 DOI: 10.2298/sarh0312437p]

18 **Vella FS**, Orlando P, Attanasi F, Simone B, Mundo A, Lopalco P, Schiraldi O, Antonaci S. [Autoantibodies in chronic hepatitis C. Markers of autoimmunity or non-specific events?]. *Recenti Prog Med* 2001; **92**: 107-112 [PMID: 11294098]

19 **Cassani F**, Cataleta M, Valentini P, Muratori P, Giostra F, Francesconi R, Muratori L, Lenzi M, Bianchi G, Zauli D, Bianchi FB. Serum autoantibodies in chronic hepatitis C: comparison with autoimmune hepatitis and impact on the disease profile. *Hepatology* 1997; **26**: 561-566 [PMID: 9303483 DOI: 10.1002/hep.510260305]

20 **Bayraktar Y**, Bayraktar M, Gurakar A, Hassanein TI, Van Thiel DH. A comparison of the prevalence of autoantibodies in individuals with chronic hepatitis C and those with autoimmune hepatitis: the role of interferon in the development of autoimmune diseases. *Hepatogastroenterology* 1997; **44**: 417-425 [PMID: 9164512]

21 **Amin K**, Rasool AH, Hattem A, Al-Karboly TA, Taher TE, Bystrom J. Autoantibody profiles in autoimmune hepatitis and chronic hepatitis C identifies similarities in patients with severe disease. *World J Gastroenterol* 2017; **23**: 1345-1352 [PMID: 28293081 DOI: 10.3748/wjg.v23.i8.1345]

22 **Badiani RG**, Becker V, Perez RM, Matos CA, Lemos LB, Lanzoni VP, Andrade LE, Dellavance A, Silva AE, Ferraz ML. Is autoimmune hepatitis a frequent finding among HCV patients with intense interface hepatitis? *World J Gastroenterol* 2010; **16**: 3704-3708 [PMID: 20677344 DOI: 10.3748/wjg.v16.i29.3704]

23 **Czaja AJ**, Carpenter HA. Histological findings in chronic hepatitis C with autoimmune features. *Hepatology* 1997; **26**: 459-466 [PMID: 9252159 DOI: 10.1002/hep.510260229]

24 **Toda G**, Zeniya M, Watanabe F, Imawari M, Kiyosawa K, Nishioka M, Tsuji T, Omata M. Present status of autoimmune hepatitis in Japan--correlating the characteristics with international criteria in an area with a high rate of HCV infection. Japanese National Study Group of Autoimmune Hepatitis. *J Hepatol* 1997; **26**: 1207-1212 [PMID: 9210605 DOI: 10.1016/s0168-8278(97)80453-9]

25 **Nakamura K**, Yoneda M, Takamoto S, Nakade Y, Yokohama S, Tamori K, Aso K, Matui T, Sato Y, Aoshima M, Makino I. Effect of ursodeoxycholic acid on autoimmune-associated chronic hepatitis C. *J Gastroenterol Hepatol* 1999; **14**: 413-418 [PMID: 10355503 DOI: 10.1046/j.1440-1746.1999.01898.x]

26 **Hasegawa N**, Matsuoka R, Ishikawa N, Endo M, Terasaki M, Seo E, Tsuchiya K. Autoimmune hepatitis with history of HCV treatment triggered by COVID-19 vaccination: case report and literature review. *Clin J Gastroenterol* 2022; **15**: 791-795 [PMID: 35716255 DOI: 10.1007/s12328-022-01654-0]

27 **Trikudanathan GV**, Ahmad I, Israel JL. Concurrent autoimmune hepatitis and grave's disease in hepatitis C during pegylated interferon α-2a and ribavirin therapy. *Saudi J Gastroenterol* 2011; **17**: 348-352 [PMID: 21912063 DOI: 10.4103/1319-3767.84494]

28 **Shah A**, Jones MP, Callaghan G, Fairlie T, Ma X, Culver EL, Stuart K, De Cruz P, O'Beirne J, Tabibian JH, Dignass A, Canbay A, Gores GJ, Holtmann GJ. Efficacy and safety of biologics in primary sclerosing cholangitis with inflammatory bowel disease: A systematic review and meta-analysis. *Hepatol Commun* 2024; **8** [PMID: 38206197 DOI: 10.1097/HC9.0000000000000347]

29 **Ballotin VR**, Bigarella LG, Riva F, Onzi G, Balbinot RA, Balbinot SS, Soldera J. Primary sclerosing cholangitis and autoimmune hepatitis overlap syndrome associated with inflammatory bowel disease: A case report and systematic review. *World J Clin Cases* 2020; **8**: 4075-4093 [PMID: 33024765 DOI: 10.12998/wjcc.v8.i18.4075]

30 **European Association for the Study of the Liver**. EASL Clinical Practice Guidelines on sclerosing cholangitis. *J Hepatol* 2022; **77**: 761-806 [PMID: 35738507 DOI: 10.1016/j.jhep.2022.05.011]

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