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Review Article

COVID-19 Associated Cholangiopathy

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Abstract

A newly described complication of severe COVID-19 is an unusual, but late-appearing form of cholangiopathy associated with a "secondary" form of sclerosing cholangitis. The aim of this evaluation was to review literature related to this disorder. Clinical features include elevated alkaline phosphatase with imaging changes typical of bile duct obstruction. In some, this was complicated by progressive jaundice often accompanied by changes of large duct obstruction and biliary casts. The precise mechanism for late biliary ductal injury still requires elucidation. In addition, Covid-19 patients require long-term follow-up, as changes may only develop late in the clinical course. Moreover, treatment has been difficult with progression to fulminant hepatic failure and requirement for liver transplantation.

Keywords: COVID-19 Bile Duct Disease; Virus-associated Cholangiopathy; Cholestatic Liver Disease; SARS-CoV-2 Infection; Coronavirus Cholestasis

Introduction

The purpose of this article was to review English-language publications on so-called Covid-19 cholangiography, only recently recognized to develop late in the course of the disease. Initially, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was described in December 2019 from Wuhan, China causing an apparently new form of coronavirus disease (Covid-19) [1]. The agent was highly transmissible and quickly spread worldwide as a pandemic. In some treatment centers, hospitalization and mortality were significant.

Vaccination was highly effective in reducing adverse outcomes from Covid-19 including hospitalization, need for intensive care and mortality [2]. Vaccines appeared to be safe with few adverse effects initially reported [3].

Discussion

Late Covid-19 complications and liver disease

Later, with additional follow-up, occasional post-vaccination organ-specific or systemic immune-based diseases were described [4,5]. These included liver injury, resembling the clinical and histopathological features of autoimmune hepatitis [6,7]. Most spontaneously resolved or responded to corticosteroid treatment [7]. In a US study, the rarity of cholestasis in a large group of patients with liver chemistry test changes was also recorded [8]. A later retrospective survey [9] of cases from multiple hospitals in 18 countries described 87 patients (18-79 years, 63% female) with a predominance of hepatocellular injury in 84% having other typical features of immune-mediated hepatitis in 57% (including elevated immunoglobulin G levels and positive autoantibodies). Median time of detection was 15 days (range, 3-65 days) post-vaccination

with 59% apparently caused by Pfizer-BioNTech vaccine, 23% Oxford-Astra-Zeneca vaccine and 16% Moderna vaccine.

A total of 46 patients received corticosteroids, usually for more severe histological disease. All patients in this series responded with resolution of liver injury, except for 1 male with fulminant liver failure requiring liver transplantation [10]. Steroids were withdrawn in 12 (26%) with complete biochemical resolution and no reported relapse of liver disease during the study period. Interestingly, even in this survey group, 5 patients were reported with a cholestatic pattern of liver injury, usually considered a rare event. In spite of these apparently good outcomes in this form of liver disease associated with Covid-19 infection, long-term studies are still needed.

Covid-19 cholangiopathy

In 2021, another interesting and detailed report from New York City retrospectively described a series of 12 patients with a distinctive syndrome of cholangiopathy in patients recovering from severe Covid-19 disease and characterized by marked alkaline phosphatase elevation with evidence of bile duct injury on imaging studies, including beading of intrahepatic ducts, bile duct wall thickening with enhancement, and peri-biliary diffusion high signal intensity [11]. In some patients in this series, further progression of these features was documented. Some were referred for liver transplantation and 1 had a successful living donor liver transplantation. Some patients with cholestasis were also later labeled with a "secondary" form of sclerosing cholangitis [12]. In these, more severe underlying Covid-19 disease with persistent jaundice was noted, usually developing late in those patients requiring prior intensive or critical care. In a study from Switzerland, 34 severely ill patients were compared to a cohort with severe influenza A. Of these, 4 patients in the Covid-19 cohort developed sclerosing cholangitis, suspected to have possibly an ischemic basis. Other considerations included hypoxic injury to the bile ducts with formation of biliary casts or direct viral infection of cholangiocytes through ACE (angiotensin converting enzyme) 2 epithelial cell receptors, similar to intestinal enterocytes [13]. In some, ischemic injury may also resulted from endothelial injury by the virus to small and large arteries and veins with or without formation of platelet-fibrin micro thrombi [14]. Similar changes were described in other case series [15-17] along with the critical need for persistent follow-up for evidence of later cholangiopathy [15] as well as the possible requirement for liver transplantation as a possible treatment measure [18,19]. More recent case series have described other biliary ductal changes including non-shadowing cylindric objects within the main bile ducts, sometimes with ductal dilation [20] along with bile duct casts visualized with endoscopic cholangiographic radiologic measures [21].

Conclusion

In conclusion, a novel form of post-COVID-19 cholangiographic disease may occur with clinical and biochemical features of cholestasis, including jaundice, imaging changes of cholangitis, biopsy features of large bile duct obstruction and dilation, often associated with strictures and biliary ductal casts. Late clinical appearance of this disease necessitates prolonged follow-up of patients with a history of severe COVID-19 disease, particularly if there were hepatic changes during the acute phase of the illness. Anecdotal reports of end-stage COVID-19 liver disease suggest that these patients may ultimately require hepatic transplantation.

Bibliography

1. Huang C., *et al*. "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China". *Lancet* 395 (2020): 497-506.

2. Barouch DH. "Covid-19 vaccines—immunity, variants, boosters". *New England Journal of Medicine* 387 (2022): 1011-1020.

3. Sharif N., *et al*. "Efficacy, immunogenicity and safety of COVID-19 vaccines: a systemic review and meta-analysis". *Frontiers in Immunology* 12 (2021): 714170.

4. Chen Y., *et al*. "New-onset autoimmune phenomena post COVID-19 vaccination". *Immunology* 165 (2021): 386-401.

5. Freeman HJ. "Collagenous colitis associated with novel sprue-like intestinal diseases". *Gastroenterology Hepatology Bedside to Bench* In press, (2023).

6. Bril F., *et al*. "Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccination: causality or casualty?" *Journal of Hepatology* 75 (2021): 222-224.

7. Shroff H., *et al*. "Liver injury following SARS-CoV-2 vaccination: a multicenter case series". *Journal of Hepatology* 76 (2022): 211-214.

8. Phipps MM., *et al*. "Acute liver injury in COVID-19. Prevalence and association with clinical outcomes in a large US cohort". *Hepatology* 72 (2020): 807-817.

9. Efe C., *et al*. "Liver injury after SARS-CoV-2 vaccination: Features of immune-mediated hepatitis, role of corticosteroid therapy and outcome". *Hepatology* (2022).

10. Efe C., *et al*. "Liver transplantation following severe acute respiratory syndrome-coronavirus-2 vaccination-induced liver failure". *Hepatology* 75 (2022):1669-1671.

11. Faruqui S., *et al*. " Cholangiopathy after severe COVID-19: clinical features and prognostic implications". *American Journal of Gastroenterology* 116 (2021): 1414-1425.

12. Butikofer S., *et al*. "Secondary sclerosing cholangitis as cause of persistent jaundice in patients with severe COVID-19". *Liver International* 41 (2021): 2404-2417.

13. Freeman HJ. "Covid-19 diarrhea". *International Journal of Celiac Disease* 8 (2020): 60-63.

14. Hamming I., *et al*. "Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis". *Journal of Pathology* 203 (2004): 631-637.

15. Cabaliero-Alvarado J., *et al*. "Post-COVID cholangiopathy: a narrative review". *Gastroenterology and Hepatology* (2022):S0210-5705(22)00221-7.

16. Shih AR., *et al*. "Persistent cholestatic injury and secondary sclerosing cholangitis in COVID-19 patients". *Archives of Pathology and Laboratory Medicine* 146 (2022): 1184-1193.

17. Ferreira FB., *et al*. "COVID-19-associated secondary sclerosing cholangitis—a case series". *Clinical Research Hepatology Gastroenterology* 46 (2022):102048.

18. Lee A., *et al*. "Liver transplantation for post-COVID-19 sclerosing cholangitis". *British Medical Journal Case Reports* 14 (2021): e244168.

19. Machado MC., *et al*. "Post-COVID-19 secondary sclerosing cholangitis: a rare but severe condition with no treatment besides liver transplantation". *American Journal of Case Reports* (2022):e936250.

20. Bazerbachi F., *et al*. "Endosonographic and ERCP findings in COVID-19 critical illness cholangiopathy". *Revista Espanola de Enfermedades Digestives* (2022).

21. Soldera J., *et al*. "Billiary casts in post-COVID-19 cholangiography". *Gastroenterology Hepatology* 46 (2023): 319-320.