Treatment response of sofosbuvir in HCV virus/ Helicobacter pylori co-infected patient a case report

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ABSTRACT

Newly developed direct-acting anti-viral drugs act as a major breakthrough in the area of HCV therapeutics. Accumulating evidence suggest that more than 99% patients achieve sustained virological response after receiving sofosbuvir-based therapy. However, we observed the first case of DAA treatment failure in HCV patient who was co-infected with H. Pylori.

Introduction

HCV is the leading cause of morbidity and mortality with global bioburden between 130–150 million infected people and approximately 700,000 deaths annually (1). The overall high prevalence of H. pylori and HCV in developing world are major bacterial and viral human disease etiologies worldwide. Gram-negative bacillus H. pylori has been associated with diverse spectrum of human enterohepatic disorders including mucosa-associated lymphoid tissue (MALT) lymphoma, peptic ulcer disease, gastritis, and gastric adenocarcinoma. Moreover, several evidences have reported the causal link of H. pylori with variety of liver diseases such as HCV-related chronic hepatitis, cirrhosis, fibrosis, and hepatocellular carcinoma (2-4).

The recent development of interferon-free regimens has revolutionized the area of HCV therapeutics by increasing sustained virological response (SVR) in more than 80% patients. However, the cure rates are not high in cases of serious liver complications and co-infections. Some evidences suggest the poor efficacy of direct-acting anti-viral (DAA) drugs in co-infections. A recent study reported the reactivation of Hepatitis B virus (HBV) infection in HBV/HCV co-infected patient treated with sofosbuvir/ledipasvir (5). Likewise, findings of Perello et al., exhibited reactivation of herpesviruses in DAA treated patients (6, 7). At present, non-responsiveness and treatment failure towards DAA therapy have not been studied properly. Despite the strong association between H. pylori and HCV, no conclusive data are available regarding the efficacy and response of DAA in bacterial and viral co-infected patient. For effective eradication of H. pylori, patients must be treated with (clarithromycin, amoxicillin, and omeprazole) for 2 weeks before starting DAA therapy (8). We experienced failed response to sofosbuvir and ribavirin in interferon ineligible HCV/H. pylori co-infected patient.

Presentation of Case

A 42-year old male patient from Lahore, Pakistan who had null response to prior interferon therapy and was ineligible for retreatment with interferon was referred by gastroenterologist to Genome Centre for Molecular Based Diagnostics & Research laboratory in 2016. The patient was diagnosed with HCV 3a genotype after undergoing two general surgeries in 2011. The

patient received pegylated interferon and ribavirin for 24 weeks in 2012 but experienced HCV relapse in 2016, four years after of interferon therapy. Laboratory evaluation revealed normal liver and spleen but mildly elevated liver function enzymes and bilirubin. His hemoglobin, total leukocytes count, and platelet count were below normal range. Viral load prior DAA treatment was 53,120 IU/ml. During first three months of treatment with sofosbuvir (400mg) and ribavirin, viral load declined slightly whereas, mild increase in the HCV viremia was observed after the completion of six-months long treatment (Fig. 1).

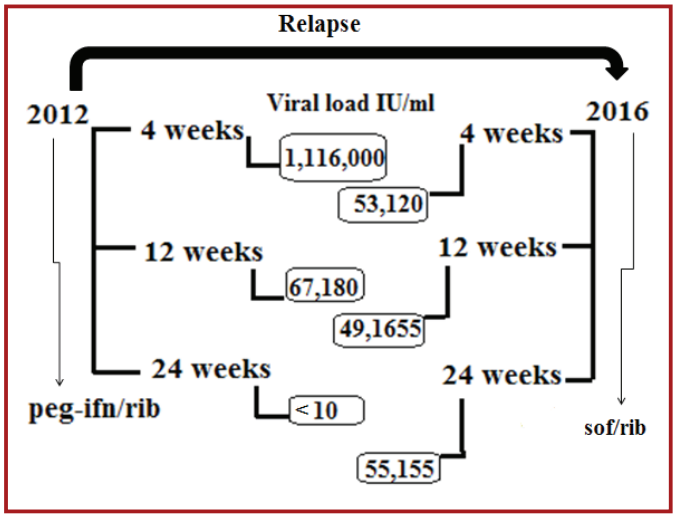

Figure 1. Treatment response towards peg-interferon/ribavirin therapy in 2012 and sofosbuvir/ribavirin therapy in 2016.

Patient was screened for other viruses (HBV, HEV, HAV & HIV) common in Pakistani population to track the underlying cause of treatment failure. The PCR was negative for other hepatitis viruses and HIV moreover, ELISA was performed to detect anti-H. pylori because patient complained of bloating, nausea, and severe heartburn for three months. The confirmed diagnosis of H. pylori infection in patient, indicates that H. pylori is implicated in treatment failure towards both interferon-based and interferon-free therapies. The patient profile and case history is provided in table below.

Table 1: Laboratory evaluation before and after DAA therapy

Variable	Measure
Age	42
Weight	55
BMI	7.9 kg/m2
Genotype	3a
ALP	151 IU/ml
ALT	131 IU/ml
AST	106 IU/ml
Hemoglobin	11.6 g/dL
Platelet	112×103/IL
Bilirubin	0.4 mg/dL
Total leukocyte count	3900 (mcL)

Discussion

More than 50% of population is infected with H. pylori and the presence of H. pylori in liver material worsens condition of HCV patients. In addition to this, H. Pylori is the universal problem in developing world that begins even from early childhood (9). Robust epidemiological data suggest high prevalence of H. pylori in HCV infected cirrhotic patients because this bacteria has been reported to play an important role in the progression of liver disease. Reportedly, it has also been clarified that H. pylori accerlates the progression of liver disease in HCV patients (10).

Few evidences have shown H. pylori induced hepatotoxicity in vitro (2, 11).

Interferon-based treatment regimens is no longer the standard of care therapy since the development of interferon-free regimens i.e, interferon-free treatment or direct-acting anti-viral drugs (DAA). Large majority of patients have achieved sustained virolgoical response and have been successfully treated with DAA but herein, we observed a non-responder patient whose HCV RNA load didn't clear even after receiving 6 months long treatment with sofosbuvir and ribavirin. After investigating we found out that the patient had another bacterial co-infection that altered the treatment outcome (12). Therefore, the physicians belonging to developing world must monitor the patient for other common infections because the presence of co-infection alters the treatment outcome with DAA therapy.

Conclusion

In conclusion, the patient profile exhibited the involvement of H. pylori in reduced efficacy of peg-ifn/ribavirin and sofosbuvir/ribavirin in HCV infected patients. Hence, it might be useful to clear H. pylori infection before starting HCV treatment. All HCV patients must be screened for identification of H. pylori because of extremely high prevalence of this bacterial infection worldwide.

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Conflict of Interest

The author declared nothing to disclose regarding conflict of interest with respect to this manuscript.

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