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Case Presentation

Acute Portal Vein Thrombosis Associated with Sofosvubir and Ribavirin Use

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Abstract

Incidence of Portal Vein Thrombosis (PVT) in cirrhosis patients varies from 0.6% to 15%, which primarily reflects the incidence of chronic PVT. Despite its association with potentially life threatening conditions, the incidence and natural history of Acute PVT in cirrhosis remains largely underreported. This unusual complication describe usually after systemic infection or in the presence of prothrobotic state. We describe here 2 cases of Acute PVT following use of Oral Direct acting antiviral against Hepatitis C infection.

Introduction

Hepatitis C Virus (HCV) infection is a major cause of end-stage liver disease and hepatocellular carcinoma. There have been rapid advances in HCV treatment with the development of oral Direct-Acting Antiviral (DAAs). Sofosbuvir is a nucleotide analog used in combination with other drugs for the treatment of Hepatitis C Virus (HCV) infection. It has been marketed since 2013. Compared to previous treatments, sofosbuvir-based regimens provide a higher cure rate, fewer side effects, and a two- to four-fold reduced duration of therapy [1,2]. This report illustrate the first experience of drug induced Acute PVT with the new DAAs. The mechanism underlying PVT is currently unknown.

Case Presentation

Case 1

A 61 year old female was diagnosed with Hepatitis C related cirrhosis 3 months before during hospitalisation for massive upper gastrointestinal bleed. Her HCV RNA was 26460IU/mL and genotype [3]. She has been taking sofosbuvir with ribavirin for past 2 months. Her liver function was stable with normal bilirubin, prothrombin time, creatinine and platelets. She had recurrent massive bleed following EVL for which endoscopic glue injection was performed. Despite that, bleed persisted and she became hemodynamically unstable. Hence, Sengstaken-Blakemore tube deployed and she was transferred to our intensive care unit. At admission she was having advance hepatic encephalopathy and moderate ascites. An emergency bedside ultrasound performed in our unit revealed an acute portal vein thrombosis. And CT Liver angiogram demonstrate hypodense nonenhancing filling defect in main portal vein lumen (thin arrows), extending up to portal confluence and proximal superior mesenteric vein (asterix) causing venous luminal distention without any evidence of space occupying lesion in the liver and collaterals (Figure 1, 2). Following the onset of acute PVT, liver decompensation had set in with rising bilirubin (>10 mg/dL) and high international normalised ratio (>3.5). Her prothrombotic work up was normal. In view of persistent bleed and coagulopathy, we could not start anticoagulation therapy for acute PVT. Transjugular Intrahepatic Portosystemic Shunting (TIPS) could not be offered as there was worsening encephalopathy and high bilirubin. Hence, after thorough family counselling, urgent living related liver transplantation was performed. The graft was the right lobe (GRWR 0.79) of liver donated by her son. Intraoperatively, there was complete portal vein thrombosis extending into superior mesenteric vein. Portal vein thrombectomy was done and soft clots removed reestablishing good portal flow of 1.6 liters per minure. Her post-operative period was uneventful and was

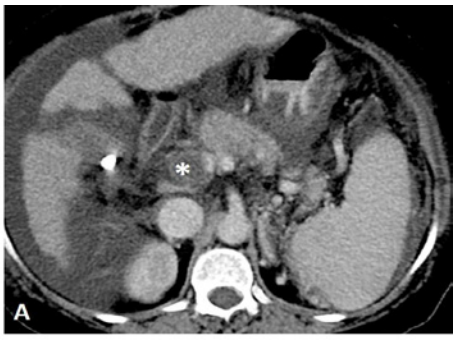

Figure 1: Contrast Enhanced CT Scan Axial view.

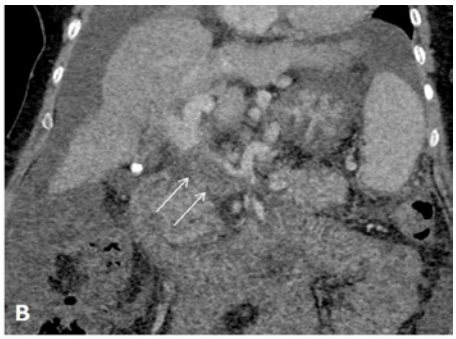

Figure 2: Contrast Enhanced CT Scan Coronel view.

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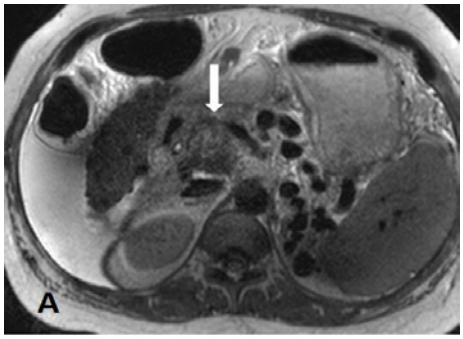

Figure 3: Non contrast MRI T2 weighted.

started on anticoagulation therapy. She discharged 3 weeks following transplantation and presently doing well.

Case 2

A 47 yr old female was diagnosed with Hepatitis C related cirrhosis in September 2014. She was apparently good and her bilirubin and INR was normal. She developed ascites in October 2015. She never had episode of hepatic enchelopathy. Her ultrasound was done in the January 2016 shows chronic liver disease with sign's of partal hypertension including dilated portal vein. She was started Sofosvubir and ribavirin in January 2016. Initially she was tolerated the drug well. But after 2nd month of starting sofosvubirpatient started having increasing serum bilirubin serially and in the last week of march it became >11 mg%. INR was also started increasing and became > 2.5. She also developed diuretic intolerant ascites and episode of hepatic enchelopathy. Patient came to us in first week of April, we started evaluating her for the cause of recent decompensation. On MR imaging Noncontrast axial T2 (Figure 3) and T1 (Figure 4) weighted images reveal presence of an in homogenouly hyper intense thrombus in portal vein lumen (thick arrows) at the level of confluence suggestive of sub acute hemorrhagic signal. We also evaluate for possible prothrombotic stated, however found to be negative. Hence, after thorough family counselling, living related liver transplantation was performed. The graft was the right lobe (GRWR 0.82) of liver donated by her son Portal vein thrombectomy was done and soft clots removed reestablishing good portal flow of 1.7 liters per minute. Her post-operative period was uneventful and was started on anticoagulation therapy. She discharged 3 weeks following transplantation and presently doing well.

Discussion

This report describes the first experience of acute PVT with the new DAAs. However reports of Oral DAAs with liver decompensation are been described earlier [3]. The mechanism underlying these drug reactions is currently unknown. They may represent idiosyncratic (Type B) drug reactions which are rare and unpredictable [4].

The common factor in these cases was treatment with sofosbuvir (NS5B inhibitor) and ribavirin. Given the timing of events it is probable that the acute PVT was drug-related. Sofosbuvir is rapidly

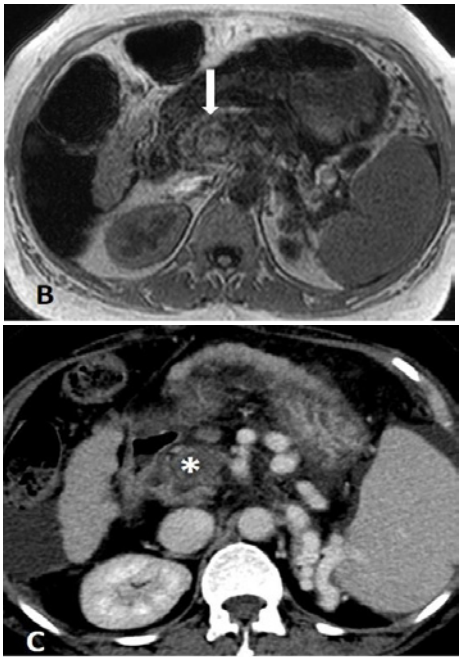

Figure 4: Non Contrast MRI T1 weighted.

absorbed and undergoes extensive first-pass hepatic metabolism. The predominant circulating metabolite, GS-331007, is formed by dephosphorylation of nucleotide metabolites, accounts for approximately 78% of total systemic exposure and is principally excreted in urine. In advanced liver disease, the metabolism of sofosbuvir may be altered leading to toxic liver injury and thereby increasing the thrombotic state or alternatively, genetic factors could play a role.

Conclusion

We report two cases of acute PVT with newer DAAs with decompensate chronic liver disease due to Hepatitis C. While the association with the DAAs is not proven, these cases highlight that patients with advanced liver disease need close monitoring while on DAA therapy and caution should be exercised. If there is a significant unexplained deterioration in liver function the DAAs should be discontinued one should also look for Acute PVT.

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