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# Emergence of resistant variants detected after Daclatasvir/Asunaprevir combination therapy in a compensated cirrhosis patient infected with HBV/HCV co-infection: a case report

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**Objective:**

We herein report a unique case of emergence of resistant variants detected after Daclatasvir/Asunaprevir combination therapy in the patient infected with HBV/HCV co-infection.

**Methods:**

A Chinese 63-year-old female patient was firstly diagnosed with Hepatitis B infection 30 years ago. She denied of the history of blood transfusion and the family history of liver disease. This patient was admitted with HCV GT-1b infection in July 2017 and HCV RNA $1.3\times10^{6}$IU/ml. Given previous HBV infection history, she was documented by positivity of HBsAg, HBeAb and HBcAb and HBV DNA $1\times10^{3}$IU/ml meanwhile. Other basic information presented here, IL28B rs12979860 genotype was CC, and rs8099917 genotype was TT. Baseline NS5A (L31M or Y93H) resistance-associated variants (RAVs) were negative either. The liver function showed ALT 23U/L， AST 42U/L， TBIL 38.2μmol/L and ALB 37.1g/L. Abdominal enhanced CT showed liver cirrhosis and splenomegaly. Gastroscopy showed mild varicosity of the esophagus. Child-Pugh grade was level A with CTP 6 points. In terms of treatment not only for anti-HBV but also anti-HCV, this patient was treated with entecavir at 0.5mg daily from July 2017, and also used daclatasvir 60mg once combined with asunaprevir at 100mg twice per day for 24 weeks from August 2017.

**Result:**

HBV DNA was less than 500 copies/ml after 2 week treated by ETV, HBV DNA was undetected at 12 weeks and 24 weeks respectively. By week 2 after the initiation of DCV/ASV treatment, HCV RNA decreased to $7.06\times10^{2}$IU/ml. At week 4, HCV RNA was $8.21\times10^{1}$IU/ml with normal liver function as well. HCV RNA became undetectable till week 6. At week 12 and 24, HCV RNA still was undetected respectively. However, at week 4 post-treatment, the patient was relapse with HCV RNA $7.54\times10^{4}$IU/ml and HCV genotype was re-tested with GT-1b. Concurrently, NS5A RAVs (L31M and Y93H) were present. HBV serologic results was still positivity of HBsAg, HBeAb and HBcAb. HBV DNA was consistently undetectable. The results of abdominal enhanced CT and gastroscope presented no significant progression compared to patient baseline situation.

**Conclusion:**

We estimate HBV/HCV co-infection may be one factor for HCV relapse and emergence of resistant variants with DAA treatment. More clinical research and study data is needed to verify this finding.