***Case report***

**HEPATITIS C DIFFICULT TO TREAT: A CASE REPORT IN JOS, NIGERIA**

**ABSTRACT**

We report a case of 60-year-old male Nigerian businessman who firstt presented to the gastroenterology unit of the Jos University Teaching Hospital (JUTH) 6years ago with systemic hypertension and subsequently tested positive for Chronic HCV. Treatment failure can occur in many situations. Some genotypes are harder to treat and hence prone to more failures. This is more with genotype 3 which is associated more with insulin resistance and alteration in lipid metabolism leading to steatosis. The presence of significant fibrosis, male gender, high viral load and deranged LFTs are usually associated with difficulty in achieving SVR12. Our patient in this report had many of these features. The Fibroscan score was 33.0kpa which was in keeping with severe fibrosis. Since our patient’s condition has worsened over the years, a liver transplant could also prove invaluable in this case at present as the patient has decompensated over time due to inability to have SVR and non availability of the suitable DAAs and financial constrain on part of the patient.

Keywords: Chronic HCV, Fibroscan, pan-genotypic, sustained virologic response

**INTRODUCTION**

The prevalence of Hepatitis C Virus (HCV) has been changing globally. The latest values put it at 1.0%, which is about 71.1milion people in the worldas of 2015 (1). In the USA, a 2013-2016 survey got a prevalence of 1.7%, which corresponds to about 4.1 million persons who were positive for HCV (2). In southwestern Nigeria, 13.3% was the prevalence of HCV in patients with Type 2 diabetes(3). In Nigeria, we have noticed more cases in middle-aged and elderly patients. This could be attributed to unsafe practices with sharps in the past and unsterilized needles for mass vaccination.

The EASL guideline for the treatment of HCV advocates the use of direct-acting antivirals (DAAS). This is either genotype-specific or pan-genotypic. For low income countries, pan-genotypic drugs are used mainly because of the cost of genotyping. Treatment failure is defined as the detection of HCV RNA 12 weeks after completion of treatment with DAAs. In other words, its lack of sustained virologic response (SVR) 12 weeks after treatment(4).

Treatment failure can occur in many situations. Some genotypes are harder to treat and hence prone to more failures. This is more with genotype 3 which is associated more with insulin resistance and alteration in lipid metabolism leading to steatosis(5). However, regardless of genotypes, cirrhosis is a common cause of the difficult clearance of the virus. This state usually warrant an extension of the most DAA regimen to 24weeks instead of the 12 weeks in compensated non-cirrhotic Child-pugh A patients(6).

Commonly used genotype-specific regimens in our environment include Sofosbuvir/ ledipasvir for genotype 1. Also, Grazoprevir/ elbasvir is effective for genotype 1. Pan genotypic drug combinations include Sofosbuvir/Velpastevir, Sofosbuvir/Daclastavir, and Glecaprevir/ pibrentasvir(6).

One of the greatest worry of HCV treatment failure is the fact that the risk of HCC is increased to 2 times compared to patients with HCV who were never treated. This was demonstrated and published in 2016 by Mei Lu et al (7).

**CASE PRESENTATION :**

A patient, 60-year-old male Nigerian businessman who firstt presented to the gastroenterology unit of the Jos University Teaching Hospital (JUTH) 6years ago with systemic hypertension and subsequently tested positive for Chronic HCV. He had no complaints and no features of decompensation.

He had a family history of Hypertension, does not smoke cigarette or consume alcohol.

His general physical examination was unremarkable and there was no stigmata of CLD.

The pulse rate was 88 beats/minute, normal volume and regular

Blood Pressure was 168/100mmHg, JVP not elevated, Heart Sounds were first and second only.

Abdomen exams was unremarkable.

**Laboratory Investigations:**

Patient declined liver biopsy. The initial Complete Blood Count (CBC) and Liver Function Test (LFT) were unremarkable.

SERUM ELECTROLYTES: sodium = 137mmol/l, potassium = 3.7mmol/l.

CREATININE = 70UMOL/L, UREA=3.2 MMOL/L.

ABDOMINAL ULTRASOUND SCAN - liver span 14cm, normal parechmal echotexture, gall bladder, portal vein not dilated, kidneys were normal. Fibroscan was 33.0kpa. HCV RNA was 168,000 copies/ml. HCV genotype was 1a.

**TREATMENT:**

 He had Sofosbuvir/Peg INF/Ribavirin for 12weeks which was what was available at that time in the country. Had SVR at end of treatment, but viral RNA was detected at 12 weeks post- treatment. This initial treatment was only for 12 weeks then because we had no privy to the fibroscan score and patient declined liver biobsy. This became widely awailable in Nigeria much later on.He has another treatment for 3months with Sofosbuvir/Ledipasvir/ Ribavirin. Also by this time, fibroscan was still not available.At 12 weeks, Viral RNA was undetected but did not have SVR 12. He then had Sofusbuvir/Velpastavir (SOF?VEL) for 6months.

 The current HCV RNA is still high at 48,700 IU/ml after DAAs for 6 months.The latest repeat Genotype is Non-1a, Non-1b, but positive for 1c,d, e,f, g and at this point patient had fibroscan 33.0kpa which showed that patient had severe fibrosis.

 **DISCUSSION**:

This patient is a typical description of difficulty to eradicate HCV due to severe fibrosis. The current drive to HCV treatment is DAAS. They are effective, oral, and mostly with fewer pill burdens. According to a recent analysis in the TARGET cohort study, the features of patients most likely to have HCV treatment failure includes Male patients with advanced fibrosis or cirrhosis and abnormal liver function tests. Also, those with certain genotypes according to regions. Like 1a in the USA, HCV-6 c-I in Southeast Asia, and genotype-4 in Europe and sub-Saharan Africa (8,9).

There is a high rate of Resistance Associates Substitutions (RAS) in the NS5A, NS5B and NS3 regions. This RAS remains in patients who fail HCV therapy even after a while in different cases. It is most persistent even after 2 years of using an NS5A drug in 90%of cases.But NS3 RAS would revert to wild type in 80% of cases after 1 year of follow-up(10).

The presence of significant fibrosis, male gender, high viral load and deranged LFTs are usually associated with difficulty in achieving SVR12. Our patient in this report had many of these features. The Fibroscan score was **33.0kpa** which was in keeping with severe fibrosis. He being a male and also had some abnormal LFTs. He was also initially genotyped 1a and had repeat treatment with different combinations of DAAs and still fail to achieve SVR12.

For this patient, what is recommended in most guidelines is to use a combination of Sofosbuvir/Velpatasvir/ Voxilaprevir (SOF/VEL/VOX) which has shown SVR12 rates of 98% according to the POLARIS 4 trial. Also relevant to our index patient is the use of SOF/VEL/VOX + Ribavirin which showed SVR 12 of 97%. This was reported in the great work done by Saxena et al(11). These responses were interestingly genotype related.

**Conclusion**

Since our patient’s condition has worsened over the years, a liver transplant could also prove invaluable in this case at present as the patient has decompensated over time due to inability to have SVR and non availability of the suitable DAAs and financial constrain on part of the patient.

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