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Case Report of HBsAg Loss in a Young Chronic Hepatitis B Patient taking Tenofovir Alafenamide

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Abstract: ***Introduction: In patients with chronic hepatitis B, loss of hepatitis B surface antigen (HBsAg) is considered a functional cure. HBsAg loss is uncommon with existing therapies, and predictive factors associated with HBsAg seroconversion are unknown. Case Report: MR.XX, 26 years old man presented withhyperpigmented macules and pruritis on 23rd August, 2017. The Laboratory findings were suggestive of hepatitis B, he was started on Tenofovir Alafenamide 25 mg on 28th March, 2018 after confirming the chronicity and was subsequently followed up. After 3 years of treatment HBV DNA was not detected on 13th March, 2021 and HBsAg was negative as tested on 25th March, 2021. Discussion: Hepatic insult by HBV resulting in chronic hepatitis B does correlate with the abnormal Sr globulin levels and reversal can be detected on proper compliance with antivirals. Conclusion: Timely detection and treatment with appropriately selected antiviral can lead to HBsAg loss and give better survival benefit to the patient.***

Keywords: Chronic hepatitis B, seroconversion, Tenofovir Alafenamide

1. Introduction

Chronic hepatitis B Chronic is characterized by the persistence of HBsAg for at least 6 months (with or without concurrent HBeAg). Persistence of HBsAg is the marker of risk for developing chronic liver disease, hepatocellular carcinoma later in life. (1)

The prevalence of HBV infection is highest in African, Western Pacific and Asian countries. In these countries the virus is acquired mainly through perinatal transmission from the chronically infected mother or through infection in early childhood. The early infections are responsible for most cases of hepatocellular carcinoma in these countries. Further in southern and eastern Europe, infection is due to perinatal transmission, needle sharing among drug users, nosocomial transmission and tattooing and body piercing. In the areas with low HBV endemicity (<2%), such as Western Europe, North America and Australia, transmission is mainly through sexual contacts and needle sharing among drug users. Now the universal hepatitis B vaccination programmes for infants and adolescents have started to show reductions in the prevalence of HBV infection. (2)

The patients who are treated with entecavir or tenofovir have very low or undetectable HBV DNA amounts, but HBsAg remains positive and at high levels. The spontaneous loss of HBsAg is a rare event in untreated patients with chronic hepatitis B infection. Patients older than 40 years had a higher likelihood of HBsAg loss (1·7%) than patients younger than 40 years of age (1·1%).(3)

Tenofovir Alafenamide was approved by FDA in the year 2016 for the treatment of Chronic hepatitis B. It is a prodrug of tenofovir and has a better safety profile with respect to renal function and bone mineral density compared to TDF. It is rapidly converted to the active metabolite intracellularly. With reduced systemic exposure to the active metabolite, the off-target kidney and bone exposure are thereby reduced. It has the same resistance profile as TDF.(4)

It seems there is a strong association between levels of serum globulin and IgG and extent of hepatic fibrosis in patients with chronic HBV infection.(5) In acute hepatitis the levels of γ-globulin are elevated and the serum albumin is normal or only slightly decreased. As the hepatitis diminishes the elevated γ-globulins gradually return to normal. If hypergammaglobulinemia persists or increases, it may indicate a transition from acute to chronic hepatitis. In chronic liver disease, particularly chronic hepatitis and advanced cirrhosis, the elevations in the γ-globulin concentrations are similar or greater than those seen in acute hepatitis but the percentage of the γ-globulin is significantly higher. This is due to hypoalbuminemia resulting in total protein concentrations which are normal or low. Particularly in chronic hepatitis, however, there is marked hypergammaglobulinemia associated with elevations in the total serum protein.(6)

2. Case report

The 26 years old man who is resident of Meghalaya came to the medicine OPD on 23rd August, 2017 with macular hyperpigmented pruritic rash on the abdomenfor the past one month which was suspected to be tinea versicolor.

He did not have any known comorbidities or any significant family history.

The general and systemic examination was insignificant. Before starting antifungals, the investigations were sent. The LFT reported slightly elevated liver enzymes with SGOT being 60U/L, SGPT being 78U/L and albumin to globulin ratio was 1.1:1. On further investigation he was tested positive for Hepatitis B by HBsAg card test on 23rd August, 2017.

For evaluation further investigations were sent. HBc IgM Antibody was positive, HBeAg was reactive and HBV DNA was 55.9×10^8IU/ml as on 26/08/2021.

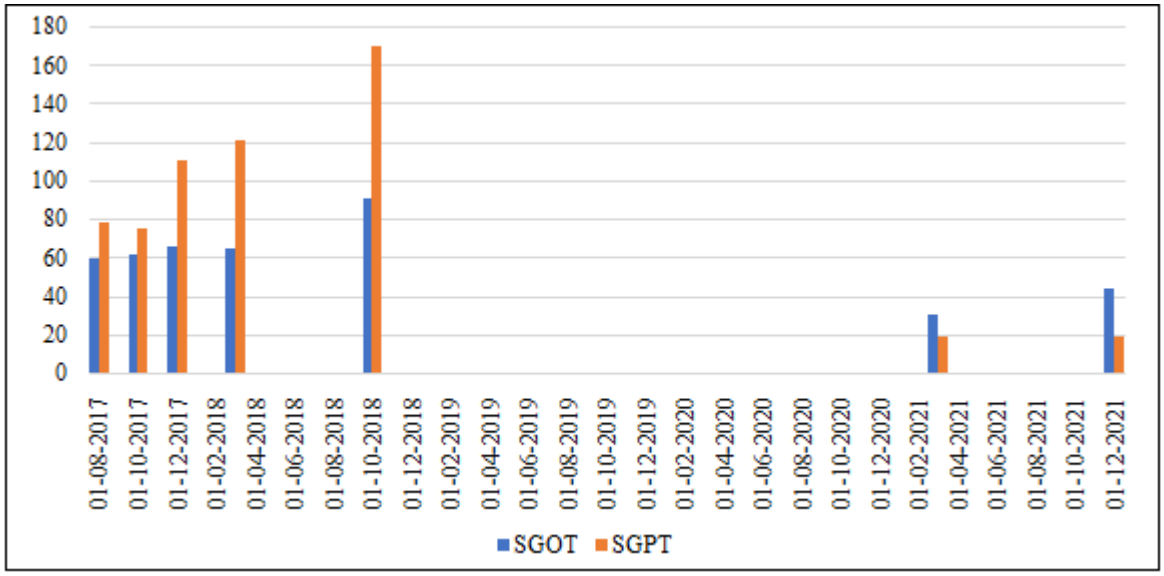
The patient was regularly followed up with SGOT and SGPT reports. On 26th March, 2018 SGPT was 121U/L and SGOT was 65U/L. On 28th March, 2018 he was started on 25mg of Tenofovir Alafenamide.

On subsequent follow up SGOT and SGPT was still high but HBV DNA values were suppressed.

On 13th March, 2021 the SGOT, SGPT values were within normal limits and HBV DNA was not detected by RTPCR, Taqman assay. HBsAg loss was reported on 25th of March, 2021.

On subsequent follow up on 15/12/2021 HBsAg, Anti-HBs was found to be non-reactive.

USG whole abdomen findings were reported normal throughout the course.



Graph 1: The serial measurement of SGOP and SGPT in the patient overtime showing significant decrease of enzymes after starting the treatment

Table 1: The serial measurement of enzymes, DNA load and protein concentration overtime.

DATE	SGOT (U/L)	SGPT (U/L)	HBV-DNA (IU/ml)	A:G ratio	Sr. Albumin (g/dL)	Sr. Globulin (g/dL)
25/08/2017	60	78	55.9×10^8	1.1:1	4.3	3.6
20/10/2017	62	75				
18/12/2017	66	111				
26/03/2018	65	121		1.3:1	4.4	3.3
10/10/2018	91	171		1.3:1	4.5	3.4
10/07/2019			2.1×10^2			
09/10/2020			1.9×10^2			
13/03/2021	30	19	Not detected	1.7:1	5.0	3.0
15/12/2021	44	52	Not detected	1.6:1	5.2	3.3

The patient has been advised to continue therapy for 1 year after HBsAg lossi.e.,till March, 2022 as per guidelines and is being advised for regular follow up. Next follow up planned in March, 2022.

3. Discussion

The patient was incidentally diagnosed with chronic hepatitis B which is a common occurrence in the developing world and needs the vigilance of the clinician to detect it timely and treat to avoid the chronic sequelae of the disease.

The patient had deranged SGOT and SGPT as well as Albumin: Globulin ratio. The follow up values of the hepatic enzymes being continuously abnormal confirmed the chronicity of the disease, and the abnormal albumin to globulin ratio indicated towards the ongoing hepatic insult and fibrosis.

Selection of antiviral has been debated, Tenofovir alafenamide having better pharmacokinetics and better bone and kidney profile was selected.

The case does reaffirm the ability of Tenofovir Alafenamide of leading to complete loss of HBsAg.

4. Conclusion

The use of Tenofovir Alafenamide can lead to HBsAg loss despite the rarity, with proper compliance and follow up.

The case also conveyed the importance of starting antiviral therapy that affectively improved the corresponding liver function profile.

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