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Case Report: An Interesting Case of Seroconversion after a Spontaneous Flare in a Patient with Chronic Hepatitis B.

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ABSTRACT

Chronic Hepatitis B is a chronic necroinflammatory disease of the liver caused by persistent infection with hepatitis B virus, India has the second highest toll of Hepatitis B infected patients, approximately 40 million, constituting about 15% of the entire pool of Hepatitis B in the world. Newer antiviral regimens are being recommended to combat this rapidly emerging disease. HBsAg seroconverison, which indicates resolved HBV infection being the goal of the treatment. Flares or acute exacerbations of Hepatits B, frequently encountered during the course of the disease can occur spontaneously or after immunosuppressive therapy. These are characterized by intermittent elevations of aminotransferase activity to more than 10 times the upper limit of normal and more than twice the baseline value. There are not many reported cases of clearing the virus following a spontaneous flare. Here we report an interesting case of Chronic Hepatitis B who had spontaneous HBsAg seroconversion following a bout of severe flare without any antiviral therapy.
Keywords: Chronic Hepatitis B, seroconversion, HBsAg, HBV DNA, hepatic flares

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Case Report

A 55 yr old male, normotensive, euglycemic, non-alcoholic, nonsmoker presented to the gastroenterology OPD in November 2013, with nonspecific complaints of vague abdominal pain and malaise for the past 15 days. He gave history of intermittent low-grade fever not associated with chills or rigors. He had normal bowel and bladder habits with no history or nausea or vomiting. He gives hisroty of high colored urine for the past 15 days. He did not give any other significant past history. General physical examination revealed icterus and minimal right hypochondrial tenderness on palpation. Investigations revealed showed elevated bilirubin and markedly elevated transaminases with total bilirubin being 6.5 mg/dL, direct bilirubin 4.8, SGOT 2130 U/L, SGPT 2430 U/L & ALP 256. His prothrombin time was 1.3. HBsAg and HBeAg were positive. IgM anti-Hbc antibodies were also positive. USG done revealed a fatty liver. Viral serology done for Hepatitis A, E & C were negative. Serum ceruloplasmin was normal and ANA was negative. In view of the above clinical picture, HBV DNA titre was sent to differentiate between Acute Hepatitis B and spontaneous flare of Chronic Hepatitis B. While HBV DNA titre report was awaited, LFTs were repeated after 7 days, which demonstrated a marked reduction in the transaminases levels, almost by half. His SGOT had come down to 1170 U/L and SGPT to1360 U/L, though there was a mild increase in the serum total bilirubin to 7.2 and patient symptomatically improved. His pro-thrombin time also normalized. HBV DNA titre was found to be 1,26,340 IU/mL. But in view of improving LFTs, he was not started on any antivirals. During his subsequent visit, he gave history of having being diagnosed as HBsAg positive in 2010 during a routine evaluation for blood donation His LFTs and HBV DNA titres were repeated on a regular basis. By the end of the first month his bilirubin markedly came down and SGOT & SGPT reduced to normal limits. His HBeAg became negative, anti HBe became positive and HBV DNA titres reduced to 24,320 IU/mL. By May 2014, sr.bilirubin came down to 1.2 mg/dL, liver enzymes normalised, HBsAg became negative, anti-HBs titres were positive and HBV DNA titres became undetectable.

Table 1: Laboratory results of the patient

Date	13.11.13	20.11.13	28.11.13	17.12.13	22.01.14	09.05.14
Total bilirubin (mg/dL)	6.5	7.2	8.6	3.2	1.6	1.2
SGOT (U/L)	2130	1170	420	38	26	22
SGPT (U/L)	2430	1360	690	26	22	14
HBeAg	+ve	+ve	+ve	-ve	-ve	-ve
Anti HBe	-ve	-ve	-ve	+ve	+ve	+ve
HBV DNA(IU/mL)	1,26,340	-	24,320	-	520	0
HBsAg	+ve	+ve	+ve	+ve	+ve	-ve
Anti HBs	-	-	-	-	-	+ve

DISCUSSION

Chronic Hepatitis B is a necroinflammatory disease of the liver, caused by persistent infection with Hepatitis B virus [1]. HBV is a DNA virus of which eight genotypes have been identified [2,3]. It causes liver damage by immune mediation. Modes of transmission include parenteral or percutaneous routes, sexual contact and vertical or perinatal transmission. India has the second most number of Hepatitis B infected patients, most of them being chronic, amounting to about 40 million cases, which is second only to China. Every year nearly 6,00,000 patients succumb to this deadly disease. All Asian countries have been categorized as high-risk areas for HBV infection [4].

Chronic Hepatitis B runs an indolent course, sometimes for decades, fatigue being the most common symptom. Chronic HBV occurs in different phases, which are outlined as follows. Patients can be immune tolerant, characterized by high rates of viral replication but normal liver enzymes and low levels of inflammation or immune active, characterized by active replication with high levels of HBV DNA & Hepatitis B e antigen (HBeAg). In addition there are also carrier states with low replication having low or undetectable HBV DNA levels, and chronic HBeAg negative states, characterized by high HBV DNA levels, elevated liver enzymes & ongoing histological activity.

Flares or acute exacerbations of Hepatitis B infection are commonly encountered during the course of chronic Hepatitis B disease, defined as intermittent elevations of aminotransferase activity to more than 10 times the upper limit of normal and more than twice the baseline value. These abrupt elevations in serum

aminotransferases are the result of an increase in intrahepatic necro-inflammation due to increased numbers of intrahepatic cytotoxic T lymphocytes. The various causes of flares in Chronic Hepatitis B include spontaneous flares, flares due to immunosuppressive therapy, flares due to antiviral therapy to Hepatitis B, flares due to super infection with other Hepatitis viruses and flares due to genotypic variations.

Spontaneous flares in chronic hepatitis B occur as a consequence of reactivated infection. HBV DNA levels increase initially followed by an increase in transaminases. During the flare, the histological picture is consistent with acute lobular hepatitis on the background of chronic viral hepatitis. The cause for these flares is unknown, but is likely related to immunological control of viral replication. These flares occur mostly during adulthood. They are common in patients co-infected with HIV and those who acquire Hepatitis B early in life.

It is imperative to differentiate a hepatic flare of Chronic Hepatitis B from acute Hepatitis B as both are characterized by positive anti-HBc IgM, positive HBsAg and ALT peak. But HBV DNA titres maybe helpful in differentiating both, HBV DNA titres being elevated in hepatic flares. Decreasing HBV DNA levels, aminotransferases levels to normal levels heralds end of hepatic flares followed by HBsAg seroconversion very rarely.

The current antivirals available for the treatment of Chronic Hepatitis B include interferon, lamivudine, tenofevir, adefovir, entecavir, telbivudine. The aim of the treatment is HBsAg seroconversion which seldom occurs after antiviral therapy or spontaneously.

Hepatic flares put the patient at increased risk of cirrhosis and hepatocellular carcinoma with a high mortality rate. Very few cases of HBsAg seroconversion following hepatic flares in patients undergoing immunosuppressive therapy have been reported. Massetto B et al. described a young patient with active chronic hepatitis B who achieved an HBsAg & HBV DNA negative with anti-HBs positive state after three hepatitic flares [5]. Villeneu et al. noted a case of HBeAg seroconversion after the third flare in a patient of Chronic Hepatitis B of 11 years [6].

HBV DNA titres are high in patients with hepatic flares in chronic hepatitis B due to resistance to antiviral therapy or mutations of HBV genome. In contrast HBV DNA titres maybe low in patients receiving interferon therapy. Akif Atinbas et al [7] reported an interesting case of a patient who had spontaneous flare presenting with high viral load followed by total Hepatitis B recovery.

The uniqueness of our case is that, HBsAg seroconversion occurred in a patient with chronic hepatitis B not on any immunosuppressive treatment, following a spontaneous flare without being subjected to any antiviral therapy. Our decision not to start on any targeted antivirals inspite of well-documented complications of hepatic flares was encouraged by the fact that his liver enzymes and HBV DNA titers were decreasing spontaneously. Not many spontaneous seroconversions have been reported in literature, ours being unique in that, he developed seroconversion following a flare without any residual cirrhosis. He is on regular follow up with us.

CONCLUSION

Flares are a well-documented entity in Chronic Hepatitis B. As a physician it is imperative to differentiate between acute hepatitis B and hepatic flares of chronic hepatitis B. It is well known that hepatic flares can lead on to dreaded complications like cirrhosis and acute liver failure, with some going on to develop complete recovery without any complications, like our case. But further studies are needed to better understand which group of patients are likely susceptible to develop complications and who may go on to recover completely.

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