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Patient with Hepatitis B Virus: From Active Acute Into Recovery Phases: A Case Report.

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Case Report

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ABSTRACT

A 24-year-old male with no prior history of liver disease was diagnosed as symptomatic active acute HBV infection with HBsA gand HBe Ag positivity with elevated HBVDNA and aminotransferase levels. The patient was followed for 18 months in order to investigate the evolution of his HBV serological profiles, HBV DNA and aminotransferase levels. Subsequently, an 18 month after the initiation of HBV, laboratory tests revealed that HBs Ag was negative, HBs Ab was positive, HBe Ag had decreased with a concomitant increase of HBe Ab, the quantity of HBV DNA was undetectable, and liver function had stabilized. I suggest that HBV-associated antigens and antibodies should be regularly tested.

INTRODUCTION

Hepatitis Bis a DNA virus that belongs to the Hepadnaviridae family [1]. It is a partially double-stranded circular DNA virus consisting of a core capsid which contains viral DNA and this is surrounded by an envelope containing surface antigen (HBsAg) that is produced during the replication of the virus [2]. The genes of HBV comprise genetic codes that create numerous protein products including Hepatitis B surface Antigen (HBsAg), Hepatitis B core Antigen (HBcAg), Hepatitis B e Antigen (HBeAg) and DNA polymerase [3]. These four proteins are of vital significance as they are measured in blood tests and aid in the diagnosis of the virus [4]. Hepatitis B virus (HBV) is one of the major diseases of mankind and is a serious global public health problem, of the 2 billion people who have been infected with the HBV, more than 350 million have chronic infections [5]. HBV infections result in 500,000 to 1.2 million deaths per year caused by chronic Hepatitis, Cirrhosis, and Hepatocellular carcinoma [6]. Here I presented a case which recovered from active acute viral hepatitis B infection.

Case Report

A 24 year old male, in 3/9/2012 was diagnosed with a 6-day history of fever, weakness, myalgia, abdominal pain in the right upper quadrant, headache, fatigue, vomiting, nausea, anorexia and jaundice. The patient developed anemia and weight loss.

The patient born and living in Basra /Iraq. Past history of any disease and drug was negative including preexisting liver disease, addiction, alcohol abuse, sexual contact, and surgery and tattooing.

He has no family history of liver disease. He was not vaccinated against HBV. Also he did not receive blood or blood product transfusion.

HBV-related serum makers and anti-HCV were detectionby ELISA test (Foresightkit, USA) that shown in detail in table(1).Furthermore, the HBV DNA titer was detected (Sacace Biotechnologies, USA)by using Real time PCR technique (Applied Biosystems, USA)with a detection limit of 250copies/Ml.

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Initial serum HBsAg, anti-HBc IgM, Total anti-HBc and HBeAg were positive, anti-HBs, anti-HBe, and anti-HCV were negative. HBVDNA was 9 × 10^6 copies/Ml. Thus I concluded that thecause of the active acute hepatitis was HBV.

Hislaboratory findings were as follows:AST:208 U/L, ALT: 131U/L, alkaline phosphatase (ALP):102 U/L, total bilirubin: 195umol/L, directs bilirubin: 157umol/L and in direct bilirubin: 38umol/L (Table, 1).

Subsequently, on a follow-up one month later, his serum HBsAg persisted as still positive but HBeAg was negative, while anti-HBe could be detected positive. Histransaminase levels and bilirubin were also still times high of the upper limit of normal, but HBV DNA was decreased from 9 × $10^6$to 4364 copies/Ml.

On the 3th month of follow up, serological markers and results of HBV DNA viral load that shown in detail in table [1] were indicated inactive viral replication. Serum aminotransferase levels were decreased in comparison with the previous values but still high. The quantity of HBV DNA was undetectable.

After a period of 6 months the patient was exposed to HBV viral load and liver enzymes assessment, HBsAg and anti-HBc IgM could be detected negative, HBV DNA was undetectable. At that time his laboratory parameters showed the liver aminotransferase levels were dramatically improved within normal ranges. After this period, the results remained stable until 18th month of follow up.

An 18th month after starting infection, follow-uptests showed that HBsAg was negative, HBsAb was positive, HBeAg was negative, HBeAb was positive, anti-HBcIgM was negative, Total anti-HBc was positive, and HBV DNA was assayed and still undetected by real-time PCR.

Table 1: Serological, molecular and biochemical parameters of the patient

Parameters	Months							
	Initial	1	3	6	9	12	15	18
HBsAg	+	+	+	-	-	-	-	-
HBsAb	-	-	-	-	-	-	-	+
HBeAg	+	-	-	-	-	-	-	-
HBeAb	-	+	+	+	+	+	+	+
Ant-HBcIgm	+	+	+	-	-	-	-	-
Total ant-HBc	+	+	+	+	+	+	+	+
HBV DNA copies/ml	9 × 10^6	4364	Un*	Un	Un	Un	Un	Un
TSB Normal value (5-17 umol/L)	195	245	42	18	12	10	7	6
SB (Direct) Normal value (<5 umol/L)	157	160	27	6	5	4	3.5	3
SB(Indirect) Normal value (<12 umol/L)	38	85	15	12	7	6	6.5	7
ALT Normal value (<12 IU/L)	131	155	40	15	12	10	11	10
AST Normal value (<12 IU/L)	208	120	12	12	11	10	10	11
ALP Normal value (21-92 IU/L)	102	91	75	64	55	40	35	33

*Undetectable ** Normal value

DISCUSSION

Both molecular and serologic testing methods are useful for interpreting the HBV status of a patient. However, because there are many different HBV markers, it is critical to understand how the appearance of a marker relates to a patient's disease or infection state. Research on HBV has clarified the clinical utility of specific HBV markers and has improved their diagnostic use [7].Outcome after acute HBV infection and its course may be influenced by the host immune response [8], host genetic factors and environmental factors including HBV genotype are widely viewed as common basis of the different outcomes of HBV infection [9].

Hereby, I report a case of hepatitis B virus infection who presented with active acute manifestations. The patient was followed for 18 months in order to investigate the evolution of his HBV serological profiles,the liver aminotransferase levels and HBVDNA. He does not given any therapy. He did not have any history of HBV.

Initial laboratory examination (Table, 1) revealed an HBsAg, HBeAg and anti-HBc antibodies were positive, HBV DNA was 9 × 10^6 copies/Ml. The liver aminotransferase levels were detected higher than normal ranges. As a result, the patient was diagnosed as active acute HBV infection. Thimme *et al*., [10] show that after inoculation, HBV does not immediately start to replicate efficiently. HBV-DNA and HBV

antigens are not detectable in serum or the liver until 4-7 weeks post-infection [11]. Following this period, HBV begins a logarithmic expansion phase that can be detected in the liver and serum, reaches levels of 10^9- 10^{10}copies / ml and infects most hepatocytes [12].

HBsAg is an antigen on the three proteins that make up the envelope of the HBV virion. HBsAg, formerly called "Australia Antigen," is the first serologic marker to appear and can be detected 1-2 weeks or as late as 11-12 weeks following exposure .It is clear within six months of onset in 90% of people who acquire Hepatitis B. HBsAg positivity persists beyond 6 months in 10% of infected individuals and is indicative of chronic hepatitis B [7, 13].

The HBV core antigen is not found as a discrete protein in the serum. In acute infection, IgM anti-HBc is found in high concentrations which gradually decline, complementing the corresponding increase in IgG anti-HBc over a three to six month period[14]. Elevation of anti-HBcIgM usually signifies acute infection, but low elevations may also occur during the reactivation of chronic HBV. It is also useful in the 'window' period, when HBsAg has become negative, and the patient has not yet developed anti-HBs [7]. Therefore, the initial diagnostic tests performed on patients presenting with a recent history of symptoms of viral hepatitis should include an IgM anti-HBc, as well as an HBsAg [13]. Most serological assays measured total anti-HBc and do not directly measure IgG anti-HBc[15]. HBeAg appears a few days after HBsAg becomes detectable and typically disappears before HBsAg is gone, although it might persist for years in a chronic carrier of hepatitis B virus[7, 13].

AST and ALT are considered hepatocellular enzymes and are released into the serum when liver cells are damaged or destroyed .In typical viral injury, the serum ALT level rises more than the AST value, reflecting the relative amounts of these enzymes in hepatocytes [16].

One month, also 3th month later, AST, ALT and serum bilirubin still high, and his serum HBsAg and HBeAb could be detected positive. Serum HBV DNA has declined to 4364copies/ml and then undetectable, respectively. In the follow-up for 6 into 18 months, HBsAg and anti-HBc IgM were negative, HBV DNA was undetectable, the liver aminotransferase levels were within normal ranges, but all the time anti-HBs remained negative.

In approximately 50% of patients with self-limited hepatitis B virus infection, there is a time interval of up to several months between the disappearance of detectable HBsAg and the appearance of anti-HBs. During this time, only the anti-HBc is detectable; this period is referred to as the "core window" or "window phase" [7]. While anti-HBe is not a protective antibody, its appearance usually coincides with a significant immune change associated with lower HBVDNA replication <10^5 copies/mL or 20,000 IU/ml [15]. The loss of HBeAg and the development of anti-HBe is termed HBeAgsero conversion, and has been used as an end-point for treatment in HBeAg-positive people, as it has been shown that sero conversion is associated with a lower risk of disease progression [17]. The serum level of HBV DNA is a dynamic parameter in chronic HBV. The level of circulating HBV has recently been shown to be the strongest predictor of the development of Cirrhosis and HCC [18]. The level of 20,000 IU/mL(around 10^5 copies/ml) has been arbitrarily selected as the level below which there is a relatively low likelihood of hepatic damage, although this can still occur [19]. Patients with HBeAg-negative chronic HBV are distinguished from inactive HBV carriers by the presence of >10^4 HBV DNA copies/ml (or >2000 IU/ml), In contrast, inactive HBV carriers usually have undetectable HBV DNA [20].

Interestingly, following 18thmonth of infection, HBsAb was positive and HBV DNA still undetected. HBsAb is a protective antibody that develops with the resolution of acute infection or following the successful vaccination against HBV [15]. Some persons who are HBsAg-positive will develop detectable anti-HBs; however, these persons are still considered infectious due to the presence of HBsAg [21]. Antibody production is critical for the neutralization of free HBV particles, the interference with virus entry into the host cells and contribute to limit cell to cell spread of viral particles, but anti-envelope antibodies are not detectable because they complexes with the excess of envelope antigens produced during virus replication [22]. This interval provided time for continued viral suppression and clinical improvement. Hereby, he healed and all abnormal laboratories as normal with a good condition. The patient was doing well. The patient's last relapse was detected 1year ago. He has been followed up inremission for 1.6 years. Ultimately, the patient was prescribed he patient made a full recovery.

In conclusion, long term follow-up of the patient in the future was recommended. My aim with this case report was to underline the importance of an early diagnosis of hepatitis B virus infection. he present

report showed that one of the best reliable markers of hepatitis B virus infection were antibodies to the core antigen (anti-HBc) and early HBeAg sero conversion was associated with recovery outcome.

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