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JSM Gastroenterology and Hepatology

Case Report

Dramatic Reduction of the Alpha-Fetoprotein Level after Entecavir Treatment of a Patient with Chronic Hepatitis B

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Submitted: 19 December 2013

Accepted: 15 January 2014

Published: 20 January 2014

Keywords
- Alpha-fetoprotein (AFP)
- Hepatitis B
- Hepatocellular Carcinoma (HCC)

Abstract

Extremely high alpha-fetoprotein (AFP) levels of 1924.7 ng/ml were found in a 43-year-old man with advanced chronic hepatitis B. After treated with entecavir (ETV) for 23 days, the AFP level was dramatically decreased to 231.4 ng/ml, and returned to normal one month later (11.4 ng/ml). No clear evidence of hepatocellular carcinoma (HCC), germ cell tumors, and metastatic cancers of the liver appears to be associated with this clinically benign disorder. In conclusion, high AFP level do not necessarily lead to HCC, and the dramatic reduction of AFP is possibly due to suppression of viral replication and associated hepatic inflammatory activities by ETV. This observation may be helpful in the diagnostic evaluation and management of chronic hepatitis B patients with markedly elevated alpha-fetoprotein levels.

INTRODUCTION

Physiologically, AFP is synthesized primarily in the fetal liver cells, and up to 4 mg/ml at 12 to 16 weeks of pregnancy, about two weeks after birth, AFP levels usually fall and disappear from the blood, so the normal serum levels of AFP is nearly undetectable (less than 12 ng/ml by RIA) [1]. However, AFP levels can rise above normal in abnormal conditions and disorders which will be discussed.

Hepatitis B is a liver disease that results from infection with the Hepatitis B virus, which causes transient and chronic infections of the liver. Acute Hepatitis B virus infection is a short-term illness that occurs within the first 6 months after exposed to the Hepatitis B virus, and may recover completely or spontaneously from the infection [2]. Acute infection can also lead to chronic infection, which is a long-term illness that occurs when the Hepatitis B virus remains in a person's body. Chronic Hepatitis B is a serious disease that can result in long-term health problems and life-threatening complications such as cirrhosis and HCC [3].

AFP is a marker of the presence of HCC, the AFP levels diagnostic for HCC are above 200 or 400 ng/ml [4]. Hepatitis B patients and HBV cirrhotic patients with rising AFP levels were at very high risk of HCC development. However, AFP is also slightly elevated in advanced chronic hepatitis B. In this report, we presented a patient with chronic hepatitis B who experienced episodes of marked elevations in serum AFP levels, which dramatically decreased to normal after treated with ETV.

CASE REPORT

In July 2013 a 43-year-old man with a 30 years medical history of hepatitis B but who was concerned that his condition might have progressed presented at our outpatient unit. He had developed intermittent right upper abdominal pain for 2 years, and had noted scleral icterus for the past 20 days. By our examination, yellow dye was found in the sclera, and the skin of whole bady is duck. The remaining physical examination was normal. His serum AFP level was elevated (1924.7 ng/ml; normal < 12 ng/ml by RIA). HBV DNA 3.06E+07 IU/ml (normal < 100 IU/ml), AST 124 U/L (normal 15-40 U/L), TBIL 200.8 μmol/L (normal 5-23μmol/L), DBIL 149.7 μmol/L (normal 0-6.8μmol/L) and IBIL 51.1 μmol/L (normal 1.7-17μmol/L). ALT, ALP tests were normal. An ultrasound found a gallstone and also showed normal liver, pancreas, spleen. An abdominal MRI was carried out, and showed no abnormality except cholecystitis.

After treated with ETV (a nucleotide analogue) receiving 0.5 mg orally daily and receive an intravenous injection of Succinic Acid Monomethyl ester (SAM) 1g daily for 23 days, the serum AFP level gradually reduced to 231.4 ng/ml. Laboratory tests showed

that HBV DNA 2.49E+06 IU/ml, AST 76U/L, TBIL 52μmol/L, DBIL 39.3μmol/L and IBIL12.7μmol/L. Another 1 month later, the serum AFP, AST, TBIL, DBIL and IBIL returned to normal (AFP 11.4 ng/ml, AST 29 U/L, TBIL 10.7 μmol/L, DBIL 5.5 μmol/L,IBIL 5.2 μmol/L, respectively) and HBV DNA was down-regulated to 4.91E+02 IU/ml.

DISCUSSION

HCC is the third leading cause of cancer related mortality worldwide, and the global prevalence and mortality resulting from HCC is directly related to underlying risk factors for primary liver cancer [5]. Although several chronic liver diseases are associated with HCC, hepatitis B Virus (HBV) is the most common cause of HCC worldwide. Disease activity may flare during the natural course of chronic HBV infection, and repeated episodes may lead to progressive fibrosis, cirrhosis, and end-stage liver disease including HCC. The longer the HBeAg-positive state is maintained, the greater the risk of developing cirrhosis and HCC, which is a reflection of active disease over a prolonged period [6].

It was confirmed that therapy for chronic hepatitis B reduces the risk of progressing to HCC [5]. Although the impact of antiviral therapy is also uncertain, there is good evidence that continuous antiviral therapy with ETV may reduce the activity of HBV in patients with chronic hepatitis B and reduce the risk of complications and disease progression in patients with chronic HBV infection, moreover, long-term ETV treatment may reduce the incidence of HCC in HBV-infected patients, and the treatment effect was greater in patients at higher risk of HCC [7,8].

The most important challenge is develop improved means of early detection and treatment of HCC in hepatitis B. Currently, HBV-related HCC is often detected too late for surgical interventions and liver transplantation. Convenient applied biomarkers for HCC in high risk patients would be helpful in identifying patients at an early stage of tumor. AFP can be used to screen for HCC in high-risk patients with chronic hepatitis B [9]. An elevation of alpha fetoprotein ≥ 200 and 400 ng/ml, or a progressive elevation of alpha fetoprotein ≥7 ng/mL/month in patients that do not reach AFP levels ≥200 ng/ml is useful for the diagnosis of hepatocellular carcinoma [10]. HBV cirrhotic patients with rising AFP levels were at very high risk of HCC development. Early detection of minute lesions may be possible by monitoring AFP levels, while patients are on treatment in conjunction with enhanced computed tomography examination [11].

In the present patient, the elevation of his AFP levels was thought unlikely to be related to the development of tumor for the following reasons: (i) the AFP level was dramatically reduced to normal after treated with ETV; (ii) detailed radiographic evaluations and ultrasound did not show the possibility of tumor; (iii) the transaminase and bilirubin was normal after treatment. This report also indicated that rapid decline in AFP after treatment is helpful for the diagnosis of specific types of chronic hepatitis B. It is well known that persistently elevated AFP levels are related to the presence of HCC, chronic hepatitis B patients with increased AFP have the possibility to develop HCC. However, since our observation is not long enough, or some extremely small lesions might be undetectable by the current means, so chronic hepatitis B patients with higher level of AFP should undergo periodic AFP and ultrasonic wave screening (every 6 to 12 months) for early diagnosis and treatment of hepatocellular carcinoma.

CONCLUSION

Our report describes a patient with chronic hepatitis B who experienced episodes of marked elevations in serum AFP levels, which dramatically decreased to normal after treated with ETV. With regard to the marked elevations in serum AFP, which can be dramatically reduced by ETV, the occurrence of this clinically benign disorder may be helpful in the diagnostic evaluation and management. To avoid inappropriate treatment decisions, this condition should be considered in patients with unexplained elevation of AFP, e.g., those screened for hepatocellular carcinoma or diagnosed for germ cell tumor. However, chronic hepatitis B patients with higher level of AFP should undergo periodic AFP and ultrasonic wave screening for early diagnosis and treatment of hepatocellular carcinoma.

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Cite this article

Liu YQ, Li JF, Qian ZP, Cui HY, Yang JQ, et al. (2014) Dramatic Reduction of the Alpha-Fetoprotein Level after Entecavir Treatment of a Patient with Chronic Hepatitis B. JSM Gastroenterol Hepatol 2(2): 1012.