

CASE REPORT

The acute hepatic flare in a patient with chronic hepatitis C infection receiving pegylated interferon alpha 2b and ribavirin

Hayati Demiraslan, Zeynep Türe, Ayşegül Ulu Kılıç

Erciyes University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Melikgazi, 38039, Kayseri, Turkey

ABSTRACT

The pegylated interferon alpha and ribavirin treatment is well established therapy for hepatitis C virus (HCV) infection. During the treatment alanine aminotransferase (ALT) flare may be observed rarely.

A 51-year-old female receiving pegylated interferon and ribavirin therapy for HCV infection, complained nausea, vomiting in seventh week of the therapy, and her ALT level was detected over 20 times above the normal level. Hepatitis B surface antigen, anti-nuclear antibody, anti-mitochondrial antibody, anti-double stranded DNA antibody and anti-hepatitis A virus IgM antibody were negative, and thyroid stimulating hormone was normal. HCV RNA level was 424 IU/ml. PEG IFN and ribavirin therapy was interrupted for three weeks, after liver enzyme level was detected less than 100U/L, the treatment was resumed. The patient was followed up for 2 months, ALT flare was not observed.

In conclusion, we present a rare case with ALT flare, while receiving pegylated interferon and ribavirin therapy for chronic HCV infection. *J Microbiol Infect Dis* 2012; 2(3): 121-123

Key words: Pegylated interferon, ribavirin, ALT flare, hepatitis C virus

Pegile interferon alfa 2b ve ribavirin tedavisi alan kronik hepatit C enfeksiyonlu bir hastada gelişen akut hepatik alevlenme

ÖZET

Pegile interferon alfa ile birlikte ribavirin tedavisi hepatit C virüs (HCV) enfeksiyonu için iyi tanımlanmış tedavidir. Bu tedavi süresince alanin aminotransferaz alevlenmesi nadiren gözlemlenebilir.

HCV enfeksiyonu için pegile interferon ve ribavirin tedavisi alan 51 yaşında kadın hasta tedavinin yedinci haftasında bulantı, kusma şikayetleriyle başvurdu ve ALT düzeyi normalin 20 katından fazla artmış olarak saptandı. Hepatit B yüzey antijeni, anti-nükleer antikor, anti-mitokondrial antikor, anti-double stranded DNA antikoru, anti-hepatit A IgM negatif ve tiroid stimulan hormon düzeyi normaldi. HCV RNA düzeyi 424 IU/ml idi. PEG IFN ve ribavirin tedavisine üç hafta ara verildi, karaciğer enzimleri 100 U/L'nin altına indikten sonra tedavi tekrar başlandı. Hastalar iki aya kadar takip edildi, ALT yükselmesi gözlenmedi.

Sonuç olarak, kronik HCV enfeksiyonundan dolayı pegile interferon ile birlikte ribavirin almaktayken ALT alevlenmesi gelişen nadir bir olgu sunuyoruz.

Anahtar kelimeler: Pegile interferon, ribavirin, ALT alevlenmesi, hepatit C virüsü

INTRODUCTION

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. Approximately 3% of the world population is chronically infected with HCV, geographically the prevalence of HCV is approximately 1.0% in Turkey.^{1,2} Early diagnosis and treatment is important to prevent progressing cirrhosis or hepatocellular

carcinoma. The combination of pegylated interferon (PEG IFN) alpha and ribavirin is well established therapy for HCV infection.^{2,3} During the therapy for HCV infection some adverse effects (psychiatric side effects or laboratory abnormalities) may induce to discontinue the treatment. Interferon induced flares have been attributed to the stimulatory effect of IFN.⁴ However, during the treatment of HCV infection ALT flare may be ob-

Correspondence: Hayati Demiraslan, Erciyes University, Faculty of Medicine,

Department of Infectious Diseases and Clinical Microbiology, Melikgazi, Kayseri, Turkey Email: tigin68@yahoo.com

Received: 06 July 2012, 2012 Accepted: 24 August 2012

Copyright © Journal of Microbiology and Infectious Diseases 2012, All rights reserved

served rarely.³ We present a case receiving HCV infection treatment with pegylated interferon alpha 2b and ribavirin with ALT flare detection.

CASE REPORT

A 51-year-old female attended our hospital with positive anti-HCV test performed before surgical operation in September 2011. There was no history of tooth extraction, surgical procedures, blood transfusion, insecure sexual intercourse or infected people in her family.

She has no hepatitis B co-infection or HIV, furthermore the alanine aminotransferase (ALT) level was 58 U/L (range 10-49), gamma-glutamyl transferase was 48 U/L (range 0-38), HCV RNA was 151,000 IU/ml (Cobas TaqMan, Germany), the HCV genotype (QIAamp DSP Virus Kit, Germany) is 1b, alpha fetoprotein was 15.1 ng/ml (range 0 to 8.1), abdomen ultrasonography was normal during hospital admission. In December 2011, liver biopsy was performed; according to Ishak's score, histological activated index was 7/18, and fibrosis was 2/6. Her body weight was

96 kilograms, accordingly every week 1.5 microgram/kg of PEG IFN alpha 2b and ribavirin 1200 mg/day were administered.

After four weeks the laboratory results were as follows; leukocyte count was 2,660/mm³, hemoglobin level 12.5 g/dl, platelet count 139,000/mm³, ALT 53 U/L, and HCV RNA 424 IU/ml in terms of rapid virological response (RVR). On the sixth week of therapy, her ALT level was increased (187 U/L), leukocyte count, platelet and hemoglobin level were decreased, 1,630/mm³, 96,000/mm³ and 11.6 g/dl, respectively. On the seventh week, she complained nausea and vomiting, an increased level of ALT 1,356 U/L, and total/direct bilirubin 2.9/2.0 mg/dl were observed, and consequently PEG IFN and ribavirin treatment were discontinued. Furthermore, during the mounting period of ALT level, she was not on any other medications such as herbal or recreational drugs, and also denied use of alcohol. Henceforward, after four days her ALT level decreased up to 965 U/L and 7 days later it was decreased to 358 U/L. Figure 1 shows the course of ALT, termination and resuming points of therapy.

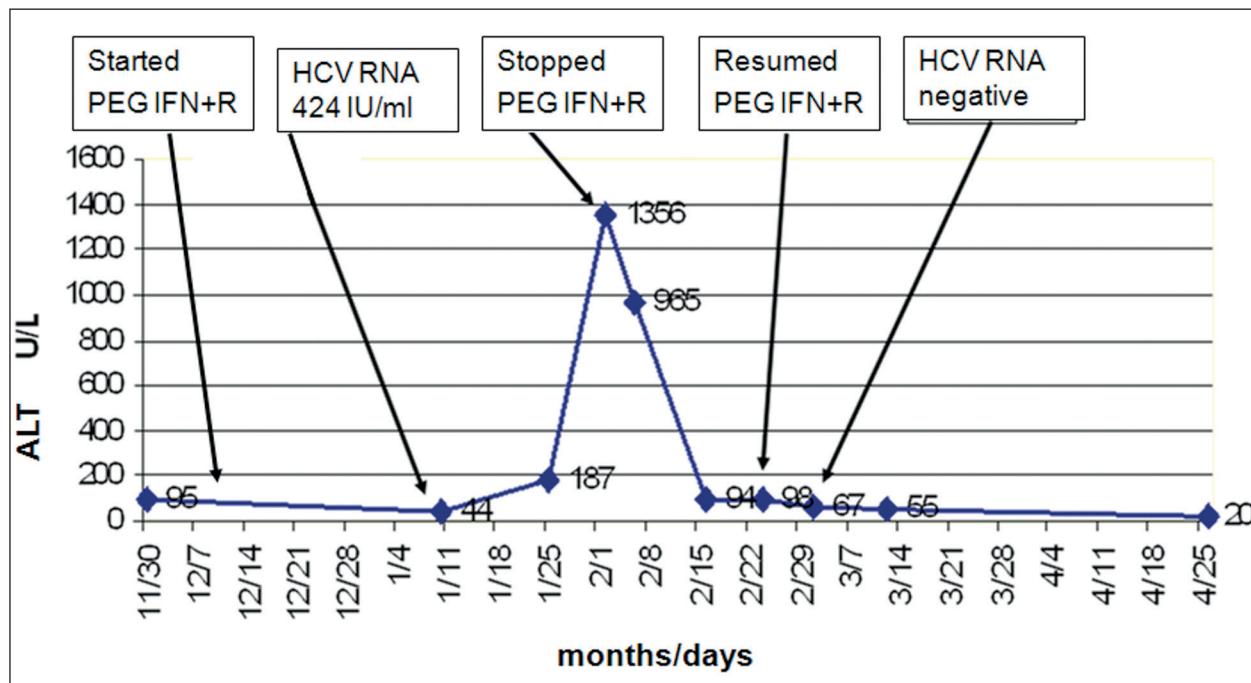


Figure 1. The course of ALT, and termination and resuming points of the therapy

PEG IFN+R: Pegylated interferon and ribavirin

Twenty-two days after the discontinuation of PEG IFN and ribavirin therapy, the laboratory results of ALT were 98 U/L, bilirubin 1.6 mg/dl, leukocyte count 2,910/mm³, platelet count 88,000/mm³ and hemoglobin 13.5 g/dl. Hepatitis B surface antigen, anti-hepatitis B core antibody, anti-hepatitis A virus IgM antibody, anti-smooth muscle antibody, anti-mitochondrial antibody, anti-nuclear antibody, anti-double stranded DNA antibody were negative. Thyroid stimulating hormone was normal, however, rheumatoid factor was 939 IU/ml (range 0 to 20), anti-hepatitis A virus IgG antibodies were positive; thereupon PEG IFN and ribavirin therapy was resumed. HCV RNA was controlled in terms of virological breakthrough and was found to be negative. The patient was followed up for two months and ALT flare was not observed.

DISCUSSION

Currently recommended therapy of chronic HCV infection is combination of PEG IFN alpha and ribavirin. About 10% to 14% of the patients have to discontinue HCV infection therapy due to adverse affects.^{3,5} The most common affects are flu-like symptoms such as fatigue, headache and fever, psychiatric side effects (depression, irritability, insomnia) and laboratory abnormalities.³ In European Association for the Study of the Liver (EASL) guidelines recommends treatment should be stopped in case of severe hepatitis flare. We know that hepatic flares occur due to stimulatory effect of interferon because of T-cell cytolytic activity and natural killer cell function. Another cause of hepatic flare during the interferon based therapy is autoimmune phenomena.² During the IFN treatment for HBV patients, interferon induced flare is observed between 25 to 40% but, the flare is unusual in HCV patients. ALT flare during IFN treatment for hepatitis B may be associated with increased virological response,⁶ however, during IFN use for hepatitis C therapy the mechanism of flare remains unknown.

Detecting the cause of ALT flare is usually difficult; three cases have been reported observing ALT flares 10-20 times above the upper level of normal in 12th week of PEG IFN alpha 2a and ribavirin. Anti-Golgi complex antibody has been detected.⁷ Moreover, a case of incomplete cirrhosis caused by HCV and HBV co-infection has

been reported, the patient suffering from hepatic decompensation in seventh month of IFN and ribavirin treatment.⁸ Another case has been reported that treated with PEG IFN 2a and ribavirin, he had ALT flare, and in 23rd week of the therapy, it had been discontinued. Virological breakthrough had been detected, and PEG IFN 2b and ribavirin had been given to patient, and ALT flare had been observed in the 12th week of therapy.⁹ In our case, the serum ALT levels of the patient increased up to 1,356 U/L at seventh week, and virological breakthrough was not observed. Moreover, most of autoimmune antibodies were found to be negative. Furthermore, the patient refrained from liver biopsy, limiting our scope from cytomegalovirus, Epstein-Barr virus, Herpes Simplex virus and toxoplasmosis serological tests. Hence, therapy was restarted and hepatic flare was not observed. As a result, the ALT flare may occur as associated with IFN treatment not only for HBV but also for HCV infection. Interruption of treatment is enough to recover ALT in HCV infection treatment with PEG IFN and ribavirin.

REFERENCES

- Cornberg M, Razavi HA, Alberti A, et al. A systematic review of hepatitis c virus epidemiology in Europe, Canada and Israel. *Liver Int* 2011;31 Suppl 2:30-60.
- Calvaruso V, Craxi A. 2011 European Association of The Study of The Liver Hepatitis C Virus Clinical Practice Guidelines. *Liver Int* 2012; 32 Suppl 1:2-8.
- Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: An update. *Hepatology* 2009; 49:1335-1374.
- Amarapurkar DN. Flares on and off therapy during chronic hbv infection: Pathogenesis, significance and management. *Hep B Annual* 2008;5:12-22.
- Demiraslan H, Aygen B, Yildiz O, Soyuer I, Gokahmetoglu S. Kronik hepatit C tedavisinde interferon- α 2a+ ribavirin ile peginterferon- α 2a ribavirin kombinasyonlarının karşılaştırılması. *Viral Hepat Dergisi* 2008;13:12-22.
- Flink HJ, Sprengers D, Hansen BE, et al. Flares in chronic hepatitis b patients induced by the host or the virus? Relation to treatment response during peg-interferon alpha-2b therapy. *Gut* 2005;54:1604-1609.
- Parana R, Schinoni MI, de Freitas LA, et al. Anti-golgi complex antibodies during pegylated-interferon therapy for hepatitis C. *Liver Int* 2006;26:1148-1154.
- Yalcin K, Degertekin H, Yildiz F, Kilinc N. A severe hepatitis flare in an HBV-HCV coinfecting patient during combination therapy with alpha-interferon and ribavirin. *J Gastroenterol* 2003;38:796-800.
- Mishra P, DeVoss A, Pai R, Hart J, Jensen DM. Marked flare in hepatic aminotransferases during treatment with pegylated interferon for chronic hepatitis C, genotype 2: A case report. *Dig Dis Sci* 2009; 54:1369-1372.