



Hepatocellular Carcinoma Developing in HIV/HBV Co-Infection: Case Presentation

Hepatoselüler Karsinom Gelişen HIV/HBV Koefeksiyonu*

Ayşe İNCİ¹, Muzaffer FİNCAKİ²

¹Artvin State Hospital, For Infectious Diseases and Clinical Microbiology, Artvin, Turkey

²Istanbul Education and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

ABSTRACT

Following antiretroviral treatment, the mortality rates associated with human deficiency virus (HIV) infection decreased, and HIV infection became a chronic disease. The hepatitis-associated liver injury in HIV-infected cases has been one of the important reasons for mortality and morbidity in these patients. The co-morbidity of HIV and hepatitis infections is common due to the fact that their routes of transmission are similar. HIV infection affects the course of hepatitis B virus infection negatively. In this study, a 68-years old case with hepatocellular carcinoma, co-infected with HIV/HBV was presented. (*Viral Hepatitis Journal* 2014; 20(1): 40-42)

Key words: CHIV, HBV, co-infection

ÖZET

Antiretroviral tedavi sonrası insan immünyetmezlik virüsü [human deficiency virus (HIV)] enfeksiyonu ile ilişkili ölüm oranları azalmış, HIV enfeksiyonu, kronik bir hastalık hâline gelmiştir. HIV enfekte olgularda hepatite bağlı karaciğer hasarı önemli mortalite ve morbidite nedenlerinden biri olmuştur. Bulaş yollarının benzer olması nedeni ile HIV ve hepatit enfeksiyonlarının birliliktebine sık rastlanmaktadır. HIV enfeksiyonu hepatit B virüsü enfeksiyonunun seyrini olumsuz yönde etkilemektedir. Bu çalışmada, hepatoselüler karsinom gelişmiş olan HIV/HBV koefeksiyonlu 68 yaşındaki bir olgu sunulmuştur. (*Viral Hepatitis Dergisi* 2014; 20(1): 40-42)

Anahtar Kelimeler: HIV, HBV, koefeksiyon

Introduction

Chronic hepatitis with hepatitis B virus (HBV) acute hepatitis is a major health issue throughout the world and in our country because of the fact it leads to liver/hepatic cirrhosis and hepatocellular carcinoma (HCC) (1).

In our country, according to the 2011 data from the Ministry of Health, it was reported that there were 5224 human deficiency virus (HIV)-infected cases (2). HCC is usually seen with chronic liver disease, increasing in prevalence in recent years and the challenges in its diagnosis and treatment still continue.

Biopsy, imaging methods and biochemical indicators are utilized in the diagnosis of HCC. Alpha-fetoprotein (AFP) is used as a biochemical indicator, while ultrasonography (USG),

computerized tomography and magnetic resonance imaging (MRI) are utilized as imaging methods (3,4).

Chronic HBV infection is commonly seen in HIV-infected people. The association of HIV with hepatitis infections is rather common due to the similarity in their modes of transmission. HIV infection enhances the course of the liver disease caused by chronic HBV infection (5,6,7).

Our country is located in an endemic region average in HBV infections and low in HIV ones (8). HIV infection affects the natural course of HBV infection in a negative way. It reduces the anti-HBe and anti-HBs seroconversion rates. The HBV replication levels increased in HIV-infected patients. More rapid progression of liver fibrosis is shown in co-infected patients. HIV hepatitis

co-infection is an important risk factor for HCC. HCC in the first HIV-infected case was reported in 1999 (9,10,11).

In this study, a 68-years-old male case with HIV/HBV co-infection has been presented.

Case

The 68-years-old male patient who admitted to our polyclinic four years ago with the complaint of fever and dysphagia (difficulty in swallowing) was referred to our service for further examination. During his examinations, the anti-HIV test was determined to be positive. The patient whose anti-HIV positivity was verified through Western Blot was followed-up with the diagnosis of HIV syndrome. No peculiarity/special feature were determined in the patient's case and family history. As for the route of transmission, a possible heterosexual contact was taken into consideration. No alcohol, drug use or smoking habits were found. No pathological finding was ascertained in his physical examination. Considering the laboratory results, in his complete blood count (CBC), the values were as follows: WBC: 4200 / μ L, Hb: 14 g/dL, platelet number: 128 000 / μ L; in his biochemical examinations, the values were as follows: ALT: 32 U/L, AST: 24 U/L, BUN: 28 mg/dL, creatinine: 0.8 mg/dL, glucose: 92 mg/dL, and in the serological analysis, they were determined as HBsAg (+), anti-HBc IgG (+), anti-HBs (-), anti-HCV (-). The CD4 lymphocyte counts during the case's application to the clinic were ascertained to be 76 cells/mm³ and HIV-RNA: 323 352 copy/mL, HBV-DNA: negative. The tenofovir/emtricitabine and efavirenz treatments were started for the patient. As the result of the 4-years-patient follow-ups, the CD4 level was increased up to 865 cells/mm³. HIV-RNA and HBV-DNA become negative in the sixth month of the antiretroviral treatment (ART), and their negativity continued throughout the patient follow-up period. Upon detecting a mass (tumor) in the liver through the USG performed in the 4th year of the patient follow-up, a dynamic MRI examination was applied. The AFP level of the patient checked at that time was seen to be 1980. Results of the dynamic MRI revealed amorphous lesions (lesions, the boundaries of which were unclear) with 5.5 cm in diameters in the liver, showing a T2A- hyperintense and a T2A- heterogenous hypointense contrast involvement. The patient was exitus in his 4th year follow-up after the diagnosis.

Discussion

As the result of the application of ART, the mortality rates associated with HIV infection decreased, and HIV infection became a chronic disease. The liver injury that occurred due to hepatitis viruses in HIV-infected cases has been one of the important reasons for mortality and morbidity in these patients (12).

In a study carried out in Western Europe and America, the rate of incidence of chronic HBV infection in HIV-infected cases was reported to be 6%-14% in heterosexuals, 9%-17% in homosexuals and 7-10% in the group using intravenous drugs (13). While the rates of incidence of hepatitis B infection in HIV-infected patients were reported to be 4.4%, 4%, 4.8% and 14.2% respectively in studies performed in our country, these rates were suggested to be 8.7%, 6.3%, 7.9%, 9.9%,

respectively considering some of the studies carried out abroad (14,15,16,17,18,19,20,21).

In a study conducted by Thio et al., when the HIV-positive cases were concerned, the mortality due to liver disease (hepatopathy) in cases with HBsAg (+) turned out to be 14.2/1000 patients per year, whereas in those with HBsAg (-), it turned out to be 1.7/1000 patients per year, and this was statistically significant (22).

In a multicenter study performed for the matter involved, it was determined that 14% of mortality in HIV-infected cases was associated with the liver and that 16.9% of it was HBV-related (23).

The HBV indicators must definitely be checked out prior to highly active antiretroviral therapy. One of the drugs, such as emtricitabine, lamivudine and tenofovir should be applied in the co-infection therapy/treatment since they are effective against both HIV and HBV. Therefore, in ART, one of the combinations of tenofovir + emtricitabine or tenofovir + lamivudine should be preferred as a nucleoside reverse transcriptase inhibitor (24).

In a study conducted by Ocoma et al., HBsAg positivity in 13 out of 15 HCC cases and the existence of HIV-hepatitis B co-infection in 3 out of these 13 cases were reported (25). For the matter involved, a case presentation reporting that a HCC case with HIV/HBV co-infection was treated/cured successfully is included in the literature (26).

A biopsy could not be performed in our case, however, the fact that the AFP value was 1980 and HBsAg was positive, along with the MRI findings, gave rise to the thought that there was HCC in the forefront.

In a study carried out by Dülger et al. in our country, the AFP value in cases with HCC was found to be 308.9±385.6 ng/mL, while this value was measured as 30.3±72.7 ng/mL in cases with liver cirrhosis, and a significant difference was determined between them (27).

Again, in some studies conducted for the matter involved, the fact that the AFP level was high was reported to be associated with a shorter-term survival and to have negatively affected it (28,29).

Consequently, it is known that HIV infection affects the course of HBV infection negatively. The response rates of the patients with HIV/HBV co-infection to treatment and the experiences on the duration of therapy are insufficient.

We are in the opinion that the hepatitis indicators in HIV-infected patients are significant in terms of both the determination and treatment of the co-infection and the planning of the hepatitis B prophylaxis under necessary conditions.

Conflict of interest: None declared.

References

1. Madendağ Y, Çöl Madendağ I, Çelen Ş Ünlü S, Danışman N. Seroprevalence Of Hepatitis B, Hepatitis C And HIV At Whole Obstetric And Gynecologic Patients Who Applied Our Hospital. Turkiye Klinikleri J Gynecol Obst. 2007; 17: 442-446.
2. Temel Sağlık Hizmetleri Genel Müdürlüğü, Bulaşıcı ve Salgın Hastalıkların Kontrolü Daire Başkanlığı, Züherevi Hastalıklar Şubesi verileri. Ankara: TC Sağlık Bakanlığı; 2012.

3. Yazıcı O, Bahar K. Hepatosellüler karsinomda yeni tanı ve tedavi yöntemleri. *Güncel Gastroenteroloji*. 2008; 12: 47-52.
4. Taş A. Hepatosellüler Karsinom Tanı ve Tedavisi. *Güncel Gastroenteroloji*. 2010; 14: 145-148.
5. Koziel MJ, Peters MG. Viral hepatitis in HIV infection. *N Engl Med*. 2007; 356: 1445-1454.
6. Soriano V, Poveda E, Vispo E, Barreiro P. Hepatitis B in HIV-infected patients. *Clin Liver Dis*. 2013; 17: 489-501.
7. Shire NJ, Sherman KE. Management of hepatitis B virus in HIV-positive patients. *Minerva Gastroenterol Dietol*. 2006; 52: 67-87.
8. Altınbaş A, Ergünay K, Calık Başaran N, Alp A, Turgut D, Hasçelik G, ve ark. HIV Pozitif Olgularda Okült Hepatit B Varlığının Araştırılması. *Mikrobiyol Bul*. 2011; 45: 353-358.
9. Puoti M, Torti C, Bruno R, Filice G, Carosi G. Natural history of chronic hepatitis B in co-infected patients. *J Hepatol*. 2006; 44(Suppl 1): 65-70.
10. Nunnari G, Berretta M, Pinzone MR, Di Rosa M, Berretta S, Cunsolo G, Malaguarnera M, Cosentino S, De Paoli P, Schnell JM, Cacopardo B. Hepatocellular carcinoma in HIV positive patients. *Eur Rev Med Pharmacol Sci*. 2012; 16: 1257-1270.
11. Merchante N 1, Merinos E, López-Aldeguer J, Jover F, Delgado-Fernández M, Galindo MJ, Ortega E, Rivero A, Minguez C, Romero-Palacios A, Padilla S, Márquez-Solero M, Amador C, Ríos- Villegas MJ, Téllez F, J Portilla, Pineda JA. Increasing Incidence of Hepatocellular Carcinoma in HIV-Infected Patients in Spain. *Clin Infect Dis*. 2013; 56: 143-150.
12. Aygen B. HIV, Hepatit B /C koenfeksiyonları epidemiyoloji klinik ve tanı. *Türk HIV/AIDS Derg*. 2005; 8: 115-120.
13. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol*. 2006; 44 (Suppl 1): 6-9.
14. İnci A, Fincancı M, Soysal F. HIV/HBV koenfeksiyonlu olguların değerlendirilmesi. *Journal of Clinical and Analytical Medicine*. 2013; 1-4.
15. Kumbasar-Karaosmanoğlu H, Aydin AÖ, İnce ER, Nazlıcan Ö. HIV/AIDS Hastalarında Hepatit B ve Hepatit C Seroprevalansı. *Viral Hepatit Dergisi* 2009; 14: 53-56.
16. Kaptan F, Örmen B, Türker N, El S, Ural S, Vardar İ, ve ark. İnsan Immün Yetmezlik Virüsü ile Enfekte 128 Olgunun Retrospektif Olarak Değerlendirilmesi. *Turkiye Klinikleri J Med Sci*. 2011; 31: 525-533.
17. Ural S, Kaptan F, Türker N, Örmen B, El S, ve ark. İnsan Immün Yetmezlik Virusıyla Infekte Olgularda Hepatit B Virüsü ve Hepatit C Virüsü İnfeksiyonu Seroprevalansı. *Klinik Dergisi* 2010; 23: 100-104.
18. Hukuk WP, Dore GJ, Duncombe CJ, Mahanonharit A, Boyd MA, Ruxrungtham K, Lange JM, Phanuphak P, Cooper DA. Risk of severe hepatotoxicity associated with antiretroviral therapy in the HIV-NAT Cohort, Thailand, 1996-2001. *AIDS*. 2003; 17: 2191-2199.
19. Lincoln D, Petoumenos K, Dore GJ; Australian HIV Observational Database. HIV/HBV and HIV/ HCV coinfection, and outcomes following highly active antiretroviral therapy. *HIV Med*. 2003; 4: 241-249.
20. Tremeau-Bravard A, Ogbukagu IC, Ticao CJ, Abubakar JJ. Seroprevalence of hepatitis B and C infection among the HIV-positive population in Abuja, Nigeria. *Afr Health Sci*. 2012 ;12: 312-317.
21. Jain M, Chakravarti A, Verma V, Bhalla P. Seroprevalence of hepatitis viruses in patients infected with the human immunodeficiency virus. *Indian J Pathol Microbiol*. 2009; 52: 17-19.
22. Thio CL, Seaberg EC, Skolasky R Jr, Phair J, Visscher B, Muñoz A, Thomas DL; Multicenter AIDS Cohort Study. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet*. 2002; 360: 1921-1926.
23. Weber R 1, Sabin CA, Friis-Møller N, P Reiss, El-Sadr WM, Kirk O, Dabis F, Hukuk MG, Pradier C, De Wit S, Akerlund B, Calvo G, Monforte Reklam, Rickenbach M, Ledergerber B, Phillips AN, Lundgren JD. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med*. 2006; 166: 1632-1641.
24. III. Viral hepatit tanı ve tedavi rehberi. *Viral Hepatitle Savaşım Derneği*. 10 Aralık 2011-Ankara.
25. Ocama P, Opio KC, Kagimu M, Seremba E, Wabinga H, Colebunders R. Hepatitis B virus and HIV infection among patients with primary hepatocellular carcinoma in Kampala, Uganda. *Afr Health Sci*. 2011; 11(Suppl 1): 20-23.
26. Chelis L, Ntinos N, Souftas V, Deftereos S, Xenidis N, Chamalidou E, Maltezos E, Kakolyris S. Complete response after sorafenib therapy for hepatocellular carcinoma in an HIV/HBV coinfected patient: Possible synergy with HAART? Case report. *Med Oncol*. 2011; 28(Suppl 1): 165-168.
27. Dülger AC, Esen R, Tuncer I, Türkdoğan K. Dekompanse Karaciğer Sirozlu Hastalarda Hepatosellüler Kanser (HSK) Açısından Tanısal Değerler. *Van Tip Dergisi* 2006; 13: 113-117.
28. Dohmen K, Shigematsu H, Irie K, Ishibashi H. Clinical characteristics among patients with hepatocellular carcinoma according to the serum levels of alpha-fetoprotein and des-y-carboxy prothrombin. *Hepatogastroenterology*. 2003; 50: 2072-2078.
29. Farinati F, Marino D, De Giorgio M, Baldan A, Cantarini M, Cursaro C, Rapaccini G, Del Poggio P, Di Nolfo MA, Benvegnù L, M Zoli, Borzio K, Bernardi E, F Trevisani. Diagnostic and prognostic role of alpha-fetoprotein in hepatocellular carcinoma: both or neither? *Am J Gastroenterol*. 2006; 101: 524-532.