Research Article

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Seroprevalence Investigation of Hepatitis B and Hepatitis B Core Antigen in Oncology Patients

Onkoloji Hastalarında Hepatit B ve Hepatit B Çekirdek Antijenin Seroprevalansının Araştırılması

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ABSTRACT

Objectives: Hepatitis B virus affects a significant part of society and is characterized by high mortality and morbidity. Hepatitis B affects approximately 350 million people worldwide, many of whom are chronic patients. Especially being under immunosuppressive therapy is a risk factor for the reactivation of the disease. The aim of this study was to investigate the seroprevalence of hepatitis B in oncology patients.

Materials and Methods: In this study, the seroprevalences of HBsAg, anti-HCV, anti-HBs, and anti-HBc IgG were retrospectively evaluated from the medical records of 84 patients who were diagnosed of cancer, and were admitted to the outpatient clinic of medical oncology in the state hospital within a period of one year (Between January and December 2017).

Results: Anti-Hbc IgG was positive in 44 patients (52.2%),16 (36.4%) have received treatment for the prevention of HBV reactivation Six of these patients were HBsAg positive No reactivation and no side effects occur in patients who received prophylactic antiretroviral treatment.

Conclusion: In our study, both the proportion of patients with HBsAg positivity and the proportion of patients with natural immunity were found to be slightly higher than those in Turkey and worldwide. No patients with hepatitis B reactivation is important evidence of necessity effectiveness of prophylactic antiviral treatment

Keywords: Hepatitis B, oncology, Hepatitis B virus reactivation

ÖZ

Amaç: Bu çalışmanın amacı immnosupresif tedavi alması planlanan onkoloji hastalarında kapsamlı hepatit panellerinin irdelenmesi, HBsAg seroprevalansı ve Anti-Hbc IgG seroprevalansının değerlendirilmesidir.

Gereç ve Yöntemler: Bu çalışma retrospektif nitelikte tanımlayıcı bir çalışma olarak gerçekleştirilmiştir. 1 Ocak-2017 ila 31 Aralık 2017 dönemi boyunca Batman Bölge Devlet Hastanesi Onkoloji Bölümü'ne başvuran 84 hasta çalışmaya dahil edilmiştir. Bu hastaların hepatit serolojileri kayıt altına alınarak hastalar aktif HBV enfeksiyonu, geçirilmiş HBV enfeksiyonu, almış oldukları profilaksiler ve reaktivasyon açısından değerlendirmiştir.

Bulgular: Hastaların 6'sı HBsAg pozitif olarak saptanmış olup, 44 hasta(52.2%) ise Anti-Hbc IgG pozitif olarak saptanmıştır. Bu 44 hastadan 28 hasta (63.6%) düşük riskli bir kemoterapotik ajan almaları nedeniyle profilaksi almamıştır, diğer hastalar ise profilaksi almıştır. HBsAg poztif olan hastalardan bir hasta dışında tüm hastalar tedavi almıştır. Tüm hastalar değerlendirdiğinde takipte hiçbir hastada reaktivasyon gelişmemiştir.

Sonuç: Kapsamlı Hepatit B serolojisi onkolojik tedavi planı olan tüm hastalara bilinmelive eğer endikasyonu varsa hastalar tedavi veya profilaksi için değerlendirmelidir. Bu değerlendirmelerde kılavuz önerileri esas alınması reaktivasyon gelişme ihtimalini en aza indirecektir.

Anahtar Kelimeler: Hepatit B, seroprevalans, onkoloji, reaktivasyon

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Introduction

Hepatitis B virus (HBV) affects a significant part of society and is characterized by a high clinical picture of mortality and morbidity. Hepatitis B affects approximately 250 million people worldwide, many of whom are chronic patients [1].

The current guidelines recommend that patients diagnosed with cancer should be screened for hepatitis B immediately after diagnosis [4], and vaccinations should be offered to individuals who have never come in contact with HBV. Patients with anti-HBs positivity should be assessed by anti-HBc IgG and natural/acquired immunity should be distinguished among all the patients. Those with natural immunity should be assessed for a reactivation prophylaxis requirement by classifying them according to the risk group of the chemotherapy regimen. While patients receiving hepatitis B treatment prior to cancer diagnosis and therapy should continue taking their prescribed drugs, patients with HBsAg positivity who receive no antiviral treatment should be evaluated for reactivation prophylaxis according to oncology treatment regimens [2].

Hepatitis B virus reactivation (HBVr) can be defined as detectable levels of serum HBV DNA in patients with a baseline undetectable level ≥ 2 log10 IU/mL, increase in HBV DNA in patients with a baseline detectable viral load, or reappearance/reversion of HBsAg [4]. Reactivation is more common in HBV than in HVC (Hepatitis C) and occurs more frequently in men than in women.

. Furthermore, individuals who come in contact with the HBV on subsequent occasions may develop a natural immunity to the virus (i.e., patients possessed anti-HBs positivity due to their previous history of hepatitis B infection and simultaneously possessed hepatitis B core antigen [anti-HBc IgG] seropositivity. HBVr may develop some symptoms or it may entirely be asymptomatic. Fatigue, nausea, and vomiting are the most common visible symptoms. However, some patients may experience liver failure and some may even die. The risk of HBVr is highest in patients who test positive to HBsAg (up to 50%). Individuals with natural immunity receiving immunosuppressive treatments are also at risk of HBVr, [3,6].

In this study, we aim to investigate the frequency of individuals with hepatitis B and naturally acquired immunity against hepatitis B, as well as demonstrate the proportion of patients requiring treatment for the prevention of HBVr by retrospectively screening the hepatitis serological assays of patients who were admitted to and diagnosed with cancer at the Medical Oncology Unit of the Xxxx Regional State Hospital in 2017.

Materials and Methods

In this study, the seroprevalences of HBsAg, anti-HCV, anti-HBs, anti-HIV, and anti-HBc IgG were retrospectively evaluated from medical records of 84 patients who were diagnosed of an oncology disease and were admitted to the outpatient clinic of Medical Oncology in the Xxxx Regional State Hospital within a period of one year (between January and December 2017).

In addition, the records of patients that applied to the Infectious Diseases and Gastroenterology Departments for oral antiviral treatment to prevent hepatitis B reactivation, according to the examination, were retrospectively examined. The treatments given and the results obtained were subsequently evaluated. Data from enrolled patients were analyzed using the Statistical Package for the Social Sciences 24 program.

Results

A total of 84 newly diagnosed cancer patients were admitted to the Department of Medical Oncology at the Xxxx Regional State Hospital in 2017, 43 (51.2%) were women .The mean age of the patients was 55.9 years (range: 17–81 years). Among the 84 patients, 26 (31%) were diagnosed with breast cancer, 15 (14.9%) with lung cancer, 9 (10.7%) with colon cancer, 6 (7.1%) with prostate cancer, 5 (5.9%) ,other patients diagnosed with other types of cancer.

The seroprevalence of HBsAg positivity was determined in six individuals (7.1%). Anti-HBs negative outcomes were observed in 39 patients (45.9%), while 46 patients (54.1%) showed anti-HBs positivity. Eight patients with anti-HBs positivity (9.5%) were considered as immunized through vaccination. Thirty-eight patients with both anti-HBs and anti-HBc IgG positivity (45.2%) were considered as previously infected with the HBV and as possessing naturally acquired immunity. No anti-HCV or anti-HIV positivity was detected in the patients.

Anti-Hbc IgG was positive in 44 patients (52.2%). Six of those patients were positive to HBsAg and 16 (36.4%) received treatment for the prevention of HBVr. One of these HBsAg-positive patients had not been treated for hepatitis B. Among the 16 patients, 7 (43.8%) received entecavir as the treatment regimen, 8 (50%) received tenofovir, and 1 received lamivudine (6.3%). All the patients with HBsAg positivity tested negative to HBeAg. None of these patients had hepatitis B treatment prior to the cancer treatment. The treatments of all the patients were initiated following the serologic screening but preceding the chemotherapy regimens. Twenty-eight patients with natural immunity (63.6%) did not receive the reactivation prophylaxis that was initiated because they had received chemotherapeutic agents in the low-risk group. No reactivation occurred in any of this patients .

Based on the immunosuppressive properties of the chemotherapies initiated, the patients' oral antiviral therapies were scheduled to be discontinued within six months to one year. One (1.2%) of the enrolled patients had isolated anti-HBc IgG positivity

In the one-year follow-up, none of the at-risk patients has developed HBVr yet. The follow-up of the patients continuing oral antiviral therapy is still ongoing. None of the patients that were admitted to the outpatient clinics of infectious diseases due to oral antiviral drugs-related adverse events started antiviral treatments.

Discussion

HBV infects close to 350 million individuals annually, while approximately 800 thousand individuals per year die due to hepatitis-related complications. Patients may present with different clinical pictures depending on the HBV types, including acute infection, chronic infection, hepatic insufficiency, fulminant hepatitis, cirrhosis, and hepatocellular carcinoma [1].

It is not possible to halt the persistence of this disease because of cccDNA. Hepatitis B affects a large number of individuals worldwide, even though it can be prevented through vaccination.

Oral antivirals can also be used to control hepatitis in certain cases, however, the development of hepatocelluler carcinoma cannot be definitively prevented even by this intervention.

Serologic screening for hepatitis B must be performed in oncology patients as well as in all other patients who will receive immunosuppressive treatment for any reason [3]. Also, HBsAg-negative patients should not be considered completely risk-free [3]. It is important that the HBsAg-negative and anti-HBs-positive patient groups are immunized either naturally or by vaccination [9]. In other words, the HBV exposure status of patients should be clearly determined by serologically testing anti-HBc IgG, particularly in regions where the disease is moderately to highly endemic because the proportion of individuals with natural immunity might be higher.

Turkey is a moderately endemic country for hepatitis B. This implies that some patients in our study require treatment to protect from the risk of reactivation. Such high rates could be because the region where the study was conducted has the highest seroprevalence rates across Turkey [8]. However, both the high proportion of individuals with natural immunity and the considerable proportion of patients receiving HBV prophylaxis due to cancer therapy suggest that HBV exposure status must be clearly assessed prior to treatment (in terms of anti-HBc IgG).

In the study performed by Köse et al., serological indicators of hepatitis in oncology patients were found as follows: The positivity of HBsAg was determined in 4.2% individuals, Anti-HBc total was positive in 38.4% patients,18.1%) patients had isolated anti-HBc total positivity, Compared to this study, HBV exposure rate was higher in our study. The main reason of this difference is thought to be that the disease is more endemic in the South Anatolia region in Turkey. This reveals the importance of investigating the disease with Anti-HBc total.

When we compare with world data, Wu-YT et al. HBV reactivation in oncology patients with the meta-analysis study, it was seen that no recoveries were associated in our study with prophylaxis in all patients who needed prophylaxis. The frequency of the disease observed in this study and therefore the different rates of reactivation in different regions seem to be related to the epidemiology of the disease and prophylactic oral antiviral administration at the right time.

The fact that the patients did not develop HBVr during our study was satisfactory; all the patients were fully screened and prophylaxis was administered to all the eligible patients in accordance with the recommended guidelines to formulate these results. Patients' prophylactic regimens, with the exception of one patient who received lamivudine, were administered using drugs with high genetic barriers in accordance with the recommended guidelines [2,3].

Conversely, some patients had low-risk chemotherapy regimens that did not require prophylaxis, and HBVr did not develop among these patients. The lack of treatment for this group of patients is still a controversial subject around the world and the algorithms in this area are often changing.

The patient with . isolated Anti-Hbc IgG positivity didn't receive any treatment aganist HBVr and noticed that this patient was not recommended for an investigation into the occult hepatitis B infection.But in the follow up we have seen that this patient didn't recativate.

Study Limitations

Biggest limitation of our study is it is performed as a retrospective data analysis in a limited cohort of patients. However, the same reason, a certain patient population of patients, minimized data loss.

Conflict of interest: The authors of this article declare that they have no conflict of interest

Conclusion

Hepaititis B serology should be evaluated in all patients with an oncologic diagnosis and treatment plan. Prophylactic treatment should be given where necessary. On the other hand, treatment should not be given when not necessary. The risk of HBVr can be minimized with the right approaches according to the guidelines.

References

1. WHO. (doi: 10.1016/j.jhep.2006.05.013) Hepatitis B.http://www.who.int/mediacentre/factsheets/fs204/en/ 2017 [cited 2018 Feb 24].
2. Reddy KR, Beavers KL, Hammond SP, Lim JK, Falck-Ytter YT. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during ımmunosuppressive drug therapy. Gastroenterology 2015;148:215–219.
3. Cancer Network. Screening and prevention of hepatitis B virus reactivation during chemotherapy. Oncology. http://www.cancernetwork.com/oncologyjournal/screening-and-prevention-hepatitis-b-virus-reactivation-during-chemotherapy [cited 2018 Feb 25].
4. Gastroenterological Association A. AGA hepatitis B virus reactivation guideline: Patient summary. Gastroenterology. 2015;149:496–497.
5. Di Bisceglie AM, Lok AS, Martin P, Terrault N, Perrillo RP, Hoofnagle JH. Recent US Food and Drug Administration warnings on hepatitis B reactivation with immunesuppressing and anticancer drugs: Just the tip of the iceberg? Hepatology. 2015;61(2):703–711.
6. Kang FB, Wang L, Sun DX. Hepatitis B virus infection in an HBsAb-positive lymphoma patient who received chemotherapy: A case report. Medicine (Baltimore) 2017;96(44):e8518.
7. CDC.gov. Hepatıtıs B. Are you at risk? https://www.cdc.gov/hepatitis/hbv/pdfs/hepbatrisk.pdf [cited 2018 Feb 24].
8. Tosun S. The Changing Viral Hepatitis Epidemiology in our Country. Ankem Derg 2013;27(2):128–134.
9. Marco Fiore, Ivo Maria Crosato, Rossana Bussani, Romina Valentinotti, Marta Mascarello, Roberto Luzzati.Reactivation of hepatatis B in a patient with breast cancer treated using capecitabine. J Gastroenterol Hepatol Res. 2016;5(2):2038–2040. doi: 10.17554/j.issn.2224-3992.2016.05.631
10. Kose S, Olmezoglu A, Gozaydin A, Ece G. Seroprevalence of hepatitis B and C among oncology patients in Turkey. J Health Popul Nutr. 2011;29(6):652–655.
11. Wu YT, Li X, Liu ZL, Xu Z, Dai W, Zhang K. Hepatitis B virus reactivation and antiviral prophylaxis during lung cancer chemotherapy: A systematic review and meta-analysis. PLoS One. 2017;12(6):e0179680.