

IZAZOVI U TERAPIJI I DJAGNOSTICI VIRUSNIH HEPATITISA KOD IMUNOSUPRIMIRANIH OSOBA

CHALLENGES IN THERAPY AND DIAGNOSIS OF VIRAL HEPATITIS IN IMMUNOSUPPRESSED PERSONS

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SAŽETAK

Procenjuje se da oko 22 % osoba koje su primale neku od imunosupresivnih terapija (IS) bilo zbog automimunih, malignih oboljenja nakon transplantacije solidnih organa su imale neko oštećenja jetre. S druge strane, preegzistentno prisustvo virusnih infekcija jetre (primarno hepatotropnim virusima, hepatitis B, D i E) često dovodi do egzacerbacije bolesti jetre kod primene IS terapije ili u stanjima imunosupresije. Dobro je poznato, da se u stanjima imunosupresije hronična HBV infekcija može reaktivirati i dovesti do razbuktavanja hepatitisa. Pravovremena primena antivirusne terapije može redukovati ovaj hepatitis a time i omogućiti primenu neophodne imunosupresivne terapije. Za razliku od monoinfekcije HBV, koinfekcija HBV/HDV je retko opisana u kontekstu reaktivacije kod imunosupresije. Međutim opisano je par slučajeva udružene HDV infekcije sa autoimunim hepatitisom i to najčešće u kontekstu terapije pegilovanim interferonom. Saznanja o postojanju hronične HEV infekcije u stanjima imunodeficiencije naročito kod primalaca transplantiranih organa bilo bubrega ili jetre je prvi put objavio Kamar sa saradnicima 2008, uz podatak da više od 66% primalaca solidnih organa razvija hroničnu, uglavnom asimptomatsku HEV infekciju uzrokovanu genotipom 3, ređe genotipom 4 HEV virusa. Primarna prezentacija HEV infekcije često je udružena sa ekstrahepatičnim manifestacijama uključujući neurološke, nefrološke, hematološke i imunoposredovane manifestacije. Stanje imunosupresije sa sobom nosi i dijagnostičke probleme jer pojedini dijagnostički testovi uglavnom serološki, koji su bazirani na detekciji specifičnih antitela na pojedine virusne antigene može biti odloženo ili odsutno u stanjima imunosupresije što dodatno komplikuje pravovremeno prepoznavanje i dijagnostikovanje hroničnih virusnih hepatitisa. Tako je važan dijagnostički marker akutne HEV infekcije detekcija anti HEV IgM antitela. Kada se testiraju ova antitela komercijalno dostupnim testovima senzitivnost je preko 97% kod imunokompetentnih osoba ali ta senzitivnost pada na 80-85% kod imunosuprimiranih - zato je neophodno testiranje na prisustvo HEV RNK u ovoj populaciji. Pravovremeni i ciljani skrining na markere virusnih infekcije jetre jedan od imperativa u planiranju IC terapije i lečenju i monitoringu imunosupresivnih stanja.

Ključne reči: virusni hepatitis, imunosupresija, HBV DNK, HEV RNK

ABSTRACT

Liver-related injuries are estimated to affect up to 22% of patients receiving immunosuppressive therapies (IS) (either due to autoimmune, malignant diseases or solid organ transplantation). Also of concern, is the risk of exacerbating liver injury in patients infected with chronic viral hepatitis: hepatitis B virus (HBV), hepatitis D virus, hepatitis E virus), as immunotherapy can damage liver function due to the immune response against viral antigens. It is well known that in conditions of immunosuppression, chronic HBV infection can be reactivated and lead to flare of hepatitis. Timely application of antiviral therapy, can prevent this hepatitis, and thus enable the application of the necessary immunosuppressive therapy. Unlike HBV monoinfection, HBV/HDV co-infection has rarely been described in the context of reactivation in immunosuppression. However, a couple of cases of combined HDV infection with autoimmune hepatitis have been described, most often in the context of pegylated interferon therapy. Knowledge about the existence of chronic HEV infection in states of immunodeficiency, especially in kidney or liver transplant recipients, was first published by Kamar et al. in 2008, that more than 66% of solid organ recipients develop chronic, mostly asymptomatic HEV infection caused by genotype 3, less often by genotype 4 HEV viruses. The primary presentation of HEV infection is often associated with extrahepatic manifestations including neurological, nephrological, hematological and immune-mediated manifestations.

The state of immunosuppression also brings with it diagnostic problems because certain diagnostic tests, mainly serological, which are based on the detection of specific antibodies to certain viral antigens, may be delayed or absent in states of immunosuppression. The detection of anti-HEV IgM antibodies is thus an important diagnostic marker of acute HEV infection. When antibodies are tested with commercially available tests, the sensitivity is over 97% in immunocompetent persons, but this sensitivity drops to 80-85% in immunosuppressed persons - that is why testing for the presence of HEV RNA in this population is necessary. Timely and targeted screening for markers of viral liver infections is one of the imperatives in planning IC therapy and treatment and monitoring of immunosuppressive conditions.

Keywords: viral hepatitis, immunosuppression, HBV DNA, HEV RNA