

Hepatitis in immunocompromised hosts

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Objectives

The aim of this presentation is make a review of the main agents responsible for hepatitis in immunocompromised hosts, namely those undergoing chemotherapy or other immunosuppressive therapies, allograft recipients and HIV positive individuals.

Summary

Hepatotropic virus infection (HBV and HCV) are common in immunocompromised hosts. Several mechanisms (humoral and cellular) play a vital role in the elimination of these viruses. Immunosuppression itself doesn't increase the prevalence of fulminant hepatitis (i.e. HBV) but the risk of reactivation is high. This risk is independent of its aetiology, but increases based on the degree of immunological compromise (i.e. HIV+). In certain settings, such as Haemodialysis Units, the risk is 40-80% for HBV and 85-95% for HCV.

Reactivation of HBV is a well-recognised complication of chronic HBV, typically occurring in immunosuppressed patients (1). The severity of hepatitis ranges from anicteric hepatitis to severe progressive hepatic failure, which may result in death (2). Hepatitis as a result of HBV reactivation may occur via two, possible linked mechanisms. First, the administration of cytotoxic/immunosuppressive agents may result in T-lymphocyte depletion and suppression of normal immunological response to viral antigens; this allows enhanced HBV replication and may cause direct hepatic toxicity. The second mechanism can occur on cessation of cytotoxic therapy, when a rebound immune response results in hepatocyte destruction (2).

Early prophylactic antiviral therapy is superior to treatment after HBV reactivation. Therefore all chronic HBV carriers should be started on oral drugs, at least 7 days before initiating immunosuppressive therapy (1). The optimal duration of anti-HBV treatment remains uncertain. For patients receiving conventional chemotherapy, Lamivudine therapy until 6 months after cessation of chemotherapy has been recommended; if a longer duration is needed (i.e. patients receiving rituximab or in those with high baseline HBV DNA before chemotherapy), use of new agents (Entecavir or Tenofovir) is reasonable, due to the potential risk of development of drug resistance with use of Lamivudine (3).

HBV /HIV co-infection is estimated in 6-10% in Europe and USA. HIV patients have high levels of HBV DNA, less spontaneous recovery after acute hepatitis and higher evolution to chronicity. According to EACS guidelines (4), if both viruses need therapy, two anti-HBV drugs should be included in HAART schedule.

Regarding HCV, there are some conditions, such as renal disease, liver transplant and HIV infection, in which it represents a worsening factor in their outcome. HCV related liver disease is the leading cause for liver transplantation (5). In case of renal allograft recipients, HCV therapy has low efficacy and increases the risk of allograft rejection. In liver transplant recipients, HCV recurrence after transplant is high (almost 100%) due to the presence of virus in extrahepatic sites. In HIV patients, HCV coinfection accelerates time to HCV-related liver disease and adversely impacts HAART therapy. If possible HCV treatment should be offered before renal or hepatic transplantation and before starting antiretroviral therapy in HIV positive patients.

All patients undergoing potential immunosuppressive therapy should be screened for HBV and HCV before initiating treatment. Prophylactic or effective treatment, are the keys to minimize the serious threat these infections may represent.

Recommended reading

- 1) Post A, Nagendra S. Reactivation of Hepatitis B: Pathogenesis and Clinical Implications. *Current Infectious Disease Reports* 2009,11: 113-119
- 2) Yeo W, Chan PKS, Chan HLY, *et al.* Hepatitis B virus reactivation during cytotoxic chemotherapy-enhanced viral replication precedes overt hepatitis. *Journal of Medical Virology* 2001, 65: 473-477
- 3) Liang R. How I treat and monitor viral hepatitis B infection in patients receiving intensive immunosuppressive therapies or undergoing hematopoietic stem cell transplantation. *Blood* 2009; 113: 3147-3153
- 4) Rockstroh JK, *et al.* European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults. *HIV Medicine* 2008, 9: 82-88
- 5) Segondy M. Infections virales chez les patients transplantés. *Revue Francophone des Laboratoires* 2008; 403: 31- 40