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Meeting report

The management of chronic hepatitis B in the immunocompromised patient: Recommendations from a single topic meeting

Keywords: Hepatitis B; Immunocompromised host; HIV; Kidney transplantation; Liver transplantation; Chemotherapy

1. Introduction

The management of chronic hepatitis B virus (HBV) infection in immunocompromised patients presents challenges above and beyond those routinely encountered in this already complex disease. With this in mind a single topic conference was convened jointly, in May 2007 by the Scottish Viral Hepatitis Group and the Scottish Diagnostic Virology Group to discuss the management of hepatitis B in the specific contexts of chemotherapy for haematological malignancy, liver and renal transplantation and HIV co-infection.

2. Methods and aims

The aim of the meeting was to generate pragmatic guidelines combining best available evidence and expert opinion. In advance of the meeting a discussion document containing draft guidelines was prepared and circulated to a participating expert panel. On the day of the meeting presentations were given on each of the topics followed by a panel discussion with questions from the floor. The discussions were transcribed and used to prepare the following guidelines which are presented in Figs. 1–4, and discussed here in turn.

2.1. Management of hepatitis B infection in patients undergoing chemotherapy for haematological malignancy (Fig. 1)

2.1.1. Background

Chemotherapy induced reactivation of hepatitis B is a well recognised phenomenon first described over 30 years ago (Galbraith et al., 1975). It is thought that chemotherapy induced immunosuppression allows a rapid increase in viral replication (Mindikoglu et al., 2006). Between cycles, or after cessation of chemotherapy, reconstitution of the immune system takes place. During this period a T cell mediated immune response may occur against the increased number of infected hepatocytes with a clinical picture ranging from elevation of ALT, through jaundice, fulminant liver failure and death (Lok et al., 1991).

Whilst no uniform definition of reactivation exists one that is commonly used is the presence of hepatitis (as suggested by an ALT > 3 ULN) in combination with either a ten-fold rise in HBV DNA viral load or an absolute value greater than 20,000 IU/ml. The risk of reactivation for HBsAg positive patients undergoing chemotherapy for haematological malignancy is between 33 and 67% (Lok et al., 1991; Nakamura et al., 1996; Markovic et al., 1999; Yeo et al., 2005), with regimes containing high dose steroid or rituximab independently increasing risk (Cheng, 1996; Takai et al., 2005; Hui et al., 2006). Patient factors conferring increased risk include high serum HBV DNA pre-chemotherapy (Lau et al., 2002; Yeo et al., 2004), male sex and high levels of ALT.

Reactivation mortality rates have been reported variously as between 5 and 37% (Lok et al., 1991; Nakamura et al., 1996; Markovic et al., 1999), with more patients developing jaundice. The latter causes significant morbidity and may necessitate interruption of chemotherapy potentially leading to a poorer treatment outcome.

Although less common, reactivation may occur in patients who are HBsAg negative but positive for other markers of prior exposure to the virus, including anti-HBc or anti-HBs alone or in combination (Lok et al., 1991; Law et al., 2005; Hui et al., 2006). Although the reactivation rate is lower amongst this group, in the region of 5%, reactivation carries a significant risk of mortality and morbidity (Hui et al., 2006). In areas of low HBV endemicity up to 20% of patients with markers of prior exposure to HBV will have anti-HBc in isolation, which may represent acute infection, occult infection, resolved distant infection or a false positive result (Grob et al., 2000). Those with occult HBV infection, defined as HBsAg

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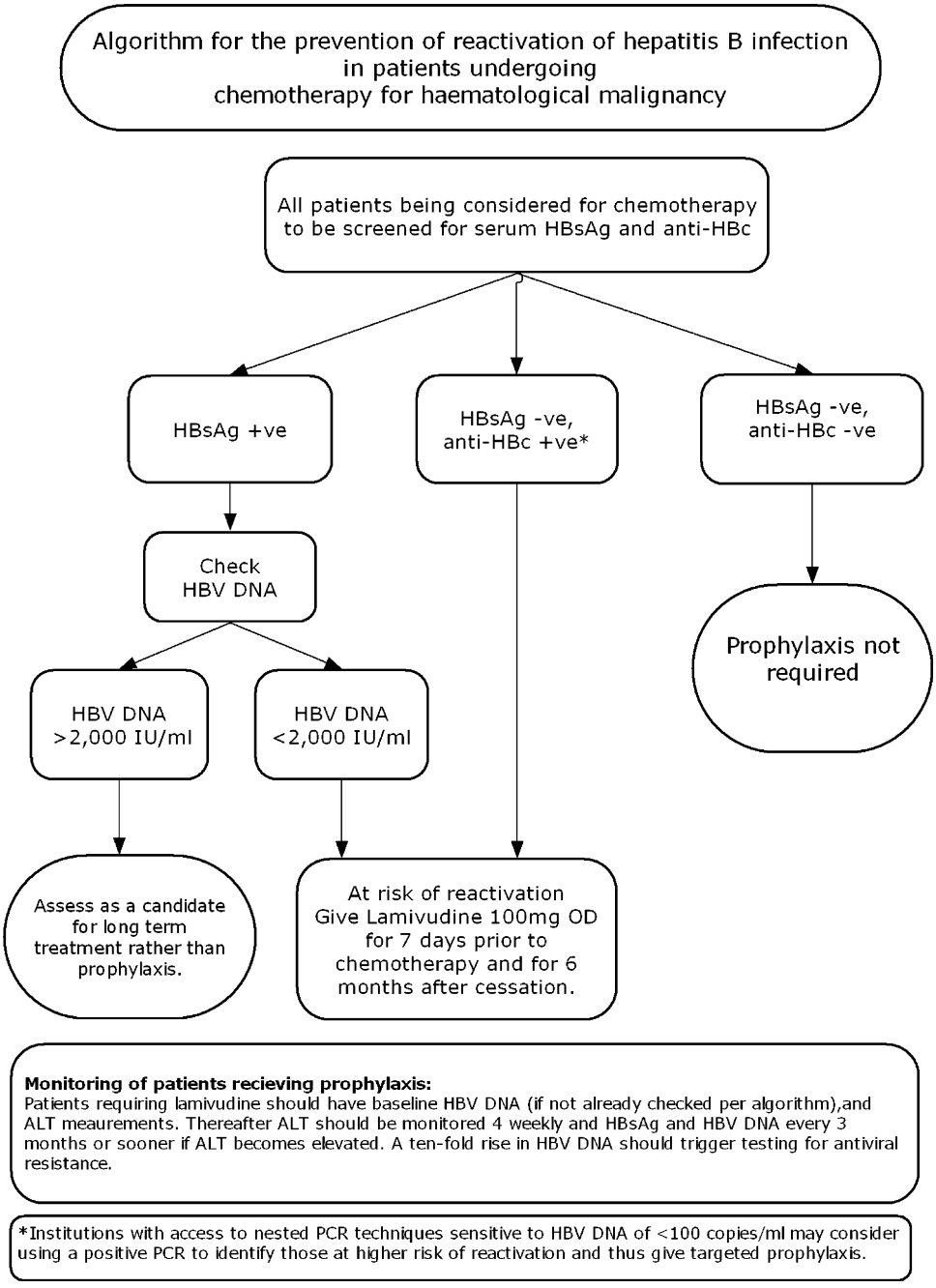

Fig. 1. Algorithm for the prevention of reactivation of hepatitis B infection in patients undergoing chemotherapy for haematological malignancy.

negative with low level detectable HBV DNA, appear to have the greatest risk (Hui et al., 2006).

2.1.2. Screening of patients undergoing chemotherapy

Given the high rate of reactivation and subsequent morbidity/mortality amongst patients with chronic hepatitis B undergoing chemotherapy it is recommended that all patients undergoing chemotherapy for haematological malignancies have their HBV status assessed by testing for serum HBsAg and anti-HBc. The rate of HBV infection may be higher amongst patients with haematological malignancy than in the background population (Pioltelli et al., 2000; Kim et al., 2002; Talamini et al., 2004; Marcucci et al., 2006) and screening is cheap and widely available.

2.1.3. Evaluation of HBsAg positive patients

HBsAg positive patients should have their serum HBV DNA levels checked. Those patients with HBV DNA levels >2000 IU/ml should be evaluated further with regards to serum ALT, e-antigen status, liver biopsy or non-invasive markers of fibrosis (Myers et al., 2003), and considered as potential candidates for treatment rather than prophylaxis.