Patients With Isolated Hepatitis B Core Antibody: Has the Time Come to Vaccinate?

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Isolated anti-HBc serological profile: has the time come to vaccinate?

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Word count: 515

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Dear Editor,

The proportion of individuals with an isolated anti-HBc (IAHBc) serological profile ranges from 1% to 32% [1], frequently observed in patients with chronic hepatitis C [2] or HIV infection [3]. The partly unsolved question is indeed how to manage these patients. Indeed, the risk of HBV reactivation can be globally and approximately estimated at between 2.0% and 3.9% [2,3]. There is increasing and recent evidence of such a risk of (re)infection - or more likely reactivation – particularly in some patients, such as those on immunosuppressive therapy (e.g. rituximab, anti-TNF [1], or more recently ibrutinib or pomalidomide), those with HIV infection and/or experiencing withdrawal from drugs with anti-HBV activity, or those treated with new direct anti-HCV agents [4].

Though there is rather a consensus to offer treatment to IAHBc patients with positive HBV DNA, whether preventive measures should be adopted in those without positive HBV DNA – if any – is still a matter of debate. Some physicians advocate the use of anti-HBV drugs, in particular in patients waiting to be treated with immunosuppressive drugs [5,6] or in those on HCV therapy with direct antiviral agents [7]. However, the duration of such a specific HBV therapy and its benefit/risk balance are still unclear, considering the long-term potential safety issues and the residual risk – albeit lower - of reactivation/(re)infection (from 0.14 to 1.1/100 person-years in HIV-infected patients [8]).

It thus seems relevant to strongly promote and systematically offer HBV vaccination to these patients (***figure***), as recently recommended in the US Public Health Service guidelines for management of HIV infected persons. An anamnestic anti-HBs response to one dose of HBV vaccine (recall) supports the presence of an immune memory to HBV with resolved HBV infection [1], and suggests that there is no need for further HBV vaccination or therapy. By contrast, the lack of an anamnestic response should lead to full vaccination in these patients. Reinforced (double-dose) schemes have been assessed in patients with this IAHBc serological profile and impaired immunity (such as cirrhosis [9] or HIV co-infection [10]), and have shown satisfactory response rates (up to 89%) and safety profiles. This vaccination strategy makes sense since most patients at risk of reactivation/(re)infection are likely to suffer from long-term immunodepression and/or liver disease.

On the other hand, another strategy, which has never been clearly assessed, could be first to see whether patients with an IAHBc profile experience an anamnestic response following a single dose of HBV vaccine, and then to assess HBV DNA in the non-anamnestic responders, to distinguish between those who need anti-HBV therapy (because of positive HBV DNA), and those who need full vaccination.

In conclusion, even though the clinical benefit of the above strategy associated with the development of immune protection in such patients has yet to be assessed, recommendations and guidelines should be upgraded and include offering HBV vaccination to these patients, at least to those with virological or drug-related impaired immunity, and to those suffering from liver diseases and/or HCV infected. The best schedule could be a recall dose, followed by a full scheme (often reinforced) in the absence of an anamnestic response.

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Figure

Suggested strategy in patients with an IAHBc serological profile and impaired immunity