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Response to Comment on: Hepatitis B virus reactivation following T-cell engager therapy in multiple myeloma despite negative hepatitis B core antibody serology: implications for screening in patients with haematological malignancies

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Dear Editor,

We thank Rago et al. for their interest in our recent case report describing hepatitis B virus (HBV) reactivation following T-cell engager (TCE) therapy in multiple myeloma.[1,2]

Rago et al. note that HBV DNA was detectable in June 2024 prior to teclistamab, and suggest antiviral therapy should have been commenced at that time. We emphasise, as stated in our report, that this HBV DNA result was obtained retrospectively through *look-back testing*. At the time of clinical care, the patient's serology (HBsAg, anti-HBc, anti-HBs) was negative and liver function tests were normal. We agree that had HBV DNA been contemporaneously available, antiviral prophylaxis would have been warranted and likely prevented this event.

The response letter suggests the possibility of de novo HBV infection. We believe this is unlikely. Throughout the patient's myeloma journey, there was no known HBV exposure risk. The more plausible explanation, consistent with our findings, is occult HBV infection with subsequent *reactivation* in the profoundly immunosuppressed setting of TCE therapy. This interpretation aligns with the biological behaviour of HBV under immunosuppressive pressure and with known risks of viral reactivation in hematology patients.

Our case highlights the limitations of conventional serological screening alone in this population. Current guidelines do not recommend HBV DNA testing in seronegative individuals – a limitation highlighted by this case.[3] Despite repeatedly negative anti-HBc, the patient harboured occult HBV detectable only by retrospective DNA testing. This highlights the need for vigilance and, in selected high-risk populations, consideration of HBV DNA testing even when serology is negative.

We welcome the discussion prompted by our report. However, we clarify that the June 2024 HBV DNA result was not known at the time of treatment, and that de novo HBV infection is unlikely. Rather, our case illustrates that HBV reactivation can occur despite negative serology, with significant implications for screening strategies in patients receiving novel immunotherapies.

References:

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