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Letter to the Editor

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Persistent Anti-Core Negative Serology during HBV Reactivation in a Recipient of Anti-Core^{+} Orthotopic Liver Transplantation

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Letter to the Editor

Dear Editor,

The risk of HBV reactivation (HBVR) requires specific monitoring in occult HBV carriers receiving immunosuppressive treatment [1,2]. The presence of anti-HBcore antibodies (HBcAb) is considered as a reliable marker of the occult carrier status and the associated risk of HBVR [3,4]. Here, we report on a patient who underwent Orthotopic Liver Transplantation (OLT) following HCV-related cirrhosis and was the recipient of an anti-HBcore positive (HBcAb+) donor liver. Eight years post-transplantation he presented with HBVR. However, he remained persistently negative for the presence of HBcAbs in the serum throughout the long period of follow up. Transplantation was performed in 2014. As a recipient of a liver from an HBcAb+ donor, the patient was given preventive antiviral therapy with Lamivudine together with anti-HBV-Abs and standard immunosuppression with Tacrolimus+Everolimus. Signs of rejection presenting in 2019 required adding high doses of Methylprednisolone to the treatment above. In January 2022 a routine check-up displayed elevated ALT and AST (5 times above reference levels), elevated HBV-DNA, HBsAg and HBeAg positivity, indicating HBVR. Surprisingly, neither IgM nor total HBc-specific Abs was ever detected. Treatment switched from Lamivudine to Entecavir and quantitative assays for HBsAg (CMIA Architect

Abbott) were introduced to better monitor therapeutic efficacy. The levels detected at initial check-up (8000 IU/ml) were comparable to those of acute hepatitis.

After 32 weeks of therapy with Entecavir, the patient still showed elevated ALT and AST (about 4 times higher than normal), while HBV-DNA was greatly reduced and HBsAg was also decreased. However both IgM and total anti-HBc Abs remained undetectable; HbeAg was still present in the serum while anti-HBeAbs were absent **(Table 1).**

Table 1: Laboratory parameters during follow up.

	At OLT (2014)	At HBVR (Jan 2022)	At remission (Sept 2022)	At hosp. readmiss. (Sept 2025)
ALT (IU/L)	93	242	186	280
Alb (g/dL)	2.6	3.7	3.7	2.9
Tot. Bilirubin (mg/dL)	3.2	1.3	1.1	1.8
PCHE	1209	6386	6158	2573
INR	1.64	1.06	1.03	1.06
HBs Ag QLT	NEG	POS	POS	POS
HBs Ag QNT (IU/mL)	0.0	8046	2507	7045
Anti- HBs	0.0	0.0	0.0	0.0
HBc Ab	NEG	NEG	NEG	NEG
HBc Ab IgM	NEG	NEG	NEG	NEG
HBe Ag	NEG	POS	POS	POS
Anti HBe	NEG	NEG	NEG	NEG
PLT ($x10^3/\mu L$)	50	87	101	136
HBV-DNA (IU/ml)	N.D.*	55700	N.D.*	N.D.*

* Non Detectable

In September 2025 the patient was again admitted to hospital because of ascites and elevated ALT. A diagnosis of chronic hepatitis, with steatosis and fibrosis, was confirmed through biopsy. Etiologies different from HBV were ruled out (negative serology for Abs anti-delta virus, anti-HAV, anti-HCV or ant-HEV). However, anti-HBc Abs was persistently negative (Table 1, left column). This case report highlights difficulties in interpreting sero-immunological profiles of individuals who are occult carriers of HBV and require immunosuppressive therapies: no single marker, including HBcAb positivity, can reliably predict the risk of HBVR and this type of patients require careful monitoring at clinical laboratory level.

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