Dear Editor,
Recent immunosuppressive and antineoplastic drugs condition a new scenario in hepatitis B virus (HBV) reactivation, in addition to traditional B-lymphocyte depletion treatments and immunosuppression associated with bone marrow transplantation (1).

Case report
We present the case of a 69-year-old male with chronic lymphocytic leukemia diagnosed in 2014 and under treatment with ibrutinib since 2017. Partial response was achieved, without significant adenopathy or splenomegaly in the computed tomography (CT) scan in November 2022. During these years, HBV serology had been monitored periodically, with negative HBsAg, positive anti-HBc, undetectable HBV-DNA and normal transaminases.

The patient was admitted in January 2023 for pneumococcal pneumonia. An elevation of aspartate aminotransferase/alanine aminotransferase (AST/ALT) and total bilirubin

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(6.7 mg/dl) was shown on laboratory tests. Abdominal ultrasound was normal. A new HBV test showed positive HBsAg and HBeAg with HBV-DNA 1,180,000 UI/ml. Treatment with tenofovir was immediately started because of HBV reactivation and ibrutinib was reintroduced afterwards. Both normalization of liver biochemistry and undetectable HBV-DNA were confirmed one month later.

**Discussion**

Ibrutinib is an antineoplastic tyrosine kinase inhibitor drug with a risk of HBV reactivation. It is a moderate risk in cases of HBsAg-positive and low-moderate if HBsAg-negative and anti-HBc-positive. According to the guidelines, the recommendation is to monitor HBV serology during and up to six months after treatment, as in our patient (1). So far, isolated cases of HBV reactivation by ibrutinib have been reported (2), including a multicenter study of more than 100 patients with chronic lymphocytic leukemia treated with this drug (3). In this last study, two reactivations were detected, one in a patient on lamivudine prophylaxis. It is important to note that cases of severe HBV reactivation have been reported (4).

The rate of occult HBV infection is 8-14% in chronic lymphocytic leukemia patients treated with ibrutinib (2,3). However, the rate of HBV reactivation due to this drug is not defined and its cumulative risk of HBV reactivation is not stipulated. In addition, HBV reactivation may be years after ibrutinib treatment, as in our case. Currently, the recommended drugs for HBV reactivation prophylaxis are tenofovir, entecavir and TAF (1). In the presence of HBV reactivation, these treatments are effective (5), as was observed in our patient.

Studies designed to assess the ability of drugs such as ibrutinib to cause HBV reactivation are needed. In our opinion, cases like the one we describe here may lead to future changes in the indication for drug prophylaxis.

**References**


