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Chronic Hepatitis B Infection Management During Long-Term Follow-Up of Chronic Lymphocytic Leukemia (CLL) Treated With Multiple Lines of Chemoimmunotherapy, Including Ibrutinib

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INTRODUCTION

Hepatitis B virus (HBV) reactivation may occur in B cell dysfunction, especially in those B cells that have previously met with HBV surface antigen (HBsAg), despite prior acquired immunity. Ibrutinib is a Bruton's tyrosine kinase inhibitor (BTKi) that regulates B-cell signaling, resulting in B-cell maturation. HBV reactivation during treatment with tyrosine kinase inhibitors is still a dilemma; there is little knowledge about how to protect against acute reactivation of HBV.

AIM

To present a case report of chronic HBV reactivation during ibrutinib treatment.

CASE

A 75-year-old man previously diagnosed with Rai stage 2 CLL and naturally immunized against HBV was admitted to our clinic. In May 2017, a rituximab + chlorambucil (R-Cl) protocol was administered with tenofovir disoproxil fumarate prophylaxis. After 6 cycles of chemotherapy, he was in remission. No HBV reactivation occurred during prophylaxis or the treatment-free follow-up interval.

RESULTS

Three years after his last dose of chemotherapy, in September 2020, he had weight loss, rapidly growing lymphadenopathy, and anemia. Due to a relatively low performance status score, ibrutinib 420 mg/d was administered. After the ninth cycle of ibrutinib, elevated liver enzymes were detected. His HBV DNA level was increased, so entecavir was administered; after the third cycle, the HBV DNA level did not decrease enough, so his treatment was switched to tenofovir alafenamide fumarate (TAF). After 3 cycles of TAF, continued follow up for chronic inactive HBV and CLL.

Time (month/year)	CLL Treatment	HBV treatment	AST/ALT (N: <35 U/L)	HBV DNA (copy/uL)
05/2017	R-Cl x6 cycle	TDF x12 months	15/20	610
09/2020	Ibrutinib at 9th cycle	None during 9 months	10/10	negative
06/2021	Ibrutinib at 15th cycle	Entecavir x3 months	150/182	1.270.000
09/2021	Ibrutinib at 18th cycle	TAF x6 cycle	25/52	581.000
02/2023	Ibrutinib at 44th cycle	TAF at 23rd cycle	12/14	negative

Table 1: *A brief proggress about HBV and CLL treatment. After initiaion of ibrutinib treatment, neither increased HBV DNA copy number, nor any sign of loss of immunity for HBV, prophylaxis did not consider Cl: chlorambucil, TDF* with tenofovir disoproxil fumarate, *TAF:* tenofovir alafenamide fumarate

CONCLUSIONS

Ibrutinib has a potential role in B-cell signaling, causing alteration of cellular immunity. On the other hand, ibrutinib also facilitates B-cell maturation, allowing immunomodulation of T cells, which are also considered amendatory for the immune system. Primary or secondary prophylaxis for HBV, especially for carriers before initiation of ibrutinib, is still controversial according to local and international guidelines. An individualized approach and risk assessment is still considered the best option for HBV prophylaxis.

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