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Citation	International Urology and Nephrology, 39(2), 461-463 <a href="https://doi.org/10.1007/s11255-006-9006-8">https://doi.org/10.1007/s11255-006-9006-8</a>
Issue Date	2007-06
Doc URL	<a href="http://hdl.handle.net/2115/28261">http://hdl.handle.net/2115/28261</a>
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Type	article (author version)
File Information	IUN39-2.pdf



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Category: Case report

Title: Reactivation of hepatitis in a bladder cancer patient receiving chemotherapy.

Running title: Reactivation of hepatitis in bladder cancer

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## Abstract

Reactivation of hepatitis is a serious complication of chemotherapy in hepatitis B virus (HBV) carriers. There are many reports of this in lymphoma patients but few in urological cancer patients.

A 59-year-old woman with bladder cancer who was an HBV carrier developed severe liver dysfunction after 2 cycles of chemotherapy. The diagnosis was reactivation of hepatitis. She improved with administration of lamivudine

with a steroid and is currently well without disease.

Conclusions: Care should be taken about the risk of reactivation when performing chemotherapy in HBV carriers and prophylaxis by lamivudine should be considered.

Key Words: hepatitis B virus, chemotherapy, reactivation, lamivudine,

## Introduction:

Reactivation of hepatitis is a serious complication of chemotherapy in hepatitis B virus (HBV) carriers. There have been a number of cases reported during treatment of lymphoma; however, only one case has so far been reported for urological cancer treatment. [1] We herein report a case of chemotherapy-induced hepatitis flare in a patient with bladder cancer.

A 59-year-old woman was diagnosed as having infiltrating bladder carcinoma with metastasis to local lymph nodes. She was an HBV carrier but had no active hepatitis and a normal alanine aminotransferase level (ALT, normal <40 IU/l), positive HBs Ag, positive anti-HBe Ab, positive serum HBV-DNA ( $4.9 \times 10^6$  copies/mL, normal < $4 \times 10^2$  copies/mL). Following cystectomy she received chemotherapy consisting of methotrexate, epiadriamycin and cisplatin. At the end of the second cycle of chemotherapy, just after the withdrawal of 4 mg/day dexamethazone for antiemesis, she presented with general fatigue and appetite loss. Laboratory tests showed ALT elevated to 2,000 IU/l (Fig. 1). Although her serum HBV-DNA level decreased to  $4.7 \times 10^2$  copies/mL, she was diagnosed as having reactivation hepatitis because a thorough evaluation did not indicate any other cause for liver dysfunction. She was started on lamivudine at 100mg/day with 500mg of steroid therapy for 3 days. One week later she developed reversible posterior leukoencephalopathy syndrome, and required an anticonvulsion agent and respiratory care for 1 month. She improved 3

months later; ALT normalized and serum HBV-DNA was undetectable when lamivudine was stopped. After the discontinuance of chemotherapy she has been well without evidence of cancer recurrence or hepatitis for 2 years of follow-up.

## DISCUSSION:

Reactivation of HBV is well known in lymphoma patients undergoing cytotoxic chemotherapy. The mechanism of flare in HBV carriers has not been clearly elucidated, though a possible mechanism is that increased HBV-infected hepatocytes due to immunosuppressive agents are disintegrated by the attack of restored activated T cells after the withdrawal of the agents. [2]

The frequency of HBV reactivation in HBsAg-positive lymphoma patients receiving chemotherapy was reported to range from 15-20%. The HBV-DNA usually rises and drops rapidly soon after ALT elevation, so the true incidence of HBV reactivation might be underestimated in retrospective studies. In fact, we did not detect a rise of HBV-DNA during the clinical course. Patients with positive HBV-DNA have a risk for flare-up. In addition, the use of steroids was reported to be a risk for reactivation. Upon withdrawal of steroids, there is an intense rebound in cytotoxic T-cell function that coincides with a surge in serum ALT and decreases in the levels of HBsAg and HBV-DNA. [3]

Lamivudine inhibits reverse transcription activity and DNA synthesis, is well tolerated and the adverse effects are mild. However, long-term lamivudine use is associated with the development of lamivudine-resistant mutant strains of HBV. Despite this risk, prophylaxis against chemotherapy-induced reactivation is recommended. [4]

There has hitherto been only one report of HBV reactivation in urological cancer chemotherapy. However, as our case demonstrates, this remains a possibility and care should be taken about reactivation when performing chemotherapy in HBV carriers; monitoring HBV-DNA is mandatory and prophylaxis by lamivudine should be considered.

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## Figure legends

Figure 1: The time courses of ALT and HBV-DNA.

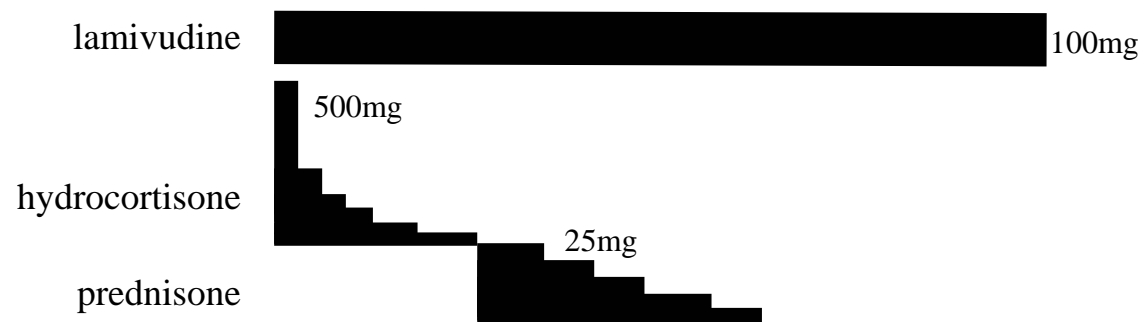
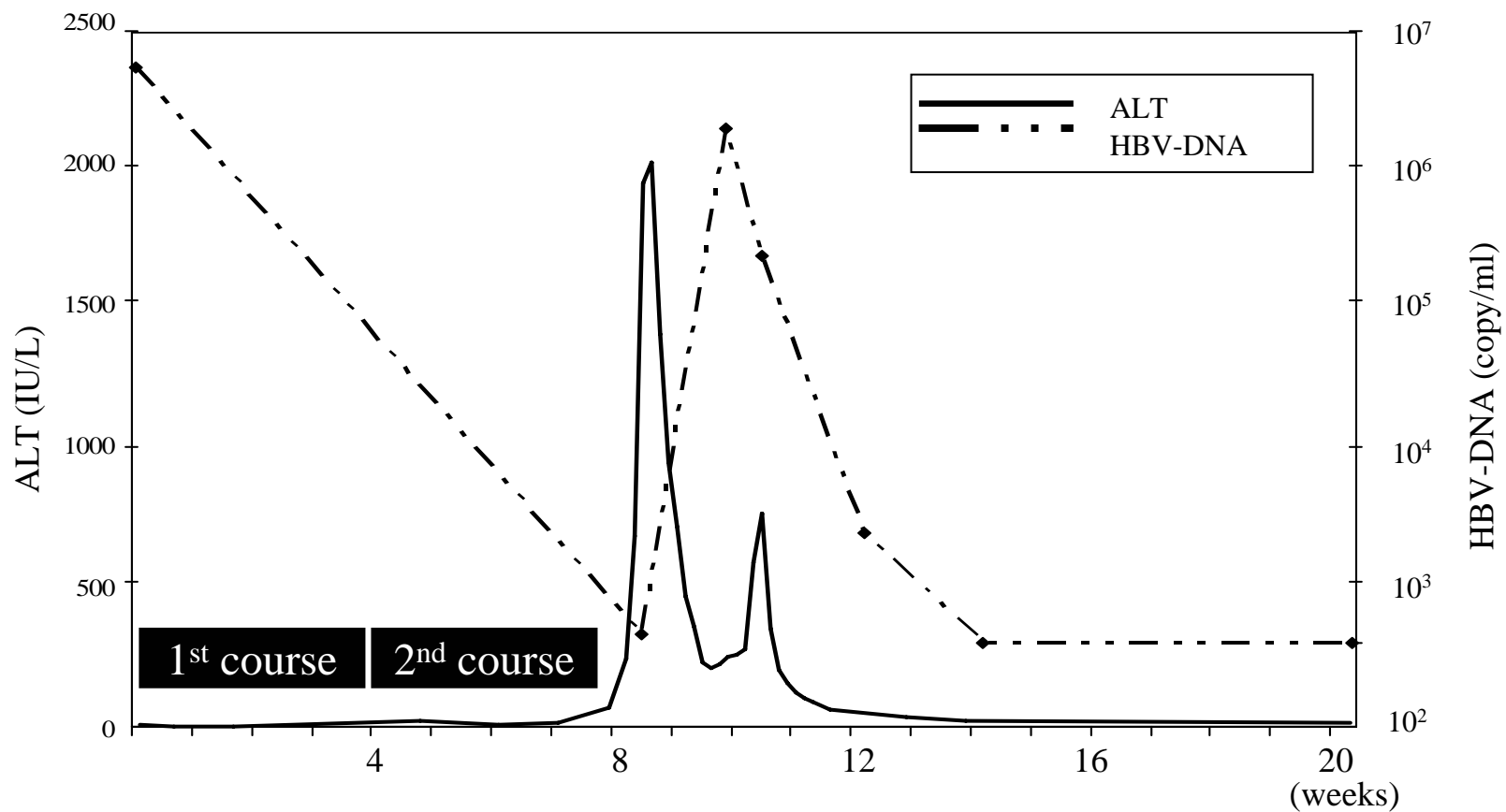


Fig. 1