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*Case Report*

# Successful HBsAg clearance without bone marrow transplantation in a patient with B-cell chronic leukemia

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## SUMMARY

**We report the case of a 55-year-old man diagnosed with B-cell chronic lymphocytic leukemia five years ago and hepatitis B three years ago who succeeded in HBsAg clearance with interferon-a 2a (4.5 MU/ three times a week) followed by lamivudine monotherapy without any kind of transplantation. At the last follow up, the patient showed HBV clearance (HBeAg negative, HBsAb positive, HBcore positive) and undetectable HBV-DNA. This is to the best of our knowledge the first case of a patient with B-cell chronic leukemia and chronic hepatitis B viral infection who succeeded in serum HBV clearance.**


**Keywords:** leukemia, hepatitis B, interferon, lamivudine, clearance

## INTRODUCTION

It is widely accepted that seroconversion of HBsAg (Hepatitis B surface Antigen) to HBsAb (antibody) indicates clearance of hepatitis B virus. Hepatitis B surface Antigen (HBsAg) clearance has been already reported in several cases of patients with peripheral blood malignancies requiring peripheral blood (PB) or bone marrow transplantation (BMT)[1]. These cases provide evidence of clearance of HBsAg in chronic hepatitis B carriers due to adoptive transfer of immunity by a hepatitis B immunized bone marrow or peripheral blood. However, BMT efforts in HBsAg carriers have also been proved fatal in a few cases where hepatitis B virus was reactivated resulting in fulminant irreversible hepatic failure.

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## CASE REPORT

We report the case of a 55-year-old man diagnosed with B-cell chronic lymphocytic leukemia (B-CLL) five years ago and hepatitis B three years ago who achieved HBsAg clearance without any kind of transplantation. At the time of leukemia diagnosis, the patient was started on therapy with chlorambucil, methylprednizolone and erythropoietin and achieved partial remission. Two years after leukemia diagnosis, transaminase levels were two-fold increased and the patient was diagnosed with chronic hepatitis B infection (HBeAg negative) and highly detectable viral load. By retrieving medical history again, the patient remembered a probably icteric episode he had thirty-five years ago.

Because of the continuously increasing transaminase levels the patient was started on interferon-a 2a (4.5 MU/ three times a week subcutaneously) while other leukemia therapy was interrupted. Liver biopsy was not performed due to the patient's unwillingness. Eight weeks later, severe thrombocutopenia lead to interferon discontinuation. At the end of this short interferon treatment although transaminase levels were normalized, HBV-DNA and HBsAg remained at highly detectable levels. Lamivudine uninterrupted monotherapy was then started on for a thirty month period and, at the last year of treatment, the patient achieved sustained virological and biochemical response. In the mean time the hematologic malignancy was in partial remission. At the last regular 3-month follow up check-up, the patient surprisingly showed HBsAg clearance (HBeAg negative, HBsAb positive, HBcore positive) and HBV-DNA below the cut-off values (400 copies/ml, branch DNA method). We decided on lamivudine discontinuation and to follow up the patient on a 6-month basis.

## DISCUSSION

Serological clearance of hepatitis B surface antigen (HBsAg) has been described after reception of hepatitis B surface antibody positive marrow, via allogenic bone marrow transplantation (BMT).[2] Clearance of HBsAg and HBV-DNA was observed in an HBsAg carrier with leukemia who received BMT from his HLA-matched anti-HBc+/anti-HBs+ brother.[3] Moreover the fact that short term interferon-a 2a or prolonged uninterrupted lamivudine monotherapy may result per se in HBsAg clearance should not be ignored. However, the presence of HBs antibodies could, probably, be against this hypothesis.

Histological changes during the clearance of HBsAg are unknown. In two chronic hepatitis B carriers (both hepatitis B e antigen negative), who cleared HBsAg after allogeneic bone marrow transplantation hepatic immunohistochemistry showed no detectable expression of hepatitis B core antigen. However, HBsAg was positive, mainly in the area of confluent necrosis. Using in situ hybridization, hepatitis B virus (HBV) DNA was detected in the nucleus of 5% of hepatocytes, but not in the cytoplasm in that study.[4] A leukemic patient with absence of HBsAg and presence of HBsAb who developed lethal hepatits B after BMT has been reported.[5] Hepatitis B virus latently existing in the liver cells before BMT proliferated during the immunosuppressed period causing fatal hepatitis. This case strongly suggests that immunosuppressed and leukemic patients cannot always express the HBV surface antigen, which is probably suppressed in terms of expression in a mysterious way. Consequently, the term clearance may only be attributed to serum but not tissue parameters.

This is to the best of our knowledge the first case of a patient with B-cell chronic leukemia and chronic hepatitis B viral infection who succeeded in spontaneous serum HBsAg clearance.

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