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# Development of hepatocellular carcinoma in a HBeAG-negative chronic hepatitis B patient without cirrhosis under the long-term virological suppression with lamivudine plus adefovir therapy

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**Objective**
The risk of hepatocellular carcinoma (HCC) is particularly high in chronic hepatitis B (CHB) patients with
cirrhosis. Studies have shown the benefits of treatment for preventing HCC with reducing disease progression in HBVrelated
cirrhosis. However, the long-term efficacy of adefovir dipivoxil (ADV) in combination with lamivudine treatment on
HCC incidence in non-cirrhotic patients is still unclear.
Background & Aims: We report a case of HCC in a HBeAg-negative CHB patient which developed 70 months following
biochemical remission and virological suppression with lamivudine plus ADV therapy.
**Case**
A 56-year-old man with CHB was treated 12 years ago with recombinant interferon (IFN) alpha-2b, 5.000.000 U by three times a week for 24 weeks. Initially, his liver histology was consistent with a moderate activity and
3\6 fibrosis stage. Lamivudine monotheraphy was started 6 years after because of sustained virological and biochemical
response couldn’t be achieved after IFN theraphy but the levels of aminotransferase and hepatitis B virus (HBV)-DNA in
serum had low-watched. Control biopsy prior to lamivudine monotherapy showed mild activity and the same stage of
fibrosis. After 8 weeks of lamivudine treatment, virological and biochemical response were obtained, and continued until
the end of second year when virological breakthrough occured due to lamivudine-resistance. Virological remission was
achieved again 4 months after ADV addition to ongoing lamivudine treatment. Patient was followed every 6 months with
alpha-fetoprotein (AFP) and ultrasound scan for HCC.
HCC was suspected by ultrasonography 70 months after the start of lamivudine. Aminotransferases and AFP
were normal, HBV DNA was undetectable in serum when HCC was diagnosed. Dynamic computed tomography identified
HCC by the finding of a focal hypervascular liver lesion (43x35x36 mm in size) in segment 4B–8. Pathological
examination revealed moderately differentiated HCC with no metastasis. Partial hepatectomy was performed, and no
recurrence was occured within 4-year follow-up.
**Conclusion**
Although excellent biochemical and virological remission were achieved with ADV addition to ongoing lamivudine treatment in our case atleast for 4 years, it wasn’t enough to suppress hepatocarcinogenesis. Long-term
treatment with more potent antivirals that have a higher resistance barrier may be more effective to reduce HCC risk in
lamivudine-resistant patients. Further and multi-centered studies are needed to clarify this topic.