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CASE REPORT

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α-Interferon therapy for HBV-related glomerulonephritis

We report a case of a patient with hepatitis B virus (HBV)-related membranous glomerulonephritis (MGN) who showed improvement after interferon-α (IFN-α) therapy. A 35-year-old man with nephrotic syndrome and HBV antigens received a 24-week course of IFN-α. At the end of therapy there was an elevation in the level of plasma aminotransferase and an increase in proteinuria, which were followed by antigen/antibody seroconversion. This "flare-up" before seroconversion suggests an increase in disease activity in the liver and kidney, demonstrating *in vivo* HBV involvement in MGN.

Uniterms: Hepatitis B virus. Membranous glomerulonephritis. Interferon.

INTRODUCTION

In addition to its role in chronic hepatitis, cirrhosis and hepatocellular carcinoma, the hepatitis B virus (HBV) has also been implicated in extrahepatic immunologic manifestations such as glomerulonephritis and polyarteritis nodosa.[1]

Over the last few years, various morphologic patterns of HBV-related renal disease have been reported, with membranous glomerulonephritis (MGN) being the most commonly described.[1,2] In adults, spontaneous remission of HBV-related MGN rarely occurs and a slow progression to chronic renal failure is reported in about 50% of patients.[2] Recently, promising results have been described in HBV-related MGN therapy with recombinant interferon-α (IFN-α), a cytokine with antiviral and immunomodulatory properties.[3,4]

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In this report, we describe a patient with HBV-related MGN who showed complete serological response and clinical improvement after IFN-α therapy.

CASE REPORT

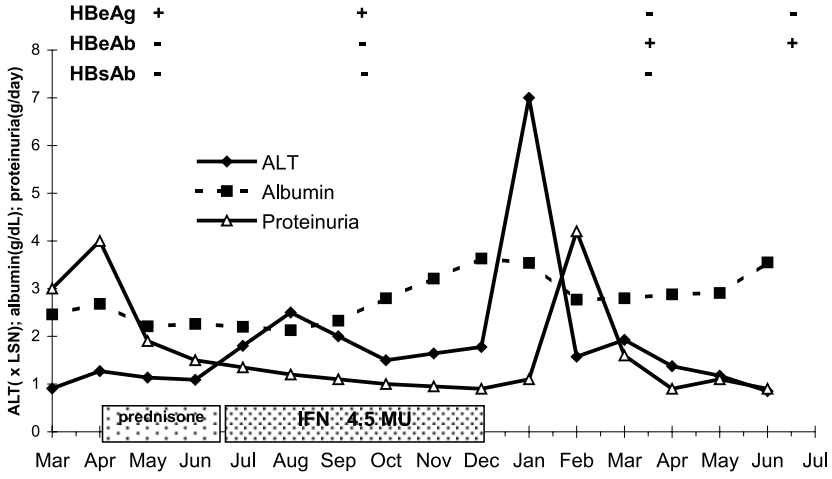
The patient was a 35-year-old white man with a 6-month history of anasarca, whose diagnosis revealed systemic hypertension and associated nephrotic syndrome. Treatment with antihypertensives and diuretics was started. A percutaneous kidney biopsy showed MGN. He was homosexual and had a past history of "acute hepatitis" following surgery for carpal tunnel syndrome 15 months earlier. Both HBsAg and HBeAg were positive by enzyme immunoassay, and anti-HCV and anti-HIV were negative. A liver biopsy showed mild portal lymphocytic infiltrate, and HBsAg was positive in the cytoplasm and HBcAg positive in hepatocyte nuclei. He received a 6-week course of prednisone orally (60 mg daily for 2 weeks, then 40 mg daily for 2 weeks, then 20 mg daily for 2 weeks), which was followed by IFN-α in a dose of 4.5 MU given subcutaneously three times a week for 24 weeks. Proteinuria decreased and serum albumin levels improved,

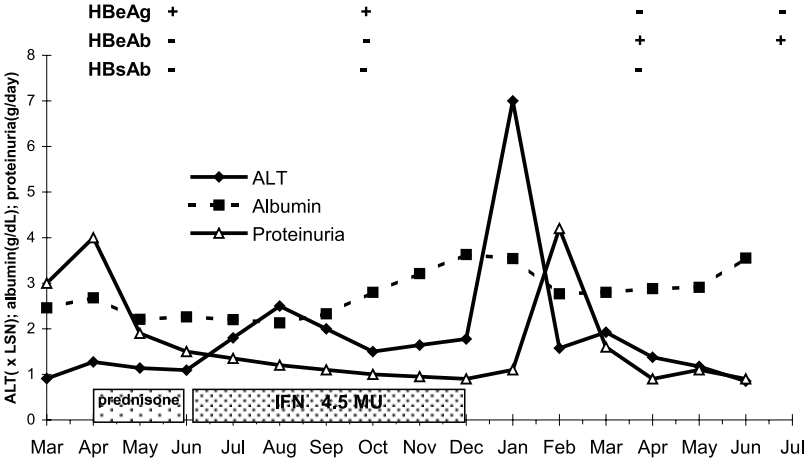
but plasma alanine aminotransferase (ALT) concentrations did not change during the period of IFN-α therapy. However, at the end of IFN therapy a sudden elevation of plasma ALT level (to about 7 times the upper limit for normality) was observed and this was followed by an elevation in urinary protein excretion (Fig. 1). After a few weeks, ALT and urine protein levels return to baseline values and seroconversion from HBeAg to anti-HBe was detected. He seroconverted from HBsAg to anti-HBs 2 months later. Six months after discontinuing IFN therapy, he had normal serum ALT concentrations, his proteinuria levels were decreasing, and he remained without edema by taking a low dosage of antihypertensive medication.

DISCUSSION

Glomerular basal membrane deposition of HBeAg seems to be one of the most important features involved in the development of HBV-related MGN.[1] In fact, remission in chronic hepatitis B, demonstrated by loss of HBeAg from the serum, can occur spontaneously or be induced by antiviral therapy, and this is usually associated with regression in the MGN.

Since HBV does not have a cytopathic effect and the pathogenesis of chronic hepatitis is thought to be mediated by the host immune system, seroconversion from





Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul
0.91	1.27	1.14	1.09	1.80	2.50	2.00	1.50	1.64	1.78	7.00	1.58	1.93	1.38	1.18	0.85	
2.46	2.68	2.21	2.26	2.20	2.13	2.33	2.80	3.21	3.63	3.54	2.77	2.80	2.88	2.91	3.55	
3.00	4.00	1.90	1.50	1.35	1.20	1.10	1.00	0.95	0.90	1.10	4.20	1.60	0.90	1.10	0.90	

Figure 1 - Seric alanine aminotransferase (ALT) levels, seric albumin concentration and urinary excretion of protein in a patient with HBV-related membranous glomerulonephritis, who was treated with a 6-week course of prednisone followed by a 24-week course of interferon-α.

HBeAg to anti-HBe can be related to hepatocyte destruction.[3] Hence, the raised serum ALT elevation activity is believed to be a result of the immuno-mediated clearance of HBV-infected hepatocytes. The short course of prednisone and its sudden withdrawal, as used in this patient, was intended to cause a rebound in the immune system. However, this immunologic response apparently was not obtained and the patient showed persistent baseline serum ALT levels (around the upper limit of normality). The use of corticosteroid before IFN therapy has been proposed for patients with chronic hepatitis B that have normal serum ALT levels, and has been used in patients with HBV-related MGN by Lai et al.[2,3]

At the end of IFN therapy, we observed an immune response characterized by a transitory elevation in serum ALT levels and increased urinary protein excretion followed by HBe and HBs seroconversion. The increase in serum ALT and proteinuria before antigen/antibody seroconversion suggests an increased disease activity in both the liver and kidney, demonstrating *in vivo* HBV involvement in MGN.

More recently, Conjeevaram et al.[4] described clinical, biochemical and serological remission in 8 out of 15 patients (53%) with HBV-related MGN who had been treated with IFN-α. In addition, the 8 responders had MGN while 4 of the 7 nonresponders had membranoproliferative GN, showing that the histologic pattern may be a predictor of therapeutic response.

Although this is an encouraging result, further clinical assessment of IFN-α therapy in controlled trials will be necessary to confirm these findings. Therefore, in patients who have glomerular disease, in particular with MGN, we would recommend investigating HBV markers to avoid prolonged immunosuppressive therapy and to provide antiviral treatment.

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RESUMO

Relata-se o caso de um paciente com glomerulopatia membranosa (GNM) associada a infecção pelo vírus da hepatite B (HBV), que apresentou melhora após tratamento com interferon-α. Trata-se de indivíduo de 35 anos, com síndrome nefrótica e hepatite B, tratado com interferon-α por 24 semanas. Ao final do tratamento, observou-se elevação nos níveis de alanina aminotransferase e de proteinúria, com subseqüente soroconversão dos marcadores virais (antígenos para anticorpos). A exacerbação que predeceu a soroconversão deve refletir aumento na atividade da doença tanto a nível renal como hepático, demonstrando *in vivo* o envolvimento do HBV na GNM.