CASE REPORT

Interferon Induced Glomerular Disease in a Patient With Chronic Hepatitis C

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Summary

Chronic hepatitis C manifests with many extrahepatic features including renal involvement. However, less commonly, interferon therapy for chronic hepatitis C can also result in renal involvement and we describe a case when interferon therapy resulted in minimal change glomerulopathy, a form of involvement which, carries a good prognosis. Our patient developed nephrotic syndrome while on interferon therapy and HCV RNA levels were undetectable at that time. The disease showed excellent response to steroid therapy.

Key Words: Chronic hepatitis C, Interferon, Renal involvement

Introduction

Both alpha and beta interferons (IFN), have been increasingly used for the treatment of many types of malignancy, and recently in the management of hepatitis C virus (HCV) with or without malignancy. We report a patient who developed nephrotic syndrome while being treated with alpha interferon for HCV infection. The renal biopsy showed minimal change glomerulopathy. This case also indicates that when renal abnormalities occur during treatment of HCV infection with alpha-IFN, kidney biopsy may define the responsible renal lesions and serve as a guideline for proper management.

Case Report

NA, a 40 year old security guard presented with a positive anti HCV on third generation Elisa testing, which was discovered when he went for blood donation. There were no identifiable risk factors such as intravenous drug abuse, blood transfusions in the past or multiple sexual partners. He was asymptomatic. Physical examination revealed a well looking man with no evidence of chronic liver disease. Biochemical testing revealed two to three fold elevations of transaminase levels and the levels showed fluctuation. Liver synthetic function was well preserved with normal albumin levels and prothrombin time. A qualitative HCV RNA polymerase chain reaction test was positive. Ultrasound of the hepatobiliary system was essentially normal. HCV viral load was measured by the branched DNA assay method and showed a viral load of 3,480,000 DNA equivalents per ml. HCV genotyping by the INN-LiPA HCV II method confirmed that this was a genotype 1a virus.

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Liver biopsy revealed expanded portal tracts with Chronic inflammatory infiltrate, focal piecemeal necrosis, bile duct damage with spotty necrosis; and was reported as chronic hepatitis C. In view of the biochemical, virological and histological features, definitive treatment was commenced and combination interferon and ribavarin therapy was planned for 48 weeks. The important aspects of therapy including success rates and potential complications were discussed with him. Treatment was commenced on 11/7/2000 and the patterns of alanine transaminase (ALT) response are depicted in Table I. He showed good response to therapy with normalization of ALT levels at week 4 and HCV RNA by qualitative PCR was negative at week 24. He had remained well throughout and tolerated therapy well. At 27 weeks of treatment he suddenly presented with generalized oedema, associated with frothy urine. He did not have any haematuria and denied using any other drugs, traditional medications or herbal products. Urine albumin was 4+ on dipstick and 24-hour quantitation of urine protein revealed a level of protein of 2.3gm. Serum albumin had dropped to 15g/l but liver synthetic function was intact with a normal prothrombin time.

In view of this, a diagnosis of interferon-induced glomerulonephritis with nephrotic syndrome was made. Interferon and ribavarin were both stopped and a repeat HCV RNA by PCR proved to be negative. He underwent a renal biopsy which confirmed minimal change glomerulonephritis and he was commenced on steroid therapy. This resulted in reduction in the degree of proteinuria and after 6 weeks of steroid therapy, a complete normalization of his albumin levels and absence of protein in his urine.

His ALT levels remained completely normal and HCV RNA checked 24 weeks after stopping combination therapy remained negative and he was thus was deemed to have a sustained response. He remains on follow up and ALT levels, urine protein levels are monitored at regular intervals while his HCV RNA is to be checked annually or earlier if there is an ALT flare.

Table I: Alanine transaminase levels at baseline and at subsequent visits after therapy had been commenced and corresponding haemoglobin and HCV RNA levels

Week	0	2	4	8	12	16	20	24	27	29	32	36	41	46	51
Hb	12.3	11.7	11.4	11.6	10.9	11.2	11.1	11.0	10.8	10.9	11.0	10.9	11.0	11.2	11.1
ALT	70	41	33	22	16	24	22	22	18	24	29	31	33	29	23
HCV RNA	0.748							PCR -ve	Therapy stopped						PCR -ve

Discussion

The use of interferon has increased significantly over the past few years, in the treatment of hepatitis B, C and in many types of malignancies. In the setting of Hepatitis C, glomerular involvement is reported and treatment is with interferon alpha. On the other hand there have been a few reports of renal involvement while patients were on interferon alpha treatment, which have been then directly linked to interferon itself [1-3]. Renal biopsy is of utmost importance when renal involvement becomes apparent in order to guide therapy and planning of proper management. The severity of renal involvement will also help define the prognosis.

In this patient renal involvement was of the milder type, namely minimal change glomerulopathy. This has resulted in a very successful outcome to therapy. However relapse may occur in keeping with the natural history of glomerulotides and therefore constant surveillance is important. It must also be emphasized here that interferon therapy is contraindicated in future. Renal biopsy is important in these cases, as it will help define the direction of therapy and serve as a guideline to treatment[1]. In addition to glomerular involvement, tubular involvement has also been reported[1].

Despite having Genotype 1 virus and being treated for only 27 weeks, he has managed to attain a sustained virological response at 24 weeks after stopping therapy. He has to be constantly monitored for virological relapse and will be subjected to an annual HCV RNA by qualitative PCR. In reports prior to this one, the glomerulonephritis has been more severe. In our case, the pattern of involvement has been of the least severe type of glomerulopathy and the outcome to therapy has been excellent. As the number of cases of Hepatitis C increase, and more cases are treated, there is greater likelihood that glomerular involvement will be detected. We would like to propose that all patients undergoing treatment with interferon, have a regular urine protein and microscopy performed to enable early detection of glomerular involvement.

References

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