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Case Report: Open Access

# Successful Treatment of Chronic Hepatitis C using Pegylated Interferon and Ribavirin in a Patient with Sheehan's Syndrome

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**Abstract**

A 50-year-old female with Sheehan's syndrome was treated for chronic hepatitis C using pegylated interferon-α2b and ribavirin. The patient's HCV-RNA status was negative by the fourth week and remained undetectable until the completion of treatment without signs that Sheehan's syndrome had been exaggerated. This case demonstrates that pegylated interferon-α2b and ribavirin does not necessarily exacerbate Sheehan's syndrome.

**Keywords**

Chronic hepatitis C, Sheehan's syndrome, Interferon

**Abbreviations**

HCV: Hepatitis C Virus; CHC: Chronic Hepatitis C; PEG-IFN-α: Pegylated Interferon-α; IFN: Interferon; SS: Sheehan's Syndrome; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase

## Introduction

Hepatitis C virus (HCV) infection is a global public health problem affecting an estimated 185 million people worldwide [1]. Chronic hepatitis C (CHC) is associated with variable degrees of hepatic inflammation and fibrosis. Without effective treatments, significant increases in CHC-associated morbidity, mortality, and healthcare costs are predicted [2]. A treatment consisting of a combination of pegylated interferon-α (PEG-IFN-α) and ribavirin was the approved and accepted standard-of-care for CHC before the advent of direct-acting antiviral agents and remains the preferred treatment for the majority of patients with CHC [3]. However, interferon (IFN) therapy has been associated with a variety of possible side effects in virtually all organ systems [4]. Thus, antiviral therapy in patients suffering from CHC and concurrent comorbidities may not be a viable option because it can reduce the likelihood of a good therapeutic response due to an increased frequency of side effects.

Sheehan's syndrome (SS) is a parturition-related pituitary disease resulting from severe postpartum hemorrhage and can present with varying degrees of pituitary insufficiency ranging from general symptoms, such as weakness and fatigue, to severe pituitary insufficiency that can lead to coma and even death [5]. Although the frequency of SS has recently declined in developed countries due to modern obstetric care, it remains a common problem in developing countries, in which epidemiological studies have reported a high prevalence [5]. The etiopathogenesis of SS is not yet fully understood but is thought to involve increased pituitary volume, small sella size, disseminated intravascular coagulation and autoimmunity [6]. Patients with SS may present concurrent HCV infection resulting from the transfusional therapy used to treat severe postpartum hemorrhage. To date, there are no data concerning IFN treatment in patients with confirmed Sheehan's syndrome. Clarifying whether the treatment of CHC with IFN is possible in patients with SS is of great clinical relevance. Indeed, a number of SS patients treated with transfusional therapy during the past decades have been exposed to HCV infection, and a portion of them exhibit advanced chronic hepatitis. In this study, we report that a patient with concurrent CHC and SS was successfully treated with a combination of PEG-IFN-α and ribavirin.

## Case Report

In September 2014, a 50-year-old female with concurrent HCV infection and SS was referred to the Liver Research Center to be considered for anti-HCV treatment. She had been in good health until the age of 22. Menstruation had been normal from the menarche at 14, and she married and had her first pregnancy in 1986. The first delivery was uncomplicated and was followed by normal breast feeding, lactation and the reestablishment of menstruation. However, at the end of a second pregnancy in 1993, she exhibited severe vaginal hemorrhage after delivery that required the transfusion of several units of blood due to circulatory collapse. Subsequently, the patient did not lactate and had permanent amenorrhea. She gradually developed generalized malaise, hair loss, intolerance to cold, and weight gain following her last delivery and was diagnosed with SS by endocrinologists at our hospital in 1994 based on her combined symptoms, abnormal endocrinological tests (low adrenocorticotrophic hormone (ACTH), thyroid-stimulating hormone (TSH) and free serum thyroxine levels), and the history of severe postpartum hemorrhage. She had taken both levothyroxine and prednisolone because the SS diagnosis and did subjectively well with hormonal supplementation.

She had been diagnosed as HCV-positive more than two years prior at another hospital, but was not treated with IFN therapy

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due to fears of exacerbating her SS and because her liver function was normal at that time. Approximately two months previously, she was found to have elevated serum transaminase levels during a routine examination. By physical examination, she was found to be moderately obese but otherwise in good clinical health: her vital signs were normal, and no hepatosplenomegaly was present. The results of a complete blood count and the glucose, electrolytes, albumin, globulin, and bilirubin serum levels were all within the normal range, as were renal function, coagulation, and thyroid function. The level of Alanine Aminotransferase (ALT) was 179 units per liter, and that of Aspartate Aminotransferase (AST) was 164 units per liter. The baseline serum HCV-RNA concentration, measured by reverse transcriptase polymerase chain reaction, was 457000 IU/mL. The HCV genotype was 1a. Given the presence of SS, a joint evaluation was performed in collaboration with the outpatient clinic for endocrinology. Before therapy her endocrinological tests were: triiodothyronine (T3): 0.96 ng/ml (normal: 0.58-1.59 ng/ml); thyroxine (T4): 6.1 μg/ml (normal: 4.87-11.72 μg/ml); Free serum Triiodothyronine (FT3): 2.23 pg/ml (normal: 1.71-3.71 pg/ml); Free serum Thyroxine (FT4): 1.1 ng/ml (normal: 0.70-1.48 ng/ml); Thyroid-Stimulating Hormone (TSH): 0.65 μIu/ml (normal: 0.35-4.49 μIu/ml). The endocrinologist considered the patient's SS to be in stable condition.

In September 2014, PEG-IFN-α-2b (80 mcg per week subcutaneously) and ribavirin (900 mg per day orally) antiviral therapy was initiated. This therapy was prolonged for 48 weeks. Close monitoring of clinical symptoms, blood counts, and liver and thyroid function were performed throughout the treatment course. The treatment was well tolerated, with the exception of flu-like symptoms that were easily controlled by paracetamol, and a mild decrease of the white blood cell, platelet, and hemoglobin counts. The exacerbation of SS symptoms did not occur during treatment. Interestingly, the HCV-RNA test was negative by the fourth week (< 25 IU/mL) and continued to be undetectable up to the completion of treatment. Similarly, ALT and AST normalized within the first 4 weeks of treatment, and the results of all other laboratory tests were normal. During and after therapy, the results of her endocrinological tests were similar to those before therapy. The patient is now receiving hormonal therapy. She is in good health and is more active and energetic. Written informed consent was obtained from the patient before the procedures. The study conformed to the 1975 Helsinki declaration and was approved by the Second Xiangya Hospital Ethics Committee.

## Discussion

IFN therapy has been associated with a large variety of possible side effects in virtually all organ systems. Thyroid disease, with the clinical manifestations of hypothyroidism or hyperthyroidism, has been reported in 5% to 12% of patients who received IFN for various diseases [4]. To the best of our knowledge, six cases of hypopituitarism developed following PEG-IFN-α therapy have been described to date in English-language literature [7-12]. Among them, two women developed symptoms related to hypopituitarism on the second and fourth days of IFN therapy for CHC and were diagnosed with latent Sheehan's syndrome, which had manifested during IFN therapy. Their symptoms improved rapidly with hormone replacement therapy. The first patient discontinued the antiviral therapy; the second patient successfully completed 12 months of therapy without other complications and achieved a sustained virological response. It is likely that the rapid development of symptoms in these two cases was caused by the acute decompensation of latent adrenal insufficiency upon the initial stress of IFN therapy [7,8]. The remaining four patients developed hypopituitarism between two weeks and one year of IFN therapy [9-12]. The patients' symptoms also improved markedly with hormone replacement therapy. Hypopituitarism ran a reversible course in two patients but was irreversible in the other two patients. The incidence and pathogenesis of hypopituitarism in these patients remains uncertain, although the involvement of the immune system is likely.

Unlike previously reported cases, our patient had confirmed SS. There are no data describing IFN treatment in patients with confirmed Sheehan's syndrome. We carefully evaluated whether to treat the patient and any possible complications that might have occurred, including a worsening of the basic pathology. Only after a thorough examination and taking into account the high risk of CHC progression, the stable condition of SS, and the strong motivation of the patient did we start anti-HCV treatment under close clinical monitoring. The patient presented a rapid virological response after four weeks of therapy and a sustained virological response after one year of therapy. This case shows that pegylated interferon-α2b and ribavirin does not necessarily exacerbate SS in patients who have been stable for extended periods. In such difficult clinical situations, anti-HCV therapy may also be attempted, especially in patients at high risk of CHC progression. However, careful monitoring remains necessary in patients with SS who receive both PEG-IFN-α and ribavirin therapy. In conclusion, the successful treatment of CHC with pegylated interferon and ribavirin was possible in a patient with SS.

## Conflict of Interests

The authors declare that they have no competing interests.


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