Case Report

Treatment of autoimmune thrombocytopenia in a case of chronic hepatitis C with ursodeoxycholic acid

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Abstract

Pegylated interferon (PEG-IFN) alpha and ribavirin therapy has become the standard treatment in chronic hepatitis C virus (HCH)-infected patients. While thrombocytopenia associated with IFN use is frequently observed among these patients, autoimmune thrombocytopenia is one of the rarely observed adverse effects. In the present report, we present a case with chronic HCV infection in which autoimmune thrombocytopenia developed at week 7 of PEG-IFN alpha 2b plus ribavirin therapy. The patient subsequently received ursodeoxycholic acid (UDCA) treatment. Although there is not an adequate number of studies on this subject, it was concluded that the use of UDCA in cases of autoimmune thrombocytopenia that have developed due to PEG-IFN treatment in chronic HCV infection is a favorable option.

Key Words: autoimmune thrombocytopenia, side effects, PEG-IFN-alpha, chronic hepatitis C, ursodeoxycholic acid

Introduction

Chronic hepatitis C virus (HCV) infection is recognized as a global health problem with 170 to 200 million people estimated to be infected worldwide [1]. Chronic HCV is one of the most common chronic viral infections worldwide and it is a major cause of cirrhosis, end-stage liver disease and hepatocellular carcinoma [2]. Pegylated interferon (PEG-IFN) alpha and ribavirin therapy has become the standard treatment in chronic HCV infected patients [3]. While thrombocytopenia associated with IFN use is frequently observed among these patients, autoimmune thrombocytopenia is one of the rarely observed adverse effects [4]. Similarly, many autoimmune thrombocytopenia cases resulting from the introduction of PEG-IFN alpha therapy have been reported [5-11]. Here we present a case with chronic HCV infection in which autoimmune thrombocytopenia developed at week 7 of PEG-IFN alpha 2b plus ribavirin therapy. The patient subsequently received ursodeoxycholic acid treatment.

Case Report

A 60-year-old female patient presented as HCV positive, with ALT 87 IU/L, WBC 6,700/µL, Hb 14 g/dL, platelet count 240 x 10^3/µl, and HCV RNA 1 038 014 IU/ml. The patient refused liver biopsy, and the FibroTest® was performed. The results of the FibroTest® were A3 (severe activity) and F2 (bridging fibrosis with septa). PEG-IFN alpha 2b 1.5 µg/kg/wk sc and ribavirin 1,200 mg/day therapy was initiated in this patient. The patient presented in our clinic due to extensive petechia and patches of ecchymosis in the upper and lower extremities at week 7 of the therapy. On detection of the platelet count as 16 x 10^3/µl, PT 12.4 sec. (10-14), PTT 29.8 sec. (24-35), INR 0.96 (0.81-1.17), the patient was hospitalized. PEG-IFN and ribavirin therapy was terminated. Peripheral blood tests showed erythrocytes were normocrom-normocytic and leucocytes were normal in number and nature. The platelet count had decreased excessively. In bone marrow aspirates, megacaryocytes were sufficient and a dwarf appearance was detected in some. Erythroid and myeloid lineage initiators were observed as normal. Anti-nuclear antibodies, anti-mitochondrial antibodies, anti-smooth muscle antibodies, anti-liver-kidney-microsome antibodies, anti-thyroid autoantibodies, and rheumatoid factor were negative, while immunoglobulin (Ig) G, IgA and IgM were normal. Cryoglobulin was not detected.

Figure 1. Patient's platelet count during treatment and follow-up period.
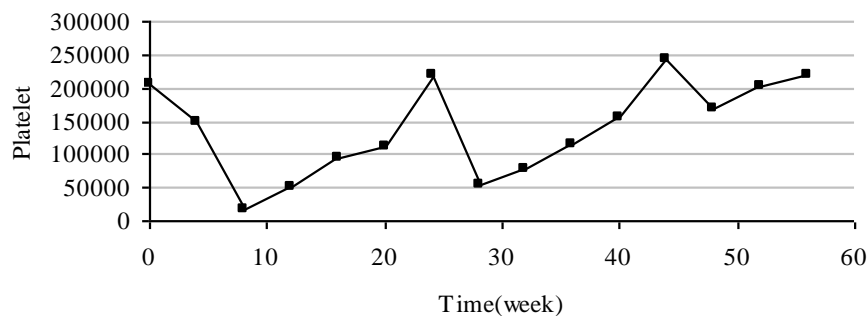
HCV RNA was positive (41 019 IU/ml). , The patient was diagnosed as autoimmune thrombocytopenia associated with PEG-IFN treatment after anti-platelet autoantibodies (anti-GPIIb-IIIa) were found to be positive. Ursodeoxycholic acid (UDCA) 1,500 mg/day (q8h) therapy was initiated. At week 16 after initiation of UDCA therapy, the platelet count was detected as $219 \times 10^3/mm^3$, HCV RNA 41 019 IU/ml, ALT 62 IU/l. UDCA therapy was terminated at week 52 of the therapy. At week 4 after the termination of UDCA therapy, the platelet count was detected as $219 \times 10^3/mm^3$ (Figure 1).

Discussion

In chronic HCV infection, many adverse effects associated with PEG-IFN plus ribavirin treatment have been observed. Hematological adverse effects are the most frequently observed, and they require dose reduction or treatment cessation [4,12]. Autoimmune thrombocytopenia, thrombotic thrombocytopenic purpura, and autoimmune hemolytic anemia have been observed in association with PEG-IFN use [8,13,14]. Our case was diagnosed with autoimmune thrombocytopenia at week 7 of PEG-IFN treatment. In the other cases, development of autoimmune thrombocytopenia was observed at weeks 4, 8, 10, and 13 and at months 6 and 12 of therapy [5-10]. In the case of Elefsiniotis *et al.*, autoimmune thrombocytopenia developed six months after the therapy was completed [11]. Therefore, clinicians should keep in mind that autoimmune thrombocytopenia can occur late after the initiation of PEG-IFN therapy. Of the previously reported cases in which PEG-IFN was used, two cases developed autoimmune thrombocytopenia after PEG-IFN alpha 2a [5-8,11]. PEG-IFN alpha 2b was used in our case. In other previously presented cases, four were given intravenous immunoglobulin (IVIG) and steroid, one case received IVIG and danazol, one received IVIG and ritoximab, and one received steroid therapy [5-11].

It has been suggested that the primary immune defect in chronic ITP is caused by autoantibodies that are specific to glucoproteins on the surface of the platelets secreted by autoreactive B lymphocytes and a decrease in the self-tolerance level of T lymphocytes [15]. An abnormal subpopulation of T lymphocytes may arise in that the proportion of CD4+ and CD8+ lymphocytes may be reversed and the number of activated CD3+ lymphocytes may be increased [15,16]. Moreover, interleukin (IL)-2 secreted by CD4+ lymphocytes stimulates the secretion of anti-platelet autoantibodies in B lymphocytes[16]. Koike *et al.* reported two cases in whom liver dysfunction with immune thrombocytopenia was detected and whose platelet counts increased after UDCA treatment was initiated. They suggested that UDCA treatment was effective in these cases by decreasing immunoglobulin production in B lymphocytes and cytokine production in T cells [17]. Since corticosteroids used in first-line therapy of autoimmune thrombocytopenia can increase viral replication, we gave 1,500 mg/day UDCA treatment to our patient. At week 16 of UDCA treatment, we observed that platelet count had become normal in our patient. At week 4 after termination of UDCA treatment, the platelet count was detected at $219 \times 10^3/mm^3$.

In summary, although there is not an adequate number of studies on this subject, it was concluded that the use of UDCA in autoimmune thrombocytopenia that has developed due to PEG-IFN treatment in chronic HCV infection is a favorable option.

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Conflict of Interest: No conflict of interest is declared