

Case Report

Successful use of splenectomy in a patient with hepatitis C virus-related thrombocytopenia

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Abstract

This case report describes a 44-year-old female with hepatitis C virus-related thrombocytopenia. The laboratory tests showed a platelet count of $3 \times 10^9/l$, positive HCV serology and high serum concentration of HCV-RNA of 6.74×10^6 copy/ml. She was refractory to standard therapies including corticosteroids, intravenous immunoglobulin (IVIG), thrombopoietin (TPO) and even interferon (IFN) regimens, due to the persistence of a low platelet count. At first, splenectomy was thought to be impossible, but then splenectomy was successfully performed and patient showed good tolerance and a constant normal platelet count after surgery. In conclusion, splenectomy is feasible in selected patients and may allow us to acquire a reasonable platelet count and completion of an anti-HCV protocol. Low platelet count itself should not be the contraindication of operation specifically for these patients. Further studies in larger numbers of patients and over a longer period of time are warranted.

Key words: hepatitis C; thrombocytopenic; splenectomy.

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Introduction

A 44-year-old female was admitted to our hospital with mucocutaneous hemorrhage for a fortnight. She had a history of unsafe blood-selling ten years before. However, she did not do any routine blood tests and seldom suffered obvious bleeding. At the moment of admission, blood tests showed severe thrombocytopenia, with a platelet count of $3 \times 10^9/l$. Virological examination showed positive Anti-HCV antibodies, and mean quantitative value of HCV-RNA were 6.74×10^6 copy/ml. Patient's liver and coagulation functions were normal, although B-ultrasonography examination revealed chronic liver disease, liver cirrhosis and splenomegaly. The results of a screening of autoimmune markers including antinuclear antibodies (ANA), anti ds-DNA antibodies and antiphospholipid antibody were negative. Bone marrow smear showed a normal number of megakaryocytes with mainly granular megakaryocytes. So the diagnosis was hepatitis C virus-related thrombocytopenia.

Firstly, the treatment was intravenous methylprednisolone 80 mg/day and oral ribavirin (1000mg/day) together with platelet transfusion at irregular intervals. Ten days later, after the patient complained of a worsening hemorrhage, high-dose

IVIG (400mg/kg) was added. Her platelet count remained in the range of $1 \times 10^9/l$ to $4 \times 10^9/l$ while HCV-RNA increased to 2.02×10^7 copy/ml with elevated serum ALT level after glucocorticoid was used for one month. Platelet growth factor therapy with romiplostim was administered for 20 days, and there was no obvious change in platelet count. Finally the low-accelerating dose regimen of IFN- α , together with ribavirin, were used. The initial IFN- α dosage was 90 MU/day, which was then increased gradually from 180 MU daily to 360 MU daily. During the first period of IFN- α treatment, the load of HCV-RNA average dropped to $4.58 \times 10^3/l$, and the platelet count increased to a maximum level of $10 \times 10^9/l$. However, as IFN- α dosage increased, platelet count decreased to the minimum level of $1 \times 10^9/l$ and the patient showed severe nasal hemorrhage, so IFN- α was discontinued after administration for 21 days.

Given her refractoriness, splenectomy was decided. One week after the termination of IFN- α therapy, with the support of platelet transfusion, the splenectomy operation was performed. There were no severe bleeding or infection complications during or after splenectomy. The patient recovered well and a rapid increase in platelet count was observed immediately after the surgery. Her platelet count

returned to normal and remained above $100 \times 10^9/l$ for more than 1 year after surgery. Splenic pathologic examination exhibited immune thrombocytopenic purpura with small focal lymphoid hyperplasia. Meanwhile, under the regular treatment of the Infectious Disease Unit, IFN- α was utilized for anti-HCV protocol without dose reduction, achieving a sustained virological response.

Discussion

Data showed that chronic active HCV infection may induce an autoimmune reaction to platelets leading to thrombocytopenia, the activation of B lymphocytes due to HCV infection might be one of main causes [1-3]. For many years, no standard treatment was established for patients with Hepatitis C virus-related thrombocytopenia [4,5]. General therapeutic strategies included corticosteroids, IVIG and TPO, and even rituximab and danazol, which all resulted partially effective. Until 2011, there has been a guideline for this [6]. The American Society of Hematology in 2011 published an evidence-based practice guideline for immune thrombocytopenia recommending that in patients with secondary ITP due to HCV infection, antiviral therapy should be considered in the absence of contraindications (grade 2C). However, the platelet count should be closely monitored due to a risk of worsening thrombocytopenia attributable to infection. If treatment for ITP is required, the initial treatment should be IVIG (grade 2C). This guideline also suggests that the presence of thrombocytopenia with a platelet count $<75 \times 10^9/l$ is a relative contraindication to interferon therapy, corticosteroids may increase the platelet count, but it may also increase the HCV viral load. In contrast, IVIG may result in a short-lived platelet-count increase, but without an increase in the HCV viral load. Thrombopoietin can increase platelet count, but it produces infrequent off-treatment sustained remissions. Splenectomy appears effective for thrombocytopenia associated with HCV.

Although thrombocytopenia can be a complication of hepatitis C virus (HCV) infection, these patients have less severe thrombocytopenia, defined as platelet count $\leq 10 \times 10^9/l$. Whereas our patient showed persistence of a low platelet count less than $\leq 10 \times 10^9/l$ in combination with high load of HCV-RNA when first diagnosed. Theoretically, this patient required urgent elevation of platelet and antiviral treatment at the same time. Yet, she showed an extremely low platelet count and obvious bleeding. Since IFN therapy may aggravate thrombocytopenia through the

inhibition of platelet production, increasing platelet count was our priority. Effective therapies were needed to increase the platelet count to a certain level that can lift the risk of life-threatening bleeding episodes and to initiate and maintain antiviral treatment with natural IFN- α as well.

Unfortunately, this patient was unresponsive to these therapies according to previous observations. Chronic HCV patients with baseline thrombocytopenia are often excluded from treatment with peginterferon alfa and ribavirin or undergo many dose reductions of peginterferon alfa because they may exacerbate thrombocytopenia. Several studies indicated treatment with peginterferon alfa and ribavirin appears to be safe in patients with platelet counts below $50 \times 10^9/l$ and severe bleedings did not occur [7,8] although in these case reports, patients with platelet counts below $25 \times 10^9/l$ were rare. Our patient was administered with IFN and only showed a minor response in the initial stage, so therapy was discontinued due to a worsening platelet count and bleeding onset; extremely low baseline thrombocytopenia and IFN adverse events may be a possible explanation for this.

Although the guidelines indicated splenectomy can be a useful way to increase platelet count for these patients, these studies were small; only a few successful cases reported specifically on these patients whose platelet count was more than $50 \times 10^9/l$, guaranteeing the success of operation [9-12]. We seldom found case reports in which platelets were as low as below $10 \times 10^9/l$ with splenectomy. Therefore, our patient was considered inoperable at the beginning. The risk of a massive hemorrhage during and after surgery, operative complications and being unresponsive to this surgery were into consideration. However, as almost all measures seemed ineffective, in agreement with the patient we had to take a risk, with the support of a good communication with surgeons and enough platelet transfusion. This patient did well intraoperatively and postoperatively and her platelet count showed a remarkable response.

Given the response seen with splenectomy in our patient and the fact that other therapies like IVIG and thrombopoietin have the inconvenience of elevated costs and duration, we propose that splenectomy is appropriate in patients with hepatitis C virus-related severe thrombocytopenia in the event that other treatments are ineffective. Most importantly, the low platelet count itself should not always create hesitancy to treat this type of patient with splenectomy.

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