Case Report

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Portal vein thrombosis as complication of romiplostim treatment in a cirrhotic patient with hepatitis C-associated immune thrombocytopenic purpura

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Background & Aims: Thrombopoietin receptor agonists are a new class of compounds licenced for the treatment of immune thrombocytopenic purpura. They are currently being studied for patients with thrombopenia in advanced liver disease or under therapy for hepatitis C. There are indications that the risk for development of portal vein thrombosis in patients with advanced liver cirrhosis might be increased under therapy with thrombopoietin receptor agonists. We report a case of a patient with Child class B liver cirrhosis with concurrent immune thrombocytopenic purpura that developed portal vein thrombosis under therapy with the thrombopoietin receptor agonist romiplostim.

Methods: A 50-year-old woman with hepatitis C virus associated immune thrombocytopenic purpura and Child class B liver cirrhosis presented in our emergency with rapidly evolving hydropic decompensation and general malaise. For immune thrombocytopenic purpura, the patient was started on the thrombopoietin receptor agonist romiplostim nine months ago.

Results: During hospitalization, the platelet count was measured above 330,000/μl and partial portal vein thrombosis was diagnosed by imaging studies. The thrombotic event was assumed to be associated with the romiplostim treatment for immune thrombocytopenic purpura via excessive elevation of platelet count. After anticoagulation with heparin and cessation of romiplostim treatment, complete recanalisation of the portal vein was achieved.

Conclusions: We conclude that romiplostim should be used with precaution in patients with hepatitis C-associated immune thrombocytopenic purpura and advanced liver cirrhosis as the risk for thrombotic complications may increase significantly.

Case report

A 50-year-old woman with Child class B liver cirrhosis due to chronic hepatitis C was admitted to the hospital in June 2010 with rapidly evolving hydropic decompensation and general malaise. The patient was on the waiting list for orthotopic liver transplantation and had a Model for End-Stage Liver Disease (MELD) score of 20. Abdominal ultrasound examination showed large amounts of ascitic fluid and a thrombus that had emerged in the extrahepatic portal vein and which obstructed approximately two third of the veins lumen. By doppler sonography, portal vein peak-flow was measured to be 22 cm/s. Liver veins showed no abnormalities. The diagnosis was confirmed by computed tomography which showed a localized thrombosis at the intersection of the superior mesenteric vein into the portal vein (Figs. 1 and 2). Previous abdominal CT scans and regularly performed abdominal ultrasound examinations had never documented an obstruction of the portal vein so that it was assumed to be a recent event.

The patient had HCV-associated immune thrombocytopenic purpura (ITP) and treatment with the thrombopoitin receptor agonist (TRA) romiplostim was started nine months ago. ITP had been diagnosed in March 2009 by the detection of IgM and IgG antibodies by platelet immunofluorescence test (PIFT). The antibodies were specified by simultaneous analysis of specific platelet antibodies (SASPA) such as IgG antibodies against GP (glycoprotein) IIb/IIIA, IX, Ia/IIA, CD32, CD62p, CD9, GPV, CD109, CD31, CD49e, CD36, and HLA-class I-attributes and IgM antibodies against GP IX. Pseudothrombocytopenia was excluded previously by blood smear examination. Bone marrow aspiration had shown increased megakaryopoiesis. As the patient experienced bleeding from esophageal varices in the past, coexisting ITP was considered as a major risk factor for re-bleeding although band ligation was performed previously and the patient was on prophylactic propranolol therapy. Therefore, ITP was treated by pulse therapy with glucocorticosteroids 2 mg/kg but no significant increase in platelet count could be observed. Glucocorticosteroids were ultimately stopped as the patient developed deterioration of blood glucose levels and hepatic encephalopathy. Since platelets dropped below 20,000/μl repeatedly, treatment with the TRA romiplostim 500 μg/week subcutaneously was initiated. Romiplostim is approved for patients with ITP in which steroids are not successful and in which splenectomy is not

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Abbreviations: HCV, hepatitis C virus; ITP, immune thrombocytopenic purpura; MELD, model for end-stage liver disease; TRA, thrombopoietin receptor agonist; GP, glycoprotein.

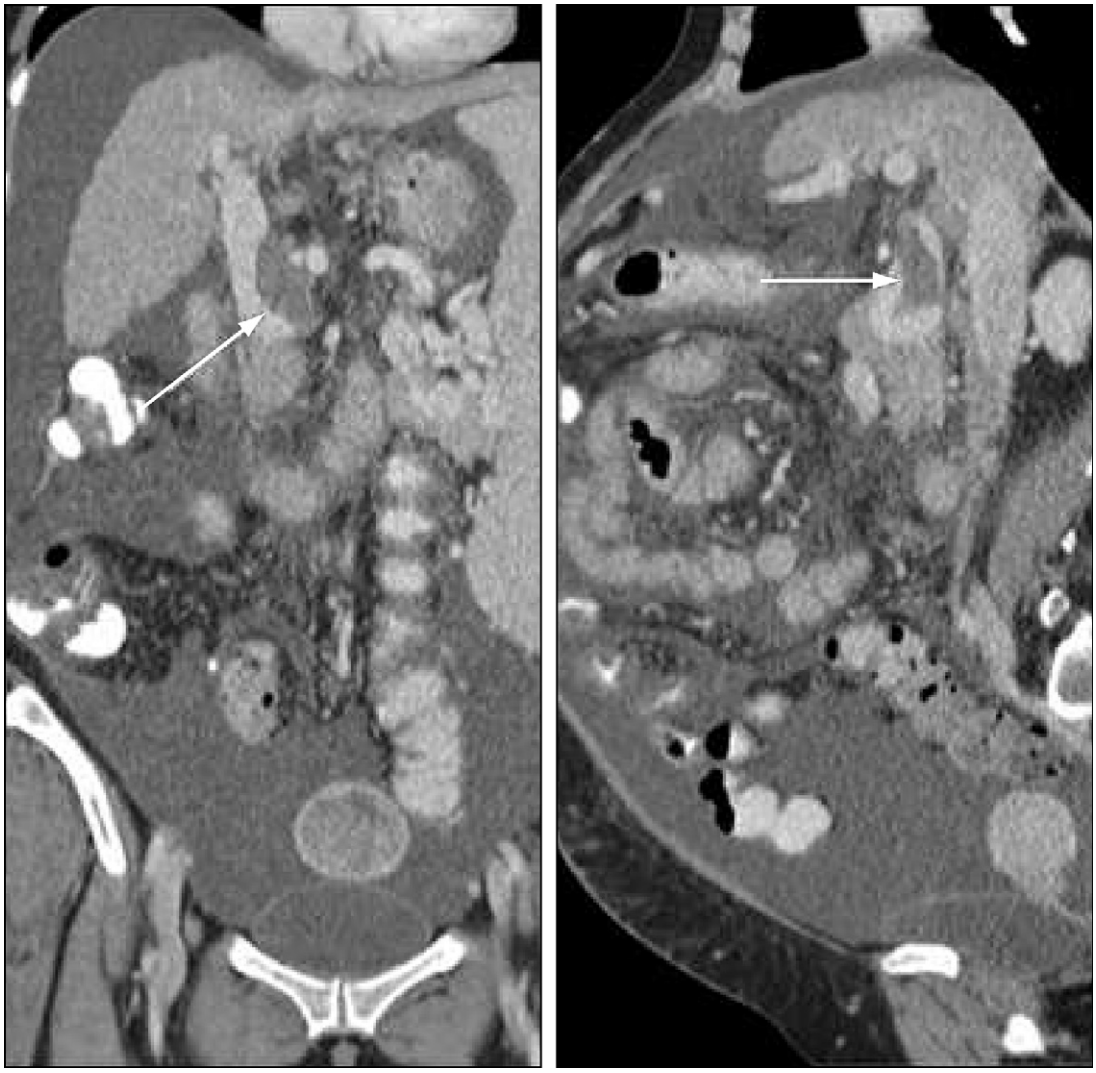

Fig. 1. The coronal and sagital view of a contrast enhanced CT in a 50-year-old female patient shows partial obstruction of the portal vein. The white arrow indicates narrowing and partial obstruction due to a huge thrombosis located in the extrahepatic portal vein.

recommended. At that time point, the patient had a Child class B cirrhosis with a MELD score of 16 without clinical signs of hepatic encephalopathy or hydropic decompensation. Weekly romiplostim injections resulted in a rapid increase in platelet count over 50,000/μl and were continued until hospital admission in June 2010.

Review of the platelet count during hospitalization revealed a peak of 331,000/μl whereas platelet count ranged between 50,000/μl and 100,000/μl during several weeks before admission (Fig. 3). Hence, coincidence of exceeding increase in platelet count and onset of portal vein thrombosis suggests a causative role of romiplostim leading to immediate discontinuation of romiplostim treatment. Thrombophilia screening including antiphospholipid antibodies, factor II/V mutations and Jak 2 genotyping did not show any abnormalities. Continuous intravenous administration of unfractionated heparin was initiated and the clinical condition of the patient improved constantly. The beneficial antithrombotic effect of heparin treatment was evaluated by intra-arterial digital subtraction angiography (DSA) of the celiac trunk and superior mesenteric arteries nine days later. Fortunately, complete recanalization of the portal vein was achieved (Fig. 4). Celiac trunk and inferior vena cava were shown to be free of thrombotic material. The patient was discharged two weeks after the diagnosis of portal vein thrombosis and low molecular weight heparin was administered subcutaneously thereafter. Finally, the patient received a liver graft in August 2010. Histologic examination of the patient's explanted liver revealed advanced cirrhosis without evidence of hepatocellular carcinoma.

Discussion

Chronic HCV infection is associated with a variety of extrahepatic manifestations including lymphoproliferative hematologic diseases as well as a wide range of immune-related disorders [1,2]. Recent reports emphasize that the incidence rate of ITP in patients with chronic hepatitis C is higher than previously