Portal Vein Thrombosis in a Chirrotic Patient with Immune Thrombocytopenic Purpura During Eltrombopag Treatment

Gül İlhan¹, Can Acıpayam²
¹Hatay Antakya Devlet Hastanesi, Hematoloji Bölümü, Mustafa Kemal Üniversitesi Tıp Fakültesi, Pediatrik Hematoloji ve Önkoloji Bölümü, Antakya, Türkiye

Abstract
Portal vein thrombosis (PVT) is a rare but serious complication in liver cirrhosis. Eltrombopag is a new, second generation agent used for immune thrombocytopenic purpura (ITP). It may cause thrombotic events. PVT has been rarely reported as a life threatening complication in some cirrhotic patients during eltrombopag using. We presented 63 years old cirrhotic and immune thrombocytopenic patient who had PVT after eltrombopag.

Keywords
Portal Vein Thrombosis; Immune Thrombocytopenia; Eltrombopag

Özet

Anahtar Kelimeler
Portal Ven Trombozu; Immün Trombositopenik Purpura; Eltrombopag
Introduction

Eltrombopag is a second generation thrombopoietin receptor agonist used for immune thrombocytopenic purpura in last years. Some studies showed that it increased deep vein and pulmonary thrombosis risk while platelet count was normal or subnormal [1].

Portal vein thrombosis (PVT) is a life threatening event caused by myeloproliferative diseases, cirrhosis, cancer and infections. It occurs acutely or chronically. Clinical features of PVT is ranged from asymptomatic disease to gastrointestinal bleeding and acute intestinal ischemia. PVT is rare but life threatening complication showed in patients with chronic liver disease and thrombocytopenia during eltrombopag treatment [2,3,4].

In cirrhotic patients, PVT frequency is 0.6-15.8%. Hereditary or acquired thrombophilic factors, bacterial infections and reduced portal vein flow increase frequency. In cirrhosis both procoagulant and anticoagulant factors decrease and coagulation balance can move to one side easily. There are some studies showing increase in factor 8 and decrease in protein C in these patients. Factor V leiden, prothrombin and methylenetetrahydrofolate mutations have minimal importance on PVT. While in case of partial PVT, patients are asymptomatic, in case of full obstruction, acute abdomen and lombar pain may occur. Bloodless diarrhea can be seen if there is additional mesenteric vein thrombosis. Patients with chronic PVT can be asymptomatic or can be diagnosed with symptoms of hypersplenism or portal hypertension. Cavernous transformation of portal veins or hepatic pedal collateral veins can be seen. Doppler ultrasonography or ultrasonography are generally sufficient for diagnosis but computerized tomography or magnetic resonance are more sensitive for showing extension of thrombus in detail. Anticoagulation must be done in acute PVT. The aim is recanalization of veins and prevention of intestinal enfarction and portal hypertension.

Antithrombin III, TIPS (transjugular intrahepatic portosystemic shunting) are other treatment options. Therapy of chronic PVT is controversial. If thrombophilic factors or risk of mesenteric veins at the first month of the treatment. Immediately, we rejected splenectomy operation. For this reason we decided to stop azatiopurine and gave him eltrombopag with low dose (15 mg/kg/day). After one month platelet count reached to 97000/µL but he complained of abdomen and back pain. Portal venous doppler ultrasonography showed ascites and thrombus in portal vein extending right main branch at intrahepatic region and in splenic veins. We gave low dose (3500 units/day) bemiparin sodium subcutaneously to him. For 3 months, he is being followed with about 50 000/µL platelet count.

Discussion

Thrombocytopenia is seen approximately 49-64% in chronic liver disease patients. Platelet levels rarely decrease under 30 000-40 000/µL. Thrombocytopenia causes is hypersplenism, impaired thrombocyte production, immune or non immune factors. Immune thrombocytopenia is seen more frequently due to hepatitis C [6].

In a phase II study, 74 HCV-related cirrhosis patients were given eltrombopag at doses of 30,50 and 75 mg/day. Platelet counts of patients were 20-70 000/µL. Most of patients reached to platelet count of 100 000/µL at 4 week [7].

Portal vein thrombosis after eltrombopag has been reported as a rare but mortal complication. Treatment and prognosis are not clear because of few number of cases. Two PVT cases were reported in two cirrhotic patients. One of them was with eltrombopag, another one was with romiplostim. In non cirrhotic patients, standart treatment of PVT is anticoagulant therapy was given and thrombosis of them were resolved [3,4].

In a randomised study, 75 mg/kg eltrombopag was given to 145 chronic liver patient at dose of 75 mg daily for 14 days before invasive procedures. Platelet requirement was 28% in eltrombopag group vs 81% of placebo group. PVT was seen in 6 patients who received eltrombopag as compared with 1 who received placebo. Study was finished early [7].

In a patient with HCV related cirrhosis and ITP, low dose (12.5 mg/day) eltrombopag was used. Fifty four days later portal vein thrombosis occurred. Although eltrombopag was stopped, subsequently pulmonary and deep vein thrombosis were shown. Heparin and antithrombin III were used and recanalization was seen. [8]. In our case, thrombosis occurred in portal and splenic veins at the first month of the treatment. Immediately, we stopped eltrombopag and started low molecular wight heparin. We had used eltrombopag with low dose but couldn't prevent thrombosis.

Mechanism of thrombosis development with eltrombopag is not clear. Increase in platelet count and activity can be causes [8]. In non cirrhotic patients, startandt treatment of PVT is anticoagulation with drugs such as antithrombin III and heparin for 14-15 months. But in cirrhotic patients, anticoagulant therapy increased bleeding [7]. In a cirrhosis case with PVT after eltrombopag, there was no bleeding [8]. In these kinds of patients, treatment must be set for each patient individually.

In conclusion, our case and other cases show that eltrombopag, there was no bleeding [8]. In these kinds of patients, treatment must be set for each patient individually.
Competing interests
The authors declare that they have no competing interests.

References

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