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Protein C in a patient with portal vein thrombosis in liver transplantation

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Abstract

Background. *The problem of thromboses, including those associated with impaired hemostasis system, is relevant in orthotopic liver transplantation.*

Aim. *To present the experience of intraoperative use of protein C during orthotopic liver transplantation in a patient with a high risk of recurrent portal vein thrombosis.*

Results. *During orthotopic liver transplantation in a patient with a high risk of recurrent portal vein thrombosis, the intraoperative administration of the protein C preparation at a dosage of 500 IU contributed to the increase in plasma level of protein C by 48%. In the post-transplant period, recurrent portal vein thrombosis was not observed.*

Conclusion. *Intraoperative administration of protein C in combination with basic therapy for orthotopic liver transplantation helps to prevent recurrent portal vein thrombosis.*

Keywords: protein C, liver transplantation, recurrent portal vein thrombosis

Conflict of interests Authors declare no conflict of interest

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APC, Activated Protein C

APTT, activated partial thromboplastin time

AT, antithrombin

FC fibrinogen determined by the Clauss assay

HAT, hepatic artery thrombosis

HVT, hepatic vein thrombosis

INR, International Normalized Ratio

LBV, linear blood flow velocity

LC, liver cirrhosis

OLT, orthotopic liver transplantation

PVT, portal vein thrombosis

Introduction

Portal vein thrombosis PVT, hepatic artery thrombosis HAT, and hepatic vein thrombosis HVT are some of the most severe complications after liver transplantation. Lacking the drug therapy effect, the inability to restore blood supply by surgical and endovascular interventional radiology techniques lead to the graft loss and a highly probable death of the recipient [1-3].

Liver cirrhosis (LC) leads to the imbalance of hemostasis factors, and in combination with hepatocellular cancer, it often contributes to the development of occlusive and/or non-occlusive PVT. The incidence of PVT correlates with an increase in the LC severity. So, the incidence of lower than 1% is recorded with compensated cirrhosis, and it can reach 4–30% with decompensated cirrhosis. Recipients with Budd-Chiari syndrome comprise a special group. An impaired outflow via the hepatic veins in this disease is often the only clinical manifestation of some hematological diseases [4, 5].

Prevention of both primary and recurrent thrombosis in orthotopic liver transplantation (OLT) is the most effective means to prevent the graft loss and the patient death [6]. Despite the ongoing therapy with unfractionated or low molecular weight heparin, with antithrombin (AT) III, the prevalence of PVT, HVT, HAT in patients undergoing liver transplantation ranges from 3 to 7% [7-9].

In this regard, the solution to the problem of thrombosis prevention, including the thrombosis cases associated with impaired hemostasis system, remains relevant in liver transplant recipients, especially in the intraoperative and early postoperative periods.

Protein C deficiency contributes to the development of venous thrombosis, while the concentration of proteins C and S in the portal blood flow is lower than in the peripheral one [10–12]. Protein C is an anticoagulant, vitamin K-dependent glycoprotein, that is synthesized in the liver. It is activated on the surface of the vascular endothelium by the thrombin-thrombomodulin complex, and turns into activated protein C (APC). APC is a serine protease that, in the presence of protein S, has a potent anticoagulant effect. APC inactivates the activated V and VIII coagulation factors, which leads to a reduced thrombin formation. APC also has a profibrinolytic effect [13]. In a recent publication, the authors

have reported on the successful use of protein C in children with its acquired deficiency for antithrombotic prophylaxis. Its use turned out to be especially effective in those patients who at the time of its administration had already had thrombosis [14].

In connection with the above, we present the experience of using protein C in the intraoperative period in a recipient with a high risk of portal vein re-thrombosis after OLT.

Clinical Case Report

Patient K., 69 years old, diagnosed with class C liver cirrhosis (13 points) according to Child-Pugh Score, portal hypertension (ascites, splenomegaly), grade 2 esophageal varices, hepatocellular insufficiency (hypocoagulation, hypoalbuminemia), grade 2 hepatic encephalopathy, hepatocellular carcinoma was hospitalized to have OLT performed from a posthumous donor.

On admission: the patient was conscious, had grade 2 encephalopathy. The skin was icteric, the lower legs were swollen. Vesicular breathing passed over to all departments, there was no wheezing. The respiratory rate was 18 breaths per minute. He had stable hemodynamics, blood pressure of 110/70 mm Hg, the heart sounds were muffled. The ultrasound examination of hepatic vessels identified PVT (Grade 1, up to Yerdel classification).

Plasma hemostasis factors on admission: AT III is 68.8%, Protein C is 52.6%. The coagulogram results are graphed in Fig. 1.

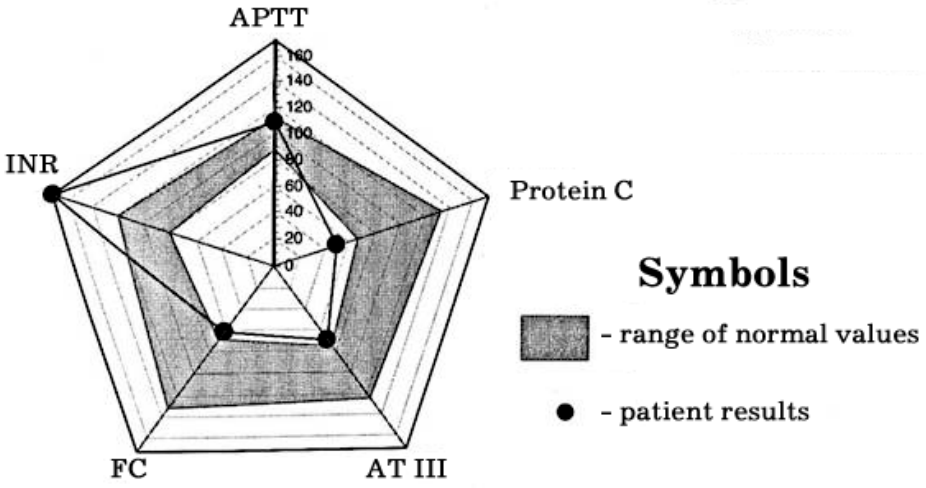

Fig. 1. Coagulogram before surgery

Notes: activation of the coagulation link against the deficiency of coagulation inhibitors; APTT, activated partial thromboplastin time; INR, International Normalized Ratio, FC, fibrinogen determined by Clauss assay

Induction in anesthesia was performed by propofol at a dose of 2.5 mg/kg, fentanyl 3 μg/kg, and cisatracurium besylate at a dose of 150 μg/kg. Anesthesia was maintained with desflurane (5 vol% to achieve MAK 1, fresh gas flow 0.5 L/min), using a Dräger anesthesia machine with a semi-closed circuit, fentanyl 2 μg/kg/h, and cysatracurim besylate 50 μg/kg/h.

Non-occlusive PVT was intraoperatively confirmed, thrombectomy was performed.

Low protein C levels, preoperative PVT, advanced age, and hepatocellular carcinoma were the factors of a high risk of developing re-thrombosis after restoring. liver perfusion. In this regard, after venous reperfusion, 500 IU of protein C was administered. After the anastomoses had been made, an intraoperative ultrasound examination was performed: no liver hemodynamic impairments were seen. Blood loss during liver transplantation was 600 mL, the fluid therapy was performed with crystalloids and albumin, a total of 4500 mL; the urine excreted by the

patient during surgery was 700 mL. The patient was delivered to the Intensive Care Unit, extubated 2 hours after the surgery completion. A continuous infusion of sodium heparin was started at a rate of 200 IU/h for 24 hours.

The results of the study for anticoagulant factors on the 1st day after transplantation showed the reference values of AT III 74%, protein C 78%.

From day 2 to day 10 after OLT, the patient received subcutaneously injected sodium parnaparin 960 anti-XA ME once a day.

The resulted coagulogram on day 2 is graphed in Fig. 2.

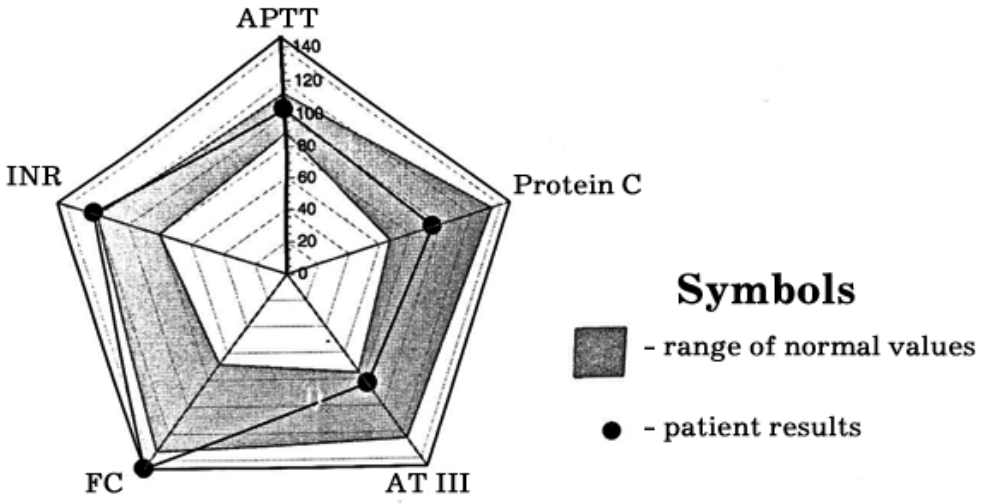

Fig. 2. Coagulogram on postoperative day 2

We present the results of the control duplex scanning of hepatobiliary system vessels performed on the 5th day (Fig. 3). Portal vein is 1.3 cm, blood flow is preserved, there are no signs of thrombosis. Linear blood flow velocity LBV 0.38 m/s. Hepatic artery is 0.4 cm, LBV is 0.46 m/s. The resistance index is 0.67. Hepatic vein is 0.8 cm, LBV is 0.20 m/s. The shape of the Doppler curve is of the monophase type.

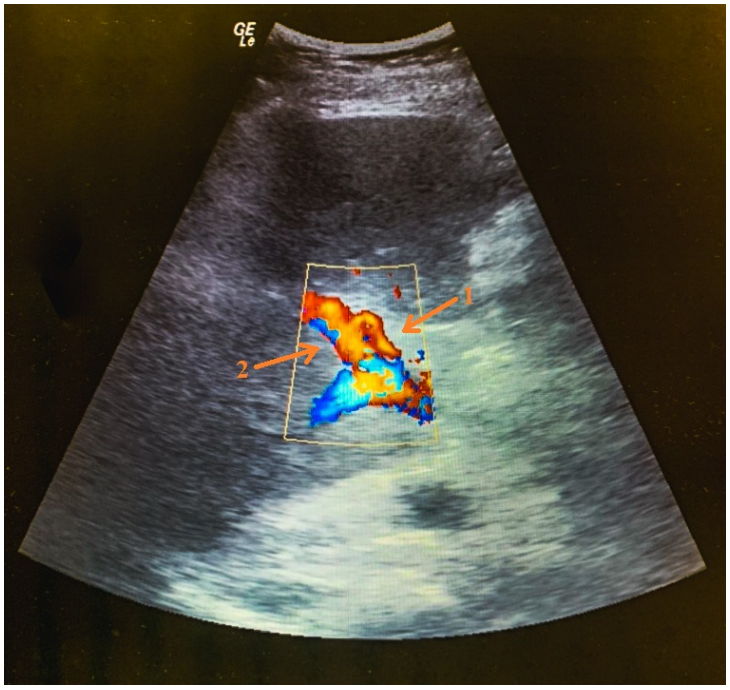

Fig. 3. Ultrasound imaging of the hepatobiliary system vessels of the on day 5 after OLT

Note: 1 - hepatic artery, 2 - portal vein

Results

With intraoperative administration of protein C at a dosage of 500 IU, the plasma concentration of protein C increased by 48% (from 52.6 to 78%). Further increment achieved with the donor liver functioning was 27.2%. On day 2 after liver transplantation, the protein C concentration was within the reference values.

In the post-transplant period, there was no recurrent PVT. The patient was discharged in satisfactory condition on day 14 after OLT.

Discussion of the results

The liver synthesizes the majority of pro-, anticoagulants, and fibrinolytic proteins, which concentrations decrease with liver dysfunction. The decrease in procoagulant factors is balanced by a simultaneous decrease in anticoagulant factors in various liver diseases.

Despite the newly formed balance between the pro- and anticoagulant system after transplantation, the patients with LC are at a higher risk of thrombosis [15].

In connection with the above, there is an urgent need for methods to correct the deficiency of plasma hemostasis factors in patients undergoing OLT.

Conclusion

Intraoperative administration of protein C concentrate during orthotopic liver transplantation helps to compensate for the factor deficiency which was caused by the native liver dysfunction in decompensated cirrhosis, and in combination with baseline therapy, to prevent recurrent portal vein thrombosis after orthotopic liver transplantation.

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