CASE REPORT

DOI: http://dx.doi.org/10.15403/jgld-1584

Local Thrombolysis in Acute and Extended Portal Vein and TIPS Thrombosis in a Patient with Decompensated Cirrhosis and Protein S Deficiency

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Received: 23.03.2020
Accepted: 27.06.2020

ABSTRACT

This report describes the use of local thrombolysis using a tissue plasminogen activator in a case of a patient with refractory ascites referred for transjugular intrahepatic portosystemic shunt (TIPS) insertion. After successful TIPS insertion, the patient developed acute extended portal vein and TIPS thrombosis, which were treated with local thrombolysis using a tissue plasminogen activator, followed by the complete resolution of ascites. Although there are only limited published data of local thrombolysis for acute splanchnic vein thrombosis, we also review the relevance of the problem in the context of advanced liver disease.

Key words: tissue plasminogen activator – splanchnic vein thrombosis – transjugular intrahepatic portosystemic shunt – prothrombotic condition.

Abbreviations: LMWH: low molecular weight heparin; PVT: portal vein thrombosis; TIPS: transjugular intrahepatic portosystemic shunt; tPA: tissue plasminogen activator.

INTRODUCTION

Portal vein thrombosis (PVT) is a frequent complication in patients with liver cirrhosis, especially in patients with decompensated cirrhosis [1]. Despite altered values of the conventional coagulation tests (increased INR, low platelet counts), patients with cirrhosis generate an adequate amount of thrombin to support coagulation [2] and, their coagulation is characterized by a fragile equilibrium [3]. In the case of inherited prothrombotic disorders in patients with advanced liver disease, particular challenges need to be addressed. We present the case of a patient with decompensated cirrhosis and inherited protein S deficiency, who developed extended portal vein and transjugular intrahepatic portosystemic shunt (TIPS) thrombosis that required local thrombolysis with a tissue plasminogen activator (tPA).

CASE REPORT

A 60-year old male patient, previously diagnosed with alcohol-induced cirrhosis and partial PVT complicated with previous recurrent variceal bleeding, refractory ascites, and a giant umbilical hernia, was referred to the Hepatology Department of the Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania for TIPS insertion. The procedure's purpose was to prevent future variceal bleeding and to treat the refractory ascites. Following the control of the ascites, the large umbilical hernia could eventually be surgically repaired. Under ultrasonographic and fluoroscopic guidance, the shunt was successfully created by placing a 68x10 mm bare stent (Wallstent®, Boston Scientific, Marlborough, Mass) into the portal vein, combined with a 60x12 mm ePTFE covered stent (Fluency®, Bard, Tempe, USA) to assure the intrahepatic part.

Two days after the initial successful intervention, the ultrasound examination detected complete thrombosis of the stent and portal vein. The complete coagulation workup revealed associated protein S deficiency (protein S activity was only 14%). The protein S levels were discordantly low comparing to the protein C (56% activity) and antithrombin III (74% activity). The rest of the prothrombotic workup was negative. The anticoagulant treatment was immediately

initiated, but after a few days, the computed tomography scan revealed the extension of the thrombosis (Fig. 1).

Fig. 1. The abdominal contrast-enhanced CT scan, venous phase, reveals complete thrombosis of the TIPS (arrow) and a large amount of ascites.

During the TIPS revision, through a 5F pigtail catheter inserted into the portal vein, 5mg bolus of tPA was administered, followed by 12 hours of continuous infusion of 1mg/hour. The portosystemic gradient decreased from 23 mmHg to 10 mmHg, and the portography revealed an efficient flow through the stent (Figs. 2 A and B). No bleeding complication occurred during the procedure and follow-up.

The patient continued long-term anticoagulant treatment with low molecular weight heparin (LMWH). One month later, the ultrasound examination indicated the permeability of the stent and a significant decrease in the ascites. Furthermore, a systematic TIPS revision confirmed the maintenance of the stent permeability and a portosystemic gradient of 10 mmHg. During follow-up, three months later, the ultrasound revealed complete disappearance of ascites. The next step was the surgical repairment of the abdominal hernia without any complications.

DISCUSSION

During the natural history of liver cirrhosis, PVT frequently develops, although its impact on the prognosis of liver disease is still a matter of debate [1, 4, 5]. The reduced velocity in the portal vein secondary to portal hypertension is the leading risk factor for thrombosis [6]. Moreover, patients with decompensated cirrhosis also have increased levels of factor VIII and von Willebrand factor (vWF), as a marker of endothelial activation, and decreased ADAMTS-13 (a vWF cleaving protease) that allow platelets to adhere and aggregate adequately [7, 8]. Patients with stable cirrhosis have a rebalanced hemostasis, despite the presence of altered levels of different coagulation factors. Under certain precipitating factors (decompensation or infections), this balance may easily be altered both in hemorrhagic and thrombotic direction [3]. Because 25% of cirrhotic patients develop PVT [1], the prothrombotic workout is not routinely recommended. However, it could be indicated in certain particular situations, as acute and extensive portal vein and TIPS thrombosis. Usually, TIPS insertion would prevent PVT because it accelerates the portal blood flow, and it would help the resolution of a previous PVT [9]. While the TIPS insertion is more difficult from a technical point of view, in most cases it leads to partial or total permeability of PVT. Although the diagnosis of an inherited deficiency of the natural anticoagulants is challenging in patients with cirrhosis, a discordant lower level of one of the factors would suggest the diagnosis. In the case of our patient, protein S was significantly and discordantly lower, which suggested an associated inherited protein S deficiency. In this case, to prevent PVT recurrence, long term anticoagulation is recommended [10].

There is limited data regarding local thrombolysis in splanchnic thrombosis, most of the data being case reports or small series [11-19] (Table I). Most of the publications discuss non-cirrhotic PVT treated with urokinase as a thrombolytic

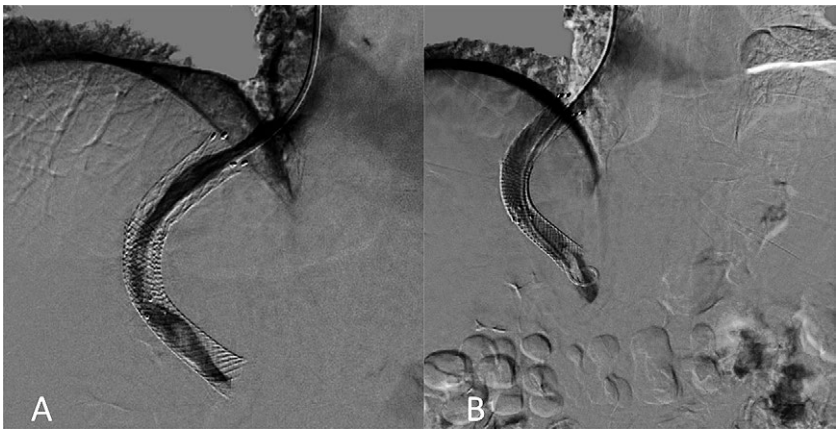

Fig. 2. During the TIPS revision, the portography reveals thrombosis inside the stent (A); after local thrombolysis with tPA the portography shows efficient flow through the stent (B).

Table I. Existing evidences for local thrombolysis for portal vein thrombosis

First author, year of publication, reference	Clinical scenario	Number of patients	Thrombolytic agent	PVT resolution
Aytekin, 2001, [11]	non-cirrhotic	1	urokinase	complete
Ciccarelli, 2001, [12]	post-OLT	1	tPA	complete
Ferro, 2007, [13]	non-cirrhotic	1	urokinase	complete
Liu, 2009, [14]	non-cirrhotic	32	urokinase	26 complete 6 partial
Wang, 2011, [15]	non-cirrhotic	12	urokinase	complete
Hilliard, 2017, [16]	cirrhosis	1	tPA	complete
Jiang, 2017, [17]	cirrhosis	20	urokinase	15 complete 4 partial 1 no change
Klinger, 2017, [18]	non-cirrhotic	17	urokinase tPA (2)	9 complete 7 partial
Wang, 2018, [19]	non-cirrhotic	13	t PA	6 complete 3 partial 4 lost of follow-up

OLT: orthotopic liver transplantation; PVT: portal vein thrombosis; tPA: tissue plasminogen activator

agent. In the majority of the cases, the treatment was efficient with complete resolution of the thrombosis. In patients with cirrhosis, even less data is published, but apparently, the treatment is similarly efficient with non-cirrhotic patients. The selection of appropriate candidates for thrombolysis is, probably, the most challenging issue in patients with cirrhosis. The difficulties lie, especially in the assessment of the risk of variceal bleeding in the context of lacking appropriate tests to evaluate the hemostasis. In the case of our patient, the main indication for TIPS insertion was refractory ascites complicated with a giant umbilical hernia. At the same time, the previous variceal bleeding episodes occurred few years earlier, and the patient was under efficient secondary prophylaxis. The local thrombolytic treatment was successfully applied without any bleeding complications.

Acute TIPS occlusion is a rare complication, occurring in 10-15% of the patients. It is caused mainly by biliary leakage (the bile is very thrombogenic), hypercoagulability or malposition of the stent [20]. However, since the introduction of covered stents (which eventually cover the biliary leakage), the acute TIPS occlusion occurs in only 4-5% [21, 22] and, it seems to be associated with preexisting PVT. Thus, our patient had the underlying prothrombotic condition and previous PVT, as factors indicating acute TIPS thrombosis.

CONCLUSIONS

Local thrombolysis using tPA may be an efficient therapeutic option in cirrhotic patients with acute TIPS or portal vein thrombosis. The recanalization of the splanchnic vascular bed may control the portal hypertension-related complications.

Conflicts of interest: None to declare.

Authors' contribution: M.R., M.I. and B.P. drafted the paper; M.R., B.P., O.N.F, H.S. and R.H. managed the patient; O.N.F, H.S. critically revised the final version of the manuscript. All authors approved the final version of the manuscript.

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