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The Challenging Management of an Intracardiac Thrombus in a Liver Transplant Patient at the Reperfusion Phase: A Case Report and Brief Literature Review

Luigi Vetrugno, MD,[1,2] Vittorio Cherchi, MD, PhD,[3] Dario Lorenzin, MD, PhD,[3] Francesco De Lorenzo, MD,[1] Marco Ventin, MD,[2] Victor Zanini, MD,[1,2] Giovanni Terrosu, MD,[2,3] Andrea Risaliti, MD,[2] Umberto Baccarani, MD, PhD,[2,3] and Tiziana Bove, MD[1,2]

Abstract: The exact origin of intracardiac thrombi formation during orthotopic liver transplant remains unknown. The altered balance between hypercoagulability, hypocoagulation, and endothelial dysfunction associated with end-stage liver disease is thought to play a pivotal role. Venous stasis, vascular clamping, and reperfusion could also contribute to clot formation. The incidence of intracardiac thrombi formation stands at 4.2%, associated with a mortality rate of 45.5%, and to date, no consensus exists regarding the best way to treat this complication. Intraoperative transesophageal echocardiography is the only effective method for diagnosing intracardiac thrombi formation early, while point-of-care coagulation testing could guide the coagulation management potentially improving patient outcomes.

Transesophageal echocardiography (TEE), a real-time hemodynamic monitoring tool, is recommended by the American Association for the Study of Liver Diseases in all cases of liver transplantation.[1] According to the literature, the most common abnormality TEE detects during orthotopic liver transplant (OLT) is right-sided microemboli.[2] By contrast, intracardiac thrombosis (ICT) is a rare but potentially catastrophic condition. A recent review article reports the incidence of ICT to stand at 4.2%, associated with a mortality rate of 45.5%.[3] The exact cause of intracardiac thrombi formation during OLT remains unknown. An alteration in anticoagulation and procoagulation processes is thought to be involved in intracardiac thrombi formation, and some advocate the use of thrombelastography.[4] However, the origin of these thrombi remains a matter of debate; for example, it is unknown whether they originate from the superior or inferior vena cava (IVC), or whether factors like the presence of a pulmonary arterial catheter (PAC) or the use of an IVC clamp constitute predisposing factors. Finally, no consensus has been reached regarding the best treatment of ICT, and the literature lacks strong evidence supporting any one approach. Case series published over the last 10 y have highlighted the use of low-dose recombinant tissue plasminogen activator (rTPA), whereas others advocate the use of a low heparin dose before vena cava clamping.[5,6] The present article presents a brief review of the literature on ICT and reports a rare case of ICT and pulmonary embolism, occurring at the reperfusion phase, diagnosed with TEE, in which the patient's coagulation profile was managed with the rotational thromboelastometry system.

CASE DESCRIPTION

A 61-y-old patient underwent orthotopic liver transplantation (OLTx) for end-stage liver disease. The patient's characteristic and clinical data are shown in Table 1. After anesthesia induction and tracheal intubation, right radial artery cannulation was performed, followed by the positioning of an internal jugular vein 8.5-Fr introducer (AVA 3Xi 8.5-Fr; Edwards Lifesciences, Irvine, CA) through which a PAC catheter was inserted (Swan-Ganz CCOmbo V CCO/SvO_2/CEDV/VIP; Edwards Lifesciences). A PAC catheter was then connected to a Vigilance hemodynamic monitor (Edwards Lifesciences) for semicontinuous cardiac output measurements. A TEE probe (GE Healthcare Vivid E95, Little Chalfont, United Kingdom) was then placed. Since higher model for end-stage

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[1] Department of Anesthesia and Intensive Care, University-Hospital of Udine, Udine, Italy.

[2] Department of Medicine, University of Udine, Italy, Udine, Italy.

[3] General Surgery Clinic and Liver Transplant Center, University-Hospital of Udine, Udine, Italy.

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Correspondence: Luigi Vetrugno, MD, Department of Anesthesia and Intensive Care, University-Hospital of Udine, P.le S. Maria della Misericordia n° 15, 33100 Udine, Italy, and Department of Medicine, University of Udine, Italy, Via Colugna n° 50, 33100 Udine, Italy. (luigi.vetrugno@uniud.it).

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TABLE 1.

Patient's clinical data, history, and surgical data

Age, y	61
Sex	Male
BMI, kg/m^2	32.4
MELD	21
Underlying disease	Alcoholic liver cirrhosis (Grade C)
	HCC (34 mm)
Complications (disease-related)	Ascites
	Esophageal varices (F2–F3)
	Portal vein thrombosis
Treatment before OLTx	TACE, complete radiological response (αFP 1720–120 mg/dL)
	Variceal endoscopic band ligation (due to bleeding)
	OLTx
Comorbidities	Diabetes mellitus type II
	Arterial hypertension
	Obesity
Surgical technique	Caval reconstruction using modified Piggyback technique by Belghiti
Relevant data from OLTx	
CIT	450 min
WIT	35 min
Clamp time	38 min
ABO-mismatch	Negative
Packed red blood cells transfused	11 U
Units of frozen plasma	5 U
Pharmacological therapy	Rifaximin, propanolol, furosemide, spironolactone, lactulose, insulin
Antibiotic prophylaxis	Meropenem, daptomycine, anidulafungin
Donor	
Age, y	69
Sex	Female
Death cause	Postanoxic encephalopathy
Comorbidities	Diabetes mellitus type II
	Hypothiroidism

BMI, body mass index; CIT, cold ischemia time; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; OLTx, orthotopic liver transplantation; TACE, trans-arterial chemoembolization; WIT, warm ischemia time.

liver disease (MELD) scores are associated with a higher bleeding risk and lower survival rate, in our center, we consider a MELD score > 15 as the threshold for placing a PAC catheter.[7,8] For the assessment of left ventricle function, we used the mid-esophageal 4-chamber view, the 2-chamber view, and the long-axis view of the left ventricle. TEE showed a slightly dilated left ventricle of normal thickness, dimension, and kinetics. The right ventricle was normal in volume and function. No other anomalies were detected. The orthotopic donor liver transplantation was performed following a difficult hepatectomy because of a massive hypertrophy of the caudate lobe that included a large circumference of the retrohepatic vena cava. The Belghiti technique was preferred for graft reconstruction. The anhepatic phase was hemodynamically stable with a mean arterial pressure of 70 mm Hg, a heart rate of 70 bpm in sinus rhythm, a central venous pressure of 5 mm Hg, and a pulmonary arterial pressure of 27/11 mm Hg (mean 16 mm Hg), and cardiac index was low (1.86 L/min/m^2). Following the reperfusion phase, the patient's blood pressure suddenly collapsed, and the patient experienced cardiac arrest. Following 1 mg of epinephrine administered and 1 min of external cardiac massage, the patient achieved the return of spontaneous circulation. TEE in the mid-esophageal 4-chamber view, performed shortly after, diagnosed a dilated and hypokinetic right atrium and ventricle, with a thrombus floating through them adherent to the pulmonary catheter (**Video 1, SDC**, http://links.lww.com/TXD/A358). After 5 min, the thrombus disappeared, suggesting its spontaneous propagation into the pulmonary bed. The patient was administered epinephrine and norepinephrine as pharmacological hemodynamical support and the surgery completed. The patient was transferred to the post-transplant intensive care unit. The patient's coagulation profile and treatment during the different phases of the surgery are shown in **Figures S1–5, SDC**, http://links.lww.com/TXD/A360.

DISCUSSION

The pathogenesis of ICT and pulmonary embolism during OLT is unknown, but it is hypothesized to arise from a complex alteration of both anticoagulation and procoagulation processes. While hypercoagulability is strongly related to endothelial dysfunction, hypocoagulation is related to the liver's reduced coagulation products[9]; however, the exact etiology remains poorly defined. During OLT, the most frequent risk factor of ICT is the use of venous-venous bypass, which is only used in some centers.

A recent survey showed that over 70% of transplant anesthesiologists were proficient in TEE monitoring and that the rate of TEE use by these physicians was very high (over 94%).[10] TEE is the only presently available tool able to identify in "real time" the acute failure of the right ventricle and show the effects of the treatment. The literature offers very few case series or single-center experiences with regard to ICT treatment during liver transplantation. In 2011, Boone et al[6] described the successful use of a low dose of rTPA (0.5–4.0 mg) administered to 4 liver transplant patients. The authors also advocated that early diagnosis with TEE and PAC could help achieve rapid thrombolysis, that the low dose of rTPA likely played a critical role in the lytic process, and that this treatment was safe and effective. The literature offers no other reports published before 2011 on the use of a low dose of rTPA in the setting of OLT. However, more recent studies suggest that rTPA in the context of OLT may be associated with a risk of massive bleeding; thus, its use should be guided by a point-of-care test with a fast turnaround time.

Other reports suggest that thrombectomy and/or thrombolysis may be associated with lower rates of patient mortality; although this trend has not been shown to be statistically significant.[4,5] Groose et al,[11] in a single retrospective study center, reported that the odds of developing ICT were significantly lower following the administration of intravenous heparin before IVC clamping and thus concluded heparin to be protective. This would suggest that venous stasis, vascular clamping, and reperfusion could contribute to clot formation (**Video 2, SDC**, http://links.lww.com/TXD/A359). The vena cava isolation maneuvers (from the caudate lobe during the hepatectomy and during liver graft reconstruction) could play an important role in clot formation under specific circumstances. For example, significant stress may be exerted on the IVC wall during these phases, resulting in injury to the endothelial layer. In our case, the severe hypertrophy of the caudate lobe of the recipient's own liver that embraced the IVC resulted in difficult hepatectomy. We applied laterolateral cavostomy, according

to the Belghiti technique, involving the construction of a laterolateral anastomosis between the graft's IVC and the longitudinally sectioned IVC of the recipient in such a way that a large part of the lumen was significantly reduced, together with blood flux, which led to vascular stasis upstream of the clamp. In our patient, the clamp remained in this position for 38 min; the graft was reperfused with sequential portal vein and hepatic artery declamping. By the end of the OLTx, 11 units of packed red blood cells, 5 units of fresh–frozen plasma, 1 g of tranexamic acid, and 2 g of fibrinogen had been administered after reperfusion and before abdomen closure.

In conclusion, ICT is a rare event and TEE is the only available tool for real-time diagnosis. POC coagulation testing, such as rotational thromboelastometry, can guide coagulation management potentially improving patient outcome.

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