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Post-hepatectomy liver failure: Should we consider venous outflow?



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ABSTRACT

INTRODUCTION: Post-hepatectomy liver failure (PHLF) is one of the most serious complications of liver resection and is associated with high morbidity and mortality rates.

PRESENTATION OF CASE: We report a case of PHLF involving clinical presentation of posthepatectomy-related 'small-for-size' syndrome (SFSS) secondary to obstructed venous outflow in the liver remnant, following extended right hepatectomy.

DISCUSSION: PHLF is similar to SFSS in liver transplantation (LT) in terms of pathogenesis, clinical presentation and outcomes. Although inflow hypertension is clearly implicated in the pathogenesis of SFSS some authors have suggested that outflow obstruction is a potential pathogenic factor.

CONCLUSION: The present case support the hypothesis that outflow obstruction could lead symptoms similar to SFSS.

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1. Introduction

Post-hepatectomy liver failure (PHLF) is one of the most serious complications of liver resection and is associated with high morbidity and mortality [1,2]. It is important to determine the risk factors for PHLF in order to identify the patients most at risk, and to facilitate implementation of strategies to reduce the incidence and associated mortality [1]. One of the main surgical risk factors is extent of resection, since extended hepatic resection can result in a small remnant liver volume (SRLV) [1]. This condition may be linked to the 'small-for-size' syndrome (SFSS) known in liver transplantation (LT) as the two conditions have similar pathogenesis, clinical presentation and outcomes. Although inflow hypertension is known to be implicated in SFSS pathogenesis it has also been suggested that outflow obstruction is a potential pathogenic factor [3]. Recent pre-clinical experimental research in rats provided support for the hypothesis [3–5].

In support of the hypothesis that outflow obstruction could lead to symptoms similar to SFSS, we report a case of PHLF involving clinical presentation of posthepatectomy-related SFSS secondary to obstructed venous outflow in the liver remnant following extended right hepatectomy.

2. Case report

In July 2014 a 64-year-old male with a history of hypertension and tobacco consumption, moderate obesity (BMI = 31 kg/m², weight = 91 kg, height = 1.71 m) and moderate alcohol consumption (30 g/day) was referred to our center for the management of a histologically confirmed 9 cm hepatocellular carcinoma of the right liver. His liver had moderate steatosis without fibrosis and the carcinoma was discovered incidentally on contrast-enhanced CT during exploration of an appendicular syndrome presenting as an abdominal pain in the right iliac fossa. Preoperative clinical evaluation revealed no liver cirrhosis, no signs of portal hypertension and normal liver function (prothrombin time, PT = 100%, bilirubinemia = 9 μmol/L, albuminemia = 43 g/L, creatininemia = 69 μmol/L, platelet count = 303 G/L). Preoperative histological evaluation of the non-tumoral parenchyma was not available. Morphological investigation using CT and MRI revealed a 9 cm tumor developing in the right liver which extended into segment I and segment IV and was in close contact with the inferior vena cava. The preoperative liver volumetry results were: total liver, 1924 cm³ (tumor-free volume: 204 cm³); left liver, 484 cm³ (25% of the total liver volume; future liver remnant-to-body weight ratio: 0.5%); and right liver, 1644 cm³ (75% of the total liver volume). Surgery consisted of an extended right hepatectomy including segment I using the Dissectron device (Integra LifeSciences Corp., Plainsboro, NJ, USA). The remaining left liver was fixed in an anatomical fashion, under perioperative Doppler ultrasound (DUS) control for vascular patency, stitched between the remnant falciform ligament and

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Fig. 1. Coronal cross-section reconstruction of contrast-enhanced hepatic MRI at tardive time showing the metallic stent (white arrow) within the remnant left hepatic vein 6 months after surgery.

the diaphragm. During the perioperative period there was intermittent portal clamping (43 min in total) associated with 20-min periods of caval clamping; the total operating time was 10 h, and there was no hemodynamic insufficiency requiring treatment with amine drugs. A total of 6 L crystalloids and 2 red blood cells transfusions were administered. Pathological examination confirmed R0 resection of a well-differentiated, encapsulated hepatocellular carcinoma (Edmondson and Steiner grade II) 9 cm at its maximum diameter, classified as pT2 according to the AJCC 2010. There was evidence of microvesicular or macrovesicular steatosis in 50% of the non-tumoral parenchyma. The post-operative course was notable for a non-severe pulmonary embolism on post-operative day (POD) 2. On POD 2 the remnant liver volume was measured at 711 cm³ (33% of the initial total liver volume; liver-to-body weight ratio: 0.8%). PHLF occurred on POD 5, defined by PT = 49%, hyperbilirubinemia of 125 μmol/L and significant ascites (2 L/24 h) complicated by sepsis from ascites infection by *Proteus mirabilis* which necessitated antibiotic treatment and transfer to intensive care. The patient remained in the ICU for 14 days.

On POD 9, the remnant liver volume was measured at 916 cm³ (43% of the initial total liver volume; liver-to-body weight ratio: 1%). On POD 18 a contrasted-enhanced CT investigation of the PHLF (bilirubin = 565 μmol/L, PT = 73%) revealed left hepatic vein stenosis which was confirmed by DUS, which showed a loss of triphasic flow. After confirmation of the diagnosis of stricture of the remnant left hepatic vein using cavography and assessment of the pressure gradient between the left hepatic vein and inferior vena cava (LHV-IVC gradient = 9 mmHg) a percutaneous transluminal angioplasty (PTA) involving placement of a metallic stent (diameter = 10 mm, length = 6 cm; Misago, Terumo Corp., Tokyo, Japan) within the remnant left hepatic vein was performed to restore normal outflow. After the procedure the LHV-IVC gradient decreased to 3 mmHg. The course of post-intervention recovery was uneventful and characterized by a progressive reduction in bilirubinemia. The patient

was discharged on POD 30. Two months after surgery the bilirubin level was 230 μmol/L with a normal PT; bilirubinemia was normal after 4 months. At 10-months follow-up there was no evidence of late surgical complication; the liver function tests were within normal limits and the patient did not complain. Morphological imaging revealed adequate regeneration of the left remnant liver (1300 cm³, post-hepatectomy liver remnant-to-body weight ratio 1.2%), with satisfactory inflow and outflow and no signs of recurrence of liver failure. The metallic stent within the left hepatic vein was permeable and in place (Fig. 1).

3. Discussion

There is no consensus definition of PHLF, however most recent reports have noted an incidence of around 5–10% [1]. The most widely used criteria for PHLF are the 50–50 criteria [6], peak bilirubin >7 mg/dL [7] and the ISGLS criteria [1,2]. In practice clinical presentation of PHLF typically includes deterioration of one or more of the synthetic, excretory or detoxifying functions of the liver and manifests as hyperbilirubinemia, hypoalbuminemia, prolonged PT or international normalized ratio (INR), elevated serum lactate level and hepatic encephalopathy during the post-operative period [1,2]. Over the past two decades, there has been a decrease in the incidence of PHLF, presumably as a result of improvements in surgical technique and perioperative care, which have also reduced mortality following hepatic resection. Over the past two decades the mortality rate following partial hepatectomy has remained at 0–6%, with PHLF contributing to mortality in the majority of cases [1]. Identifying risk factors for PHLF would help to identify those patients most at risks and would also facilitate development and implementation of strategies to reduce the incidence of PHLF and the associated mortality [1]. To date several independent predictors of PHLF have been identified; they can be classified into three main categories: patient-related, liver-related, and surgical or

post-operative related factors [1]. Extent of resection is one of the main surgical risk factors as extended hepatic resection can result in SRLV [1]; however, Yigilter et al. reported that incidence of PHLF was not closely correlated with remnant liver volume [8], reflecting the complexity of the mechanisms leading to PHLF. Nevertheless, PHLF is similar to the SFSS recognized in LT in terms of pathogenesis, clinical presentation and outcomes. The initial description of SFSS were based on experience of living-donor liver transplantation (LDLT) and it was defined as a graft-to-recipient weight ratio (GRWR) of less than 0.8–1% or less than 30–50% of standard/estimated liver volumes [1,5,9]. The mechanisms underlying SFSS involve increased portal blood flow and portal hypertension, which lead to histological injuries in the form of sinusoidal congestion and disruption of the sinusoidal lining and hence liver graft insufficiency and, if the condition remains untreated, liver graft failure [5]. It has been suggested that outflow obstruction contributes to the genesis of SFSS [3] and recent pre-clinical experimental research corroborate this hypothesis [4]. In a rat model involving ligation of the median hepatic vein combined with 50% partial hepatectomy the authors demonstrated that focal obstruction of venous outflow obstruction in the remnant liver causes confluent centrilobular necrosis and may be critically involved in development of SFSS [4]. In the case presented here the PHLF symptoms met the 50–50 criteria and were associated with a postoperative liver volume of <1% of body weight (or <50% of initial total liver volume) and abundant postoperative ascites, leading us to advocate a diagnosis of SRLV or posthepatectomy-related SFSS. DUS allowed us to rule out portal hypertension and confirm the outflow hepatic vein obstruction, but diagnosis was delayed (until POD 18) because of the unusual PHLF presentation. In conclusion, this report provides further evidence that outflow obstruction is implicated in the pathogenesis of PHLF and/or posthepatectomy-related SFSS. We therefore advocate the systematic investigation of hepatic vein outflow when PHLF occurs after extended liver hepatectomy.

Conflict of interest

Each authors have no conflicts of interest related to this manuscript to disclose.

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Patient's consents

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

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Author's contribution

Martin Lhuire: study concept, data collection, data analysis, writing the paper.

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Onorina Bruno: data collection, data analysis.

Annie Sibert: data collection, data analysis.

Reza Kianmanesh: data analysis.

Daniele Sommacale: study concept, data analysis, writing the paper.

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