All about diagnostic imaging and minimally invasive treatment of liver graft arterial thrombosis

Poster No.: C-1134
Congress: ECR 2014
Type: Scientific Exhibit
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Keywords: Interventional vascular, Arteries / Aorta, Liver, Catheter arteriography, CT-Angiography, Ultrasound-Colour Doppler, Thrombolysis, Recanalisation, Catheters, Acute, Embolism / Thrombosis, Transplantation
DOI: 10.1594/ecr2014/C-1134

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Aims and objectives

Aim:

We have chosen this topic because our hospital is the main liver transplantation center in Romania, with an experience of more than 400 liver transplantations since the year 2000.

The objectives of this paper are:

- to display the imaging methods of choice in the diagnosis and evaluation of hepatic artery thrombosis (HAT) following liver transplantation;
- to describe the minimally invasive (endovascular) treatment of this vascular complication (intraarterial thrombolysis, mechanical thrombolysis);
- to evaluate the outcome of patients with HAT treated by intraarterial thrombolysis in our department.
Methods and materials

Patients:

Retrospective study carried between January 2001 to December 1012 including 14 patients (M:F 8:6), with ages between 6 and 61 years, out of 389 liver transplants performed in Fundeni Clinical Institute. In these patients, hepatic artery thrombosis was detected following imaging tests in our department. A total of 49 patients had vascular complications following liver transplantation (hepatic artery thrombosis, hepatic artery stenosis and hepatic artery pseudoaneurysm, portal vein thrombosis, portal vein stenosis, liver infarction, hepatic vein or inferior vena cava thrombosis or stenosis).

Various types of liver transplantation were performed depending on the availability of donor organ: deceased donor, living donor split grafts. In our study, 7 patients with HAT had orthotopic liver transplantation and 7 patients had living-related liver transplantation.

The patients detected with HAT had chronic liver failure prior to liver transplantation, due to chronic viral hepatitis (hepatic virus B, or associations between hepatic viruses B and D or B and C), alcoholic hepatitis (2 patients), Wilson’s disease (1 patient), Caroli’s disease (1 patient) and hereditary fructosemia (1 patient).

Knowledge of the type of anastomosis was important because thrombosis frequently occurs at this site.

In orthotopic liver transplantation: The arterial anastomosis is performed generally at the level of the common hepatic artery bifurcation, or at the cuff created with the gastroduodenal artery take-off (Fig. 1 on page 6). If the recipient hepatic artery is not adequate to perform a safe anastomosis, then direct anastomosis or the placement of an arterial conduit (donor iliac artery) between the aorta (supraceliac or infrarenal) and the donor hepatic artery is performed (1). Many surgical techniques are described for donors with standard hepatic artery anatomy and replaced or accessory right or left hepatic artery. Also, the main concern is that any excessive length can lead to twisting and looping that can lead to an increased incidence of hepatic artery thrombosis.

In living donor transplantation: Hepatic arterial reconstruction is technically more difficult and troublesome than in orthotopic liver transplantation, mainly because of the need to reconstruct thin, short, and/or multiple arterial branches in limited surgical fields. The main concern is the caliber discrepancy, which is dealt with dilatation of the vessel edge, enlargement of the circumference of the smaller lumen by cutting artery obliquely or in fish-mouth, making a longitudinal side-cut, funnelization, suturing with wider bites on the larger vessel (2). When the size mismatch is greater than 1:3, the alternatives are: the
interposition of an arterial graft (superior rectal artery, ovarian artery, radial artery (3)) or venous conduct, the construction of an end-to-side anastomosis or anastomosis with a side branch of a larger vessel.

**Hepatic artery thrombosis can lead to biliary ischemia, since the hepatic artery is the only source of vascular supply to the bile ducts***(4). Biliary ischemia may in turn lead to a nonanastomotic biliary stricture or a biloma, which are often associated with hepatic artery complications.

**Methods and Protocols:**

The protocol used for monitoring liver transplant patients includes Doppler ultrasound (US), CT angiography and conventional angiography (**Fig. 2** on page 6).

Contrast enhanced ultrasonography and MR angiography were not used for evaluation (contrast-enhanced MR imaging places greater demands on patients than does ultrasonography or CT: longer scanning time, and longer breathhold sequences).

**CT angiography (CTA) protocol** (**Fig. 3** on page 7):

- 16-row MDCT scanner.
- A non-enhanced CT scan was obtained, then we used bolus triggering (set in the descending abdominal aorta, at the level of the coeliac trunk), a volume of contrast media of 1,5 ml/kg of high iodine concentration and a flow rate of 3-4 ml/s.
- The arterial phase had a 6 s delay after the aortic peak (100 UH), with the following scanning parameters (16x0,6 mm/5/p0.8). Additional portal venous phase and equillibrium phase scans were obtained.
- 0.75 mm axial reconstructions were used for diagnosis, and also multiplanar reformats (MPR), maximum intensity projections (MIP), volume rendering technique (VRT).

**Conventional angiography (CA) and transcatheater intraarterial thrombolysis protocol** (5,6):

- CA uses local anesthesia and usually a right femoral artery approach (Seldinger technique), 5-6 F introducer sheaths and hydrophillic guide wires.
- A large catheter (cobra/SIM 4/5F) is placed in the coeliac trunk or common hepatic artery and a diagnostic angiogram is performed. Then a microcatheter (2,5/3F)/cobra 4F catheter and 0,018/0,035 inch guidewire is used to bypass the thrombus.
• A bolus of thrombolytic agent is injected or mechanical thrombolysis and aspiration is performed (Fig. 4 on page 8). A large catheter is placed proximal to the anastomosis, and it will be used as an infusion catheter for thrombolytic agents (rt-PA) and prostacyclin.
Fig. 1: Hepatic artery anastomosis technique in orthotopic liver transplantation

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Fig. 2: Imaging evaluation of liver transplant patients.

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Fig. 3: CTA protocol

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Fig. 4: Step one (a): Digital substraction angiography (DSA) using a cobra 4F catheter placed in the common hepatic artery, proximal to the anastomosis, with confirmation of the complete thrombosis of the liver graft hepatic artery Step two (b): surpassing the thrombosis area with a coaxial system (3F microcatheter and 4F cobra catheter) Step three (c): A bolus of thrombolytic agent was injected and control angiogram shows complete revascularization of the liver graft artery
Results

HAT was the most common vascular complication of liver transplantation (14 cases), representing 3.5% of all posttransplant liver complications (Fig. 5 on page 12).

12 patients were diagnosed with early hepatic artery thrombosis (at 4 to 15 days after liver transplantation, averaging 8.5 days) and 2 patients with late HAT (at 1.5 months and 1.5 years after liver transplantation).

HAT was detected by postoperative Doppler ultrasound screening that showed nonvisualization of the hepatic artery (Fig. 6 on page 12) and a high-resistance flow at the hilum (RI = 1) if the Doppler waveform is obtained in the main hepatic artery before the thrombus (7).

Doppler ultrasound screening proved to be essential for early detection of HAT, allowing a successful endovascular treatment.

Confirmation of the HAT was required by CTA, which revealed both the lack of enhancement of the hepatic artery, and also the related parenchymal ischemic changes (Fig. 7 on page 13, Fig. 8 on page 13). All patients with late HAT and 10 patients with early HAT showed complete thrombosis of the liver graft artery (at the level of the anastomosis) and 2 patients with early HAT had partial thrombosis of the hepatic artery.

Endovascular treatment was available for 6 patients with early HAT.

After CTA, we performed a diagnostic conventional angiogram. The next step is to perform intraarterial thrombolysis or mechanical thrombolysis. The endovascular treatment can be applied if HAT is recent (< 24 hours) (Fig. 9 on page 14, Fig. 12 on page 16). Doppler US and CTA are used to monitor the status of endovascular treated patients (Fig. 10 on page 14, Fig. 11 on page 15, Fig. 13 on page 16).

Transcatheter arterial thrombolysis and mechanical thrombolysis was performed in 6 cases of HAT, with successful revascularization and graft salvage in 3 cases (Fig. 14 on page 17). In 3 cases the revascularization of the hepatic artery was unsuccessful. After intraarterial thrombolysis, the control angiogram can show an irregular lumen of the liver graft artery, or smooth contour with an even caliber. The patency of the hepatic artery was shown to be transient (rebound thrombosis was found in 2 out of 3 patients), so the need for retransplantation is high (the transient revascularization can maintain a good liver function until a donor liver is available).
One patient had a good response to endovascular treatment, maintaining a good permeability of the hepatic artery. Two patients had rebound thrombosis (in one patient, a surgical direct anastomosis was performed, by placing an arterial conduit between the infrarenal aorta and the donor hepatic artery). In this patient, the arterial graft showed also signs of thrombosis and, after intraarterial thrombolysis, a successful revascularization was obtained.

**Discussions**

According to WHO, liver cirrhosis accounted for 1.8% of all deaths in Europe. In the last decades of the 20th century, a very strong east-west gradient in mortality rates was observed, with the level of liver cirrhosis mortality in south-eastern Europe (especially in Hungary and Moldova but also in Slovakia, Slovenia and Romania) achieving rates never before seen in Europe (8).

Liver transplantation is currently the treatment of choice for patients with severe acute liver failure (9) (due to viral hepatitis, drug-induced hepatitis, or hepatotoxins) or chronic liver failure (autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, metabolic diseases, cholestatic liver disorders) for which no other therapy is available (10). Potential candidates are patients with hepatocellular carcinoma or inoperable neuroendocrine metastases.

Our results are similar to other authors (11), considering the small study group. Also, some authors describe the use of percutaneous transluminal angioplasty (PTA) and drug eluting stents, that do not provide a long term patency of the hepatic artery (12).

HAT has different treatment approaches depending on the age of the thrombus. Early HAT can be treated by surgical revascularization or retransplantation or endovascular treatment (intraarterial thrombolysis, mechanical thrombolysis or percutaneous transluminal angioplasty (PTA) or stenting). Late HAT benefits from conservative treatment (Fig. 15 on page 17).
Fig. 5: Vascular complications of liver transplantation. *1 case of venous graft thrombosis

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**Fig. 6:** Doppler ultrasound shows the absence of flow in the hepatic artery at the level of the hepatic hilum.

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**Fig. 7:** Axial arterial phase(a) and coronal MIP reformat (b) showing the abrupt cut-off of the hepatic artery (chevron).

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Fig. 8: a. Peripheral areas of liver graft infarction (chevron). b. Two weeks later, the infarcted zone became infected.

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Fig. 9: a. DSA - lack of enhancement of the hepatic artery (chevron); b. thread-like opacification of the liver graft hepatic artery after intraarterial thrombolysis.

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**Fig. 10:** M, 44 y.o., orthotopic liver transplantation. CTA after intraarterial thrombolysis shows enhancement of the hepatic artery (chevron).

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Fig. 11: MIP(a)/MPR(b) coronal plane reformatted images showing a good permeability of the hepatic artery.

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Fig. 12: Complete thrombosis of the liver graft hepatic artery (a) and revascularization of the liver graft artery and intrahepatic branches after intraarterial thrombolysis (b).

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Fig. 13: M, 56 y.o., orthotopic liver transplantation. CT angiography after intraarterial thrombolysis shows recanalization of the liver graft hepatic artery.

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Fig. 14: Transcatheter arterial thrombolysis.

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**Fig. 15:** Management of hepatic artery thrombosis.

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Conclusion

1. HAT is the most significant post-transplant liver complication, being associated with graft dysfunction.
2. Early imaging detection using a correct diagnostic algorithm (Doppler US, CTA and conventional angiography) allows a minimally invasive therapeutic approach, reducing morbidity and providing graft salvage.
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