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EARLY DIAGNOSIS AND TREATMENT OF SPLENIC ARTERY STEAL SYNDROME AFTER LIVER TRANSPLANTATION

A.A. Kirshin[1, 2], A.Yu. Teregulov[1, 2], A.R. Kirshina[1]

[1] Republican Clinical Hospital, Kazan, Russian Federation
[2] Kazan Federal University, Kazan, Russian Federation

Objective: to study the incidence of splenic artery steal syndrome (SASS) in our own series of liver transplant surgeries and to determine diagnostic and therapeutic tactics. **Materials and Methods.** During the 3.5 years of existence of the liver transplant program in the Republic of Tatarstan, 77 cadaveric liver transplantations (LTx) have been performed. Postoperative SASS occurred in 4 cases (5.2%). Among the patients were 3 women and 1 man; mean age was 38 years. Doppler ultrasonography of the liver vessels and celiacography were used for diagnosis. Proximal splenic embolization was used as a way to correct the syndrome. **Results.** In all clinical cases, SASS was timely diagnosed and corrected by endovascular image-guided intervention. The patients were discharged with good hepatic graft function. The complication did not affect the length of hospital stay. **Conclusion.** SASS remains a severe vascular complication of LTx, which can lead to graft dysfunction and possible loss. Timely detection and treatment prevent severe consequences for the liver recipient.

Keywords: liver transplantation, splenic artery steal syndrome, splenic embolization.

INTRODUCTION

LTx remains the only radical treatment for end-stage liver diseases. However, such high-tech interventions come with specific vascular complications. These complications can be initiated both by primary problems in the area of venous and arterial anastomoses, and by changes in hepatic hemodynamics caused by postoperative cirrhosis. Insufficient arterial or excessive portal perfusion of the graft can lead to severe consequences, even to graft loss.

SASS is still not a well understood vascular complication following LTx. The reported incidence of SASS in LTx recipients ranges from 0.6% to 10.1% [1]. It is characterized by decreased blood flow through the hepatic artery in the absence of occlusive disease of the hepatic artery, associated with increased blood flow through the dilated splenic artery or more rarely through the gastroduodenal artery [2]. Hypoperfusion develops in the graft, which can lead to severe ischemic injury of the organ up to the need for retransplantation [3, 4].

There are no clear ideas about the pathogenesis of SASS and its diagnostic criteria that allow for early prevention of graft dysfunction by timely image-guided surgery. In this paper, we want to demonstrate SASS cases with active treatment tactics.

MATERIAL AND METHODS

From December 2018 to May 2022, 77 cadaveric liver transplants were performed at the second surgical ward of Republican Clinical Hospital, Kazan. Postoperative SASS occurred in 4 cases (5.2%). All patients who developed this syndrome were operated on using the same technique (J. Belghiti's side-to-side cavo-caval anastomosis, end-to-end portal anastomosis, arterial reconstruction using the recipient's gastroduodenal artery, and end-to-end biliary anastomosis). Among them were three women and one man; the mean age was 38 years. Evaluated were the indicators of X-ray computed tomography (CT) performed in patients with up to one month before LTx – splenic and hepatic artery diameters, variant anatomy of branches of the celiac trunk and superior mesenteric artery.

After LTx, we used Doppler ultrasonography of hepatic vessels as a screening – twice a day during the first week after surgery, then when indicated and before discharge. General clinical and biochemical laboratory indicators were studied (twice a day during the stay in the intensive care unit, daily for 3–5 days after transfer to the ward, then when indicated and before discharge). The tables below mainly show the data on the day of SASS detection, as well as on days 1, 3, 5, and 10 after image-guided correction of this complication. The final diagnosis of splenic steal syndrome was established by celiacography, which in all cases revealed depleted blood flow with late filling of the hepatic artery with preferential blood flow through the splenic artery. Control celiacography immediately after splenic artery occlusion in the proximal part showed increased blood flow in the hepatic artery with improved blood supply

Corresponding author: Alexandr Kirshin. Address: 10-222, B. Urmanche str., Kazan, 420064, Russian Federation.
Phone: (912) 467-52-79. E-mail: kirshinalex80@mail.ru

to the peripheral parts of the liver parenchyma. Below we describe clinical case.

CLINICAL CASE 1

Male patient A., 34 years old, diagnosed with liver cirrhosis that resulted from primary sclerosing cholangitis, Child–Pugh class B, esophageal varices grade 3 complicated by repeated bleeding, ascites, bilateral hydrothorax, splenomegaly. MELD score 13. According to X-ray CT conducted on March 19, 2022, the spleen size was 15.5 × 15 × 7.3 cm, diameters of the splenic artery and hepatic artery were 7.5 mm and 5.5 mm, respectively. Transjugular intrahepatic portosystemic shunt was performed on March 23, 2022. Orthotopic LTx (OLTx) was carried out on March 26, 2022 due to availability of a compatible deceased donor. On day 1 after surgery (March 27, 2022), SASS was suspected via Doppler ultrasonography, which was confirmed by celiacography (Fig. 1). The splenic artery was embolized proximally for SASS (Fig. 2). Control celiacography after embolization showed good contrasting of the hepatic artery and its distal bed (Fig. 3). The postoperative period further proceeded smoothly; the patient was discharged on day 17. Laboratory and instrumental data are presented in Table 1.

CLINICAL CASE 2

Female patient A., 33 years old, presented with liver cirrhosis that resulted from autoimmune hepatitis; Child–Pugh class C, varices grade 3, three times complicated by bleeding, ascites, bilateral hydrothorax. MELD score 17.

According to X-ray CT conducted on February 30, 2022, the spleen dimensions were within normal values, the diameter of the splenic artery was 7.5 mm, that of the hepatic artery was 7.8 mm. Transjugular intrahepatic portosystemic shunt was performed on March 11, 2022. OLTx was performed on March 30, 2022. On day 8 after the surgical intervention, there was decreased peak systolic hepatic artery flow velocity with no diastolic velocity. At the same time, splenic artery velocity increased. On day 9 after the operation, due to deterioration in Doppler ultrasonography of the liver vessels, celiac trunk angiography was performed, in which the splenic embolization syndrome was confirmed, and proximal splenic embolization was performed. Control angiography showed good filling of the hepatic artery. Biochemical parameters and ultrasound data are presented in Table 2. The postoperative period further proceeded smoothly; the patient was discharged on day 14.

CLINICAL CASE 3

Female patient C., 27 years old; on April 19, 2022 underwent OLTx for cirrhosis that resulted from autoim-

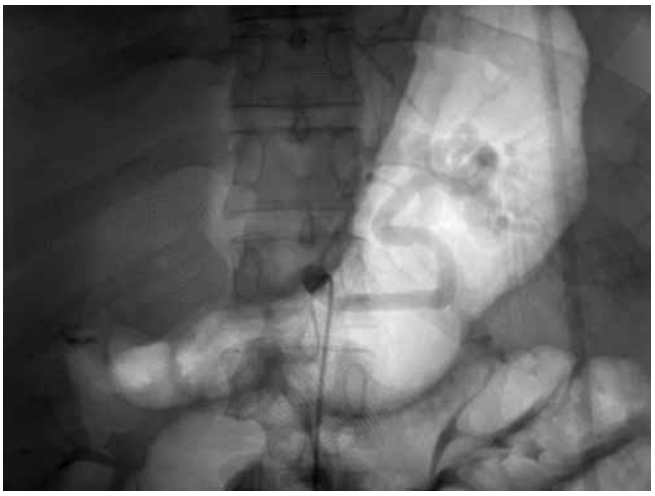

Fig. 1. Celiacography. The splenic artery is contrasted, the hepatic artery and its distal bed are not contrasted

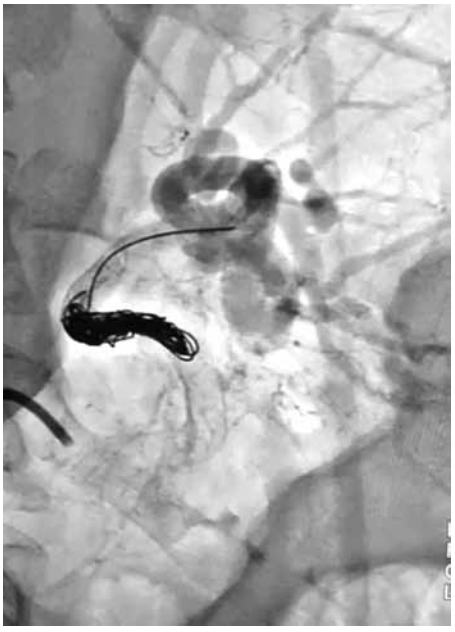

Fig. 2. Proximal splenic embolization using stent and coils

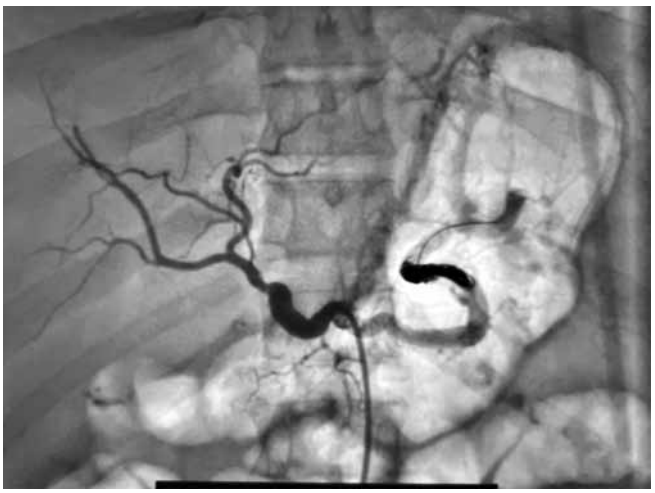

Fig. 3. Control angiography showing good filling of the hepatic artery

mune hepatitis; Child–Pugh class B, esophageal varices grade 1, ascites, grade 1 recurrent hepatic encephalopathy. MELD score 16.

According to X-ray CT conducted on April 19, 2022, the spleen size was 16 × 6 × 12 cm, diameters of the splenic artery and hepatic artery were 7 mm and 3 mm, respectively. On day 1 after surgery (April 20, 2022), SASS was suspected via Doppler ultrasonography, which was confirmed by celiacography. Proximal splenic embolization was performed. Control angiography showed good filling of the hepatic artery. The postoperative period further proceeded smoothly; the patient was discharged on day 22. The dynamics of the parameters are presented in Table 3.

Table 1

Dynamics of biochemical parameters and ultrasound data (clinical case #1)

	26.03.22	27.03.22	28.03.22	30.03.22	01.04.22	06.04.22
Biochemical markers		embolization				
Alanine aminotransferase	30	1123	879.4	554	236	116.1
Aspartate aminotransferase	33	1023	388	134	28	17.3
Alkaline phosphatase	295	138	70.9	150	164	92
Gamma-glutamyl transferase	68	114	93.8	228	229	123
Total bilirubin	50.5	68.5	37.9	31.5	22.6	10.7
Doppler ultrasound data						
VP velocity		36.8	26	26	24	24
Vertebral artery peak systolic velocity	not visualized	24	20	63	29.9	72.9
Vertebral artery end-diastolic velocity		absence	absence	26	6.4	16.5
Vertebral artery resistance index				0.59	0.78	0.79
Carotid artery peak systolic velocity	65	135		48	40	75.7

Table 2

Dynamics of biochemical parameters and ultrasound data (clinical case #2)

	03.04.2022	06.04.2022	07.04.2022	08.04.2022	10.04.2022	12.04.2022
Biochemical markers			embolization			
Alanine aminotransferase	189.6	100	50.7	69	32.9	32.1
Aspartate aminotransferase	66.9	19	13.8	19	9.3	10.6
Alkaline phosphatase	179	139	67.6	123	88	86.4
Gamma-glutamyl transferase	596	434	228	351	273	269
Total bilirubin	58.9	27.1	12.9	27.1	22.7	25.32
Doppler ultrasound data						
VP velocity	58	33	26	32	31	
Vertebral artery peak systolic velocity	118	20	16.9	69.2	46.1	
Vertebral artery end-diastolic velocity	49.4	absence	4.4	28.2	24.9	
Vertebral artery resistance index	0.58		0.74	0.59	0.46	
Carotid artery peak systolic velocity	63	84.2	133	89.5	56.9	

Table 3

Dynamics of biochemical parameters and ultrasound data (clinical case #3)

	20.04.2022	21.04.2022	23.04.2022	25.04.2022	30.04.2022
Biochemical markers	embolization				
Alanine aminotransferase	265.3	228.6	303	264	60
Aspartate aminotransferase	477.6	192.1	161	111	15
Alkaline phosphatase	68.3	68	101	104	87
Gamma-glutamyl transferase	49.2	47	247	236	79
Total bilirubin	65	46.8	49.2	44.7	28
Doppler ultrasound data					
VP velocity	55	40	45	50	68
Vertebral artery peak systolic velocity	not visualized	22	32	35	61.2
Vertebral artery end-diastolic velocity			5.5	6	11.8
Vertebral artery resistance index			0.83	0.83	0.81
Carotid artery peak systolic velocity	103	52	85	57	104

CLINICAL CASE 4

Female patient A., 58 years old, on March 29, 2022 had OLTx for cirrhosis that resulted from overlap syndrome (primary biliary cirrhosis combined with autoimmune hepatitis, Child–Pugh class C, esophageal varices grades 2–3, ascites. MELD score 26. According to X-ray CT conducted on March 28, 2022, the spleen size was 13.5 × 8.5 × 5.8 cm, diameters of the splenic artery and hepatic artery were each 6 mm. On April 1, 2022, celiacography with subsequent splenic embolization was performed due to suspected SASS. Laboratory and instrumental data are presented in Table 4. The postoperative period further proceeded smoothly; the patient was discharged on day 24.

DISCUSSION

The SASS phenomenon was first described by Manner in 1991 [5]. The authors suggested that the delayed filling of the hepatic artery with contrast according to arteriography was associated with preferential outflow of blood into the dilated splenic artery in patients with severe splenomegaly. However, in 2008, Quintini C. et al. proposed an alternative theory of portal hyperperfusion [6]. According to their data, hepatic artery narrowing in these patients occurred in response to increased portal blood flow. Transplant hyperperfusion along the portal vein causes sinusoidal damage due to the direct effect of increased portal pressure on liver cells and due to hepatic artery buffer response (HABR). HABR allows adequate hepatic blood flow to be maintained by vasodilator adenosine. A decrease in portal flow washes away less adenosine, which accumulates to dilate the hepatic artery and increase arterial blood flow. In the case of SASS, increased portal venous blood flow accelerates adenosine washout, which causes relative vasoconstriction of the hepatic artery [7]. A clinical case with a rare anatomical anomaly supports this theory [8]. In a patient with SASS, there was an absence of the splenic trunk with the splenic artery branching separately from the common hepatic artery directly from the aorta, which excludes the very process of "stealing". In 2012, Saad W.E.A. et al. suggested that HABR is only one of the potential causes of SASS, along with splenic or gastroduodenal artery steal syndrome and proposed a new name – post-transplant nonocclusive hepatic artery hypoperfusion syndrome [9]. Thus, there are no studies, which would reliably determine the pathogenetic aspects of reduced blood flow along the hepatic artery in patients after LTx.

SASS is a diagnosis requiring the exclusion of other vascular complications (thrombosis, hepatic artery stenosis), graft rejection, and infections [4, 10]. The timing of SASS ranges from a few hours to 5.5 years after surgical intervention, but more often in the first 3 months [10]. The clinical picture is nonspecific, ranging from the absence of symptoms to manifestations of severe graft dysfunction. Biochemical findings may include hyperbilirubinemia, increased levels of transaminases, alkaline phosphatase, and gamma-glutamyltransferase [4, 10].

Ultrasound examination of hepatic vessels is the method of choice for screening of the pathology. According to studies, SASS is characterized by decreased hepatic artery blood flow velocity less than 35 cm/s, resistance index more than 0.8, low or reversed diastolic blood flow [11]. At the same time, there is increased velocity along the portal vein and splenic artery. Given the presence of splenomegaly in most patients with cirrhosis, the detection of enlarged spleen has no diagnostic significance for SASS verification.

The most reliable data for diagnosis of hepatic artery hypoperfusion can be obtained by computed tomographic angiography. Kirbas I. et al. reported that a splenic artery size ≥4 mm or >150% of the hepatic artery diameter was associated with SASS [12]. Such multidetector CT signs as splenic volume >829 mL, splenic

Table 4

Dynamics of biochemical parameters and ultrasound data (clinical case #4)

	30.03.22	31.03.22	01.04.22	02.04.22	04.04.22	06.04.22	11.04.22
Biochemical markers			embolization				
Alanine aminotransferase	382.3	217.2	187.4	150.9	109.2	121	43.1
Aspartate aminotransferase	428	134	65.9	40.9	43.3	31	19
Alkaline phosphatase	170	107	110	55.3	45.9	132	170
Gamma-glutamyl transferase	70	41	49	54	35.4	41	22.9
Total bilirubin	178.9	138.8	118.2	96.4	68.8	70.7	40.4
Doppler ultrasound data							
VP velocity	80	49	33	33	74	34	25
Vertebral artery peak systolic velocity	61	100	32	79	53.5	81	48
Vertebral artery end-diastolic velocity	15	14	absence	19.8	16.5	29	21
Vertebral artery resistance index	0.75	0.86		0.75	0.69	0.64	0.56
Carotid artery peak systolic velocity	52	86	116		80		79

artery diameter >4 mm and differences of 6 mm between splenic and hepatic artery diameters are described as preoperative predictors of SASS [12, 13, 14].

Slow and delayed blood flow in the hepatic artery, early perfusion of the splenic or gastroduodenal artery are the key angiographic findings. In severe cases, portal venous blood flow is contrasted simultaneously with splenic arterial blood flow or even before complete filling of the hepatic artery [4, 9].

The aim of SASS therapy is to increase blood flow in the hepatic artery. The preferred method is splenic embolization due to its minimal invasiveness and effectiveness. According to the literature, more proximal placement of coils preserves collateral blood flow to the spleen, thus reducing the risk of complications such as spleen infarction and sepsis [4, 10, 15]. However, Fleckenstein et al., in a comparison of laboratory parameters of 75 liver transplant recipients with SASS, revealed no reliable differences in long-term outcomes depending on the place of splenic embolization [16]. Thus, the place to embolize the splenic artery is left for the physician to decide. If interventional treatment is ineffective or impossible, surgical options – splenic artery ligation or splenectomy – are considered [10].

Splenic artery ligation during LTx in the presence of risk factors is used as SASS prevention.

In our study, all patients had a splenic artery dilation >4 mm according to CT scans before LTx. This is consistent with literature data on identification of SASS predictors.

It is generally accepted that SASS is associated with graft dysfunction manifested by elevated liver function values with or without clinical signs (ascites). However, early after liver transplantation, ischemia-reperfusion injury may mask the biochemical changes suggestive of SASS. Therefore, the main focus for screening of this syndrome should be Doppler ultrasonography of the liver.

In addition, our small experience shows that timely celiacography to verify SASS with endovascular image-guided proximal occlusion of the splenic artery helps to avoid ischemic manifestations and severe graft dysfunction. In the early postoperative period, there were no complications associated with splenic embolization; all patients were discharged with satisfactory graft function.

We consider the following SASS diagnostic algorithm to be optimal. If blood flow linear velocity along the hepatic artery is reduced and that of the splenic artery and portal vein is simultaneously increased according to Doppler ultrasound of hepatic vessels, the study is repeated after 6 hours. If the tendency to changes in blood flow persists, celiacography is performed. Proximal splenic embolization is performed if typical SASS angiographic signs are revealed.

CONCLUSION

Thus, SASS remains a severe vascular complication of LTx that can lead to graft dysfunction and possible loss. Timely detection and correction of SASS could prevent severe consequences for the liver recipient. The issue of prevention of this complication remains debatable, which undoubtedly requires further research in the study of visceral venous and arterial blood supply in cirrhosis and after LTx.

The authors declare no conflict of interest.

REFERENCES

1. *De Carlis L, Sansalone CV, Rondinara GF et al.* Splenic artery steal syndrome after orthotopic liver transplantation: diagnosis and treatment. *Transplant Proc*. 1993; 25 (4): 2594–2596.
2. *Geissler I, Lamesch P, Witzigmann H, Jost U, Hauss J, Fangmann J.* Splenohepatic arterial steal syndrome in liver transplantation: clinical features and management. *Transpl Int*. 2002; 15 (2–3): 139–141.
3. *Pinto S, Reddy SN, Horrow MM, Ortiz J.* Splenic Artery Syndrome after orthotopic liver transplantation: a review. *Int J Surg*. 2014; 12 (11): 1228–1234.
4. *Uflacker R, Selby JB, Chavin K, Rogers J, Baliga P.* Transcatheter splenic artery occlusion for treatment of splenic artery steal syndrome after orthotopic liver transplantation. *Cardiovasc Intervent Radiol*. 2002; 25 (4): 300–306.
5. *Manner M, Otto G, Senninger N, Kraus T, Goerich J, Herfarth C*. Arterial steal: an unusual cause for hepatic hypoperfusion after liver transplantation. *Transpl Int*. 1991; 4: 122–124.
6. *Quintini C, Hirose K, Hashimoto K, Diago T, Aucejo F, Eghtesad B et al.* "Splenic artery steal syndrome" is a misnomer: the cause is portal hyperperfusion, not arterial siphon. *Liver Transpl*. 2008; 14: 374–379.
7. *Eipel C, Abshagen K, Vollmar B.* Regulation of hepatic blood flow: the hepatic arterial buffer response revisited. *World J Gastroenterol*. 2010; 16 (48): 6046–6057.
8. *Terra C, Furtado E, Agostinho AG, Donato P.* Splenic Artery Steal Syndrome – a Misleading Term: An Independent Artery Origin Supporting Portal Hyperperfusion Theory. *Journal of Vascular and Interventional Radiology*. 2020; 31 (11): 1916–1918.
9. *Saad WEA.* Nonocclusive hepatic artery hypoperfusion syndrome (splenic steal syndrome) in liver transplant recipients. *Semin Intervent Radiol*. 2012; 29: 140–146.
10. *Nüssler NC, Settmacher U, Haase R, Stange B, Heise M, Neuhaus P.* Diagnosis and treatment of arterial steal syndromes in liver transplant recipients. *Liver Transpl*. 2003; 9 (6): 596–602.
11. *Vit A, De Candia A, Como G, Del Frate C, Marzio A, Bazzocchi M.* Doppler evaluation of arterial complica-

tions of adult orthotopic liver transplantation. *J Clin Ultrasound*. 2003; 31 (7): 339–345.
12. *Kirbas I, Ulu EMK, Ozturk A, Coskun M, Harman A, Ogus E, Haberal M.* Multidetector computed tomographic angiography findings of splenic artery steal syndrome in liver transplantation. *Transplant Proc*. 2007; 39 (4): 1178–1180.
13. *Grieser C, Denecke T, Steffen IG et al.* Multidetector computed tomography for preoperative assessment of hepatic vasculature and prediction of splenic artery steal syndrome in patients with liver cirrhosis before transplantation. *Eur Radiol*. 2010; 20 (1): 108–117.
14. *Dokmak S, Aussilhou B, Belghiti J.* Liver transplantation and splenic artery steal syndrome: the diagnosis should be established preoperatively. *Liver Transpl*. 2013; 19 (6): 667–668.
15. *Madoff DC, Denys A, Wallace MJ, Murthy R, Gupta S, Pillsbury EP et al.* Splenic arterial interventions: anatomy, indications, technical considerations, and potential complications. *Radiographics*. 2005; 25 (Suppl 1): 191–211.
16. *Fleckenstein FN, Luedemann WM, Kücükkaya A, Auer TA, Plewe J et al.* Splenic artery steal syndrome in patients with orthotopic liver transplant: Where to embolize the splenic artery? *PLoS One*. 2022; 17 (3): e0263832.

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