Journal of Cardiology Cases 23 (2021) 103–107

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

Portosystemic shunt with hyperammonemia and high cardiac output as a complication after Fontan surgery

Kiyotaka Takefuta (MD)[a,b,*], Hideaki Senzaki (PhD, FJCC)[b], Atsuya Shimabukuro (MD)[a], Masahiro Nishibata (MD)[a], Seiichi Sato (MD)[a], Mami Nakayashiro (MD)[a]

[a] Department of Pediatric Cardiology, Okinawa Prefectural Nanbu Medical Center, Children's Medical Center, Okinawa, Japan
[b] Department of Pediatrics, International University of Health and Welfare, Narita, Japan

ARTICLE INFO

Article history:
Received 1 January 2020
Received in revised form 23 September 2020
Accepted 23 September 2020

Keywords:
Portosystemic shunt
High cardiac output
Fontan-associated liver disease

ABSTRACT

In the late phase after Fontan surgery, organ dysfunction due to high central venous pressure (CVP) is a major clinical problem. We have described the cases of two patients with portosystemic shunts who exhibited hyperammonemia and high cardiac output associated with peripheral vasodilatation after Fontan surgery. A high CVP in these patients may have resulted in the formation of a portosystemic shunt. We performed coil embolization and balloon-occluded retrograde transvenous obliteration for each case. The possibility of a portosystemic shunt as a postoperative complication of Fontan surgery should always be considered. Early detection and therapeutic intervention seem necessary from the viewpoint of stabilizing the Fontan circulation and delaying the progression of liver disorder.
<**Learning objective:** Learning objectives: A portosystemic shunt may develop due to the high central venous pressure after Fontan surgery independent of hepatic disorder and should be considered as a potential cause of unexplained hyperammonemia and high cardiac output status. Transcatheter closure of the portosystemic shunt may improve the clinical status.>

Introduction

In a portosystemic shunt formed by an increased portal pressure, various toxic substances increase in concentration in the blood without being detoxified and metabolized. As a result, cytokines and oxidative stress increase secondarily, causing various pathological conditions. In this study, we describe two cases of portosystemic shunts with hyperammonemia and high cardiac output associated with peripheral vasodilatation in the remote phase after Fontan surgery. A portosystemic shunt could develop through a mechanism different from that of portal hypertension associated with liver damage and is an important complication associated with increased venous pressure after Fontan surgery.

Case reports

[Case 1] A 33-year-old man was diagnosed with tricuspid atresia, transposition of the great arteries, and ventricular septal defect. At the age of 5 years, he underwent an atriopulmonary connection-type Fontan surgery. The postoperative course was good, but atrial tachycardia began to recur at the age of 18 years, and total cavopulmonary connection (TCPC) conversion and ablation were performed at the age of 20 years. Following that, refractory atrial arrhythmia was observed, and his cardiac function gradually deteriorated. He developed protein-losing enteropathy (PLE) at the age of 23 years, and was frequently hospitalized thereafter for the same. At the age of 32 years, he developed acute kidney injury due to sepsis. In addition, he developed treatment-resistant hyperammonemia. He was unable to withdraw from continuous hemodiafiltration, and thus, he was transferred to our hospital. On admission, his blood pressure, heart rate, respiratory rate, and oxygen saturation level were 75/25 mmHg, 80 bpm, 20 breaths/min, and 95% (nasal oxygen, 2 L), respectively. Table 1 summarizes the laboratory findings and medications given at the time of hospitalization. The findings from the abdominal computed tomography (CT) scans and abdominal ultrasonography were consistent with liver cirrhosis (LC). Cardiac catheterization (Table 1) revealed a decreased cardiac function with a left ventricular ejection fraction of 30%. His central venous pressure (CVP) was not as high as 14 mmHg, but a high cardiac output

* Corresponding author at: 852 HatakedA, Narita, Chiba 286-0048, Japan.
E-mail address: kiyotaka-takefuta@umin.ac.jp (K. Takefuta).

https://doi.org/10.1016/j.jccase.2020.10.011
1878-5409/

Table 1 Clinical data for Case 1 and Case 2.

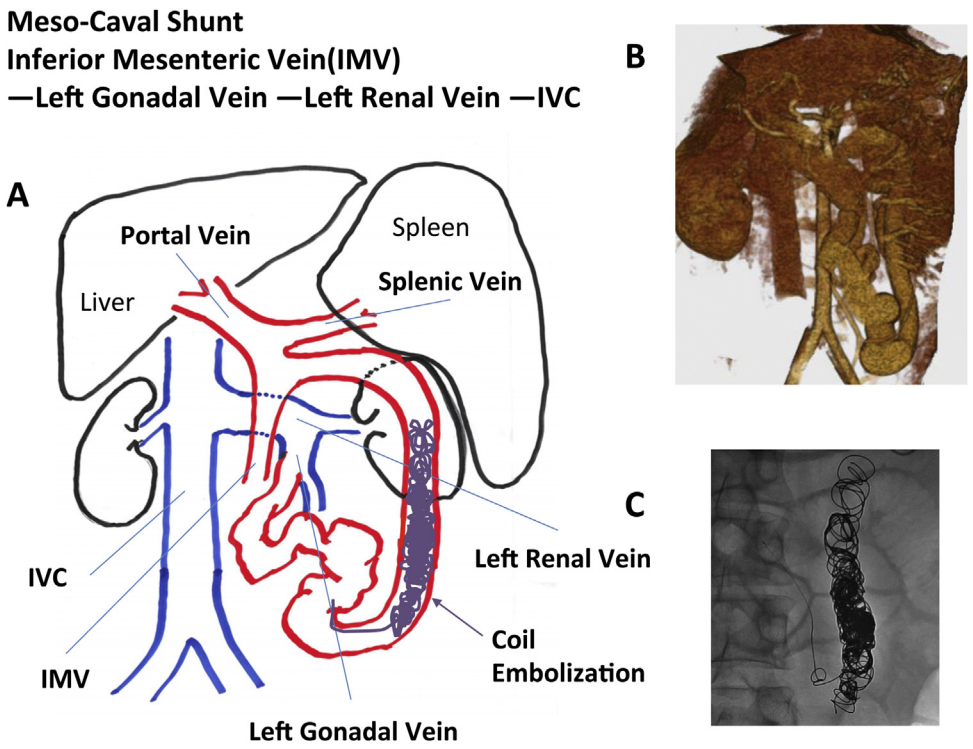
	Case 1	Case2
Medications	Amiodarone 200mg	Procainamide 875 mg/3
	Verapamil 60 mg	Aspirin 100 mg/1
	Furosemide 80mg	Enalapril Maleate 2.5 mg/1
	Spironolactone 150mg	
	Trichlormethiazide 4mg	
	Tolvaptan 15 mg	
	Macitentan 10mg	
Laboratory Data		
Blood Urea Nitrogen	84 mg/dL	8 mg/dL
Creatinine	1.86 mg/dL	0.60 mg/dL
Aspartate transaminase	56 IU/L	55 IU/L
Alanine transaminase	52 IU/L	62 IU/L
Total Bilirubin	1.9 mg/dL	4.8 mg/dL
Ammonia	345mcg/dL	120mcg/dL
Cholinesterase	139IU/L	224IU/L
Total Protein	5.4 g/dL	7.1 g/dL
Albumin	3.0 g/dL	4.6 g/dL
Hemoglobin	13.2 g/dL	16.1 g/dL
Platelet	159,000/mcL	97,000/mcL
Prothrombin Time(%)	64%	45%
Hyaluronic Acid	84 ng/mL	41 ng/mL
Type4 Collagen 7S	8.8 ng/mL	9.31 ng/mL
Catheterization data		
Central venous pressure	14mmHg	15mmHg
Ventricle pressure	80/EDP 10 mmHg	105/EDP 8 mmHg
Aortic pressure	80/29/45 mmHg	103/63/83 mmHg
Pulmonary to systemic flow ratio	1.0	1.0
Pulmonary vascular resistance index	0.60 Wood unit·m^2	0.90 Wood unit·m^2
Systemic vascular resistance index	4.7 Wood unit·m^2	14.40 Wood unit·m^2
Cardiac index	6.6 L/min/m^2	4.4 L/min/m^2
Ventricular end-diastolic volume index	75 mL/m^2	80 mL/m^2
Ejection fraction	34%	51%

associated with a marked decrease in the peripheral vascular resistance was observed. The abdominal CT scan showed a portal vein shunt from the inferior mesenteric vein to the left renal vein (Fig. 1A-C). The wedged hepatic vein pressure of 17 mmHg did not change with the temporal occlusion test of the shunt. As a result of the hyperdynamic condition due to peripheral vasodilatation, metridine and vasopressin as vasoconstrictors were administered, and the blood pressure increased from 90/30 mmHg to 100/60 mmHg. The cardiac index (CI) calculated using the Fick method of cardiac catheterization was decreased to 4.6 L/min/m^2, and the urine volume was elevated accordingly. As the portosystemic shunt was considered to have an adverse effect not only on the peripheral vasodilatation, but also on hyperammonemia, we performed coil embolization of the shunt. Immediately after the shunt closure, the ammonia level decreased from 300 μg/dL to 100 μg/dL. Subcutaneous injection of octreotide acetate and intermittent hemodialysis made six weeks of home care possible for the patient; he died from the exacerbation of PLE six months following the treatment.

[Case 2] A 19-year-old man was diagnosed with single right ventricular pulmonary stenosis. At the age of 9 years, he underwent a bidirectional Glenn procedure and extracardiac TCPC simultaneously. In the routine outpatient blood tests, hyperbilirubinemia and hyperammonemia (ammonia 120 μg/dL) were confirmed, and cardiac catheterization was performed for detailed examination. On admission, his blood pressure, heart rate, and oxygen saturation level were 100/50 mmHg, 80 bpm, and 97%, respectively. Table 1 summarizes the laboratory findings and medications given at the time of hospitalization. During the cardiac catheterization, his CVP was not as high as 15 mmHg, but CI calculated using the Fick method was elevated. Angiography revealed a shunt from the left gastric, posterior gastric, and short gastric veins to the left renal vein (Fig. 2A,B). The wedged hepatic vein pressure changed from 17 mmHg to 18 mmHg after the portal vein shunt closure test. Thus, the shunt was occluded by a balloon-occluded retrograde transvenous obliteration (Fig. 2C). The serum bilirubin level decreased from 4.5 g/dL to 3.1 g/dL, and the ammonia level decreased from 81 μg/dL to 47 μg/dL after the closure. Liver biopsy revealed hepatic congestion; however, no severe cirrhosis that could have caused secondary portal hypertension was observed. His condition, including the bilirubin and ammonia levels, have been stable for over a year after the closure.

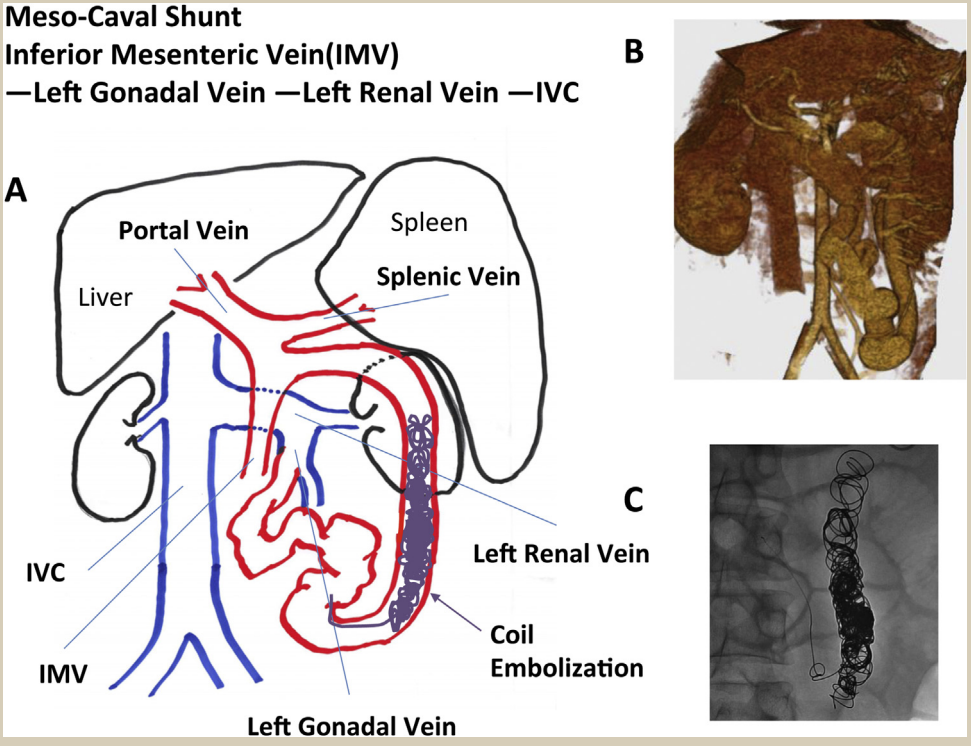
Discussion

High CVP is a compensatory mechanism in the establishment of the Fontan circulation; however, in the long term, it has been found to cause systemic organ damage of varying degrees due to congestion [1,2]. Fibrosis of the liver sinusoid progresses to fibrosis of the portal vein region, followed by LC, and finally to liver cancer [3,4]. In general, LC is accompanied by a portosystemic shunt as a compensatory pathway for the increased portal pressure; however, the high CVP in Fontan circulation inevitably causes portal hypertension immediately after Fontan completion even in the absence of LC. Of the two cases reported herein, Case 2 showed mild progression of the Fontan-associated liver disease (FALD), which strongly suggests that the portosystemic venous shunt may not be associated with LC, but could have resulted from congestion due to high CVP. In addition, the fact that the shunt developed from the splenic vein to the left renal vein in both cases is interesting considering the developmental mechanism. These sites are common with the congenital portosystemic shunt [5]. This suggests that the shunt is formed as follows: during the embryonic stage, the subcardinal vein, which differentiates into the inferior vena cava, is anastomosed with the omphalomesenteric vein, which differentiates into the portal vein, and the already formed anastomotic channel enlarges with the increased portal pressure and turns into a shunt [5]. Herein, the shunt morphology did not



(A) Schematic illustration of the portosystemic shunt in Case 1. (B) Computed tomography showing the portosystemic shunt in Case 1. (C) Coil embolization of the portosystemic shunt in Case 1.
IVC, inferior vena cava.

Fig. 1.



show the marked tortuosity typical of portal hypertension associated with LC, and the shunt was detected at a relatively mild stage of the liver disorder (especially in Case 2). Instead of flowing to the pulmonary vein or atria, where the blood pressure is lower than the CVP and portal pressure, blood flowed to the renal vein, where the blood pressure level is similar to that of the CVP and portal pressure. These findings suggest that a congenital anastomotic channel may have gradually enlarged with the inevitable increase in portal pressure after the establishment of the Fontan circulation and become a shunt.

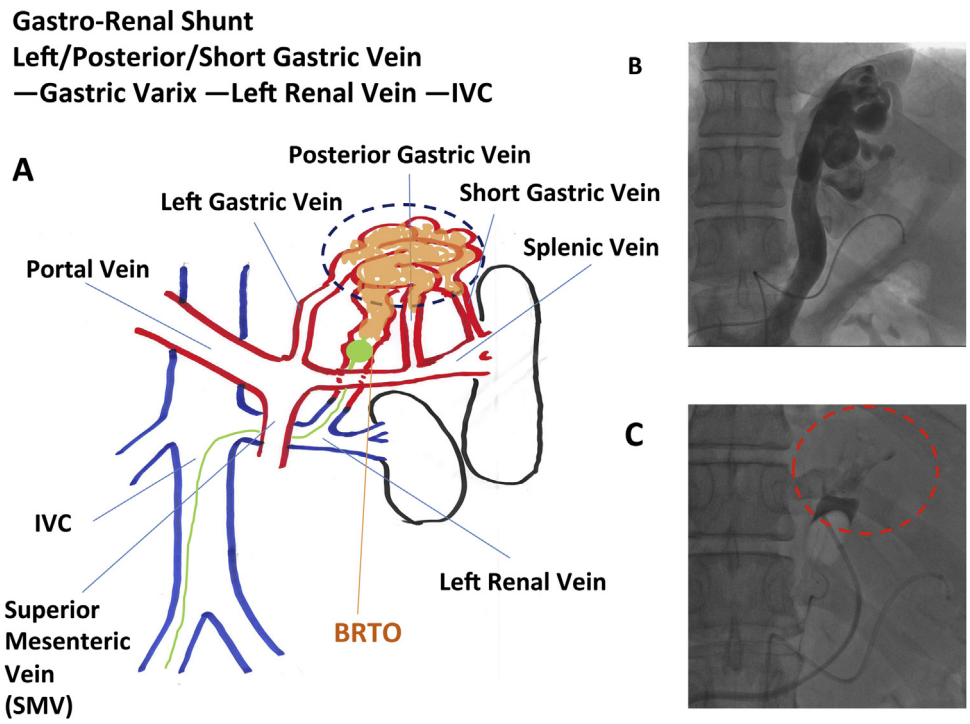


Fig. 2. (A) Schematic illustration of the portosystemic shunt in Case 2. (B) Angiography showing the portosystemic shunt in Case 2. (C) Balloon-occluded retrograde transvenous obliteration (BRTO) of the portosystemic shunt in Case 2.
IVC, inferior vena cava.

In a portosystemic shunt, regardless of whether a cirrhotic or a non-cirrhotic portosystemic shunt, portal blood does not pass through the liver, which metabolizes and breaks down various substances. Consequently, the blood concentrations of numerous non-metabolites and toxic substances cause various pathological conditions. For example, ammonia, branched-chain amino acids, false neurotransmitters, and gamma-aminobutyric acid carried into the brain may cause portosystemic encephalopathy. Indeed, Case 1 presented with hyperammonemia and encephalopathy, which may have exacerbated LC. The decreased ammonia concentrations after coil embolization of the shunt confirmed this. In Case 2, although no clinical symptoms of encephalopathy were observed, the blood ammonia concentrations were elevated, but decreased after the shunt closure. Furthermore, in the presence of a portosystemic shunt, hepatic metabolic vasoconstrictors may result in portopulmonary hypertension [6]. These conditions may adversely affect the Fontan circulation. Layangool et al. reported a case of rapidly progressing cyanosis caused by an intrapulmonary shunt after Fontan surgery [7]. Moreover, Fontan circulation generally exhibits a low cardiac output because of the high afterload and decreased preload reserve [8,9]. Ohuchi et al. reported the CI and systemic resistance in patients 10-15 years after Fontan surgery as 2.5 L/min/m^2 and 28 RUm^2 [10]. However, our patients exhibited a high cardiac output accompanied by decreased peripheral vascular resistance. Although in Case 2, one may argue that the cardiac output was not exceedingly high and the systemic resistance was not exceedingly low as compared with those of the general population, we believe that the patient's condition was in a relatively high output status as a Fontan patient. Therefore, the portosystemic shunt may have increased the blood concentrations of the vasodilatory substances, thus contributing to the peripheral vasodilatation. Finally, the portosystemic shunt may have reduced the intrahepatic portal blood flow, thus promoting the progression of liver disorder [5].

We believe that our report presents valuable findings because they suggest the importance of considering the presence of a portosystemic venous shunt as a postoperative complication of Fontan surgery regardless of the presence or absence of FALD. In this sense, monitoring the blood levels of bilirubin and ammonia appears to be necessary after the Fontan procedure. If the presence of a portosystemic venous shunt is confirmed, consideration of aggressive treatment (closure) may be appropriate from the viewpoint of avoiding the various associated complications and preventing the progression of FALD. As a portosystemic shunt may be a compensatory adaptation in patients with complication of LC, checking the transhepatic pressure gradient or test occlusion of the shunt should be necessary to safely close a portosystemic shunt in Fontan patients.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

We presented this article at the 55th Annual Meeting of the Japanese Society of Pediatric Cardiology and Cardiac Surgery.

References

[1] Liang F, Senzaki H, Kurishima C, Sughimoto K, Inuzuka R, Liu H. Hemodynamic performance of the Fontan circulation compared with a normal biventricular circulation: a computational model study. Am J Physiol Heart Circ Physiol 2014;307. H1056–72.
[2] Kurishima C, Saiki H, Masutani S, Senzaki H. Tailored therapy for aggressive dilatation of systemic veins and arteries may result in improved long-term Fontan circulation. J Thorac Cardiovasc Surg 2015;150:1367–70.
[3] Sugimoto M, Saiki H, Tamai A, Seki M, Inuzuka R, Masutani S, et al. Ventricular fibrogenesis activity assessed by serum levels of procollagen type III N-

terminal amino peptide during the staged Fontan procedure. J Thorac Cardiovasc Surg 2016;151:1518–26.
[4] Alsaied T, Possner M, Lubert AM, Trout AT, Szugye C, Palermo JJ, et al. Relation of magnetic resonance elastography to Fontan failure and portal hypertension. Am J Cardiol 2019;124:1454–9.
[5] Franchi-Abella S, Gonzales E, Ackermann O, Branchereau S, Pariente D, Guerin F. Congenital portosystemic shunts: diagnosis and treatment. Abdom Radiol (NY) 2018;43:2023–36.
[6] Hoeper MM, Krowka MJ, Strassburg CP. Portopulmonary hypertension and hepatopulmonary syndrome. Lancet 2004;363:1461–8.
[7] Layangool T, Kojaranjit V, Promphan W, Kirawittaya T, Sangtawesin C, Prachasilchai P. An unusual cause of progressive cyanosis post Fontan operation: congenital extra-hepatic porto-systemic shunt. J Med Assoc Thai 2014;97 (Suppl. 6):S176–81.
[8] Senzaki H, Masutani S, Ishido H, Taketazu M, Kobayashi T, Sasaki N, et al. Cardiac rest and reserve function in patients with Fontan circulation. J Am Coll Cardiol 2006;47:2528–35.
[9] Saiki H, Kuwata S, Iwamoto Y, Ishido H, Taketazu M, Masutani S, et al. Fenestration in the Fontan circulation as a strategy for chronic cardioprotection. Heart 2019;105:1266–72.
[10] Ohuchi H, Ono S, Tanabe Y, Fujimoto K, Yagi H, Sakaguchi H, et al. Long-term serial aerobic exercise capacity and hemodynamic properties in clinically and hemodynamically good, "excellent", Fontan survivors. Circ J 2012;76:195–203.