Peripheral Arterial Coil Embolization for Hepatic Arteriovenous Malformation in Osler-Weber-Rendu Disease; Useful for Controlling High Output Heart Failure, but Harmful to the Liver

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A 55-year-old Japanese housewife, who had Osler-Weber-Rendu disease, was admitted to our hospital because of frequent epistaxis and worsening exertional dyspnea. The computed tomography and hepatic arteriography revealed large hepatic arteriovenous malformation, which was considered to be the leading cause of her high output heart failure. Two series of hepatic arterial coil embolization procedures were performed to reduce hepatic shunt flow. They temporarily improved her cardiac condition, but gradually induced progressive hepatic failure due to intrahepatic cholangitis. Hepatic dysfunction restricted her quality of life and lead to a fatal clinical course one year after the second coil embolization. (Internal Medicine 38: 962-968, 1999)

Key words: hereditary hemorrhagic telangiectasia (HHT), arteriovenous malformation (AVM), cardiac failure, intrahepatic cholangitis, hepatic dysfunction

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is an autosomal dominant hereditary disorder, characterized by epistaxis, mucocutaneous telangiectasia, and arteriovenous malformations (AVMs) in multiple organ systems (1). The linkage analysis demonstrated that the disease gene was mapped to chromosome 9q33-q34 (2) and 12q11-q14 (3), with the mutations in the endoglin gene (4) or activin receptor-like kinase 1 gene (5). Arteriovenous malformations usually occur in the lungs, brains, kidney and gastrointestinal tract, but hepatic involvement is relatively rare (1, 6). In this reported case of HHT, the patient had a large hepatic arteriovenous malformation, which lead to high output heart failure. Two series of hepatic arterial coil embolization improved both her cardiac status and epistaxis, but they lead to gradually progressive hepatic failure due to intrahepatic cholangitis. Hepatic dysfunction restricted her quality of life and lead to a fatal clinical course one year after the second coil embolization.

Case Report

A 55-year-old Japanese housewife was admitted to our hospital because of exertional dyspnea and epistaxis. She had been given a diagnosis of HHT at the age of 44 due to frequent epistaxis and telangiectasia. One unit of packed red cell blood (200 ml) was transfused because of anemia, which caused post-transfusion hepatitis at the age of 40. Her family history revealed that her mother and elder sister had also suffered from HHT. Her father died of hepatocellular carcinoma. During the last several years, she had complained of worsening shortness of breath and palpitation on exertion. Cardiomegaly was also noted on the chest X-ray. Because of more frequent epistaxis and worsened exertional dyspnea since April 1997, she was admitted to our hospital on May 26, 1997.

Upon physical examination at her first admission, her weight was 44 kg and her height was 148 cm. Multiple telangiectatic lesions on the lips, tongue and on the top of the fingers were noted. A grade 4/6 pansystolic ejectional type murmur was audible at the apex. Bruits were heard widely on the epigastrium. No rhonchi were audible in the bilateral lung fields. Hepatomegaly, extending 3 centimeters below the right costal margin and 8 centimeters below the xiphoid was noticed on

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abdominal palpation. The liver had a smooth surface, a dull edge and a soft elasticity without any tenderness. Splenomegaly was not observed. No pretibial edema was observed on the lower extremities.

The blood examination at admission (Table 1) showed macrocytic anemia with a normal white cell and thrombocyte count, mildly elevated total bilirubin concentration, γ glutamyltranspeptidase and decreased choline esterase and plasma protein concentration. A serological test for hepatitis C viral antibody was positive.

The chest X-ray examination revealed cardiomegaly (cardiothoracic ratio, 67%) with moderate pulmonary congestion (Fig. 1). The electrocardiogram revealed a normal sinus rhythm (86 beats per minute), a left atrial overload and a high voltage of QRS in the left pre-cordial leads (Fig. 2). The echocardiography showed dilation and hyperdynamism of the left ventricle with an end-diastolic dimension of 60 mm, an ejection fraction of 66% and a cardiac output of 9.6 l/min. The color Doppler flow mapping showed mild mitral regurgitation. The right atrium and ventricle were normal size. The estimated right ventricular systolic pressure of 35 mmHg, calculated us-

ing the velocity of tricuspid regurgitation, revealed a slightly elevated pulmonary arterial pressure. The abdominal dynamic computed tomographic scans (CT) showed anomalously dilated hepatic vasculatures of the artery and portal and hepatic veins (Fig. 3A). The rapid enhancement effect of the hepatic vein was observed during dynamic contrast CT examination, which indicated arteriovenous malformation in the liver (Fig. 3B). In other organs, such as the brain and lungs, we could not detect any arteriovenous malformation on dynamic CT scans.

Cardiac catheterization, hepatic arteriography and portography were performed to examine her cardiac condition and hepatic vascular malformation, which we assumed to be the leading cause of her high output heart failure. The hepatic arteriogram (Fig. 4A) revealed a markedly enlarged common hepatic artery of 17 mm in diameter with high blood flow speed, tortuous hepatic arteries and early contrast filling of dilated hepatic veins, indicating large hepatic arteriovenous shunt. The cardiac functional study with a Swan-Ganz catheter revealed a calculated cardiac output of 10.1 l/min, a cardiac index of 7.7 l/min/m² and a mean pulmonary wedge pressure of 11 mmHg, indicating high output cardiac failure. To reduce large hepatic

Table 1. Laboratory Data on Admission

Peripheral blood		Biochemistry	
WBC	3,200/ μ l	T. Bil	0.9 mg/dl
RBC	260 $\times$ 10 ⁴ / μ l	D. Bil	0.1 mg/dl
Hb	9.0 g/dl	AST	29 IU/l
Hct	27.6%	ALT	16 IU/l
MCV	106.2 fl	ChE	85 IU/l
MCH	34.6 pg	ALP	278 IU/l
MCHC	32.6 g/dl	LAP	34 IU/l
PLT	16.0 $\times$ 10 ⁴ / μ l	γ -GTP	57 IU/l
Coagulation		LDH	132 IU/l
APTT	44.5 sec	ZTT	8.6 U
PT	52.4%	AMY	39 IU/l
Fibg	352 mg/dl	TP	5.7 g/dl
TT	66.3%	T. CHO	139 mg/dl
Arterial blood gas (room air)		TG	38 mg/dl
pH	7.469	BUN	8.0 mg/dl
PaCO ₂	37.3 mmHg	Cr	0.8 mg/dl
PaO ₂	89 mmHg	Na	136 mEq/l
SaO ₂	97.4%	K	3.7 mEq/l
Serological test		Cl	104 mEq/l
HCV Ab	(+)	Ca	9.2 mEq/l
HBs Ag	(-)	CRP	0.1 mEq/l
		Liver function test	
		ICG-R ¹⁵	72.3%

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, PLT: platelet, APTT: activated partial thromboplastin time, PT: prothrombin time, Fibg: fibrinogen, TT: thrombin time, T. Bil: total bilirubin, D. Bil: direct bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ChE: cholinesterase, ALP: alkaline phosphatase, LAP: leucine amino peptidase, γ -GTP: γ glutamyltranspeptidase, LDH: lactate dehydrogenase, ZTT: Zinc sulfate turbidity test, AMY: amylase, TP: total protein, T. CHO: total cholesterol, TG: triglyceride, BUN: blood urea nitrogen, Cr: creatinine, CRP: c-reactive protein, ICG: indocyanine green.

Figure 1. Chest X-ray examination on the initial admission, showing cardiomegaly with moderate pulmonary congestion.

arteriovenous shunt flow, we chose hepatic arterial coil embolization. Full medical information about the estimated beneficial and adverse effects was explained to the patient and her family, as an informed consent. They were also informed of another choice of treatment, surgical ligation of the hepatic artery. The patient preferred coil embolization because it is a less invasive procedure. The first percutaneous trans arterial coil embolization was performed on July 3. A Swan-Ganz catheter, connected to a Vigilance® (Baxter, CA USA) continuous cardiac output monitor, was inserted for hemodynamic monitoring during the procedure. A total of 29 Tornado® coils (Target, IN USA), 15 of 10 mm-4 mm (proximal-distal diameter), 4 of 8 mm-5 mm and 10 of 8 mm-4 mm sized coils, were released into the right, middle and left hepatic arteries (Fig. 4B, C). The right and left hepatic arteries were almost completely occluded, but the middle branch was partially obstructed because of an anatomically difficult arterial structure. The continuous cardiac output monitoring showed a 30% reduction of cardiac output after coil embolization from 15.5 l/min to 10.7 l/min. The effect of the first embolization was evaluated by chest X-ray and echocardiography. The cardiothoracic ratio on the chest X-ray, diastolic left ventricular diameters, ejection fraction and cardiac output on echocardiography decreased from 67%, 60 mm, 66% and 9.6 l/min, to 58%, 56 mm, 54% and 6.4 l/min, respectively (Table 2). She complained of epigastralgia for one month, but less frequently for other symptoms such as shortness of breath, palpitation and epistaxis.

Figure 2. Electrocardiogram on the initial admission, showing a normal sinus rhythm (the heart rate was 86 beats per minute), a left atrial overload and a high voltage of QRS in the left pre-cordial leads.

Six months later, her chest X-ray showed a reenlarged cardiothoracic ratio of 67% and pulmonary congestion. Her epistaxis had also become more frequent. The echocardiography revealed re-increased cardiac output. The abdominal ultrasound tomography and Doppler study also showed increased hepatic arterial and venous flow. Her hemoglobin concentration was 9.7 g/dl, indicating no progression of anemia. She was admitted again on December 12, 1997. The second hepatic angiography was performed to re-examine her hepatic vasculature. The left and right hepatic arteries were partially obstructed, and the shunt flow through the middle hepatic artery, particu-

Figure 3. Abdominal dynamic CT scans on the initial admission, showing the dilated hepatic artery and portal and hepatic veins (A). The hepatic vein was greatly dilated and quickly enhanced by contrast material only 30 seconds after the start of injection (B).

Figure 4. Hepatic arteriogram on the initial admission, showing a markedly enlarged common hepatic artery of 17 mm in diameter (A). All branches of the hepatic artery were almost completely occluded with 29 coils, except for the partially obstructed middle branch (B, C).

larly around the non-obstructed small branch was increased. Small new collateral vessels from the superior mesenteric artery into the liver were also observed. The second coil embolization was performed on the same day using 19 Tornade coils to obstruct the middle hepatic artery. Nearly complete obstruction of the hepatic artery was achieved. The cardiothoracic ratio, left ventricular end-diastolic dimension and cardiac output were reduced from 67%, 57 mm and 12.4 l/min to 60%, 53 mm and 6.6 l/min, respectively (Table 2). The patient was dis-

charged 19 days after the operation. However, because of prolonged epigastralgia, edema in the face and legs, general fatigue and fever, she was admitted to the hospital for the third time on January 11, 1998. The blood chemistry revealed elevated total bilirubin (2.5 mg/dl), alkaline phosphatase (1,099 IU/l), γ glutamyltranspeptidase (83 IU/l), reduced choline esterase (48 IU/l) and total protein concentration (5.4 g/dl). Ultrasound abdominal tomography revealed intrahepatic bile duct dilatation in the middle hepatic lobe, indicating intrahepatic

Table 2. The Hemodynamic Parameters before and after the Coil Embolization

		1st embolization (Jul 3/97)		2nd embolization (Dec 9/97)	
		pre	post	pre	post
CTR	(%)	67	58	67	60
LVDd	(mm)	60	56	57	53
LVDs	(mm)	38	41	32	32
EF	(%)	66	54	82	67
CO	(l/min)	9.6	6.4	12.4	6.6

CTR: cardiothoracic ratio on chest X-ray, LVDd: diastolic left ventricular diameters, LVDs: systolic left ventricular diameters, EF: ejection fraction, CO: cardiac output on echocardiography. The patient's hemoglobin concentrations were 9.2 and 10.3 g/dl at the first and second embolization, respectively.

Figure 5. Computed tomography of the liver, showing anomalous vessel structures in the liver (black arrow and white arrow) (A). The contrast enhancement study revealed non-enhanced channels, indicating enlarged intrahepatic bile ducts (black arrow and white arrow) (B).

biliary tract obstruction and infection. Systemic antibiotics, supplemental albumin and vitamins were administered to revitalize her hepatic status. Her cholangitis could be controlled by the antibiotics, but she needed regular albumin administration because of her continuous lower albumin concentration.

She was admitted to our hospital for the fourth time because of progressive jaundice and general fatigue on August 31. The blood chemical examination showed further elevated total bilirubin (7.2 mg/dl), aspartate aminotransferase (131 IU/l), alanine aminotransferase (82 IU/l), alkaline phosphatase (1,756 IU/l), γ glutamyltranspeptidase (646 IU/l) and C reactive protein (0.77 mg/dl). It also showed a reduced choline esterase (35 IU/l) and total protein (5.9 g/dl) concentration. The abdominal computed tomography revealed not only large tortuous hepatic vessels but also a markedly enlarged intrahepatic biliary duct (Fig. 5), which indicated biliary duct stagnation. We administered antibiotics, albumin, vitamins, and frozen

flesh plasma but could not revitalize her hepatic function. She died of progressive hepatic failure on November 23, 1998. The necropsy specimen of the liver showed telangiectatic hepatic fibrosis, which is reported to be typical for HHT (7), partial hemorrhage in the parenchyma and bile duct dilatation. In this case, no evidence of piecemeal necrosis indicating type C viral chronic hepatitis was found in the liver parenchyma.

Discussion

Hereditary hemorrhagic telangiectasia is a congenital disorder leading to telangiectasia on the skin and mucosal surfaces which bleeds easily, and is frequently associated with the presence of AVMs in multiple organ system (1). The frequency of the presence of AVMs in the liver widely differs among reports, between 8% and 31% (6, 8). Hepatic involvement sometimes caused high output heart failure (9–23). In the present

reports, the patient had large hepatic arteriovenous malformation, which caused high output heart failure. Systemic examination in other organs could not detect any other large vascular malformations. Several cases of surgical and interventional treatments of AVMs in the liver have been reported (Table 3). In the late seventies, surgical arterial ligation was the sole choice. Radtke et al described two patients who had undergone an operation in attempt to reduce the size of their large left-to-right shunts and to relieve some of the cardiac burden (10). The reported patients were successfully treated with ligation of the common hepatic artery. In the eighties, embolization of the hepatic artery using metallic coils, gelatin sponge and polymer particle was added to the choice of treatments. In the last several years, because of the progression of interventional radiology, coil embolization has been more frequently selected, but the effects have varied. Zentler-Munro et al chose intervention (the trans-arterial coil embolization) initially, but it was unsuccessful because of the development of collateral circulation (15). In the end, they chose open hepatic artery ligation, which was successful. In the recent reports of five HHT patients with hepatic AVMs, embolization successfully improved their high output heart failure (22, 23). Liver transplantation, which is considered to be the fundamental treatment for hepatic AVMs, was first reported in 1995 (17), and several reports followed in 1998 (19, 20). Odorico et al re-

ported that their first attempt at coil embolization induced biliary necrosis and hepatic failure, resembling our case report, but they were able to save the patient by liver transplantation (19).

In this case, interventional therapy of transarterial coil embolization was selected to reduce the large intrahepatic arteriovenous shunt flow because it was a less invasive method. The main reason we selected the coil embolization was the patient's preference, but we were also concerned about her basic low hepatic function, excessive perioperative bleeding due to peritoneal telangiectasia, and progressive anemia before operation. When we informed the patient and her family in 1997, there were some affirmative but only a few negative reports about the effects of the coil embolization for AVMs in HHT. We had scheduled a second surgical treatment if the coil embolization failed. Though the abdominal pain persisted for one month, her symptoms, which were related to heart failure and epistaxis, improved remarkably after the first embolization. However, her exertional dyspnea and epistaxis recurred a half year later, due to increased collateral flow around the coil-embolized region of the liver. Vascular regeneration is prominent in a HHT patient. The second hepatic arteriography revealed newly developed collateral vessels not only around the middle hepatic artery but also from the superior mesenteric artery through the liver surface. The second hepatic arterial coil embolization was

Table 3. Summary of Treatments for the Hepatic Arteriovenous Malformation in Osler-Weber-Rendu Disease

Author	Treatment	No. of Patients	Clinical outcome for the high output heart failure	Reference
Radtke WE, et al (1978)	Hepatic artery ligation	2	Both effective	10
Göthlin J, et al (1982)	Embolization (Spongostan plugs, coils)	2	One patient died due to GI bleeding one patient, effective.	11
Allison DJ, et al (1985)	Embolization (gelatin sponge)	1	Effective	12
Derauf BJ, et al (1987)	Embolization (Ivalon particle)	1	Effective, complication with GI bleeding.	13
Roman CF, et al (1987)	Coil embolization	1	Effective	14
Zentler-Munro PL, et al (1989)	Coil embolization then hepatic artery ligation	1	Embolization was not effective to reduce repeated hemorrhage. Ligation was effective.	15
Bourgeois N, et al (1990)	Steel coil embolization	1	Temporary improvement, but died 3 weeks after the second embolization due to massive GI bleeding	16
Bauer T, et al (1995)	Liver transplantation	1	Effective	17
Rambusch EG, et al (1996)	Embolization	1	Effective	18
Odorico JS, et al (1998)	Embolization, then liver transplantation	2	Embolization caused biliary necrosis and hepatic failure, needed following transplantation	19
Neumann UP, et al (1998)	Liver transplantation	1	Effective	20
Zieren J, et al (1998)	Adjustable banding of hepatic artery	1	Effective	21
Caselitz M, et al (1998)	Embolization (PVA and coil)	5	4 patients showed improved heart failure One patient suffered cholangitis One died from variceal bleeding	22
Chavan A, et al (1998)	Embolization (PVA and coil)	5	One ischemic cholangitis one patient died of sepsis	23

GI: gastrointestinal tract, PVA: poly vinyl alcohol particle.

performed to decrease the middle hepatic arterial flow. It successfully improved her hemodynamic data, but lead to prolonged epigastralgia, intrahepatic cholangitis, and progressive hepatic insufficiency. We suspected that the causes of intrahepatic cholangitis and hepatic dysfunction were; 1) reduction of arterial oxygen supply to hepatocyte, 2) stagnation of the bile duct and 3) reduction of portal venous flow to parenchyma. These events happened due to the mechanical disturbance of portal venous and bile duct flow by the re-shaped tortuous metallic coils in the nearby hepatic arteries. Additional surgical ligation after the second embolism could not be considered because of the low hepatic functional reserve. The recent report of Chavan et al described five cases of successful treatment of HHT by embolization (23). They induced cholangitis in only one case. The main difference from our case is that they embolized the peripheral hepatic arteries and arterioles by polyvinyl alcohol and used large coils to embolize the main hepatic artery. The reshaped coils did not restrict the nearby portal vein or bile duct. The fundamental treatment of AVMs in HHT patient is liver transplantation, but it is quite difficult in Japan because of the social situation. Recently in Japan, we seem to have 2 choices for the treatment of high output failure in the HHT patient, that is; 1) embolization of the hepatic artery; proximal arterial coil embolization and peripheral polymer embolization, to avoid restriction of portal and biliary flow, 2) surgical ligation of the main hepatic artery, which could maintain good portal venous flow into the liver. Peripheral arterial coil embolization might be temporarily useful for high output heart failure, but it is harmful to the liver.

Conclusion

The high output heart failure due to large hepatic arteriovenous malformation in a patient with Osler-Rendu-Weber disease was treated with hepatic arterial coil embolization. Coil embolization of the peripheral hepatic artery temporarily improved the patient's cardiac function, but was harmful to the liver because of induced intrahepatic cholangitis and hepatic insufficiency.

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