□ CASE REPORT □

Development of a Pulmonary Arteriovenous Fistula after a Modified Glenn Shunt in Tetralogy of Fallot and Its Resolution after Shunt Takedown in a 57-Year-Old Patient

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Pulmonary arteriovenous fistula (PAVF) is a complication of the Glenn shunt. A 57-year-old tetralogy of Fallot (TOF) patient, who had undergone a Glenn shunt and TOF total correction, complained of dyspnea and cyanosis. PAVFs were present in the right lung, and right lung perfusion was nearly absent. After coil embolization, takedown of the Glenn shunt, and reconstruction of the right pulmonary artery, the patient's symptoms were relieved. Extrapulmonary radioisotope uptake caused by the PAVFs shown in lung perfusion scans decreased, and right lung perfusion increased gradually. Although the development and resolution of PAVFs after a Glenn shunt have been reported in the pediatric population, this may be the first report on this change in old age.

Key words:
1. Fontan procedure
2. Hepatopulmonary syndrome
3. Pulmonary arteriovenous fistula
4. Tetralogy of Fallot
5. Angiogenesis inhibitor

Case report

A 57-year-old female, born with tetralogy of Fallot (TOF), visited an outpatient clinic due to dyspnea. At the age of 9 years, she underwent a palliative modified Glenn shunt operation, where the right pulmonary artery (RPA) was divided from the main pulmonary artery (MPA) and anastomosed to the superior vena cava (SVC) in an end-to-side manner with the SVC-right atrium connection preserved. At the age of 31 years, she developed cyanosis and dyspnea, and thus underwent correction of TOF, including ventricular septal defect patch closure and infundibulum and MPA patch augmentation, without takedown of the previous modified Glenn shunt. Not having been followed up, she visited Seoul National University Hospital, complaining of progressive dyspnea of New York Heart Association (NYHA) functional class II and exercise intolerance.

With preserved right-ventricle function on echocardiography, tricuspid regurgitation was mild, with a peak velocity of 4.35 m/sec. Residual pulmonary stenosis was mild, with a peak velocity of 2.35 m/sec. The pulmonary regurgitation grade was mild to moderate. On computed tomography (CT) angiography, right-lung volume was decreased, with the RPA interrupted from the MPA, and multiple pulmonary arteriovenous fistulae (PAVFs) were observed as
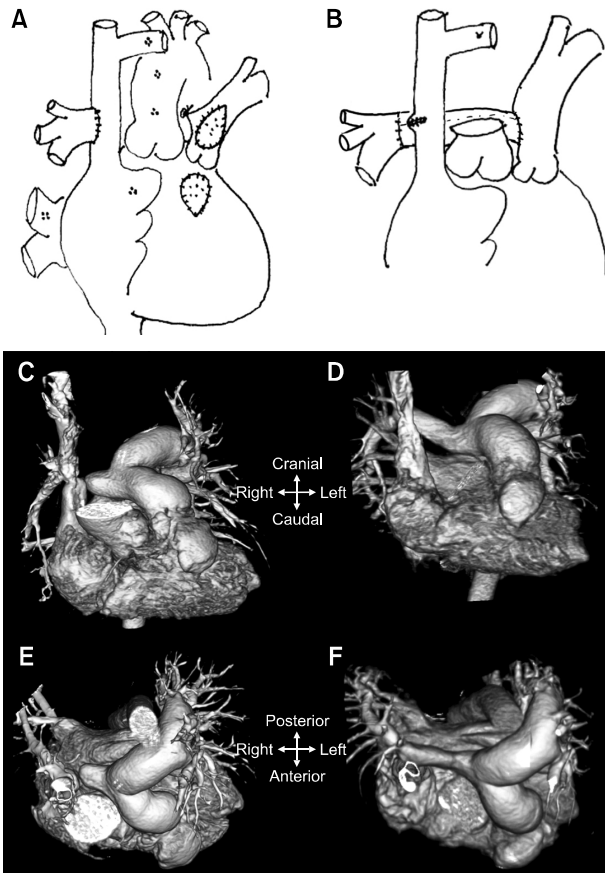
Fig. 1. (A) Preoperative anatomical status of a previous modified Glenn shunt and tetralogy of Fallot total repair. (B) Takedown of a modified Glenn shunt and reconstructed right pulmonary artery –main pulmonary artery connection with a 14-mm polytetrafluoroethylene conduit. (C and E) Anterior and superior view of the 3-dimensional reconstruction of a preoperative CT scan. (D and F) Anterior and superior view of the 3-dimensional reconstruction of an immediate postoperative CT scan. CT, computed tomography.

a long-term complication of the Glenn shunt (Fig. 1C, E and Fig. 2E). The left-to-right lung perfusion ratio was 98.5 to 1.5 on a lung perfusion scan (Table 1). Cardiac catheterization showed that systemic arterial oxygen saturation was 83%, which was probably caused by the right-to-left shunt through PAVFs in the right lung (Fig. 2A). Left pulmonary arterial hypertension was observed. For the treatment of her desaturation and dyspnea, we planned multiple-coil embolization of the PAVFs and reconstruction of the RPA after taking down the previous Glenn shunt.

Two weeks before the operation, the right-lung systemic-pulmonary artery shunt was embolized using polyvinyl alcohol (PVA) particles, via the right

bronchial, internal thoracic, inferior phrenic, and second to seventh intercostal arteries (Fig. 2B). After PVA embolization, the patient's oxygen saturation (SpO$_2$) showed no change. During the operation, the RPA–SVC anastomosis was taken down and the SVC end was repaired primarily. A polytetrafluoroethylene graft 14 mm in diameter (GORE-TEX Stretch Vascular Graft; W. L. Gore & Associates Inc., Flagstaff, AZ, USA) was interposed between the RPA and MPA (Fig. 1A, B). The right-ventricle to left-ventricle pressure ratio decreased to 0.21 immediately after the operation, compared to 0.60 before the operation. However, desaturation persisted at the intensive care unit immediately after the operation. With the patient dependent on ventilator support, SpO$_2$ was 81%–90% with a fraction of inspired oxygen (FiO$_2$) of 70%. Right lower-lobe PAVFs were noted on pulmonary angiography (Fig. 2C), and thus multiple-coil embolization was performed on postoperative day 3 (Fig. 2D). After embolization, the SpO$_2$ rose up to 94% with a FiO$_2$ of 70%, and the patient could be weaned from ventilator care and extubated. On postoperative day 7, she was transferred to the general ward and uneventfully discharged on postoperative day 16, with her SpO$_2$ at 88% on room air.

Although there was no significant stenotic lesion in MPA–RPA anastomosis on immediate postoperative CT angiography (Fig. 1D, F), a postoperative lung perfusion scan showed an unbalanced left-to-right lung perfusion ratio of 74.1% to 25.9%. When extrapulmonary uptake caused by the remaining PAVF was compared to lung perfusion, the ratio of left lung–right lung–extrapulmonary uptake was 60.8 to 19.8 to 19.4 (Table 1, Fig. 2G).

Lung perfusion scan results were aggravated at the 6-month postoperative follow-up (with a left lung–right lung ratio of 86.5 to 13.5), which persisted until the 2-year postoperative follow-up. Follow-up CT angiography showed no significant stenosis in the RPA. However, the lung perfusion scan result improved thereafter and reached a ratio of 68.3 to 31.7 at the 3.5-year follow-up. At that time, the ratio of left lung–right lung–extrapulmonary uptake was 63.9 to 31.1 to 5.0, which implied increased right-lung capillary perfusion and regressed PAVFs (Table 1, Fig. 2H). The patient had complained of dyspnea of NYHA functional class II in the immediate postoperative phase, but the dyspnea gradually resolved and com-
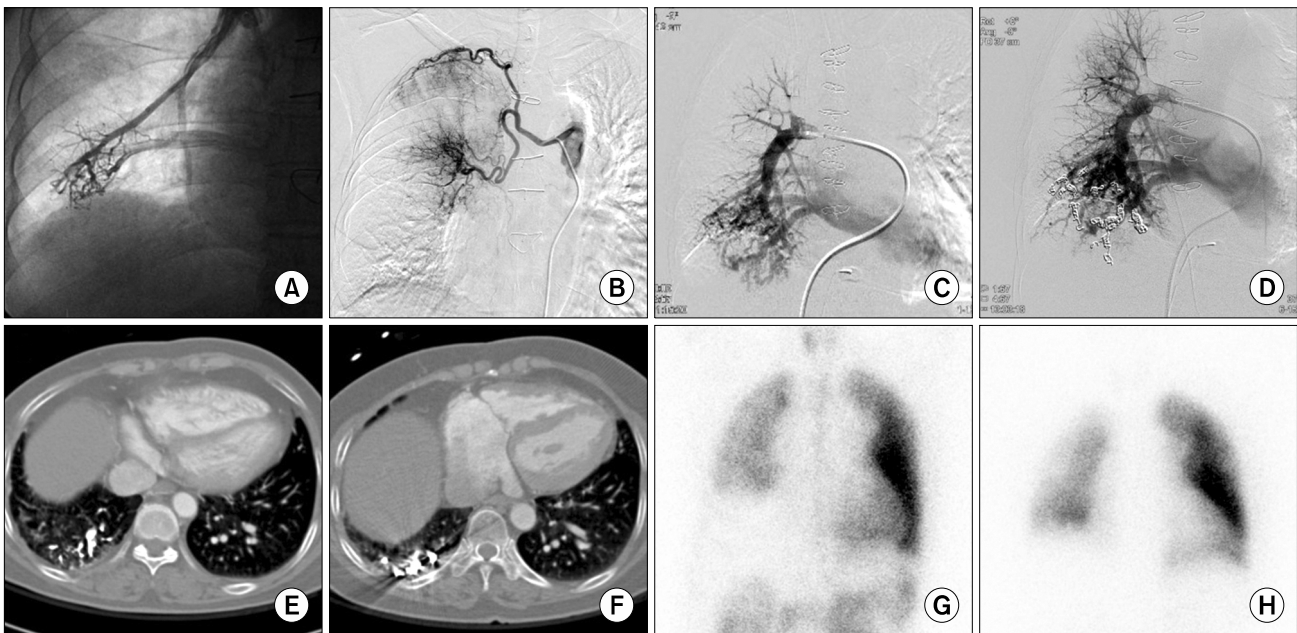
Fig. 2. (A) Initial pulmonary angiography showed pulmonary arteriovenous fistulae in the right lower lobe. (B) Preoperative systemic angiography showed systemic to pulmonary collaterals, which were embolized with polyvinyl alcohol. (C) Immediate postoperative angiography showed right-to-left shunt flow of a pulmonary arteriovenous fistula in the right lower lobe. (D) Demonstrable pulmonary arteriovenous fistulae were embolized with multiple coils. (E) Preoperative CT angiography showed pulmonary arteriovenous fistulae in the right lower lobe. (F) Two-year postoperative CT angiography showed embolized and regressed pulmonary arteriovenous fistulae. (G) Lung perfusion scan performed 2 weeks postoperatively. (H) Lung perfusion scan performed 3 years and 6 months postoperatively. CT, computed tomography.

pletely disappeared at the 2-year follow-up, with her SpO$_2$ increasing to 97% on room air at the 3-year follow-up.

Discussion

As a bridge to the Fontan operation, the bidirectional Glenn shunt plays an important role in relieving volume overload of the heart and in raising systemic oxygen saturation. However, when the next-stage Fontan operation is delayed, the Glenn shunt results in PAVFs due to the lack of direct hepatic venous flow to the pulmonary circulation, causing hypoxia, cyanosis, and exercise intolerance [1]. In a recent cohort study, PAVFs were reported to occur in 31% of patients who had undergone the classic or modified Glenn shunt [2].

Major PAVFs can be obliterated by coil embolization, which is a well-established treatment option. In our case, angiographically demonstrable PAVFs were embolized immediately after the operation. However, hepatic venous inclusion is also known to play a role

in the regression of PAVFs.

Diverted hepatic venous flow away from the pulmonary circulation has been suggested as a mechanism for the development of PAVFs after a Glenn shunt. Some PAVF patients demonstrate resolution with redirection of hepatic venous flow toward the lung with PAVFs [3,4]. Systemic arteriovenous fistulae, including brachiocephalic and axillary arteriovenous fistulae, have also been shown to effectively improve cyanosis in pulmonary arteriovenous malformation (PAVM) patients, which is likely a result of the reintroduction of hepatic venous blood into the pulmonary circulation [5]. These clinical findings provide indirect evidence that the liver and its venous flow have an effect on the pathogenesis of PAVMs.

The pathogenesis of PAVFs is currently explained by uninhibited angiogenesis due to the lack of hepatic venous efflux. Angiotensin and endostatin are potent angiogenesis inhibitors whose precursors, collagen XVIII and plasminogen, are produced in the liver. Related to their action in regulation of endothelial cell proliferation and angiogenesis, elimination of

Table 1. Preoperative and postoperative lung perfusion scan results

	Preop	Postop 10 day	Postop 4 mo	Postop 9 mo	Postop 1 yr	Postop 2 yr	Postop 3 yr	Postop 3 yr 6 mo
Left lung	98.5	74.1 (60.8)	86.5	79.7	83.0	81.8	75.0	68.3 (63.9)
Right lung	1.5	25.9 (19.8)	13.5	20.3	17.0	18.2	25.0	31.7 (31.5)
Extrapulmonary		(19.4)						(5.0)

Values are presented as %. Ten days, 3 years and 6 month after operation, the extrapulmonary shunt fraction was compared in parentheses. Preop, preoperative; Postop, postoperative.

these molecules by hepatic venous flow diversion from the pulmonary arterial circulation can cause vascular malformations such as PAVFs [1,6].

Direct hepatic venous efflux into pulmonary circulation is known not only to prevent the development of PAVFs but also to reverse this change to a variable extent. However, the exact conditions for the resolution of preformed PAVFs are not known. How long PAVMs persist or at what age they can spontaneously regress remains in question. Liver cirrhosis patients also develop PAVFs, known as hepatopulmonary syndrome. That kind of PAVF also regresses after liver transplantation. However, the reversal of PAVFs after a Glenn shunt has been reported only in young pediatric patients. Shah et al. [7] reported 3 cases of PAVFs that developed due to the interruption of hepatic venous return to the pulmonary circulation. In all their cases, the hemi-Fontan operation was conducted before the age of 1 year, and hepatic venous efflux was included earlier than year 7 after the hemi-Fontan operation. McElhinney et al. [4] presented a case series of 16 patients who developed significant PAVFs after the Kawashima procedure. In their study, follow-up catheterization was performed in 7 patients after hepatic venous inclusion. All those patients were diagnosed as having PAVFs at ages between 6 months and 10 years by using catheterization. Three out of the 7 patients showed resolved PAVFs postoperatively. However, another 2 patients still presented with persistent PAVFs, and the other 2 patients had partial resolution at the follow-up catheterization 1.5–8 years postoperatively. Even though the Fontan operation was conducted and hepatic venous rerouting was additionally performed, some patients persistently presented with PAVFs [8]. Due to these findings, some physicians concluded that those PAVFs were already irreversibly established and that there were some limitations to the reversibility of PAVFs by hepatic vein inclusion. Interrupted inferior vena cava, heterotaxy syndrome,

and the presence of an SVC bilateral or contralateral to the hepatic vein have been demonstrated to be risk factors for persistent PAVFs even after hepatic vein inclusion in Fontan operation patients. As this reversibility is regarded as possible at a young age and during an early period after the Glenn operation, they believed that after a certain period, PAVFs become irreversible. However, our patient demonstrated that PAVFs could be reversed even as late as the sixth decade of life and 26 years after the Glenn operation. This means that there may be other explanations regarding the failure of some PAVFs to resolve even after hepatic vein inclusion.

In our patient, right-lung perfusion was initially rather compromised early after the operation. A simultaneously taken simple chest X-ray showed no significant atelectasis. The reason lung perfusion scan results were aggravated during the first 6 months is not easy to identify, although the regression of PAVFs and the restoration of normal pulmonary circulation possibly had an effect on these results.

This rare case demonstrated the long-term outcome of a Glenn shunt that excluded hepatic venous flow, and the reversibility of PAVFs even in old age. Although this is an anecdotal report, further collection of this kind of patient data is necessary, because the understanding of the impacts and outcomes of cavopulmonary shunts is incomplete. With an accumulation of such cases, the factors associated with the reversibility of PAVFs could be further identified.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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