Successful laparoscopic pheochromocytoma resection in an adult patient with Fontan physiology: a case report

Yume Nohara-Shitama 1, Jinya Takahashi1, Takehiro Homma1, Tsukasa Igawa2, and Yoshihiro Fukumoto1

1Division of Cardio-Vascular Medicine, Department of Internal Medicine, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830-0011, Japan; and 2Department of Urology, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830-0011, Japan

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Background
Pheochromocytoma is a rare tumour producing catecholamines and has been more frequently reported than expected in patients with a Fontan physiology.

Case summary
The patient was a 39-year-old woman born with a univentricular atrioventricular connection and pulmonary valve stenosis. A Fontan operation was performed when she was 22 years old. At the age of 38, she was diagnosed with pheochromocytoma. The most serious problem was the increased occurrence of supraventricular arrhythmias, which easily caused heart failure. We decided to perform a laparoscopic resection. Postoperative recovery was good. There were no findings of malignancy and all postoperative catecholamine levels normalized. She was discharged home on the 14th day after the surgery, walking unaided.

Discussion
Diagnosis and treatment by tumour resection in the early phase are crucial in patients who undergo the Fontan procedure. However, patients after Fontan surgery have a very low cardiac reserve. Thus, the decision to perform a surgical treatment is a very difficult one to take. In this case, fenestration had been naturally closed. As fenestration provides a consistent source of systemic ventricular preload, we performed transcatheter fenestration dilatation to improve heart failure management before surgical pheochromocytoma removal. Although laparoscopic surgery is generally considered to be less invasive, pneumoperitoneum may interfere with venous return in Fontan physiology patients. There is also a risk of thrombosis via fenestration. Here, we reported the case of a successful laparoscopic pheochromocytoma resection in an adult Fontan patient.

Keywords
Fontan physiology • Pheochromocytoma • Laparoscopic pheochromocytoma resection • Adult congenital heart disease • Case report

ESC Curriculum
9.7 Adult congenital heart disease • 2.1 Imaging modalities

Learning points
• To understand early diagnosis and treatment of pheochromocytoma is crucial in Fontan patients to prevent heart failure.
• To understand surgical options for pheochromocytoma.
Introduction

The Fontan procedure was introduced in 1968. Presently, patients who undergo this procedure may hope for long-term survival due to technical advances. In 2018, up to 70,000 patients who underwent the Fontan procedure worldwide may have survived. Several late complications can occur in such patients, among which, pheochromocytoma has been more frequently reported than expected. Diagnosis and treatment by tumour resection in the early phase are crucial in patients who undergo the Fontan procedure, not only to protect against haemodynamic deterioration but also to prevent heart failure.

Timeline

| Time                        | Events                                                                 |
|-----------------------------|------------------------------------------------------------------------|
| Age 22 years                | Fontan procedure                                                      |
| Around age 32 years         | She has been repeatedly hospitalized for heart failure                |
| Age 38 years                | She was hospitalized for heart failure due to supraventricular arrhythmia and diagnosed as pheochromocytoma |
| A year before operation     | Transcatheter fenestration dilatation                                 |
| A month before operation    | Ventricular fibrillation cardiopulmonary arrest occurred outside the hospital, and she was resuscitated by using an automatic external defibrillator |
| The day of operation        | Laparoscopic pheochromocytoma resection                               |
| 14 days after the operation | She was discharged home, walking unaided                              |
| More than a year after the operation | No ventricular arrhythmias have occurred so far                      |

Case presentation

A 39-year-old female patient was born with a univentricular atrioventricular connection, pulmonary valve stenosis, and great artery transpositions. A modified right Blalock–Taussig shunt was performed at 18 months, an aorta-pulmonary shunt at 7 years, bidirectional Glenn anastomosis at 11 years, and the Fontan operation at 22 years of age. In the Fontan procedure, the main pulmonary artery (PA) was closed and an extracardiac connection (20 mm Gore-tex tube) was anastomosed to the inferior vena cava (IVC) and under the right PA surface. Finally, a 4 mm hole is made in the tube as a fenestration to the atrium. Postoperatively, a pacemaker (PM) implantation was performed for sick sinus syndrome. She had been repeatedly hospitalized for heart failure since she was ~32 years old. She had moderate or severe atrioventricular valve (AVV) regurgitation and coronary PA fistula, which were difficult to surgically repair.

At 38 years old, she was hospitalized due to heart failure. Upon admission, she suffered from fatigue and nausea but did not have hypertension. Initial blood pressure was 86/64 mmHg, heart rate (HR) was 80 beats per minute (b.p.m.) in PM tuning, and oxygen saturation was 95% on room air, with no leg oedema. Chest X-ray revealed pulmonary congestion, and blood tests showed mildly elevated hepatic enzymes [aspartate aminotransferase: 41 IU/L; alanine aminotransferase: 29 IU/L; and N-terminal pro-brain natriuretic peptide (NT-proBNP) 2918 pg/mL]. This NT-proBNP was the highest value in the years. Echocardiography revealed reduced ventricular ejection function (EF: 36%) and moderate common AVV regurgitation. At the time of admission, she was treated with carvedilol 7.5 mg daily, losartan 12.5 mg daily, furosemide 40 mg daily, spironolactone 150 mg daily, bepridil hydrochloride hydrate 100 mg daily, and warfarin as an anticoagulant. Her fatigue, headache, and nausea symptoms persisted although the congestive findings improved with intravenous furosemide. Additionally, supraventricular tachycardia episodes, including atrial fibrillation, paroxysmal supraventricular tachycardia, and atrial tachycardia were frequent. We examined the cause of persistent symptoms. Computed tomography scan detected a left adrenal tumour (3.2 cm × 2.4 cm; Figure 1A), as shown by 123I-MIBG scintigraphy at the same site (Figure 1B). Catecholamine concentrations by a 24 h urine collection test were elevated at the time of diagnosis (Figure 2). We diagnosed the patient with pheochromocytoma based on these findings. Her quality of life (QOL) was impaired due to sound and light hypersensitivity and insomnia. The most serious problem included the increased supraventricular arrhythmia occurrence, which easily caused heart failure. We started metyrosine (tyrosine hydroxylase inhibitor) and α-blocker doxazosin for pheochromocytoma. Furthermore, the fenestration had been naturally closed, and transcatheter fenestration dilatation was performed to improve heart failure management before pheochromocytoma removal. The total cavopulmonary connection (TCPC) conduit and interatrial puncture were performed using a Brockenbrough needle under transoesophageal echocardiography guidance and after guidewire placement and balloon (3 × 20 mm) dilatation, and 8 × 27 mm stent was implanted after the hospital ethics committee approval since it is not covered by insurance. We confirmed a postoperative fenestration flow in the stent and the decreased conduit pressure from 20 to 15 mmHg (Figure 3A and B). Right heart catheterization showed that cardiac output (CO) remained low with CO and cardiac index (CI) of 2.15 L/min and 1.42 L/min/m² postintervention, respectively, but heart failure hospitalizations were reduced under metyrosine (Figure 2). However, she gradually refused to take the medication due to abdominal distension and urinary incontinence, thus metyrosine was discontinued. Shortly thereafter, her symptoms flared up again, with elevated catecholamine levels (Figure 2).

The patient went into ventricular fibrillation (VF) and cardiopulmonary arrest outside the hospital while waiting for pheochromocytoma resection and was resuscitated by an automated external defibrillator. There were no findings that suspected ischaemic heart disease, and coronary angiography was not performed. Additionally, her serum potassium level was 3.4 mEq/L, which was low but was comparable with that before the VF onset. The serum potassium level was considered low due to pheochromocytoma. This patient was considered to indicate implantable cardioverter defibrillator (ICD) therapy because VF was possibly caused by underlying low cardiac reserve, which could not be ruled out. Moreover, our team had repeatedly discussed tumour resection, but this cardiac accident confirmed that the strongest prognostic factor for this patient was sudden cardiac death due to a fatal arrhythmia caused by pheochromocytoma.

On a surgical day, the patient’s initial blood pressure was 72/52 mmHg, HR was 88 b.p.m., and arterial saturation on room air was 93%. Standard monitors, including an arterial catheter, and defibrillator pads were placed. Anaesthesia was induced with midazolam and fentanyl, and she was intubated after muscle relaxation with rocuronium and ventilated with pressure-controlled ventilation. The positive end-expiratory pressure was 4 cmH₂O, and the rate adjusted to maintain the end-tidal carbon dioxide was 31 mmHg. Anaesthesia was maintained with a low sevoflurane concentration. Arteriovenous sheaths were inserted from the inguinal region as planned after anaesthesia and intubation, and a circulatory support system was placed to respond in case of rapid haemodynamic deterioration. Central venous pressure...
Figure 3C. We adopted a 45° right lateral recumbency to avoid pressure drainage of the IVC and allow rapid transfer to the operating theatre. The surgery was started in the right half-lateral recumbent position to minimize the effect of the surgical position on the circulatory system, and the intra-abdominal pressure was set up to 8 mmHg. The circulatory condition was stable and both CVPs were up to 19–20 mmHg although intra-abdominal pressure temporarily increased to 14–15 mmHg during surgical port placement. Small amounts of noradrenaline (0.04–0.06 μg/kg/min) and carperitide (0.013 μg/kg/min) were used. We used nitric oxide inhalation of 10 p.p.m. to reach the tumour and process the adrenal veins. Bleeding occurred when we manipulated around the adrenal vein, and we temporarily increased the insufflation pressure up to 10 mmHg. During adrenal vein ligation, the blood pressure transiently increased, which was treated by nitroglycerine and nicardipine. Milrinone, which is a phosphodiesterase-3 inhibitor, was also used. Noradrenaline (0.04 μg/kg/min), carperitide (0.013 μg/kg/min), milrinone (0.25 μg/kg/min), and dobutamine (2 μg/kg/min) were titrated to maintain normotension after the tumour removal. The operation time was ~3 h, with an estimated blood loss of 74 mL.

Postoperative recovery was good. The removed tumour was a well-demarcated 3.0 × 2.5 × 1.5 cm nodular tumour (Figure 1C). There were no findings of malignancy, and all postoperative catecholamine levels have normalized (Figure 2). She was discharged home on the 14th postoperative day, walking unaided. At discharge, bepridil hydrochloride hydrate was switched to amiodarone 200 mg daily. No ventricular arrhythmias have occurred so far for more than a year.

Discussion

We decided to perform the surgical treatment due to the following. First, the presence of pheochromocytoma was a significant prognostic factor in Fontan’s low cardiac reserve and presented a high risk of decompensated heart failure in the future. We were unable to rule out the possibility that the underlying disease caused the condition because the incidence of supraventricular tachycardia in patients who underwent extracardiac connection, as in the present case, has been reported at 5–15%,1,2 and moderate or greater AVV regurgitation is indicated as its risk factor.2 However, in patients who underwent the Fontan procedure, elevated plasma norepinephrine is associated with heart failure, fatal arrhythmias, thromboembolism, and mortality.4

Second, the patient’s symptoms associated with pheochromocytoma were not controlled by medical treatment, which highly impaired her QOL. She was unable to tolerate oral metyrosine, and her catecholamine levels were not controlled. Therefore, we decided to perform tumour resection.

Pheochromocytoma has two surgical options, including laparotomy and laparoscopic resection.7 Our team had repeatedly discussed the surgical technique and mechanical support intra- and postoperatively. The team consisted of cardiologists, anaesthesiologists, urologists, and endocrinologists. Here, fenestration had been naturally closed. A fenestration provides a consistent source of systemic ventricular preload11; thus, we performed transcatheter fenestration dilatation to improve heart failure management before surgical pheochromocytoma removal. However, it is considered a risk of thrombosis via fenestration,16 and the pneumoperitoneum may interfere with venous return in the physiology of patients who underwent the Fontan procedure.11 Meanwhile, her heart function was insufficient to withstand surgery due to the following findings. The echocardiography revealed reduced ventricular EF (~40%) and moderate common AVV regurgitation. Additionally, right heart catheterization showed that CO was low (CO: 2.15 L/min, CI: 1.42 L/min/m²) because laparoscopic surgery is generally considered less invasive, with shorter surgical time, less blood loss, and smaller wound size. Then, we finally decided to perform a laparoscopic resection.

The most important monitoring parameter for surgery was CVP in two locations, including the left internal jugular vein and the right femoral vein, because the Fontan circulation is haemodynamically compromised by a decreased preload. We kept the increased insufflation pressure up to <10 mmHg based on previous reports.11 We adopted a 45° right lateral recumbency to avoid pressure drainage of the IVC and allow rapid transfer to the circulatory support system in case of rapid haemodynamic deterioration, although the usual position for laparoscopic pheochromocytoma resection was complete right lateral recumbency. We prepared but avoided the use of extracorporeal membrane oxygenation during anaesthesia induction and intraoperatively. Hence, only the arteriovenous sheath was

(CVP) was monitored from two locations, namely, the left internal jugular vein and the right femoral vein (13–15 mmHg). Transoesophageal echocardiography was monitored to confirm the blood flow in the fenestration area (Figure 3C). The surgery was started in the right half-lateral recumbent position to minimize the effect of the surgical position on the circulatory system, and the intra-abdominal pressure was set up to 8 mmHg. The circulatory condition was stable and both CVPs were up to 19–20 mmHg although intra-abdominal pressure temporarily increased to 14–15 mmHg during surgical port placement.

Discussion

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inserted from the inguinal region and a system was in place to respond to sudden changes after induction of preoperative anaesthesia.

Preoperative metyrosine administration resulted in no significant changes in blood pressure pre- and postoperatively although concerns about catecholamine storm during resection and catecholamine loss after resection on cardiac dynamics occurred.

Furthermore, we confirmed beforehand that preoperative administration of 0.1 μg/kg/min or more noradrenaline could raise blood pressure because the blood pressure may not be raised by noradrenaline administration due to prolonged hyper-catecholaminaemia.

We considered this patient to indicate ICD therapy. A scientific statement from the American Heart Association showed that the risk factors for the late incidence of arrhythmias were older age at the time of the primary Fontan procedure, atiopulmonary type repair, preoperative and early postoperative tachycardia, moderate or greater AVV regurgitation, and longer follow-up. Additionally, sudden cardiac
death predictors are reported to include previous AVV replacement, postoperative Fontan pressures of >20 mmHg, and myocardial fibrosis, which was identified on cardiac magnetic resonance imaging (MRI). This patient had undergone extracardiac TCPC, which was performed relatively late, and the pressure in the conduit before the fenestration enlargement was as high as 20 mmHg. Additionally, she had moderate or greater AVV regurgitation. Considering the other findings, the possibility that VF was caused by underlying low cardiac reserve could not be ruled out, although we were unable to take MRI because PM was not MRI conditional. Patients who have undergone the Fontan procedure have benefited from subcutaneous ICD (S-ICD) because ICD is difficult to administer due to inadequate vascular access. However, S-ICD was not recommended because of concerns about over-sensing due to the unipolar pacing of the existing PM. The existing leads would need to be changed to bipolar if S-ICD was selected, which would require a re-thoracotomy in such patients.

Surgical ICD requires a re-thoracotomy as well. The patient had undergone four open thoracotomies and would not tolerate further re-thoracotomy, although we had explained the ICD procedure. The patient ultimately did not receive the ICD implantation, even though it was considered indicated. We need to continue to inform her about the indication of ICD implantation for preventing sudden death and confirm her intentions in the future.

### Conclusion
We reported here a case of successful laparoscopic pheochromocytoma resection in an adult patient who underwent the Fontan procedure.

### Lead author biography
Dr Yume Nohara-Shitama graduated from Kurume University School of Medicine and became a medical doctor in 2007. She was a resident of National Hospital Organization, Kyushu Medical Center until 2009. Thereafter she has belonged to Division of Cardio-Vascular Medicine, Kurume University School of Medicine, and started to research of Epidemiology in 2013. She received her PhD in 2018. Now she is working as a visiting faculty in Department of Epidemiology Bloomberg School of Public Health, Johns Hopkins School of Medicine Welch Center for Prevention, Epidemiology, and Clinical Research.

### Supplementary material
Supplementary material is available at European Heart Journal – Case Reports.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in accordance with COPE guidelines.

**Conflict of interest:** The authors declare no conflict of interest.

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