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Tetralogy of Fallot with Absent Pulmonary Valve Syndrome: A Case Series

Fallot Tetralojisi ve Pulmoner Kapak Yokluğu Sendromu: Vaka Serisi

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ABSTRACT

Tetralogy of Fallot (TOF) with absent pulmonary valve syndrome (APVS) is an extremely rare variant of TOF, with a ratio of 3-6%. Significant pulmonary insufficiency due to this valvular absence promotes dilation of the pulmonary arteries, and this can lead to airway compression during intrauterine life and after birth. The degree of compression is relative to the degree of hypoplasia of the respiratory tract. The severity of the respiratory problems indicates high mortality rates. This study aimed to present the short and mid-term outcomes following surgical repair of three TOF-APVS patients. One patient also had associated Townes-Brock Syndrome, which is extremely rare by itself. On follow-up, one patient could not be separated from cardiopulmonary bypass (CPB), and she was placed on arterio-venous extracorporeal membrane oxygenator (A-V ECMO) support before she died on the 5th day post-operatively. The patient with Townes-Brock syndrome died post-operatively 3.5th months due to pulmonary complications.
Keywords: Tetralogy of Fallot; absent pulmonary valve; pulmonary valved conduit.

ÖZ

Fallot tetralojisi (tetralogy of Fallot, TOF) ve pulmoner kapak yokluğu sendromu (absent pulmonary valve syndrome, APVS) TOF'un oldukça nadir olarak %3-6 oranında görülen bir varyantıdır. Kapakçık yokluğu nedenli gelişen belirgin pulmoner yetmezlik pulmoner arterlerin dilatasyonuna sebep olur ve bu durum da intrauterine yaşamda ve doğum sonrasında hava yolu basısına yol açar. Bası derecesi ve solunum yolu hipoplazisi derecesi arasında doğrudan ilişki mevcuttur. Eşlik eden solunum yolu problemlerinin ciddiyeti, yüksek mortaliteye yol açar. Bu çalışmanın amacı, cerrahi onarım yapılan üç TOF-APVS hastasının kısa ve orta dönem sonuçlarının sunulmasıdır. Bir hasta, kendi içinde de oldukça nadir görülen Townes-Brock sendromuna sahipti. Takipte, bir hasta kardiyopulmoner bypasstan (cardiopulmonary bypass, CPB) ayrılamadı ve arteriyo-venöz ekstrakorporeal membrane oksijenatörü (arterio-venous extracorporeal membrane oxygenator, A-V ECMO) desteğine bağlı olarak 5 gün takip edildikten sonra kaybedildi. Townes-Brock sendromuna sahip hasta, postoperatif 3,5 ay sonra, solunumsal komplikasyonlara bağlı olarak kaybedildi.
Anahtar kelimeler: Fallot tetralojisi; pulmoner kapak yokluğu; pulmoner kapaklı kondüit.

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INTRODUCTION

Absent pulmonary valve syndrome (APVS) is a rare disease that is present in 3 of 10,000 live births (1). It was first described by Royer and Wilson in 1908 (2). It is characterized by a dysmorphic pulmonary valve and dilatation of the pulmonary arteries (1). Of all tetralogy of Fallot (TOF) patients, 3-6% have AVPS. This entity includes anterior malalignment ventricular septal defect (VSD), aortic overriding, pulmonary stenosis (PS), right ventricular hypertrophy, rudimentary or absent pulmonary valve tissue, and severe pulmonary valve insufficiency (1). Because of the

aneurysmal main pulmonary artery and its dilatated branches, airway compression can subsequently progress. The severity of the airway stenosis or tracheobronchomalacia contributes to respiratory distress due to tracheomalacia and bronchomalacia developed in intrauterine life. After birth, TOF-APVS is associated with high rates of respiratory failure and mortality (15-25%) related to the severity of hypogenesia in the respiratory tract (3). TOF-AVPS can be divided into two groups: those with respiratory compromise in early infancy and those without. This study aimed to report and evaluate the short and mid-term outcomes of three patients after surgical repair of TOF-APVS.

CASE REPORT

A retrospective analysis was performed of three patients diagnosed with TOF-APVS who were operated on by the same surgeon in Muğla Sıtkı Koçman University Medical Faculty, Department of Cardiovascular Surgery, using data collected from the hospital database between 2018 and 2024. Demographic data on gender, age, weight, and preoperative and postoperative evaluations of transthoracic echocardiography, co-existing cardiac anomalies, and associated genetic syndromes were recorded. In cases of severe bronchomalacia, bronchoscopy was performed. One of the patients had respiratory problems requiring preoperative ventilatory support after birth. All of the patients had mild cyanosis on exertion. Electrocardiography showed right axis deviation and/or right ventricular enlargement in all patients. Computed tomography (CT) was performed to detect aneurysmal pulmonary arteries and tracheal compression.

Approval for the study was obtained from the Muğla Sıtkı Koçman University Ethics Committee (19.03.2024, 240049-20). All of the study procedures were in compliance with the Helsinki Declaration. Informed consent was obtained from the parents or legal guardians of all the patients.

Only one patient had an associated genetic syndrome, Townes-Brock syndrome, who was carrying the most common SALL1 gene mutation c.826C>T (p.R276X) (4). There were no other genetic associations or intracardiac or extracardiac anomalies in the other patients.

All operations were performed via a sternotomy approach, under cardiopulmonary bypass (CPB), with systemic hypothermia of 32°C and Del Nido cardioplegia used to establish diastolic cardiac arrest. Operations included VSD repair with polytetrafluoroethylene patch and right ventricular outflow tract reconstruction with a valved bovine jugular vein conduit (Contegra pulmonary valved conduit, TM Medtronic, Minneapolis, USA) reconstruction of bilateral pulmonary artery branches (posterior plication of aneurysmal pulmonary artery branches and anterior wall resection). Baseline demographics for all of the patients were reported in Table 1. Between 2018 and 2024, three patients underwent total correction.

Case 1

This 11-month-old, 7.8 kg male patient was referred to our clinic due to the progressive enlargement of the pulmonary arteries. He was suffering from recurrent pulmonary infection and had a medical history of hospitalization due to the infections. No additional genetic or other cardiac pathologies were found. Echocardiogram showed TOF, APVS, aneurysmal pulmonary branches, and tricuspid valve insufficiency. TOF total repair, posterior plication of aneurysmal pulmonary artery branches and anterior wall resection, pulmonary valved conduit replacement (Contegra pulmonary valved conduit, TM Medtronic, Minneapolis, USA), and cordal repair of the tricuspid valve was performed under CPB and Del Nido usage. The aortic cross-clamping time (ACT) was 201 minutes, and the CPB time was 254 minutes. The patient was extubated 18 hours postoperatively. The postoperative period was uneventful. The patient was discharged on the 12th day postoperatively.

Case 2

A 2.5-month-old, 3 kg female patient was referred to our clinic. She had been born in our institution. After birth, she was intubated due to severe respiratory problems on the 60th day of life. Pulmonary infection occurred after a long intubation period. Moreover, she had some stigmata of genetic disorders. After many genetic tests, the patient was diagnosed with Townes-Brock syndrome (SALL1 gene mutation c.826C>T (p.R276X, Figure 1). Echocardiography revealed TOF, APVS, and aneurysmal pulmonary branches. Bronchoscopy and CT were performed to investigate the degree of compression (Figure 2A). The right and left bronchi were both hypoplastic. On the 80th day of life, total repair (TOF total repair, posterior plication of aneurysmal pulmonary artery branches, and anterior wall resection, pulmonary valved conduit replacement: Contegra pulmonary valved conduit, TM Medtronic, Minneapolis, USA) was performed. Pulmonary arteries were extremely dilatated (Figure 2B), and she had rudimentary pulmonary cusps (Figure 2C). The ACT and CPB times were 190 and 291 minutes, respectively. She was extubated four times during the postoperative period; however, after 24 hours, she required mechanical respiratory support due to the bronchospasm and obstructive effects of secretion. In her 6th month of life, she died due to multiple complications of long-term intensive care unit admission.

Case 3

A 9-month-old, 4 kg female patient was admitted to our clinic due to recurrent pulmonary infections and severe pulmonary edema. On echocardiogram, TOF, APVS, aneurysmal pulmonary branches, perimembranous malalignment, and VSD were observed. She underwent diuretic therapy in the intensive care unit. An inadequate response to medical treatment required us to perform surgery. Total repair (TOF total repair, posterior plication of aneurysmal pulmonary artery branches and anterior wall resection, and pulmonary valved conduit replacement: Contegra pulmonary valved conduit, TM Medtronic, Minneapolis, USA) was performed. Exposure of the malignment VSD through the right ventriculotomy and tricuspid valve was inadequate. The two papillary muscles of the tricuspid septal leaflet were transected to reach the VSD border. After the patch closure, the papillary muscles were properly reimplanted. Tricuspid valve coaptation was checked. The ACT and CPB times were 257 and 406 minutes, respectively. Spontaneous sinus rhythm was restored; however, in the short term, ventricular dysfunction occurred, and the weaning process was extended. A-V ECMO support was initiated, and on the 5th day postoperatively, the patient died due to ventricular failure despite ECMO support.

Table 1. Demographic features of patients

Patients	Case 1	Case 2	Case 3
Gender	Male	Female	Female
Age at surgery time	11 month-old	2.5 month-old	9 month-old
Weight	7.8 kg	3 kg	4 kg
MPA (mm) / Z score	23 / +4.72	15 / +4.11	20 / +5.13
RPA mm / Z score	22.5 / +7.32	9.2 / +4.25	19.24 / +7.81
LPA mm / Z score	16.4 / +5.98	14.2 / +7.18	20.26 / +8.5
Preoperative intubation	No	Yes	No
Genetic syndrome	None	Townes-Brock	None
CPB time (minutes)	254	291	406
ACT (minutes)	201	190	257
Mortality (postoperative)	No	3.5th month	5th day

MPA: main pulmonary artery, RPA: right pulmonary artery, LPA: left pulmonary artery, CPB: cardiopulmonary bypass, ACT: aortic cross-clamping time

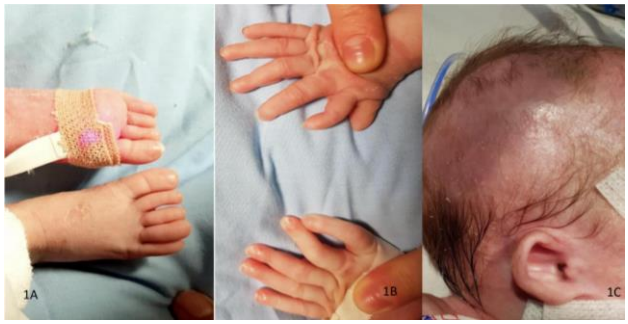

Figure 1. A, B) Polydactyly on hands and feet, and **C)** ear abnormality of the Townes-Brocks syndrome

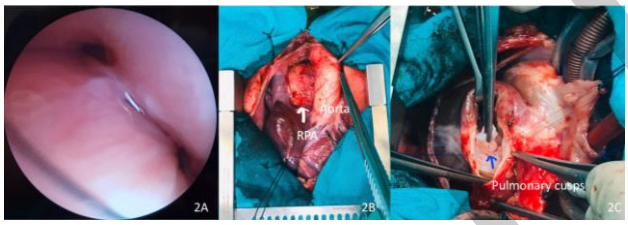

Figure 2. A) Bronchoscopic view of the compression of a pulmonary aneurysm, and intraoperative view of **B)** dilatated right pulmonary artery, and **C)** rudimentary pulmonary cusps

DISCUSSION

This study aimed to present the short and mid-term outcomes following surgical repair of three TOF-APVS cases. One patient died despite ECMO support, one patient diagnosed also Townes-Brock syndrome died 3 months later due to pulmonary complications, and the other patient could be discharged in a reasonable condition.

TOF-APVS is found in 3 to 6% of all patients diagnosed with TOF (1). Pulmonary valve agenesis leads to dilatation of the pulmonary artery and its branches in the intrauterine period. Intrauterine pulmonary artery enlargement causes compression of the tracheobronchial structure. Finally, a spectrum of airway hypoplasia progresses (4). Regarding respiratory symptoms, TOF-APVS can be classified into two groups: i) patients with life-threatening dyspnea in the neonatal period, and ii) those who are asymptomatic or frequently suffer from pulmonary infections until the infantile period (3).

In the present case series, each patient showed different outcomes due to their preoperative and intraoperative features. Case 1 was admitted following a close follow-up period at the age of 11 months, which meant the compression of pulmonary arteries was still permissive to airway flow. In conclusion, after the surgical repair, the airway, which was underdeveloped but still enough, gave the chance to wean from mechanical ventilatory support. Case 2 was admitted to the hospital after birth and was intubated subsequently. At the time of surgery, the patient was 2.5 months old, 3 kg in weight. The early intubation requirement showed the very poor development of airway structures and let us foresee the poor outcome and difficulties in the weaning process from mechanical ventilatory support. Case 3 was 9 months old. The patient needed additional repair for a tricuspid abnormality. CPB time was longer. Due to the postoperative ventricular failure, the patient died despite ECMO support.

The surgical indications are compression of the trachea and adjacent structures. If patients remain asymptomatic, they can be monitored periodically. To ensure that there is compression of the airway, CT and bronchoscopy can be performed. In this case series, cases 1 and 3 were monitored for a while until the airway compression symptoms occurred.

In the literature, many previous studies have shown that preoperative intubation and mechanical ventilation support requirement are strong risk factors for early postoperative complications and higher mortality (4). In the present series, case 2 had the same feature, and due to an additional Townes-Brock syndrome, which is related to poor outcome by itself, the patient died despite several weaning processes from the mechanical ventilator.

The aim of surgical repair is to eliminate the compression by performing plication and reduction of the anterior/ posterior wall of the pulmonary artery branches and the main pulmonary artery. In addition, the recently described Le Compte maneuver can be useful (5). A pulmonary valved conduit is also crucial to provide the competence of the pulmonary valves (5,6). If required, bronchioplasty should be performed (5). However, long-term outcomes are not always satisfactory (6).

Avdikos et al. (3), McDonell et al. (7), and Yong et al. (8) reported an early mortality of 15%, 21%, and 13.5%, respectively. Dorobantu et al. (6) reported late mortality as 8%. Yong et al. (8), Nørgaard et al. (9), and Hew et al. (10)

reported the late mortality in ratios of 18%, 5%, and 15%, respectively, in their studies. The present case series included only three patients, and two patients died due to pulmonary and cardiac reasons.

CONCLUSION

Although the mortality rate is decreasing over time, the TOF-APVS is still a challenging condition in congenital heart surgery. Particularly, newborn patients suffering from airway compression are likely to have poor outcomes.

Informed Consent: Written informed consent was obtained from the patient for publication and accompanying images.

Ethics Committee Approval: The study was approved by the Medical Science Ethics Committee of Muğla Sıtkı Koçman University (19.03.2024, 240049-20).

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