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REVIEWS

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Patient with tetralogy of Fallot at 30-year follow-up – a historical overview of the treatment of the defect

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary The authors present the case of a patient with tetralogy of Fallot. The patient underwent surgery to correct the defect 30 years ago. Our patient remains in good condition, currently reporting only poorer exercise tolerance.
The authors attempted to analyse the development of treatment methods for tetralogy of Fallot based on world literature with reference to the case described in this paper. This paper presents the history and advances that have been made in the treatment of Fallot syndrome. Numerous details and dates are cited regarding the history of the treatment of the defect. Due to the vastness of the subject of tetralogy of Fallot, the article does not discuss contemporary treatments for the defect.
Key words: tetralogy of Fallot, history of medicine, patient.

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Background

Tetralogy of Fallot (TOF) is the most common congenital cyanotic heart defect. It is characterised by the coexistence of four components: ventricular septal defect (VSD), right ventricular outflow tract stenosis (RVOTO at the conical, valvular or supravalvular level), aortic dextroposition (a.k.a. rider aorta) and secondary right ventricular hypertrophy (RVH). TOF has an incidence of 1 in 10,000 live births and accounts for about 7–10% of all congenital malformations [1]. Approximately 20% of patients with tetralogy of Fallot have co-occurring genetic abnormalities, such as 22q11 microdeletion, trisomy 21, Alagille, Noonan, Williams and Klippel and Feil syndromes [2]. The number of adult patients with congenital heart disease is increasing by about 5% each year.

Case presentation

A 4-month-old boy was admitted to the Paediatric Cardiology Clinic for an anoxaemic seizure. During his stay at the Clinic, the child's general condition deteriorated. The boy underwent an ECG, which described a sinus rhythm of about 140/min and a normogram of 1,100. In addition, features of right ventricular hypertrophy and high T-waves in the V_1–V_4 leads were evident. A chest X-ray showed an enlarged cardiac silhouette, right ventricular enlargement and smoothing of the cardiac waist. A cardiac ultrasound performed on the boy showed an aortic hypertrophy of about 40–50% with pulmonary artery stenosis with a transvalvular pressure gradient of about 128 mm Hg. The vessel diameters were: RPA (right pulmonary artery) 5.5 mm, LPA (left pulmonary artery) 5 mm. VSD (ventricular septal defect) approximately 13 mm. The patient was diagnosed with tetralogy of Fallot.

The child underwent a systemic-pulmonary anastomosis of the Blalock-Taussing type (anastomosis between the subclavian artery and the corresponding pulmonary artery by means of an artificial vessel) on the right side. The postoperative period was uncomplicated.

At the age of 14 months, the child was referred to the Clinic again due to cyanotic seizures. On admission, the child's general condition was average. Physically, there was deficient weight and a systolic murmur at the left sternal edge and in the auscultation field of the pulmonary artery. In addition, a quiet Blalock-Taussing type systemic-pulmonary anastomosis murmur was audible on the right side. During the hospital stay, an anoxaemic seizure (rapidly increasing cyanosis with anxiety and dyspnoea) was observed, and the onset of bronchiolitis was then diagnosed. Treatment included an antibiotic and continued administration of propranolol. After clinical equilibration, the child was discharged home in good general condition on the 16th day of hospitalisation.

At age 3, the boy was admitted to the Department of Paediatric Cardiac Surgery for complete correction of tetralogy of Fallot. The patient had generalised cyanosis and a systolic murmur along the left sternal edge (3/6 on the Levine scale). The boy underwent total heart defect correction under extracorporeal circulation and hypothermia. The ventricular septal defect was patched with a Dacron patch. The right ventricular outflow tract was dilated with a pulmonary homograft. After 40 days of hospitalisation, the boy left the hospital in fairly good general condition.

After two more years, a follow-up UKG (ultrasound cardiography) showed right ventricular outflow tract stenosis with a gradient of up to 50 mm Hg. A single ventricular extrasystole was recorded on the Holter ECG.

Three years after surgery to correct the total defect, a left-right leak in the area of the patch in the interventricular septum was observed on the ECG.

At 10 years of age, no arrhythmia was detected in the Holter ECG nor during the exercise test. A follow-up ECG showed an acceleration of outflow tract blood flow to 2.8 m/s with a maximum gradient of up to 30 mm Hg (mean gradient 17 mm Hg) and right ventricular enlargement.

At age 13, the ECG showed complete right bundle branch block. No cardiac arrhythmia was observed on holeter's examination. ECHO detected right ventricular enlargement and systolic-diastolic flow in the pulmonary trunk with an insignificant gradient.

At 15 years, complete right bundle branch block without right ventricular hypertrophy was still present on follow-up echocardiography.

The patient remains at a 30-year follow-up after correction of tetralogy of Fallot. He currently reports only worse exercise tolerance. A systolic-diastolic murmur is noted along the left sternal margin. No cardiac arrhythmia is observed in the ECG recording. ECHO diagnoses first-degree tricuspid regurgitation with accelerated blood flow through the MPA (pulmonary trunk). The right ventricular-right atrial systolic gradient is about 40 mm Hg.

The patient has persistent pulmonary artery regurgitation and right bundle branch block on the ECG. The patient shows no features of systemic stasis and in the pulmonary circulation. His heart failure is rated as NYHA class I, first degree. Currently, he is not taking permanent medication.

Discussion

The first description of this congenital heart defect (later named tetralogy of Fallot) dates back to 1673, when Nicholas Steno of Denmark observed abnormalities on examination of the heart of an aborted foetus [3]. In 1888, the French physician Fallot combined pathomorphological information with clinical signs seen in older children. At a time when no treatment was known, people with this heart defect were called "blue babies" due to the cyanosis they exhibited. The term "tetralogy of Fallot" was first used in 1924 by Maude Abbott (a Canadian pioneer in cardiology and paediatric pathology) [4]. Previously, the condition was called blue disease or cyanosis of the heart [5, 6].

In the past, when no treatment for the defect was known, patients died mainly from anoxaemic seizures (62%), cerebrovascular incidents (17%) and brain abscesses (13%). Mortality rates were 25% by the first year of life, 40% by the third year, 70% by the 10th year and 95% by the 40th year [7].

In 1940, Helen Taussig (director of the cardiology clinic at the Harriet Lane Home for Invalid Children) noted that children with cyanotic heart disease did better when their arterial conduit remained open. In contrast, the condition of children with PDA (ductus arteriosus) closure deteriorated and died shortly thereafter. Taussig turned to Alfred Blalock (chief of surgery) with the idea of producing a conduit [8]. Blalock and Vivien Thomas (a laboratory surgical technician) created a cyanotic animal model. They removed the flaps of one lung or both lungs from the animal and connected the proximal ends of the pulmonary artery and vein. They then made a connection between the subclavian artery and the pulmonary artery, making the cyanosis disappear [9]. In 1944, surgical treatment of children with TOF began. This was made possible by the development of the systemic-pulmonary anastomosis by Blalock, Taussig and Thomas. On 29 November 1944, Blalock and Thomas operated on a four-pound, 15-month-old girl with a severe form of tetralogy of Fallot. The child survived the operation and was discharged home after two months [10]. Between 29 November 1944 and 1 January 1951, Blalock and colleagues performed similar surgeries on 1,034 patients, 779 of whom had TOF. A 20-year follow-up showed that about 50% of the patients who underwent successful initial surgery were still alive [11].

In the case we described, a Blalock-Taussing systemic-pulmonary anastomosis was performed at the age of 4 months due to deterioration of the general condition. No complications were observed after the operation.

In the following years, there were descriptions of other anastomoses, including Potts in 1946 (connection of the descending aorta to the left pulmonary artery), Waterson in 1962 (anastomosis of the ascending aorta to the pulmonary artery) and Cooley in 1966 (intracardiac connection of the ascending aorta to the right pulmonary artery) [12–14]. All the anastomoses mentioned as central connections were at lower risk of thrombosis compared to the Blalock, Taussig and Thomas anastomoses.

In 1948, Brock described a method that relieved pulmonary truncus stenosis in cases of pulmonary valve stenosis or conus arteriosus. The procedure consisted of dilating the valve stenosis by valvulotomy using a cutting knife [15]. In 1952, Lewis and Taufic performed the first intracardiac procedure to close an atrial septal defect (ASD). Hypothermia and inflow closure were used during the operation [16].

In 1954, Lillehei was the first to perform a total TOF correction. He used cross circulation for this, since the use of early pulmonary-cardiac machines did not have the desired effect. He performed open-heart surgery using a pump that controlled the reciprocal exchange of blood between the patient and a living, group-compatible donor [17]. John Kirklin and colleagues performed a total defect correction at the Mayo Clinic in 1955. For this, they used a modified Gibbons lung-heart machine, which was the prototype of the extracorporeal circulation (CPB) machine used today. The success rate of the operation was initially 60% [18]. He performed this procedure both as a primary operation and as a secondary operation in patients who had previously undergone anastomosis [19]. By the early 1960s, the mortality rate had decreased to 7–14%. VSD closure was performed through the right ventricle (RV) using a pericardial or plastic patch. Intracardiac pressures were often measured, wanting the ratio of right to left ventricular systolic pressures to be below 0.5–0.75. It was considered important to monitor and maintain right atrial pressure above normal values (18–20 mm Hg) [20]. Complete correction of the heart defect was performed in the case we presented in the 3rd year of life. Extracorporeal circulation and hypothermia were used during the procedure. The ventricular septal defect was closed with a Dacron patch, and the right ventricular outflow tract was dilated with a pulmonary homograft.

At the end of the 1960s, the effects of surgery were evaluated, and the complications that occurred were described. Among the most common were: pulmonary valve regurgitation, cardiomegaly, aneurysmal dilatation of outflow tract patches (when the material used was a pericardial fragment) [21].

The results of the study made it possible to develop recommendations for surgical treatment. Surgical intervention was indicated in patients of all ages. In children younger than 5 years of age, surgery with the creation of an anastomosis was recommended, as a total repair procedure was associated with too high a risk of patient death. After creating an anastomosis, patients should undergo reoperation with complete correction of the defect before the age of 20. Patients over the age of 5 can undergo corrective surgery, but it has been indicated that the best time to perform this procedure is between the ages of 8 and 12 [22]. With these recommendations, survival in the late 1960s was 85–90%.

Bonchek et al. conducted a study that showed that it was better to perform total correction at a younger age rather than waiting until the child reached the age of 5 [23]. The results indicated an increased mortality rate for children in whom surgery was postponed until the patient reached 2 years of age. Early surgery prevented obstruction caused by fibrosis and inadequate development of the right ventricular (RV) outflow tract.

In the early 1970s, studies by Barratt-Boyes, Kirklin and Castaneda showed that surgery for complete correction of the defect could be performed in newborns and infants with a low mortality rate. The operation was performed in deep hypothermic cardiac arrest or using low-flow hypothermic extracorporeal circulation (CPB). Barratt-Boyes and Neutze described that performing a total correction in one stage is associated with

reduced mortality compared to two-stage surgery (with the creation of a systemic-pulmonary anastomosis first) [24].

Fraser et al. developed an individualised surgical treatment regimen based on information about the treatment of 2,175 patients at their centre. Only asymptomatic patients weighing less than 4 kg with threatening pulmonary artery isolation had a two-stage procedure with the creation of a BT (Blalock-Taussing) anastomosis, followed by total correction surgery at 6 to 12 months of age [25].

In 1978, Zavanella et al. developed the monocusp valve (single-lobe transcatheter homogeneous patch), which is now used in the group of infants over 6 months of age with an extreme form of tetralogy of Fallot who require pulmonary ring dilatation. Since the 1990s, valves have been made from autologous or bovine pericardium, a pulmonary valve allograft or a polytetrafluoroethylene (PTFE) membrane rather than from the patient's own bicuspid or tricuspid valve, as was originally used [26, 27].

Pulmonary or aortic homografts are implanted in infants with a 50% risk of reoperation within 5 years and in newborns with the same risk within 3 years.

Postoperative complications described during long-term follow-up include right ventricular volume overload (the result of postoperative pulmonary artery regurgitation), RV outflow tract obstruction, right ventricular aneurysms arising at the patch or ventriculotomy site, distal pulmonary trunk obstruction, atrial and ventricular incision scars, ventricular septal defects, ventricular hypertrophy and dysfunction, aortic valve regurgitation and aortic dilatation [28, 29]. Arrhythmia, heart failure and complications after reoperation are among the most common late causes of death in adults with TOF after complete correction of the defect. The risk of death 30 years after surgery is 6–9% [30].

Conclusions

Tetralogy of Fallot was, for a long time, an incurable heart defect. Historically, TOF has had a very high mortality rate. The development of the systemic-pulmonary anastomosis by Blalock, Taussig and Thomas gave many children a chance for prolonged and improved quality of life. The development of methods for treating tetralogy of Fallot made it possible to perform surgery on younger and younger patients. Continuous improvements in surgical techniques have made it possible to perform increasingly less invasive procedures.

The treatment of the patient described by us was in accordance with the therapeutic possibilities of those years and did not differ from the standard methods of treating such patients, thus showing exactly how this defect was treated in Poland in those years.

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