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Review Article

Tetrlogy of Fallot with Pulmonary Atresia

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Definition and Epidemiology:

This deformity represents the extremes of the anatomic spectrum of right ventricular outlet stenosis and is only one of the special cases of tetralogy of Fallot with the absence of direct communication between the cavity of the right ventricle and the cavity of the pulmonary trunk. (1) Although this deformity is sometimes referred to as pulmonary atresia with ventricular septal defect, it is a nomenclature. It is unfair because the main anatomical findings belong to the spectrum of tetralogy of Fallot malformations and it is also inaccurate because there are many other malformations in which pulmonary atresia is associated with a VSD but whose anatomy and management are completely different (eg single ventricle and congenital corrected vascular exchange). It was also found through monitoring fetuses by echocardiography during pregnancy that tetralogy of Fallot may develop into pulmonary atresia during fetal life, as the previously passable right ventricle outlet develops into complete atresia. (2,3)

The prevalence of tetralogy of Fallot with pulmonary atresia is about 2% of congenital cardiac lesions and 20.3% of all forms of tetralogy of Fallot, (4) and there is no known predisposition to sex or race in these patients.

Genetics and Risk Factors:

Many patients with tetralogy of Fallot with pulmonary atresia have extracardiac syndromes and malformations, the most important of which is microdeletion of chromosome 22q11.2, which is found in a third of patients (5), and other syndromes such as Alagille and trisomy 21, (6). Also, the presence of some diseases in the mother, such as diabetes and polyuria. Phenylketonone increases the risk of pulmonary atresia, as the presence of diabetes in the mother increases the risk about 20 times.

The risk of recurrence of this deformity in siblings is 3-4%, but the risk of recurrence increases in the event of association with hereditary syndromes. Increased surgical mortality and morbidity have also been reported when pulmonary atresia is associated with a deletion of chromosome 22q11.2.

Anatomical Study:

The extent of pulmonary atresia is highly variable, most commonly involving the pulmonary valve and the proximal portion of the pulmonary trunk. It may also involve the conus muscularis or central pulmonary

arteries either proximally or distally.

When studying the anatomy of tetralogy of Fallot with pulmonary atresia, it is important to determine whether the central pulmonary arteries are discontinuous or discontinuous, as well as to identify alternative sources of perfusion of the pulmonary vascular tree either by remaining patent ductus arteriosus or by pulmonary-systemic circulation.

The pulmonary arteries are anatomically classified into central, lobar, and segmental arteries. The diameter of the central pulmonary arteries varies greatly and appears to be directly related to the amount of pulmonary flow and its source. When the ductus arteriosus or collateral circulation connects with the proximal part of the central pulmonary arteries, then these vessels are of acceptable size. In contrast, these central arteries tend to be atrophic when The collateral circulation connects more distally at the segmental or lobar levels of the pulmonary arteries.(7) Also, stenosis of the ductus arteriosus, whether acquired or congenital, may be associated with atrophy of the central pulmonary arteries.

Tandem Rotation:

Uncommon in patients with tetralogy of Fallot in the absence of pulmonary atresia. Perfusion from the posterior circulation can be associated with the ductus arteriosus in the same patient but rarely in the same lung. In the presence of a posterior circulation, it arises more commonly from the descending thoracic aorta, less commonly from the subclavian arteries, and rarely from the abdominal aorta or from its branches or from the coronary arteries. (7-9) The number of parallel vessels ranges from 1 to 6 and their diameter ranges from 1 to 20 mm.(7) There is stenosis in approximately 60% of the collateral circulation. The stenosis tends to occur near its connection with the aorta or with the pulmonary branches. This stenosis may be isolated or segmental, congenital or acquired.

Single-source tangential circulation to the lung is called monofocal tandem circulation, and multi-source tangential circulation to the lung is called multifocal tandem circulation. Isolated perfusion is also used if the pulmonary vascular tree is irrigated from the collateral circulation only or from the true pulmonary arteries only, and dual perfusion if the perfusion comes from the true pulmonary arteries and the parallel circulation together.

When the lungs are perfused by multiple confluent circulation and the ductus arteriosus is absent, abnormalities in the pulmonary vascular tree are the norm, but when the ductus arteriosus supplies the

communicating central pulmonary arteries, the pulmonary arteries in both lungs are normal. When there are unconnected central pulmonary arteries, then the lung perfused by the ductus arteriosus will have monofocal circulation and normal arterial distribution, but the contralateral lung will have multifocal perfusion from the lateral circulation and variable pulmonary arterial distribution (7).

Although the posterior circulation may appear to be a more stable source of pulmonary flow due to its versatility, nevertheless, narrowing of the posterior circulation can gradually develop and become insufficient as the patient grows. The pattern of branching of the collateral circulation within the lung cannot be predicted as it may cause hypervascularization in some bronchopulmonary segments, and ischemia in other segments in the same patient. Thus, the pulmonary bed may show diverse histological alterations ranging from pulmonary hypertension to cholestatic thrombosis.

Ductus Arteriosus:

The ductus arteriosus is often unilateral and is associated with the presence of connected pulmonary arteries in more than 80% of cases, and in rare cases we may find a bilateral ductus arteriosus with unconnected pulmonary arteries. The ductus arteriosus does not branch before it connects with the central pulmonary arteries, as it happens in the collateral circulation, and it tends to be less tortuous than it, and given that the ductus arteriosus is wide during fetal life, so the pulmonary arteries tend to be of normal size at birth. (7) Anyway, Distal narrowing of the ductus arteriosus usually occurs in 35-50% of cases. As a result, blood flow to the lungs is diminished and relative hypoplasia of the pulmonary arteries develops as the child grows. Therefore, the ductus arteriosus is the only unstable source of pulmonary blood supply, and its tendency to close requires surgical intervention in early childhood in more than 50% of cases.

Clinical Findings:

Although most patients with tetralogy of Fallot with pulmonary atresia present for neonatal age, the range of symptoms and clinical manifestations varies and depends on the ratio of pulmonary flow to systemic flow (ratio of Qp to Qs). The clinical approach and management decisions depend on the nature of the MAPCAs and whether or not pulmonary runoff is dependent on the presence of a patent ductus arteriosus.

1- If the MAPCAs are large, the blood flow to the pulmonary vascular bed is usually non-blocking and patients may have little or no cyanosis (ie appear pink). In some patients with profuse flow, heart failure

may develop after postpartum pulmonary vascular resistance decreases, resulting in left ventricular volumetric overload. These patients may require medical treatment for heart failure.

2- Patients with insufficient MAPCAs develop reduced pulmonary flow resulting in severe cyanosis and therefore will require emergency intervention in the neonatal period.

3- In some newborns, the patent ductus arteriosus may provide pulmonary flow to one or both lungs, and these patients usually have moderate degrees of cyanosis. In these cases, intravenous infusion of prostaglandin E1 is required to maintain ductal and pulmonary flow behavior; In the event of closure of the ductus arteriosus, the cyanosis increases sharply due to the decrease in pulmonary flow.

Cardiac Examination:

Cardiac examination generally reveals a single second heart sound (S2) and a loud, continuous murmur that is the murmur of the tandem circulation or ductus arteriosus and is heard along the cardiac murmur with extension to the back and axilla.

Diagnostic Procedures:

Most babies with suspected coronary heart disease undergo initial testing, including postnatal pulse oximetry, chest radiography, and electrocardiogram (ECG). Findings in these tests are diagnostic and nondiagnostic, and TOF/PA/MAPCAs are usually diagnosed by cardiac echo and confirmed with computed tomography angiography (CTA) and/or cardiac catheterization.

Cardiac echo: It is the primary means of confirming the diagnosis by identifying the distinctive anatomical features of tetralogy of Fallot with pulmonary atresia and determining the size and anatomy of the central pulmonary arteries through two-dimensional sections and color Doppler, through which the origin of the collateral arteries or the ductus arteriosus can also be determined, if present.

However, this procedure is still limited in its ability to study the precise anatomy of the collateral circulation and the branches of the distal pulmonary arteries, which is essential for surgical management.

Angiography: It is necessary to determine the presence or absence of confluence of the central pulmonary arteries. In addition, a detailed identification of the sources of perfusion for all segments of the pulmonary vascular tree must be performed, which includes determining the origin and contributions of all the collateral

vessels to pulmonary perfusion, and the degree of communication between the collateral vessels and the branches of the true pulmonary arteries because Surgical planning depends on whether each part of the lung receives blood flow from MAPCAs, true pulmonary arteries (isolated supply), or both (dual supply).(10)

Historically, initial aortography was necessary to clarify the number and location of the collateral arteries. Currently, it may be sufficient to predetermine the origin of the collateral arteries at least by echo or other imaging studies. The goal of selective injections into the pulmonary systemic collateral arteries is to determine the presence of stenosis in these vessels and to determine the size of the extension of the pulmonary vascular tree perfused by each collateral vessel and the pattern of pulmonary arterial connection present. These collateral injections can be enhanced by selective balloon occlusion techniques. Occasionally, if the connectivity of the pulmonary arteries cannot be assessed by collateral arteriography, a retrograde wedge injection into the pulmonary vein can be performed selectively, which may help in identifying atrophy of the central pulmonary arteries. Some patients with complex patterns of pulmonary arterial abnormalities may require multiple contrast injections during imaging, so it is important to pay attention to their contrast load.

High-resolution Computed Tomography:

Recent studies have shown that CT and cardiac MRI can provide detailed preoperative information about the sources of pulmonary perfusion in neonates with tetralogy of Fallot with pulmonary atresia. When comparing these results with cardiac catheterization and surgical findings, CT was found to be the most accurate method. (11) Although both methods can provide the surgeon with clear 3D images of the original anatomy, computed tomography remains preferable for detailed evaluation of the pulmonary arteries and for tracking the trajectory of the collateral circulation. (12) The only drawback of this technique may be the lack of widespread use of the equipment and technical skills required for the use of a CT and cardiac resonator in developing countries such as those used for cardiac catheterization. Therefore catheterization is still an essential part of the preoperative evaluation of tetralogy of Fallot with pulmonary atresia in those countries.

Measure:

Newborns with tetralogy of Fallot and pulmonary atresia should be cared for in a tertiary medical center with expertise in the management of congenital heart disease.

- Initial medical management: aims to maintain sufficient blood flow to survive.

Final measure: Aims to obtain a low-pressure pulmonary circulation completely independent of systemic circulation and to close the interventricular hole.

Initial Medical Management:

It aims to stabilize cardiopulmonary function and to ensure adequate pulmonary blood flow and systemic oxygenation. The method of intervention varies depending on the patient's oxygenation.

In patients with hypoxia due to insufficient pulmonary flow: treatment aims to increase the ratio of pulmonary flow to systemic flow QP/QS. An infusion of prostaglandin E1 (alprostadil) should be initiated to maintain the behavior of the ductus arteriosus if present. Sufficient volume of intravenous fluids must also be given to increase preload, in addition to transfusion of red blood cells when needed to maintain hematocrit above 40% to improve the ability to transport oxygen, and sometimes we may need to use medical therapy with adrenaline or noradrenaline to increase systemic vascular resistance and enhance flow through the corresponding arteries. stenosis.

Cardiac catheterization can be used to place a stent in the ductus arteriosus, and in some other selective cases, a puncture of membranous atresia can be performed by means of radiofrequency catheters, after which balloon dilation is performed, and later, at an older age, the final repair is performed (13,14).

- Pulmonary congestion and heart failure may occur in some patients with increased pulmonary flow due to the presence of copious circulation, especially with reduced pulmonary vascular resistance after birth. Intervention in this situation depends on the severity of the symptoms and may include the use of angiotensin-converting enzyme inhibitors and diuretics

- In patients with adequate but not excessive pulmonary flow, intervention may not be necessary in the neonatal period because these patients may maintain acceptable oxygenation in the range of 75-85% without treatment.

Nutritional Support:

Infants who have abundant collateral circulation and symptoms of heart failure due to increased pulmonary flow should be provided with a high calorie intake to ensure normal growth, and may reach 150 kcal/kg/day. Children who have undergone palliative procedures also need to improve their calorie intake and should also be provided Whole nutritional supplements in the form of parenteral nutrition are recommended for these patients in the perioperative period as they have a long road to recovery after surgery.

Surgical Intervention:

It depends on the size of the central pulmonary arteries, their relationship to each other, and the presence of collateral circulation:

- Newborns with hypoplastic pulmonary arteries:

When the pulmonary arteries are atrophic and discontinuous with systemic pulmonary circulation, multistage repair is often required, (15) where a palliative shunt is performed to allow these atrophic arteries to expand and grow so that they can be successfully combined into a complete repair. These palliative shunts can be unilateral or bilateral, such as modified Blalock-tossing or central shunts.

- Neonates who have connected pulmonary arteries with appropriate size:

A palliative procedure with pulmonary systemic shunt can be performed to promote regrowth of the central pulmonary arteries before complete repair later, or definitive primary surgical repair can be performed directly. Definitive surgical goals include: (16)

1- Unifocalization: which involves separating the collateral vessels from the aorta and its branches and re-anastomosing them to the central pulmonary arteries to obtain a low-pressure pulmonary arterial system.

2- Reconstruction of the right ventricular outlet (RVOT) using a non-valved connection between the right ventricle and the pulmonary artery, allowing blood to flow from the right ventricle to the pulmonary vascular tree.

3- Closing the interventricular opening (VSD).

Postoperative Complications:

- Bronchospasm: occurs in many infants and children in the period after unifoclization surgery, and is thought to be caused by damage to the lymphatic vessels and blood vessels around the pulmonary bronchi. (17)
- Pulmonary edema resulting from return of blood flow: It occurs in children who had significant preoperative stenosis of the collateral vessels.(18)
- Other pulmonary complications including pneumonia, pulmonary hemorrhage, or compression of the great airways.

Endocarditis prophylaxis: Endocarditis prophylaxis should be given to all patients for six months after surgical repair. Subsequently, antibiotics are recommended for patients with a previous episode of endocarditis, for patients who have undergone repairs involving prosthetic heart valves or other prosthetic materials, for those who have an intracardiac shunt remaining after surgical repair, or for cyanosis or leakage from the patch.

Prognosis: If these patients are not treated, the mortality rate reaches 50% by the age of two years. But when appropriate management is provided, the five-year survival rate is about 85% and the 14-year survival rate is about 75%. (19)

In some cases, patients with pulmonary atresia with tetralogy of Fallot may not reach full repair due to the presence of severely hypoplastic and discontinued pulmonary arteries. These patients often suffer from chronic hypoxia and must be followed carefully due to complications associated with erythroderma and iron deficiency.

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