Chapter

64

Tetralogy of Fallot

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A four-week-old infant presents to the emergency room with agitation and cyanosis. His mother says he has been doing this for shorter periods of time for the past couple of weeks whenever he cries for food. These episodes resolve when she takes him in her lap and breastfeeds him. However, he started running a fever yesterday and had a few episodes of diarrhea this morning. And this current episode has been going on for several minutes and he is only getting more agitated and inconsolable.

Vital signs are: blood pressure unmeasurable due to worsening agitation as the cuff inflates, heart rate 180/min, respiratory rate 60/min, oxygen saturation reads 40–50% during times of agitation but improves when the patient is calm.

What Condition Are You Most Worried About? What Are Tet Spells?

This child is experiencing a hypercyanotic "tet" spell characteristic of tetralogy of Fallot (ToF).

Tetralogy of Fallot is the most common cyanotic congenital heart disease. Often, ToF is prenatally diagnosed or detected by the newborn congenital heart defect (CHD) screen. However, occasionally ToF may present with worsening spells of cyanosis, also known as hypercyanotic or "tet" spells, during which there is severe obstruction of blood flow to the lungs. In conditions that increase the pulmonary vascular resistance, more blood shunts from right-to-left through the VSD, resulting in worsening cyanosis. Tet spells are ominous indicating the acute need for palliative intervention to provide pulmonary blood flow and improve oxygenation.

What Is the Underlying Anatomy in Tetralogy of Fallot?

The tetralogy in ToF develops due to anterior deviation of the interventricular septum or infundibular tissue (Figures 64.1 and 64.2). The remainder of the tetralogy occurs following this movement. The anterior movement of the infundibulum compresses the right ventricular outflow tract (RVOT). This shift also results in an anterior malalignment VSD for which the aorta "overrides" or sits over the VSD. The compression of the RVOT ultimately results in compensatory right ventricular hypertrophy (RVH) (Figure 64.3).

Identify the Anatomic Spectrum That Is Encompassed by Tetralogy of Fallot

Tetralogy of Fallot is a spectrum of anatomy and physiology manifestations, depending on the degree of the obstruction to the right ventricular outflow tract, and the subsequent pulmonary blood flow limitation. ToF can include varying degrees of pulmonary stenosis (mild to severe). In its most extreme form, there is complete pulmonary atresia in which no blood flows from the RVOT; hence the patient is dependent on a patent ductus arteriosus (PDA) to supply blood to the lungs. If not detected prenatally, these patients may present with worsening cyanosis and may be found to have a closing PDA on echo. This cohort of patients will benefit from prostaglandin infusion and usually undergo either a modified Blalock–Taussig shunt (BTs) or PDA stent placement in the catheterization laboratory, to provide stable pulmonary blood flow. After a few months the patient will undergo completion of the repair with a takedown of the shunt or stent, and closure of the VSD, and placement of a conduit from the right ventricle (RV) into the main pulmonary artery, to create normal septated anatomy.

Considering a slightly lower less degree of pulmonary outflow obstruction, there may be a very small amount of blood flow through the pulmonary valve but this may not be adequate in the absence of supplementation from the PDA. These ToF patients with severe pulmonary stenosis (PS) follow the course of the ToF with pulmonary atresia and undergo shunting or stenting initially, prior to complete septation and repair later in infancy.

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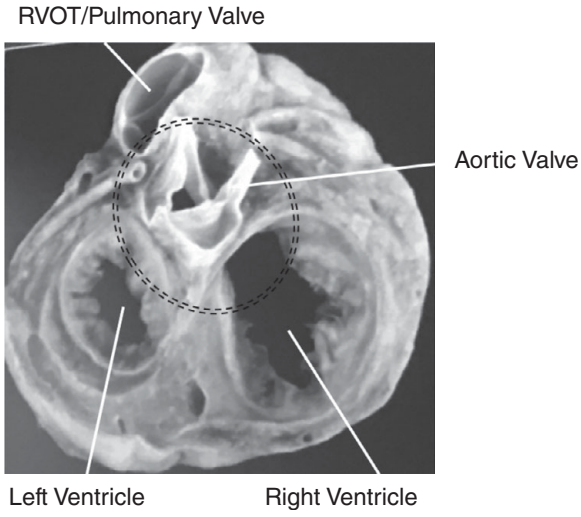

Figure 64.1 Cardiac specimen highlighting the infundibulum region (dashed circle). The region between the aortic valve and right ventricular outflow tract (RVOT) is underdeveloped leading to anterior shift of structures.

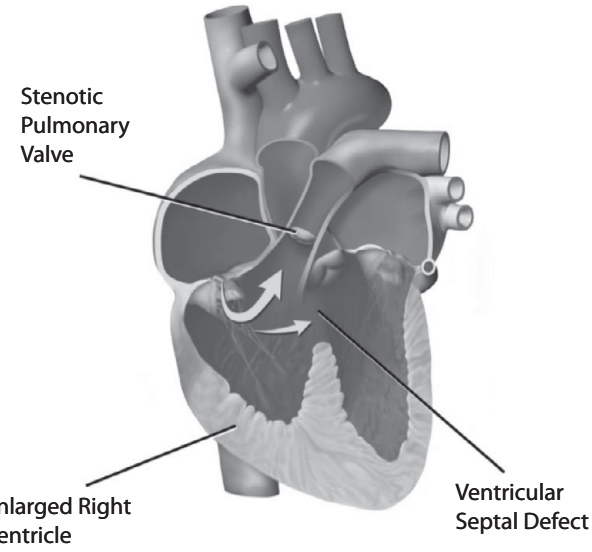

Figure 64.3 Drawing of characteristic components of tetralogy of Fallot: Reproduced from Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". *WikiJournal of Medicine* 1 (2) under CC BY-SA 4.0 license https://creativecommons.org/licenses/by-sa/4.0/.

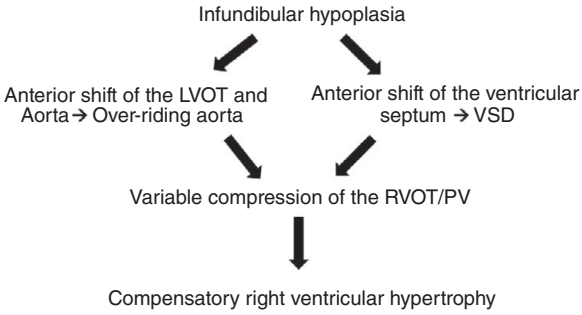

Figure 64.2 Schematic identifying the primary and compensatory changes seen in patients with tetralogy of Fallot. LVOT, left ventricular outflow tract; RVOT, right ventricular outflow tract; PV, pulmonary valve; VSD, ventricular septal defect.

Moving further along the spectrum, there are patients that may have mild to moderate obstruction initially and be able to manage without a PDA. However, as time passes the RV muscle hypertrophy just under the narrow pulmonary valve worsens and adds a dynamic component of RV outflow obstruction to the mix. This dynamic obstruction is worse when the patient is dehydrated and volume deplete, as the hypertrophied RV does not have adequate preload and generates dynamic obstruction from all the thick muscle bundles collapsed together. It is also worse when the heart rate is higher, and the RV is unable to relax completely in diastole and fill. Episodes of agitation and higher pulmonary vascular resistance or intrathoracic pressures would further limit the ability of the RV to push blood through the narrow outflow tract. Hence patients having a "tet" spell prefer to shunt blood across the VSD through the aorta, instead of being able to send it to the lungs. Thus, while they do not lose cardiac output, they become hypoxemic and cyanotic and more inconsolable and tachycardic, getting into a vicious cycle.

A final category of ToF, which manifests very differently from the usual cyanotic CHD, are ToF with pulmonary atresia and major aortopulmonary collateral arteries (MAPCAs). These MAPCAs originate from various spots on the descending aorta or from the aortic arch or its branches, and supply various segments of the lungs (Figure 64.4). The patients with MAPCAs will not present with cyanosis, rather they may have pulmonary overcirculation and manifest with tachypnea, tachycardia, and failure to gain weight normally. Their surgical planning is more precarious, as the MAPCAs may be physically far apart and difficult to unifocalize to a central main pulmonary artery. The MAPCAs also expose the pulmonary vascular bed to systemic blood pressures and predispose to development of pulmonary hypertension.

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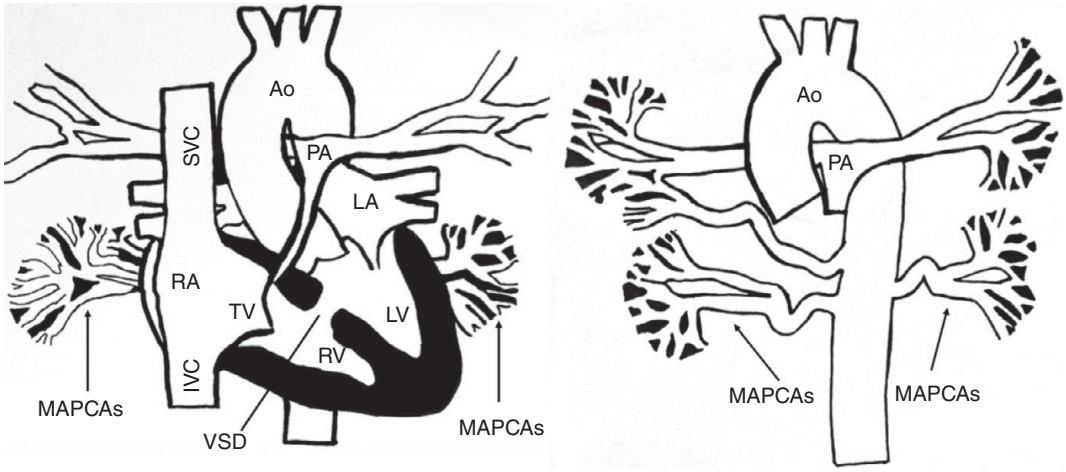

Figure 64.4 (Left) Diagram of tetralogy with pulmonary atresia and major aortopulmonary collaterals. (Right) Image demonstrating the major aortopulmonary collaterals coming off the aorta. LV and RV, left and right ventricles respectively; LA and RA, left and right atria respectively; IVC and SVC, inferior and superior vena cava respectively; VSD, ventricular septal defect; PA, pulmonary artery; Ao, aorta; TV, tricuspid valve; MAPCAs, major aortopulmonary collaterals. Illustration by Adam C. Adler MD

How Are "Tet Spells" Managed?

Acute "tet spells" are managed by firstly helping calm the patient (e.g., by handing the child to the mother to hold, allowing to feed, or sedation if needed), placing the child in a knee-chest position (to increase systemic vascular resistance, and may be achieved by mother holding the baby in her arms and cradling the knees and chest together), initiating oxygen (preferably through the least noxious route for the child, e.g., blow-by or face-mask), administering a bolus of intravenous fluids, and finally intravenous metoprolol (to slow down the heart rate) and phenylephrine (to increase systemic vascular resistance). Some will require anesthesia (on the way to the operating room). Obtaining a blood pressure may be further annoying to the child and is hence not necessary at this time. Instead a minimal intervention strategy to allow the child to recover is prudent, while remaining alert to act in case of needing more support. Rate control, volume repletion, sedation, and peripheral vasoconstriction all come together to boost blood flow through the narrow RV outflow tract.

What Are the Classic Exam Findings of a ToF Patient?

ToF patients manifest a harsh ejection systolic murmur loudest over the pulmonic area and radiating into axillae, indicating pulmonic stenosis. As the stenosis becomes worse, initially the murmur is slightly louder, but eventually it starts becoming softer as the obstruction increases. For example, during a ToF spell, the pulmonary stenosis murmur may not be audible at all. Higher saturations indicate less RV outflow obstruction. "Tet spells" may become a vicious cycle and require a combination of heart rate control and vascular resistance manipulation to break. The murmur during a hypercyanotic or "tet spell" becomes softer due to decreased pulmonary flow. Iron deficiency anemia will accelerate the onset of these spells.

Management

The time of presentation and intervention for ToF is determined by the degree of RV outflow obstruction, and the limitation of pulmonary blood flow. These clinical indicators are the O_2 saturation levels and the development of hypercyanotic spells. The Doppler-echocardiographic indicators are the pressure gradients observed across the RV outflow tract. Children with saturations less than 80% or those having hypercyanotic spells are scheduled for surgery. Surgical management includes palliative procedures like a modified Blalock–Taussig–Thomas shunt (mBTT shunt) to help provide consistent pulmonary blood flow in the setting of significant stenosis or atresia at the pulmonary valve.

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Complete repair of the heart comprises closure of the VSD as well as resection of the RV obstruction, resulting in normal saturations. Complete repair is replacing the palliative approach in many centers. Even after complete ToF repair, the patients need lifelong cardiology follow up, as their pulmonary valve may become more regurgitant (depending on the surgical approach and the intervention on the valve annulus itself) leading to RV dilation.

They may also develop arrhythmias due to the RV dilation/hypertrophy and scarring (as a result of the pulmonary valve regurgitation as well as the primary surgery), with an increase in risk of sudden cardiac death in pediatric patients with QRS $>$ 170 ms on the EKG. Cardiac MRI is used to estimate the volume of the RV to determine the time for pulmonary valve replacement (catheter-based or surgical). While complete ToF repair ensures that these children have normal saturations, a majority of patients have a prolonged QRS and features of right bundle block on the EKG due to the intervention on the interventricular septum.

A two-week-old 3 kg female infant was diagnosed with ToF with pulmonary atresia and underwent right-sided 3.5 mm mBTT shunt placement through a lateral thoracotomy. Her saturations were around 85–90% after this surgery. You respond to a code that is called as the baby is "fussy and cyanosed" over the past 20 minutes, and now her saturations are in the 40s.

What Is the First Medication You Would Like to Administer? What Exam Finding Would Be Concerning for You?

This child may have a clotted shunt, which is limiting her pulmonary blood flow. The shunt is especially critical for her, as she has pulmonary atresia, making the shunt her solitary source of pulmonary blood flow. The first medication, which has hopefully already been administered by the time you arrive, is 100 U per kilogram of a heparin bolus to try and open up the shunt. A volume bolus of colloid or crystalloid may also be considered. The lack of a loud harsh murmur on exam is extremely concerning for a shunt obstruction.

What Are the Major Anesthetic Considerations for ToF Surgery? What Are the Differences of Shunt or a Complete Repair?

ToF surgery has some unique considerations based on the procedure planned. For any ToF patient, it is imperative to have checked an ionized calcium level preoperatively, as ToF falls in the category of conotruncal anomalies that are commonly associated with DiGeorge syndrome.

Further, for a ductal stent, it is important to turn the prostaglandin infusion off a few hours prior to the procedure if possible to help the PDA constrict a little and allow the stent to fit well. During ductal stenting, there may be spasm of the PDA when the wire crosses it, hence the team must always be prepared with a stent on the wire to prevent the PDA from collapsing entirely.

A complete repair is done through a median sternotomy, with its usual considerations. In the perioperative transesophageal echocardiography, it is very important to assess for residual VSDs.

What Are the Most Common Complications Associated with ToF Surgeries?

The complications after ToF surgery vary with the kind of surgery.

- After a mBTT shunt, the patient may have significant symptoms of pulmonary overcirculation (tachypnea, tachycardia) along with lower diastolic pressures as the shunt offers runoff for the systemic flow. If the shunt is performed from a lateral thoracotomy, they can be more painful. A ductal stent may have similar features.
- A shunt (surgical or catheter-based) can never be trusted. Clotting of a shunt causing limitation of pulmonary blood flow is a dreaded complication, and usually patients are started on at least low dose heparin or other anticoagulation, and anti-platelet therapy once feeds are tolerated.
- A complete repair with a VSD patch may be complicated by arrhythmias postoperatively. While heart block of varying degrees may be

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possible due to the proximity of the patch to the normal conduction system of the heart, one of the classic arrhythmias after ToF repair is junctional ectopic tachycardia (JET). JET is often attributed to the physical stretching of the junction during the VSD repair; however, it has also been seen in patients without any intra-cardiac surgery, so a component of intrinsic arrhythmogenicity is suspected. Due to the potential for arrhythmias, patients benefit from being left with atrial as well as ventricular wires for the perioperative period.

- ToF patients have very hypertrophied RVs which have significant diastolic dysfunction. Hence it is not uncommon to see higher than usual central venous pressure (CVP) being tolerated for these patients. One must resist the urge to diurese a number, since the RV hypertrophy is still a set-up for dynamic outflow tract obstruction if the patient is volume depleted and the RV is under filled. Similarly, a volume depleted ToF will be tachycardic which also does not bode well for dynamic RV outflow tract obstruction. The tachycardia may be more prominent in patients who have been on a beta-blocker preoperatively.
- If there has been significant manipulation and augmentation of branch pulmonary arteries, especially if they were discontinuous to begin with, always be suspicious of desaturations, unilateral oligemia on the chest x-ray or a widening end tidal-pCO_2 gradient. Residual ductal tissue or scarring and inflammation may cause stenosis of a branch PA and may need catheter-based intervention if clinically significant.
- ToF with pulmonary atresia and MAPCAs is a unique condition in the ToF family. After a MAPCA unifocalization, patients may have very non-compliant lungs that have borne the brunt of the imbalanced Qp:Qs for so long. They may also demonstrate pulmonary hypertensive crises as the MAPCA vascular architecture is abnormal with thicker media and has also been exposed to systemic blood pressures for so long.
- Thoracic duct injury can lead to chylothorax, which manifest as the child starts feeding more after surgery.

What Is the Management of Junctional Ectopic Tachycardia (JET)?

JET is a classic postoperative arrhythmia manifesting in the first 72 hours after ToF repair. The initial management is to minimize the sympathetic stimulation with cooling and sedation. If the rate of JET is within normal limits of heart rate for age, one may elect to wait and watch, or intervene with overdrive pacing at a few beats above the JET rate to achieve atrioventricular synchrony.

Preemptive use of dexmedetomidine by infusion and magnesium repletion may help to reduce the incidence of postoperative JET following these repairs.

What Is the Natural History of Patients with RV-PA Conduits?

Over time, the artificial conduits undergo a number of changes that may affect their function. Of course,

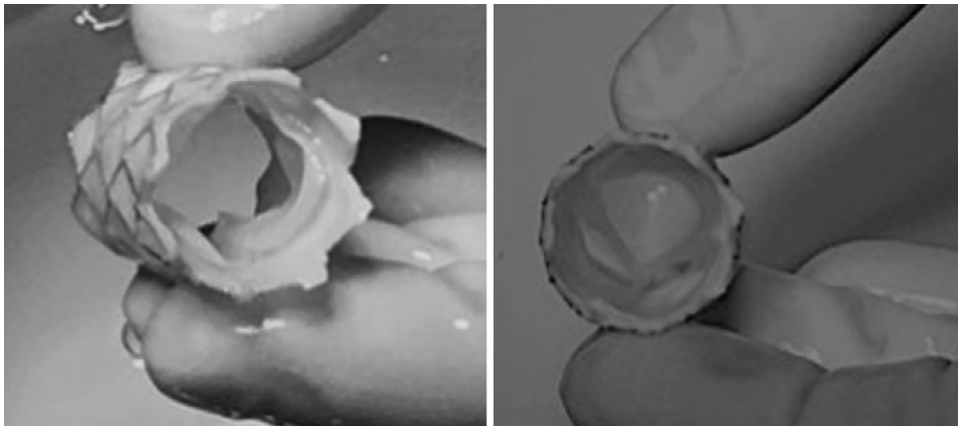

Figure 64.5 Transcatheter pulmonary valve in the open (left) and closed positions (right)

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these artificial conduits do not grow over time. When placed in small children, these conduits often require replacement with larger conduits as they become flow limiting. Additionally, internal calcifications and/or narrowing at the proximal or distal end may restrict flow.

Additionally, the native valve within the conduit eventually becomes incompetent leaving pulmonary insufficiency, which can be severe or even freely regurgitant.

What Is a Melody Valve or Transcatheter Pulmonary Valve?

This device is a trans-catheter pulmonary valve that can be deployed into an RV-PA conduit. Provided the conduit is of an appropriate size and length for the patient, a Melody valve can be deployed into the conduit in cases where severe or pulmonary regurgitation exists and functions as a pulmonary valve (Figure 64.5).

Suggested Reading

Downing TE, Kim YY. Tetralogy of Fallot: general principles of management. *Cardiol Clin*. 2015;33 (4):531–41. PMID: 26471818.

El Amrousy DM, Elshmaa NS, El-Kashlan M, et al. Efficacy of prophylactic dexmedetomidine in preventing postoperative junctional ectopic tachycardia after pediatric cardiac surgery. *J Am Heart Assoc*. 2017 Mar; 6(3): e004780. PMID: 28249845.

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