An overview of abnormal pulmonary venous connection in children

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Abstract

Abnormal pulmonary venous connection represents a rare variant of congenital heart disease, in which the pulmonary veins fail to make their normal connection to the left atrium. Instead, they connect and drain anomalously into the systemic venous circulation. The abnormal connection could be partial, when one or more but not all the pulmonary veins connect anomalously or total, when all the pulmonary veins connect anomalously. Total anomalous pulmonary venous connection (TAPVC) is by far the most common and most severe lesion, with a reported prevalence ranging between 1.5% and 2%. Its hemodynamics and clinical features are variable, and diagnosis can be challenging especially in resource-limited setting. This review discusses the embryology and pathogenesis of abnormal pulmonary venous connection, with emphasis on TAPVC. The clinical manifestations and various diagnostic options are also highlighted.

Key words: Anomalous, connection, pulmonary veins

INTRODUCTION

The earliest description of abnormal disposition of the pulmonary veins in medical literature was by Winslow in 1739 but was first confirmed by cardiac catheterization over Two centuries later in 1950 by Friedlich *et al*.[1]

Common Pulmonary venous anomalies include those related to abnormal connections and drainage. The term "drainage" is sometimes used interchangeably with "return" but "connection" and "drainage" should not be used interchangeably. According to Edward,[2] connection refers to an anatomical relationship while drainage refers to a physiologic or hemodynamic phenomenon. Drainage is the physiologic pathway of blood from the pulmonary veins into the left or right atrium (RA), while connection describes the anatomical contiguity of the pulmonary veins with a morphological left or RA. In summary, pulmonary veins that connect anomalously also drain anomalously while those that connect normally (appropriately to the left atrium) may drain anomalously, due to some left-sided structural obstruction or atresia. This is a common finding in atrial septal defects (ASDs).[2,3]

Anomalous pulmonary venous connection could be partial, when one or more but not all the pulmonary veins connect anomalously or total, when all the pulmonary veins connect anomalously. In these conditions, the pulmonary veins connect directly to the systemic venous circulation through persistent splanchnic connections.

EPIDEMIOLOGY

These conditions are rare congenital diseases. Krabil and Lucas[4] reported that partial anomalous pulmonary

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venous connections (PAPVC) accounted for 0.4%–0.6% of total autopsies, while Hirsch and Bove[5] reported a prevalence of 2% for total anomalous pulmonary venous connections (TAPVC). In the Baltimore-Washington infant study,[6] it accounted for 1.5% of all patients with cardiovascular malformations. Furthermore, in the study, TAPVC was significantly associated with intrauterine growth retardation, low birth weight and prematurity when compared with control subjects. According to Snellen *et al.*,[7] TAPVC was 10 times more common than the PAPVC.[7] Several studies[8-10] have found a male preponderance in anomalous pulmonary connections. About 90% of PAPVC are associated with sinus venosus septal defects.[7] There is a scanty report of TAPVC in the West African subregion.[8]

EMBRYOLOGY

The primitive heart can be detected by the end of the 3rd week of conception. By day 20, the first intraembryonic blood vessels can be seen, with the subsequent formation of the single median heart tube, the circulation begins about days 27–29.[11,12]

The developmental anatomy of the pulmonary veins is an intricate process that like the embryonic heart develops early *in utero*. Blom *et al.*[13] proposed some theories based on works carried out on human and animal embryos. A widely accepted theory proposes that blood from the lung buds drains into the splanchnic plexus, which is thus conveyed through the paired cardinal and umbilicovitelline veins. Subsequently, the right superior vena cava (SVC) is developed from the right cardinal venous system, while the left cardinal venous system vanishes but in <1% of individuals remains as a left SVC. The inferior vena cava (IVC), ductus venosus, and portal venous system are derived from the umbilicovitelline veins.[5] An outpouching on the dorsal wall of the left atrium is believed to give rise to the primitive common pulmonary veins. These veins eventually communicate with the lungs through the splanchnic plexus. With time, there is involution of the pulmonary venous connections to the umbilicovitelline and cardinal veins, and subsequently, the common pulmonary veins become intergrated into the dorsal wall of the left atrium. The common pulmonary veins eventually give rise to the four (two right and two left) pulmonary veins.[14,15] The incorporated pulmonary veins form the smooth posterior wall of the left atrium, and the trabeculated part of the left atrium subsequently occupy a more ventral aspect.[16] Total or partial anomalous venous drainage and/or connections arise from failure or abnormalities of any of these processes, e.g. failure of the left atrium to link to the pulmonary venous plexus with the eventual retention of connections to the primitive cardinal and umbilicovitelline drainage systems.

TYPES WITH EMBRYOLOGIC BASIS

The abnormalities involving the pulmonary veins include a wide spectrum of disorders. Krabil and Lucas[4] classified them based on the embryonic principles.
i. Atresia of the common pulmonary veins (early), while pulmonary–to– venous connections are still present
   a. Partial anomalous pulmonary venous connections
   b. TAPVC
ii. Atresia of the common pulmonary veins (late) while pulmonary –to– venous connections are obliterated
iii. Stenosis of the common pulmonary venous
   a. Cor triatriatum
iv. Abnormal absorption of the common pulmonary vein into the left atrium
   a. Stenosis of individual pulmonary veins
   b. Abnormal number of pulmonary veins.

This review will focus on class 1, partial and TAPVC. According to Neill,[17] the abnormalities of pulmonary venous drainage are broadly classified into four:
1. Drainage into the RA: This type occurs if the atrial septum develops abnormally to the left with a relatively small left atrium. The pulmonary veins enter the atrium at the superoposterior wall at the immediate right of the septum
2. Drainage into the right common cardinal system (SVC, azygos vein) secondary to the persistence of the communication between the pulmonary venous plexus and the right horn of the sinus venosus and default in the development of the normal pulmonary vein
3. Drainage into the left common cardinal system (left SVC, coronal sinus or left innominate vein)
4. Drainage into the umbilicovitelline system (portal vein and ductus venosus): According to Butler,[18] sequel to the failure of the development of the common pulmonary vein, the pulmonary plexus drains into vascular channel near the esophagus, pierces the diaphragm with it or with the vagus nerve through the foramen of Blair and communicates either with the portal vein or the ductus venosus.

The classification by Darling *et al.*[19] is widely acknowledged. The classification is based on the anatomical location of the pulmonary venous drainage in relation to the heart. They classified TAPVC into four types:

Type 1: Supracardiac connection, drainage into the SVC l system. This is the most common type accounting for 45%–50%. The common pulmonary vein drains superiorly

into the innominate vein, SVC or azygous vein via an ascending vertical vein.[5]

Type 2: Cardiac connection, drainage directly into the coronal sinus or the RA. Drainage to the coronal sinus is said to be as a result of the persistence of pulmonary to systemic venous connections to the left common cardinal vein, the embryonic precursor of the coronal sinus. This type of TAPVD is said to be secondary to an absent or impaired mesenchymal contribution to atrial septation.[20]

Type 3: Where the connection is below the diaphragm. In this type, the pulmonary venous confluence drains into a descending vertical vein through the diaphragm into the portal vein or embryonic ductus venosus. Less commonly, are connections to the gastric vein, the hepatic veins and the inferior caval veins. These systemic veins are derived from the umbilicovitelline veins. Types 2 and 3 each account for about 25%.[5]

Type 4: Where the connection is at >1 anatomical level.

In TAPVC, there is no open connection of the veins to the left atrium either due to nonlumenization of the midpharyngeal endothelial strand or the atresia of an initially lumenized common pulmonary vein.[21] An alternative classification system consists of two groups; supra – diaphragmatic with or without pulmonary venous obstruction and infradiaphragmatic or infracardiac connections with pulmonary venous obstruction. In both groups, an interatrial communication in the form of a nonrestrictive ASD or a restrictive patent foramen ovale is commonly seen. This communication is the only form of access of oxygenated blood from the RA to the left atrium.[3] Obstruction may be secondary to either an intrinsic obstruction of the vertical vein or a hemodynamic consequence of the vertical vein being sandwiched between the pulmonary trunk anteriorly and the left bronchus posteriorly.[22] Obstruction may also arise from the stenosis of the right atrial ostium of the coronal sinus and rarely at the junction of the SVC with the RA. In the infradiaphragmatic or infracardiac connections, obstruction is invariable and may be due to intrinsic obstruction, compression as the venous channel penetrates the esophageal hiatus or resistance to flow in the capillary bed of the liver.[22]

PATHOPHYSIOLOGY

In utero, the hemodynamic consequence of TAPVC is not significant since only little amount of blood flows through the pulmonary veins and lungs. At birth, there is mixture of oxygenated blood (pulmonary circulation) from

the pulmonary veins and deoxygenated blood (systemic circulation) from the great systemic veins in the RA. The subsequent hemodynamics depends on the size of the interatrial communication and the pulmonary vascular resistance. A restrictive patent foramen ovale will lead to rise in right atrial and pulmonary venous pressures with eventual pulmonary hypertension and decrease flow to the left atrium.[3] On the other hand, a nonrestrictive ASD allows easy flow of blood from the right to the left atrium depending on the compliance of both ventricles. The increased blood flow leads to a dilated right ventricle and increased pulmonary circulation. The increased pulmonary circulation results in increased return to the RA and mild cyanosis with equal oxygen saturation of the RA, right ventricle, pulmonary trunk, left atrium, and left ventricle. Eventually, an increased pulmonary vascular resistance causes right ventricular (RV) hypertrophy with poor compliance with a resultant fall in pulmonary blood flow and increasing cyanosis.

For those with venous obstruction, there is a resultant pulmonary hypertension, reduced pulmonary blood flow, and increased concentration of deoxygenated blood with marked cyanosis. A vicious circle of severe obstruction, pulmonary hypertension, and pulmonary trunk dilation is triggered, when a left vertical venous channel is compressed between the pulmonary trunk and left bronchus.[3]

Clinical features

The clinical presentation varies widely depending on adequacy of interatrial communication, the degree of pulmonary vascular resistance and whether there is obstruction to the pulmonary venous return or not.[23,24] At one end of the spectrum, symptoms are mild and often overlap with those of other noncardiac disease.[3] At the other end, patients become very symptomatic soon after birth and may have a stormy clinical course.[23,25]

In the absence of pulmonary venous obstruction, the signs and symptoms of TAPVC resemble those of a large secundum ASD.[23] Affected patients are typically asymptomatic at birth, but majority develop signs and symptoms of heart failure within the 1st year of life including dyspnea, tachypnea, and diaphoresis during feeding.[23,26,27] Recurrent respiratory tract infection is quite common, and many patients have failure to thrive due to combination of anorexia, inadequate intake, and increased metabolic demand. Cyanosis may be so mild (SpO_2 >80%) as to be clinically in apparent.[26,28] Some patients with uncorrected lesions may occasionally present later in life or during adulthood.[29-34] Such patients may acquire obstructive pulmonary vascular disease, and then manifest with severe cyanosis and symptoms of low cardiac out.

When pulmonary venous obstruction is present, severe respiratory distress and cyanosis occur within days after birth.[24,34] Usually, there is rapid onset of tachypnea, gasping, and retractions indicative of pulmonary edema.[34] The more severe the obstruction, the earlier the infant is symptomatic and discovered to have heart disease.[34] In patients with infradiaphragmatic TAPVC, cyanosis and dyspnea may be aggravated by straining, crying or swallowing because the anomalous venous channel is further compressed at the esophageal hiatus.[5,35]

Cardiovascular examination shows precordial bulge with prominent left parasternal heave as a result of RV volume overload.[28] Similar to a large nonrestrictive ASD, the second heart sound is widely split and fixed with loud pulmonic component (P2). There is also a soft ejection systolic murmur along the upper left sternal border due to rapid ejection of a large RV stroke volume into a dilated pulmonary trunk.[27,35,36] Mid-diastolic murmur over the lower left sternal border is common and is due to increased flow across tricuspid valve.[35,36] In a few cases, a continuous murmur mimicking venous hum is audible over the left upper sternal border.[1] It occurs due to continuous flow through the venous confluence, the left vertical vein, and left innominate vein.[36]

In infants with pulmonary venous obstruction, auscultatory signs are governed by pulmonary hypertension rather than increased pulmonary flow.[36] The signs are that of pulmonary artery hypertension including absence of cardiac enlargement with diffuse apical impulse (RV type), single or closely split second heart sound (S2), loud P2 and an early diastolic murmur of pulmonary regurgitation.[23] A high frequency holosystolic murmur of tricuspid regurgitation, hepatomegaly and peripheral edema accompany pulmonary hypertensive RV failure.[26,36]

Without surgical repair, two-thirds of infants with unobstructed TAPVC die before reaching 1 year of age. They usually die from superimposed pneumonia. Patients with infracardiac (infradiaphragmatic) type rarely survive for longer than a few weeks without surgery. Most die before 2 months of age.[35]

Chest X-ray
The radiologic features in unobstructed TAPVC resemble that of a nonrestrictive ASD.[35] There is moderate to marked cardiomegaly involving the RA and RV, with increased pulmonary vascular markings and prominent pulmonary artery segment [Figure 1].[23,26,35] In patients with supracardiac type of TAPVC, X-ray may reveal a pathognomonic cardiac silhouette known as "figure-of-8," "snowman" or "cottage loaf" appearance.[1] The upper portion of the figure-of-8 is composed of the anomalous
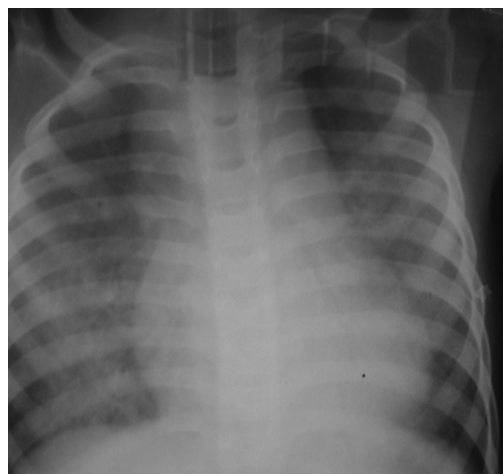
Figure 1: Chest radiograph of a 9-year-old girl with supracardiac total anomalous pulmonary venous connection showing cardiomegaly with widened mediastinum, simulating figure-of-8 appearance

vertical vein on the left, the left innominate vein superiorly, and the SVC on the right.[4] The lower portion is formed by the dilated RA and right ventricle [Figure 1].[33] The figure-of-8 radiographic appearance is not usually present before the age of 4 months because the venous channels need time to develop sufficient size and radiodensity to be visible in the X-ray.[26,36]

In obstructed TAPVC, the heart size is normal or only slightly enlarged. Pulmonary vascular markings are mottled and show reticular appearance. Lung fields reveal features of pulmonary edema such as diffuse reticular nodular "ground glass" appearance and Kelly B lines.[35] These findings may be confused with those of pneumonia or respiratory distress syndrome (Hyaline membrane disease).[35]

The radiologic features in patients with partial anomalous venous return also reflect the increased pulmonary blood flow and RV dilatation, typical of ASD. However, distinctive features may additionally be observed depending on the number of pulmonary veins that are anomalously connected and the site of anomalous connection.[26] For example, patients with anomalous connection of right pulmonary veins to IVC (scimitar syndrome) have a crescentic shadow in the right lower lung field. The term "scimitar syndrome" was coined because the X-ray shadow resembles the shape of a Turkish sword (Scimitar).[36] The roentgenogram in scimitar syndrome may also show hypoplasia of the right lung with secondary dextrocardia and pulmonary parenchymal abnormalities.[26,36]

Electrocardiography
Right axis deviation, right atrial enlargement, and RV hypertrophy with occasional incomplete right bundle branch block are the typical features [Figure 2].[33]
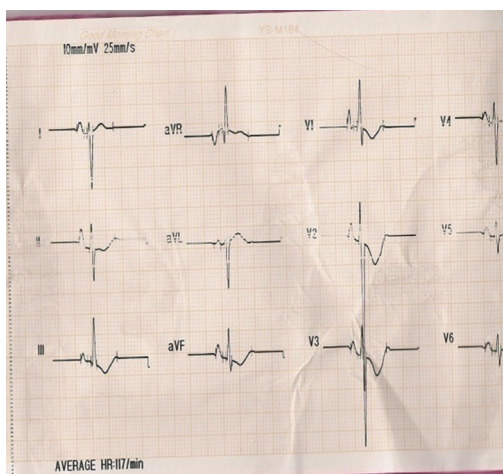
Figure 2: Electrocardiography tracings of the 9-year-old girl with total anomalous pulmonary venous connection. Note the presence of right axis deviation, right atrial enlargement, and right ventricular hypertrophy

Echocardiography

Echocardiography is an invaluable tool for evaluation of a patient with anomalous pulmonary venous connection. It is generally noninvasive and has good diagnostic sensitivity.[37-39] A major disadvantage is its limited field of view (echo window), which may hinder complete assessment of pulmonary venous structures and detection of more distant associated vascular anomalies in some patients.[14] To ensure accurate and reliable result, a careful step-by-step examination using multiple echocardiophy windows is necessary. The goals of echocardiography in patients with abnormal venous connection are to establish the diagnosis, locate the four pulmonary veins and their drainage sites, identify the venous confluence and its connection, determine whether there is obstruction to pulmonary venous flow and its mechanism, and identify the location and size of interatrial communication.[26,36] It also entails performing a complete anatomic and functional survey of all cardiovascular structures so as to exclude additional cardiovascular anomalies.[26]

The features common to all types of TAPVC are signs of RV volume overload: the most striking findings being a large RV with a compressed LV, a large RA with a small LA, and evidence of dilated pulmonary arteries (PAs). The interatrial septum bows toward the left while the interventricular septum deviates leftward and may show paradoxical motion.[26,35]

Another supportive evidence for diagnosis of TAPVC, besides RV volume overload, is inability to image the pulmonary veins entering the left atrium.[26] The course and diameter of the individual pulmonary veins, the orientation of the pulmonary venous confluence (and its relationship to left atrium), and the venous channels that connect with the systemic veins are assessed using

two-dimensional (2-D) echo and color flow Doppler mapping.[26] In supracardiac TAPVC, the abnormal pathways can be imaged in suprasternal notch short axis view while in infra cardiac type, the venous channel is best evaluated from the subcostal sagittal and transverse windows.[25,26,35] When TAPVC connects to the coronary sinus, the dilated sinus is easily imaged in the parasternal long axis or apical four chamber view.[26,35] For patients with pulmonary venous obstruction, 2-D echo reveals luminal narrowing with proximal dilatation of the pulmonary venous channel while color flow Doppler interrogation shows increased flow acceleration (turbulence) with loss of phasic variations. This is in contrast to the obstructed TAPVC where the pulmonary venous flow is characterized by a low velocity, phasic laminar flow pattern with brief flow reversal during atrial systole.[35]

Magnetic resonance imaging

Cardiac magnetic resonance imaging (MRI) has emerged as an increasingly useful technique for a complete noninvasive evaluation of the structure and function of the heart.[40] It is the preferred imaging technique for the evaluation of pulmonary venous structures especially in older, larger patients with poor echo windows.[14,26,34] It provides a wide-field imaging of the pulmonary veins and blood flow within them as well as adjacent cardiovascular and noncardiac structures.[26] The additional advantages of this imaging technique include lack of ionizing radiation, multiplanar capability, and the ability to acquire multiple imaging phases using a single intravenous (IV) bolus of gadolinium-containing contrast material.[14] The pulmonary venous system can be evaluated using a variety of MRI techniques.[14] Electrocardiography-gated spin-echo imaging and contrast enhanced MR angiography is used for anatomic information, while functional information is obtained from Cine Trufi (steady-state free precession), Cine Flash (gradient-echo), and Cine phase-contrast (Cine PC) sequences.[40] Multilevel steady state free precession cine MRI in axial, coronal, and oblique planes is performed across the chest and demonstrates the dynamic nature of blood flow, cardiac chambers, and AV and semilunar valves. Cine PC is used to determine flow direction and to quantify flow velocity and flow rate.[26]

Computed tomography

Computed tomography (CT) may be useful for imaging pulmonary venous structures in patients who are incompletely evaluated by echocardiography and who cannot, for whatever reason, undergo an MRI examination.[14] Axial and 3D reconstructed images both excellently depict anomalous pulmonary venous structures. The primary disadvantage of CT is that it requires the use of ionizing radiation. CT also requires the use of IV iodinated contrast material, which may adversely

affect renal function or, rarely, result in acute allergic-like reactions. Suboptimal timing of contrast bolus may result in poor opacification of pulmonary venous structures.[14]

Cardiac catheterization

The accuracy of echocardiography and the increasing availability of MRI have significantly reduced the need for diagnostic catheterization in the initial evaluation of patients with abnormal pulmonary venous connection.[26,37] Diagnostic catheterization and angiography are now used occasionally when a more detailed assessment of hemodynamic parameters and anatomic substrate is required. It is also indicated when significant pulmonary hypertension or vascular obstruction is suspected, to quantitate resistance and to study responses to vasodilators.[34] In a patient with TAPVC, the oxygen saturation in the RA (80%–95%), right ventricle, pulmonary artery, left atrium, left ventricle, and systemic arteries are nearly identical.[26] The RV and pulmonary artery pressures may be slightly elevated, equal to or higher than systemic pressure.[26] When selective pulmonary arteriography is performed, it is usually diagnostic and clearly outlines the anomalous pulmonary venous channel and its connections. Cardiac catheterization should be avoided as much as possible in patients with obstructed TAPVC as it may aggravate the already compromised clinical condition of the patient.[26]

MANAGEMENT

Children with TAPVC require surgery for survival. Medical management should be instituted to stabilize the patients before surgical intervention. Prostanglandin (PGE1) infusion should be commenced. PGE1 is believed to maintain the patency of the ductus venosus which encourages the decompression of an obstructed infradiaphragmatic TAPVC.[41] Balloon atrial septostomy or septectomy may be carried out if surgery cannot be done immediately.[35]

The goals of surgery include the creation of an unrestricted side to side anastomosis between the pulmonary venous confluence and left atrium.[42] The timing of the surgery depends on the type of TAPVD. Immediate surgery is indicated for those with pulmonary venous obstruction while those without obstruction but with intractable heart failure can be operated on between 4 and 6 months of life.[35]

PROGNOSIS

Factors that determine the prognosis of TAPVD include the size of the interatrial defect, the presence of

obstruction. Most unoperated cases die before their first birthday.[35,42] Surgical outcome is better with favorable sized pulmonary veins and confluence and long-term outcome is excellent with about 10% developing pulmonary stenosis requiring reoperation.[42,43]

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