Congenital Malformations Leading to Paradoxical Embolism

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KEYWORDS

• Paradoxical embolism • Congenital defects • Cyanosis • Shunt

KEY POINTS

- Any congenital cardiovascular malformation affording a bypass of the filtration of blood by the pulmonary circulation, a right-to-left shunt, can be associated with paradoxical embolism.
- The formation of the systemic venous system and the septation of the heart are complex embryologic processes that, when aberrant, create unusual connections and pathways.
- After correction or palliation, potential or residual right-to-left shunts may develop owing to leaks, changes in physiology, collateral formation, or pulmonary arteriovenous fistulae.
- Anticoagulation is essential to prevent paradoxical emboli; however, the hematologic disturbances and the most appropriate anticoagulation therapy in these patients require further evaluation.
- Surgery and transcatheter interventions are a major cause of stroke/paradoxical emboli in patients with congenital heart defects and preventive actions are of major importance.

INTRODUCTION

The role of the lungs and the pulmonary circulation as both oxygenator and filter of the systemic venous return was first described by *Ibn Nafis* Damashqi in his 'Commentary on the Anatomy of Canon of Avicenna' written in 1242.[1] A translation from the Arabic has been published as follows:

> … *after the blood has been refined in the right ventricle of the heart, it must reach the left ventricle where in it is impregnated with the vital spirit (pneuma) but there is no opening between these two ventricles as the septum between them is thick and solid and in contrast to what some people have imagined, there is no visible pores and also contrary to what Galen has said there are no invisible pores connecting them. And thus this blood after it is refined must flow via the vena arteriosa (pulmonary artery) to the lungs where it must spread and be mingled with air and its most delicate substance be refined and then flow through the arteria venosa (pulmonary vein) so that the blood that has been mixed with air and is ready to receive the vital spirit reaches the left chamber of the heart.*

This absolute separation of the right and left circulations and the "*refinement*" of blood in the pulmonary circulation are essential to prevent the passage of thrombotic material from the systemic venous system in to the systemic arterial circulation. Any breach of the intracardiac septae or circumvention of the pulmonary capillary network has the potential to cause a paradoxical embolus.[2,3] The most common causes are a patent foramen ovale (PFO), atrial septal defects (ASDs), and pulmonary arteriovenous malformations, which are discussed extensively in other sections of this issue (see Suradi HS, Hijazi ZM: Patent Foramen Ovale: Stroke and device Closure, in

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this issue; Leppert M, Poisson NS, Carroll JD: Atrial Septal Defects and Cardioembolic Strokes, in this issue; and Holzer RJ, Cua C: Pulmonary Arteriovenous Malformations and Risk of Stroke, in this issue). The purpose of this article is to discuss other forms of congenital cardiovascular malformations that are associated with paradoxical emboli and the possible pathophysiology in both untreated and corrected or palliated defects.

ISOLATED SYSTEMIC VENOUS ABNORMALITIES AND PARADOXICAL EMBOLI

The complex embryology of the systemic veins in the developing fetus affords many unusual malformations.[4] Three different paired venous systems—the cardinal, vitelline, and umbilical systems—undergo a series of staged organized processes of involution and attachment to each other, the sinus venosus, and other developing organs so that after birth the systemic venous return from the upper body drains via a right-sided superior vena cava (SVC) to the right atrium and a right-sided inferior vena cava (IVC) drains the lower body similarly.[5]

Persistent Left Superior Vena Cava

The most common form of isolated systemic venous abnormality is the persistence of the left SVC (LSVC) owing the failure of involution of the left common cardinal vein, which occurs in 0.3% of the population.[6] The persistent LSVC drains to the coronary sinus, which runs behind the left atrium to drain normally in to the right atrium and is, therefore, asymptomatic. However, rarely, there is partial or complete unroofing of the coronary sinus and the systemic venous return drains directly in to the left atrium. Persistent LSVC to the left atrium has been described as a cause of paradoxical emboli causing stroke after upper extremity trauma and there are a number of case reports of brain abscesses.[7,8] A connection between the innominate vein and the left upper pulmonary vein has also been described as a cause for transient ischemic attacks as have collaterals that have developed after right SVC obstruction.[9–13] These are probably not true LSVC, but a different persistent embryonic connections such as a vertical vein or levoatrial cardinal vein.

Right Superior Vena Cava Draining to the Left Atrium

This is a very rare anomaly, especially when it appears as an isolated finding, and may be owing to a sinus venosus defect of the RSVC in fetal life causing preferential flow to the left atrium with hypoplasia or involution of the proximal RSVC.[14] The right SVC, therefore, may drain solely to the left atrium or to both atria and is a very uncommon cause of cyanosis and paradoxical embolus.[15]

Inferior Vena Cava "Draining to the Left Atrium"

The formation of the IVC is more complex than the SVC and depends on 5 different segments, of which 4 have a bilateral presence, to connect and involute appropriately.[4,16] Even though multiple abnormalities of the IVC have been described there is no proven case of an IVC connecting directly to the left atrium.[5] In the fetus, oxygenated blood from the placenta flows through the IVC to the right atrium and is deflected across the foramen ovale, by the Eustachian valve, to the left atrium. The persistence of a large Eustachian valve associated with a patent foramen ovale after birth can similarly deflect some systemic venous blood to the left atrium, giving the impression that the IVC is directly connected.[4,5] Lampropoulos and colleagues[16] described a right-sided dual IVC drainage with anterior IVC draining to the right atrium and the posterior channel draining via a venous collateral to a right pulmonary vein into the left atrium. The patient presented with cyanosis and a transient ischemic attack and had had a cerebellar infarct documented on MRI 6 months previously. The pathologic specimen of a case report by Gardner and Cole[17] of a woman with cyanosis and an IVC directly connected to the left atrium was reevaluated by Geva[5] and demonstrated to be the incorrect diagnosis.

In situs solitus and situs inversus totalis, the anatomic relationships of the systemic veins are typically intact. However, in visceral heterotaxy–atrial isomerism the systemic, and pulmonary, venous connections can be anomalous and often are associated with complex intracardiac defects. The drainage of the IVC to the "left-sided" atrium has been described, but this is in fact a morphologic right atrium with or without anomalous pulmonary venous return.[4,5]

Ductus Venosus

The ductus venosus forms in the fetal liver and connects the (left) umbilical vein to the right hepatic vein to the suprahepatic segment of the IVC to deliver the oxygenated blood from the placenta to the right atrium.[4] The ductus venosus acts as a sphincter of the low resistance placental circuit to prevent excessive shunting and fetal cardiac volume overload and also directs blood in to the developing portal venous system.[4,18]