Congenital coronary artery fistulas: three different presentations in catheterization laboratory and review of literature

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Introduction

Coronary artery fistulas (CAF) are defined as a sizable connection between a large sub-epicardial coronary artery and a great vessel, a cardiac chamber or pulmonary circulation, bypassing the capillary bed. They are usually found incidentally during angiographic evaluation for coronary artery disease and are associated sometimes to other congenital defects; most of them are small and of no clinical relevance. We present three different clinical cases and the review of the literature discussing the prevalence of CAF, their morphology, clinical presentation and complications, diagnosis techniques and treatment possibilities.

Case 1

73 years old male patient, hypertensive, dyslipidemic, type 2 diabetic, ex-smoker, overweight (BMI 28.2), came to our outpatient clinic for a treadmill stress test, referring recurrent episodes of oppressive chest pain. His cardiovascular history began in January 2000 when, for angina associated to a positive stress test, he underwent a coronary angiography (CA) that showed significant proximal right coronary artery (RCA) disease, treated with percutaneous transcatheter coronary angioplasty (PTCA) plus stent implantation (3.0 x 13 mm). As collateral finding CA showed multiple coronary artery to-left ventricle fistulas. In February 2008 after a positive treadmill stress test and several recurrent episodes of chest pain, CA demonstrated atherosclerotic disease progression involving the middle part of left anterior descending (LAD) artery, so an other PTCA plus stent implantation (3.5 x 13 mm) was performed. In March 2010, because of new return of angina, he was newly referred to CA that showed coronary artery disease (CAD) of the second diagonal branch, so that another PTCA plus stent (3.0 x 15 mm) was executed. Subsequently, in September 2010, for

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unstable angina and evidence of in-stent restenosis of the stent previously implanted on the second diagonal branch, a drug eluting balloon (DEB) (2.75 x 14 mm) procedure was carried out. Between February 2011 and November 2011 another two CA were performed and showed no progression of CAD with good patency of stents and of the coronary treated with DEB technique. However, during all this period the patient complained multiple and recurrent angina episodes with moderate effort, so in June 2014 he came to our outpatient clinic for another functional evaluation. The electrocardiogram (ECG) at rest was normal (Fig. 1A) but during effort, at the second minute of the second step of Bruce protocol, ECG showed ST segment depression in lateral leads, V4 to V6 (Fig. 1B). His pharmacological treatment was composed by acetylsalicylic acid 100 mg/die, clopidogrel 75 mg/die, ramipril 10 mg/die, amlodipine 10 mg/die, atorvastatin 80 mg/die and oral hypoglicemic therapy. So we decided to perform another CA that confirmed good patency of the stent and diffuse fistulas connecting LAD to left ventricle (Figure 1C/D, Video 1). Because of the persistence of angina, inducible myocardial ischemia at functional tests and evidence of no progression of CAD, a “coronary steal” phenomenon through CAF was hypothesized. Because of the dimensions and number of the fistulas, it was not possible the closure (percutaneous or surgical approach), so pharmacological treatment with beta blockers was the best available option for this patient.

**Case 2**

62 years old patient, hypertensive, dyslipidemic, smoker, come to our attention for an arrhythmologic evaluation for an implantable cardioverter defibrillator implantation (ICD). He had during last years several syncopes preceded by palpitations and a previous diagnosis of obstructive hypertrophic cardiomyopathy (HC). A transthoracic echocardiogram was performed and confirmed the diagnosis of HC, mainly apical, with septum thickness of 21 mm, posterior wall of 14 mm (Fig. 2A), a dynamic ventricular gradient of 40 mmHg and a moderate mitral insufficiency. After the execution of a 24-hours ambulatory ECG Holter monitoring that showed multiple episodes of ventricular tachycardia, the patient underwent to CA evaluation to exclude the ischemic origin of the arrhythmias. CA study showed no CAD but evidence of multiple small coronary fistulas connecting LAD artery and circumflex artery to left ventricle and two large fistulas connecting proximal tract of LAD (Fig. 2B, Video 2) and RCA (Fig. 2C, Video 3) to pulmonary artery (PA). This was an incidental finding of a coronary anomaly associated to a cardiomyopathy. Patient subsequently underwent to ICD implantation; there was no indication for the closure of the fistulas.

**Case 3**

73 years old patient, hypertensive, dyslipidemic, previous smoker, overweight, was admitted to our ward for
ingravescent dyspnoea in the last month and nocturne paroxystic dyspnoea in the last days. His domiciliary medical therapy was: acetylsalicylic acid 100 mg/die, ramipril 2,5 mg/die, metoprololo 200 mg/die, simvastatin 20 mg/die and furosemide 50 mg/die. His history includes two heart attacks; the first one in 2006 managed with medical therapy and the second one in 2008, where CA showed bivascular CAD and a PTCA plus stent implantation on the proximal part of LAD artery was performed; a transthoracic echocardiogram showed a slight reduction (50%) of ejection fraction (EF). In our department he underwent to an echocardiographic evaluation that showed global hypokinesia, akinesia of the apex with an aneurysmatic shape and severe left ventricular dysfunction with an EF of 35% (video 4). We decided to perform another CA exam to evaluate the coronary disease and the possible revascularization strategy. The exam showed complete occlusion of right coronary and a marginal branch, good patency of the previously implanted stent on the proximal part of the LAD artery and significant stenosis in the middle part. The angiography also showed multiple large coronary artery fistulas (CAF) from the LAD artery to the right ventricle (Fig. 3A, video 5). The patient underwent to a second PTCA plus stent implantation in the middle tract of LAD artery.

Definition and Epidemiology

Coronary arteriovenous malformations (or CAF) are defined as a sizable connection between a large subepicardial coronary artery and a great vessel, a cardiac chamber or pulmonary circulation, bypassing the capillary bed. The first
The published description of a coronary fistula was done by Krause in a post-mortem case dated 1865 [1]. Haller and Little [2] described the diagnostic triad for CAF: an abnormal localization for a murmur thought to be due to a patent ductus arteriosus; a left to right shunt at the atrial or ventricular level; and a large, tortuous coronary artery at coronary angiography. It is a rare abnormality observed in 0.3% of autopsy series, in 0.2-1% of adults undergoing angiographic examinations [3] and 0.06% of children undergoing echocardiography [4]. At least 75% of CAF found incidentally are small and clinically silent. Their etiology is most frequently congenital (they represent only 0.4% of all congenital cardiac malformations) [5]. Approximately 10-30% of patients with a CAF also have another congenital cardiovascular anomaly [6]. The most commonly seen defects include variations of Tetralogy of Fallot, patent ductus arteriosus, and atrial septal defect. During the embryonic development, coronary arteries communicate with the great vessels and the chambers of the heart via sinusoids. Along with the development of myocardium the sinusoid gap are compressed and downgrade into normally calibrated capillary network. But if sinusoid gap persisted instead of being degraded it would turn to be CAF [7]. Occasionally may be detected after heart valve replacement, coronary artery bypass graft and cardiac transplantation [8], attributable to cardiac trauma [9] or to iatrogenic factors such as therapeutic chest irradiation [10], surgery for congenital defects [11], PTCA [12], repeated endo-myocardial biopsies after heart transplantation [13] or permanent pacing-lead erosion.

**Morphology and Pathophysiology (Shunt Issues)**

CAF vary widely in their morphological appearance and presentation. The feeding artery of the fistula may drain from a main coronary artery or one of its branches and is usually a dilated and tortuous artery terminating in one of the cardiac chamber or a vessel [14]. There may be multiple feeding arteries to a single CAF drainage point or there may be multiple drainage sites [15]. Fistulas originate from the RCA in about 52% of cases, from the LAD coronary artery in about 18% of cases and the circumflex coronary artery in about 18% of cases [16]. Over 90% of the fistulas from either coronary artery drain to the right sided heart chambers, coronary sinus, superior vena cava or the PA and less of 10% drain to the left side of the heart [17]. In some cases, especially adults, fistula may originates from both the coronary arteries and drain into the pulmonary trunk. Dual coronary artery fistulas involving both right and left coronary trees are uncommon accounting for only 5% of all cases [18]. Most of the fistulas originate proximally in the coronary tree, in the first segment of the involved coronary artery. Such an origin facilitates their closure by endoluminal or surgical intervention. Those located in the middle or distal segment usually drain into the ventricular chambers [3]. In an old classification Wearn et al. categorised CAF into three anatomical types [19]. I. Arterioluminal type: originates directly from the coronary arteries to the lumen of a heart chamber. They appeared to be more numerous in the ventricles than in the atrial. II. Arteriosinusoidal type: from the coronary arteries via myocardial sinusoids into the lumen of a ventricle. The communication is through the myocardial sinusoidal network. III. Arterio-capillary type: the fistula drains into the capillaries and then through the Thebesian system into a cardiac chamber. In a majority of cases the shunt is small and has no hemodynamic consequences; in other cases, the severity of the shunt, is responsible for hemodynamic abnormalities and the development of symptoms. The size of the shunt is determined by the size of the fistula and the pressure difference between the coronary artery and the chamber into which the fistula drains. When the fistula drains into the right side of the heart, the volume load is increased to the right heart as well as to the vascular bed, the left atrium and the left ventricle, having a circulatory physiology similar to an atrial septal defect; those that drain to the PAs are similar hemodynamically to a patent ductus arteriosus. When the fistula drains into the left atrium or the left ventricle, there is volume overloading of these chambers but no increase in the pulmonary blood flow. A coronary fistula that drains to the left atrium results in no left to right shunt, but does cause a volume load similar to mitral regurgitation; similarly, a CAF that drains to the left ventricle produces haemodynamic changes similar to aortic insufficiency [20]. Occasionally congestive heart failure occurs and rarely, myocardial ischemia [14]. It is clear that many of the symptoms and complications of the fistulas are greatly affected by size. Latson [20] in his review considered “small” fistulas those that result in little or no dilatation of the proximal coronary artery from which they arise, and are themselves no larger at any point than twice the normal expected proximate coronary artery diameter for the patient. Fistulas that, at any point, are larger than two times but less than three times the expected proximate normal coronary artery diameter, are considered to be “medium” size. Those with bigger dimensions are considered “large”.

**Clinical Findings and Consequences**

CAF are usually asymptomatic; they are sometimes discovered in children admitted for investigation of a continuous heart murmur; a small number of them may close spontaneously during childhood or may increase in size over time. Accumulating evidence suggests that the majority of patients do become symptomatic with advancing age, during the fifth or sixth decade of life in relation to the slow, progressive enlargement of the fistula and shunt
augmentation [21]. Only about 20% of patients < 20 years of age and with coronary fistulas are symptomatic versus nearly two thirds of those > 20 years of age, with an overall incidence of symptoms of 39% in a series of 174 patients [21]. Symptoms may include dyspnoea, angina and more rarely palpitations. Differential diagnosis include persistent duc tus arteriosus, pulmonary arteriovenous fistula, ruptured sinus of Valsalva aneurysm, aortopulmonary window, prolapso of the right aortic cusp with a supracristal ventricular septal defect, internal mammary artery to pulmonary artery fistula, and systemic arteriovenous fistula [22]. The most common clinical finding is the presence of a cardiac murmur over the mid-chest, that typically peaks in mid to late diastole rather than systole. If the fistula connects to the left ventricle, an early diastolic murmur is heard. The place where the continuous murmur is loudest depends on where fistula enters in the heart. With entry into the right atrium the murmur is loudest lower along the sternal border, with entry into the left ventricle the murmur is loudest near the apex [23]. Several complications are described in literature; one of them is “coronary steal phenomenon” from the adjacent myocardium causing myocardial ischaemia. Increased blood flow over the sistemic-to-pulmonary fistula may lower the distal intracoronary diastolic pressure and result in ischemia in absence of CAD [24, 25]. Most of these patients develop exercise angina and much less frequently myocardial infarction. Occasionally a coronary fistula may coexist with an atherosclerotic stenosis of the same coronary artery, contributing to the pathophysiology of myocardial ischaemia [26]. The location of the coronary fistula respect to the coronary stenosis may play a significant role in the pathophysiology of myocardial ischemia. When the fistula is located proximally to the coronary stenosis, ischemia occurs because of the coronary steal phenomenon associated with the diminished coronary flow over the stenosis. If the fistula is located distally to the stenosis, instead, ischemia is induced because of the reduction in coronary flow over the stenosis and myocardial irrigation with oxygen deprived blood from the PA. Anginal symptoms have disappeared with closure of the fistula in most patients with no distal disease [21]. Other complications include thrombosis, embolism (especially in young patient with cryptogenic stroke) [27], congestive heart failure, especially in patients with large left-to-right shunts, atrial fibrillation, pulmonary hypertension, endocarditis [28, 29], aneurysmal dilatation and rupture causing haemopericardium, which is the most dramatic, but fortunately rare, life threatening complication necessitating urgent surgery [30]. Endocarditis is a risk for any type of arterio-venous fistula and has been reported in 3% of patients (both pediatric and adult) with a medium to large CAF [21]. Standard endocarditis prophylaxis precautions shoud probably be observed by any patient with any type of CAF.

**Diagnostic Technique**

ECG may show the effects of left (or right) ventricular volume overload or ischaemic ST-segment changes may become apparent when the patient exercise on the treadmill [31]. Chest X ray is usually unhelpful; occasionally moderate cardiomegaly may be present when there is a large left-to-right shunt accompanied by signs of pulmonary congestion. Two dimensional and colour Doppler echocardiography are helpful, but it is difficult to define the detailed anatomy of the fistula; is more successful in children, in whom optimal acoustic windows are obtained. Multiplane transesophageal echocardiography can more accurately define and provide a high quality panoramic view of the origin, course, and drainage site of CAF [32, 33]. Magnetic resonance and computed tomography may help as the proximal coronary arteries or even the whole length of the fistula may be seen. Although non invasive imaging may facilitate the diagnosis and identification of the origin and insertion of CAF, the main diagnostic technique remains cardiac catheterization and CA. It helps to assess the haemodynamic significance of the fistula, to provide detailed anatomy and show the presence of concomitant atherosclerosis and other structural anomalies. In particular, the size, the origin, the course, presence of any stenoses and the drainage site; all characteristics that helps to plan the appropriate treatment strategy [14]. Several angiographic classification of CAF have been reported. One of these divides them into two types. Type 1: the fistula consists of one large channel or one or more small but discrete channels terminating into the pulmonary trunk. Type 2: the fistula is composed of a plexiform network of vessels [34].

**Management and Treatment: When and How to Close It**

There is controversy about the best management because both spontaneous regression and life threatening complications have been seen. Medical therapy with calcium channel blockers or beta blockers may be effective in controlling symptoms or angina [35, 36]; antiplatelet therapy is recommended, especially in patients with distal CAF and abnormally dilated coronary arteries [37] but the aim of treatment is the occlusion of the fistula preserving normal coronary blood flow. Symptoms, complications and significant shunt are the main indications for the treatment; including the presence of a large or increasing left-to-right shunt, left ventricular volume overload, myocardial ischaemia, left ventricular dysfunction, congestive heart failure and for prevention of endocarditis [14]. A rapid increase in size of cardiac fistulas is indicative of imminent rupture, and patient should therefore be referred to urgent
surgery. If fistulas are detected in infancy and are asymptomatic, conservative management with regular echocardiographic follow-up is appropriate, since several cases of spontaneous closure of small fistulas has been reported [38]. Instead, all those patients with moderate to severe shunt, large fistulas, even if asymptomatic, should be treated since the potential long-term complications are serious. Treatment options include surgery or transcatheter closure. Böörck and Crafoord [39] performed the first successful surgical closure in 1947 and the first therapeutic embolization of abnormal thoracic vessels was performed in 1974 by Zuberbuhler et al. [40]. Prior to the decision regarding the method of closure, surgical or percutaneous, the pathological presentation and precise anatomy of the fistula should be obtained by angiography. As most of these anomalies originate in the proximal vessel segments, as a single conduit that later develops into a maze of capillary vessels, they are easily accessible for endoluminal or surgical closure. Sometimes fistulas have multiple origins in the coronary artery and presents as a complex, plexiform, diffuse vascular anomaly resembling hemangiomas. In these cases fistula closure raises difficult technical problems for both the surgeon or the interventionist [3]. Surgery is associated with a low morbidity and mortality rate ranging from 0 to 6% [41]; myocardial infarction may occur in less than 5% of cases. Perioperative complications are directly related to the age of the patient: the incidence of complications reaches 23% for patients > 20 years whereas it is < 1% among those < 20 years old [21]. Complete occlusion may be achieved in >95% of cases after surgery [42]. Two techniques may be employed for definitive surgical closure of coronary fistulas: external ligation (“epicardial approach”) or direct suture of the fistulous ostium from within the recipient chamber (“endocardial approach”). In a group of 21 patients the incidence of angiographically confirmed long term fistula recurrence was 16.6% for patients submitted to the endocardial approach and 22.2% for patient in whom an epicardial approach closure was performed [6]. The risk of recurrence is due to the fact that there may be multiple fistulas present which are difficult to deal with by surgery. Surgical procedure is reserved to patients who are not suitable for coil embolization for the presence of a complex and distally located fistula, or for adjacent vessels at risk, or a large fistula, or in patients with associated congenital defects or severe CAD that require surgery. Catheter closure of the fistulas is considered an effective and safe alternative to surgery; it reduces the morbidity and mortality associated with open chest surgery, intervention related costs and hospital stay. The aim is to occlude the fistula artery as close to its termination point as possible, so to avoid any changes to occlude branches of the normal myocardium. Different types of embolization materials can be used such as detachable balloons, stainless steel coils or platinum microcoils or different chemicals, such as pure alcohol [43, 44]. In patients with coexisting CAD can be used covered coronary stent in the main coronary vessel. There are several determinants for the success of the procedure including the size of the fistula, its tortuosity, the presence of high flow in the fistula, aneurysmal dilatation of the feeding vessel and the choice of the exact point for the closure. With catheter closure techniques, complete occlusion may be achieved in >95% of the patients; catheter techniques may be difficult or impossible in a small percentage of patients due to extreme vessel tortuosity and inability to deliver a catheter far enough distally, presence of multiple drainage sites, presence of normal coronary branches too close to the drainage site to allow selective occlusion, or very small size of the patient [20]. Most patients remain asymptomatic for several years after a closure procedure; small residual leaks appear to be present in about 10% of cases; other residua and sequelae of the fistulas and closure procedure include persistent dilatation of the coronary artery, late stenosis in tortuous coronary arteries, arrhythmias, and late occlusion of dilated and tortuous coronary arteries with or without myocardial infarction [20]. Endoluminal closure should be performed in patients with a single proximal fistula origin, in case of advanced age and in the absence of other cardiac disease necessitating surgery. The risk of closure may be less, and the risk of late giant aneurysm higher, in CAF that arise near the coronary artery origin. Complications are rare and include coil embolisation [45] (especially in high-flow large fistulas or with undersized coils), ischaemic ECG changes, transient bundle branch block and myocardial infarction.

Conclusions

CAF are a rare congenital abnormality. The major part of them are not clinical relevant and are usually found incidentally during angiographic studies. Symptoms (angina, coronary artery steal phenomenon), complications and significant shunts are the main indications to closure. CA is the diagnostic choice’s procedure to evaluate the morphology and the characteristics of the anomaly and it allows to obtain informations about the preferred technique for closure. There are several therapeutic modalities for the large spectrum of clinical manifestations of CAF, including conservative pharmacological strategy, percutaneous transluminal embolisation and surgical ligation.

References


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