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EDITORIAL

The Mystery and Enigma of Spontaneous Coronary Artery Dissection☆

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First described in 1931 [1], spontaneous coronary artery dissection (SCAD) is a non-atheromatous disease of the coronary arteries that presents as an acute coronary syndrome (ACS) or death [2]. Primary or isolated SCAD, the focus of this editorial, is an idiopathic, non-syndromic disorder due to an intramural haematoma (IMH) and/or a dissection with an associated intraluminal thrombosis obstructing coronary artery blood flow, which is not iatrogenic or related to trauma. It is underdiagnosed as a cause of ACS as it is often not considered as a diagnosis in younger women presenting with chest pain, or a diagnostic angiogram or troponin levels are not obtained. Previously considered rare, SCAD is now recognised to be the cause of 2–4% of all cases of ACS, 24–36% of myocardial infarcts (MI) in women <50 years, and the commonest cause of an MI associated with pregnancy. SCAD predominantly affects women (92–98% of cases), who are relatively young (42–52 yrs) and have a low incidence of traditional risk factors [2–9].

In addition to primary or isolated SCAD, spontaneous dissection of coronary arteries can occur in association with connective tissue disorders [10] [e.g., Marfan's syndrome (fibrillin, FBN1, gene defect), Ehlers Danlos, type 4 (collagen, COL3A1, gene), cystic medial necrosis, Loeys-Dietz syndrome (LDS), type II (transforming growth factor B receptor, TGFBR2, or SMAD3 genes); atherosclerotic coronary artery disease; aortic dissection with coronary artery extension, or inflammatory disorders (e.g., systemic lupus erythematosus (SLE), Crohn's disease, ulcerative colitis). There are also isolated case reports of SCAD occurring in conjunction with Alport's syndrome, polyarteritis nodosa or autosomal dominant polycystic kidney disease [11–13].

Pathophysiology

Spontaneous coronary artery dissection results from a spontaneous tear in the intima of a coronary artery with a classical 'intimal flap' being evident by angiography, giving rise to the appearance of two lumens (true and false). This typical 'inside-out mechanism' results in an IMH that may also lead to an intraluminal thrombus. Alternatively, SCAD can be due to an IMH without intimal tear as a result of rupture of vasa vasora. With this 'outside-in' mechanism, there is no communication between the true and false lumens.

There is no single unifying disease process leading to SCAD, although, based on the finding of familial clustering of SCAD cases with involvement of mother-daughter, identical twin sisters, sister-sister, aunt-niece, and first-cousin pairs [14], and strong association of SCAD with fibromuscular dysplasia (FMD) (observed in 45–86% of cases), another vaso-occlusive disorder occurring predominantly in women, for which a genetic variant has recently been identified [15], as well as with migraine [16], it is likely that SCAD is a manifestation of a systemic arteriopathy due to a genetic predisposition that is manifested by the superimposition of an environmental factor. Such environmental factors might include exercise [increased shear stress due to enhanced sympathetic nervous system (SNS) activity], hypertension (increased shear stress), pregnancy (Valsalva; sudden drop in vasodilatory oestrogen levels postpartum), migraine medication (vasoconstriction), stress associated with bereavement (increased SNS activity), or increased progesterone (increased capillary fragility of the arterial media) etc.

Precipitating Factors

Risk factors for SCAD include intense physical exercise (isometric or aerobic), Valsalva manoeuvre (e.g., retching,

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vomiting, bowel movement, coughing), pregnancy (most commonly in the peripartum period) and/or a history of miscarriages, bereavement or other major stress, drug use (mainly cocaine), hormone therapy (oestrogen, progesterone, β-HCG, testosterone, corticosteroids), or coronary artery spasm, whereas the presence of joint hypermobility (present in ~30% of SCAD cases [10]), velvety and translucent skin, easy bruising or atrophic scars, might suggest an underlying connective tissue disorder, such as LDS.

Presentation

As with other causes of ACS, SCAD presents classically with chest pain, shoulder, or epigastric pain (96% of cases), with or without radiation to the arm (52%), less frequently with nausea or vomiting (24%), radiation to the neck (22%), diaphoresis (21%), dyspnoea (20%) and infrequently with back pain, dizziness, fatigue, headache or syncope (<20% each) [2]. Symptom severity can vary from mild to severe and cardiac dysfunction can cause heart failure, hypotension and dysfunction of other organs.

Diagnosis

Spontaneous coronary artery dissection manifests as an ACS and thus is diagnosed by electrocardiogram (ECG) findings and serial troponins. ECG changes may be absent or subtle (minor ST/T changes), or may show a typical ST-segment elevation MI (STEMI). The ratio of SCAD presentations with STEMI versus non-ST-segment elevation MI (NSTEMI) varies from ~1:1 to 1:3. The standard test to diagnose SCAD is coronary angiography ± intracoronary nitroglycerin. Diagnostic angiographic features include: absence of atheroma, a radiolucent flap, contrast staining of the arterial wall; the beginning and end of an angiographic abnormality (a stenotic segment ± contrast staining) being on a side branch, and long narrowing of lumen calibre (either smooth and linear or stenotic)—three of these five criteria being present in 93% of cases [5]. Based on angiographic features [2], lesions are classified as type 1, 2 or 3 (Table 1, Fig. 1).

With type 3 lesions and to enhance visualisation of the IMH or intimal tear, intravascular imaging using intravascular ultrasound (IVUS) or optical coherence tomography (OCT) is helpful. IVUS provides good visualisation of the IMH and false lumen, but is poor at delineating the lumen-intimal interface. OCT is superior to IVUS for visualising the intimal tear, intramural thrombi, false lumens and IMH, but has more limited optical penetration and shadowing.

Non-invasive tests, such as computed tomography (CT) or magnetic resonance (MR) coronary angiography, have limited utility as they may miss small and distal lesions. However, non-invasive imaging limits the risk of iatrogenic (catheter-related) coronary dissection, and may be useful for assessing healing after SCAD. Typically, SCAD affects the left anterior descending coronary artery (LAD; 60% of cases), left circumflex (38%), left main coronary artery (LMCA; 8%), right coronary artery (RCA; 7%) and, less commonly, more than one vessel (>1%), with the LAD being involved more commonly in women and the RCA in men [2]. Recurrent episodes of SCAD invariably affect different arterial segments than the initially dissected vessel [17].

Clinical Management

Conservative medical management is recommended in patients without ongoing chest pain or ECG changes and usually is associated with spontaneous healing of the affected segment on subsequent angiography [18]. Long-term aspirin and β-blockers are commonly prescribed, although the rationale for using anti-platelet or anti-coagulant therapy, including aspirin, in patients with an IMH without an intimal tear, is tenuous, given that such therapy may increase bleeding within the vessel wall. Intravenous heparin should not be given or should be stopped in such patients once the diagnosis has been made. Thrombolytic therapy, dual antiplatelet therapy and glycoprotein IIb/IIIa inhibitors should be typically avoided. There is also little rationale for the use of statins unless the patient is dyslipidaemic. Angiotensin converting enzyme inhibitors or angiotensin receptor blockers

Table 1 Angiographic types of SCAD.

Type of SCAD	Percentage of cases	Angiographic description
Type 1	29-48%	False lumen readily identifiable with a linear filling defect or dissection flap.
Type 2	52-67%	Diffuse stenosis of varying severity and length with the IMH-induced narrowing being bordered by normal artery segments both proximally and distally (Type 2A lesion), or the narrowing extending to the apical tip of the artery (Type 2B lesion).
Type 3	2-4%	Focal or tubular stenosis (length typically <20 mm) that mimics atherosclerosis. Importantly, apart from the culprit lesion the remainder of the coronary tree looks normal, or there may be increased tortuosity of the coronaries but no plaque.

Abbreviation: IMH, intramural haematoma.