

# Spontaneous Coronary Artery Dissection in a Woman on Fenfluramine

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*Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome, cardiogenic shock, and sudden cardiac death in women of reproductive age who have no traditional risk factors for coronary artery disease. The etiology, prognosis, and treatment of SCAD remain poorly defined. Coronary angiography is the gold standard for diagnosis. Management includes medical therapy and revascularization procedures using percutaneous intervention and coronary artery bypass grafting. Possible mechanisms of SCAD include rupture of atherosclerotic plaque or vasa vasorum, hemorrhage between the outer media and external lamina with intramedial hematoma expansion, and compression of the vessel lumen. We report a case of SCAD in a 39-year-old woman presenting with ST-elevation myocardial infarction midway through her menstrual cycle. Her medications included fenfluramine for obesity and hydrochlorothiazide, amlodipine, and atenolol for hypertension.*

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• Fenfluramine • Oral contraceptives

A 39-year-old woman with obesity (body mass index of 34 kg/m<sup>2</sup>) and hypertension presented to the emergency department complaining of sustained substernal pain with irradiation to the left arm and diaphoresis. The patient had no angina or signs of heart failure. In the previous 5 years, she had lost 30 pounds while on fenfluramine therapy. Her hypertension had been poorly controlled by hydrochlorothiazide, amlodipine, and atenolol. The patient had no history of estrogen replacement therapy, recent pregnancy,

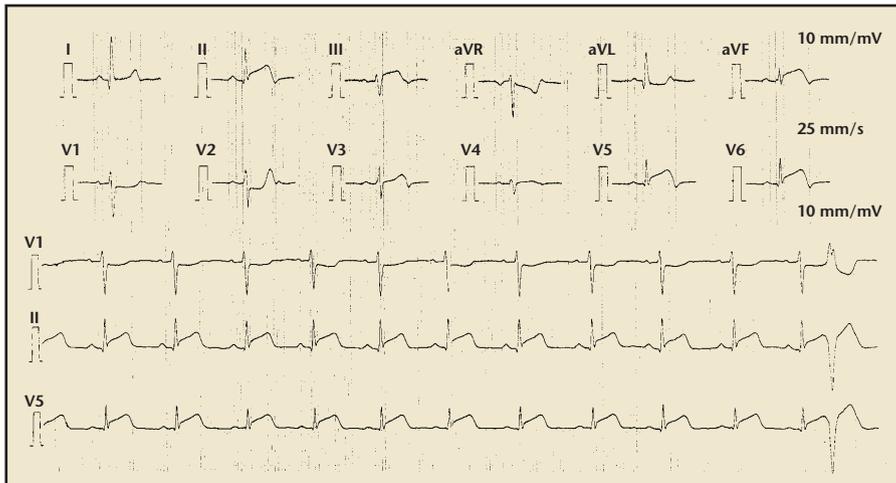


Figure 1. Twelve-lead electrocardiogram demonstrating ST elevation over inferior and lateral leads.

smoking, alcoholism, or addiction to drugs, including cocaine. She had no family history of connective tissue disorders, premature coronary disease, or sudden cardiac death.

The admission electrocardiogram scan exhibited an inferolateral ST segment indicative of inferolateral ischemia (Figure 1). The patient was in the middle of her menstrual cycle, but otherwise had no contraindication to thrombolytics. She received a recombinant plasminogen activator followed by heparin, aspirin, intravenous nitroglycerin, and beta-blockers. She was transferred by airplane to a tertiary center 60 miles away, where she continued to have chest pain for 2 hours after arrival, with persistent ST-segment elevation. She was taken emergently to coronary angiography, which revealed a spiral spontaneous coronary artery dissection (SCAD) of a distal, large, obtuse marginal branch of the left circumflex artery (Figure 2). The rest of the coronary vasculature was disease-free. The left ventricular ejection fraction was calculated as 60%.

An attempted percutaneous coronary intervention (PCI) was unsuccessful due to the spiral nature of the dissection. The large vessel size and

the failed PCI prompted suggestion of coronary artery bypass grafting, but the patient declined in favor of medical treatment. She received glycoprotein IIb/IIIa inhibitors for 18 hours. The peak troponin I level was 210. She did well during the hospital course and had no heart failure symptoms. Upon hospital discharge, she discontinued use of fenfluramine. Four weeks later, an adenosine sestamibi stress test showed normal results.

**Discussion**

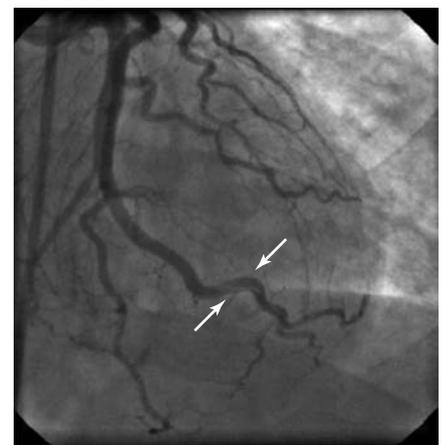
SCAD is a rare cause of acute coronary syndrome, cardiogenic shock, and sudden cardiac death in women of reproductive age who have no traditional risk factors for coronary artery disease.<sup>1</sup> The first case was described in 1931 by Pretty,<sup>2</sup> during an autopsy of a 42-year-old woman who had died suddenly after experiencing chest pain. The incidence of SCAD varies between 0.1% and 1.1%;<sup>3</sup> it is twice as common in women as in men.<sup>4</sup> Because sudden death occurs in up to 50% of cases, the true incidence of this abnormality in the general population is underestimated.<sup>1</sup> The left anterior descending artery is the most commonly involved artery

in women (66% to 75% of cases), whereas the right coronary artery predominates in men (50% of cases).<sup>3-5</sup>

SCAD has been reported in association with multiple factors, including the peripartum period, the early puerperium period, connective tissue disorders, vasculitis, extension of aortic dissection, chest wall trauma (Table 1),<sup>1</sup> and use of certain medications, such as oral contraceptives (Table 2). A recent systemic review reported that 41% of cases of SCAD occurred in women in the peripartum period, predominantly within 2 weeks after delivery.<sup>1,3,4</sup> Another study found that 22% of SCAD cases in women occurred during pregnancy and 78% occurred in the postpartum period.<sup>6</sup>

The pathogenesis of SCAD is unclear, and various mechanisms have been proposed. Rupture of atherosclerotic plaque or vasa vasorum is a possible mechanism.<sup>3</sup> Hemorrhage between the outer media and external lamina with intramedial hematoma expansion and compression of the vessel lumen has been noted.<sup>7</sup> Other suggested mechanisms include increased shear stress, connective tissue necrosis, and

Figure 2. Coronary angiogram revealing spiral dissection of the distal obtuse marginal branch (arrows).



**Table 1**  
Factors Associated With Spontaneous Coronary Artery Dissection

Middle age
Female sex
Peripartum or puerperium period
Use of oral contraceptives
Connective tissue disorders
Vasculitis
Fibromuscular dysplasia
Hypertrophic cardiomyopathy
Cocaine abuse
Blunt chest trauma
Intense physical exercise
Sexual intercourse
Presence of atherosclerotic disease and risk factors for atherosclerotic disease
Traumatic cardiac catheterization and cannulation for percutaneous coronary intervention
Extension of aortic dissection

localized vasculitis with eosinophilic infiltration.<sup>1,3</sup>

The patient described in this report sustained a SCAD about 2 weeks postmenstrually after long-term therapy with fenfluramine and a combination of hydrochlorothiazide, amlodipine, and atenolol for apparently refractory hypertension. SCAD and, in general, arterial dissection appear to occur frequently during pregnancy and peripartum. We

**Table 2**  
Medications Associated With Spontaneous Coronary Artery Dissection

Combined oral contraceptives <sup>14-20</sup>
5-Fluorouracil <sup>21</sup>
Thrombolytic therapy <sup>13</sup>
Heparin <sup>22</sup>

surmise that the occurrence of SCAD midway through the menstrual cycle was related to the periovulatory hormonal dynamics that typically involve a surge in luteinizing hormone, estradiol, and progesterone. Effects of such hormonal changes on the biology of arterial cells are complex and may determine both endothelial and vascular smooth muscle changes accounting for arterial vasorelaxation. Whether acute loosening of matrix proteins under the release of metalloproteinases contributes to the acute arterial response is uncertain.<sup>8</sup>

Another contributing factor could be that the patient developed resistant hypertension while taking fenfluramine. Hypertension alone is an independent contributor to the etiology of SCAD.<sup>9</sup>

Coronary angiography is the gold standard in diagnosing SCAD. Even when coronary angiography is performed, SCAD may go undiagnosed if the vessel is totally occluded or if classic signs of dissection, like a radiolucent intimal flap or the presence of extraluminal contrast after washout of dye from the remainder of the vessel, are not appreciated.<sup>10</sup>

**Management**

Management of SCAD includes medical therapy and revascularization procedures using percutaneous intervention and coronary artery bypass grafting. The optimal treatment is unknown. There are favorable outcomes with medical treatment using antiplatelet therapy, beta-blockers, and nitrates.<sup>11</sup> Alternatively, immunosuppressive therapy in patients who are not candidates for revascularization has been reported.<sup>12</sup> Thrombolytic therapy has been a successful treatment. However, the theoretical risk of propagating the intramural hematoma and dissection as a complication of thrombolytic

therapy has been documented.<sup>13</sup> Angioplasty alone, intracoronary stenting, and surgical revascularization have all been reported as therapy for SCAD.

**Conclusion**

SCAD should be considered in patients presenting with angina during the periovulatory or postovulatory phase of the menstrual cycle. In addition, this case illustrates that conservative medical treatment is an alternative for coronary artery bypass surgery in patients unsuitable for PCI. ■

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### Main Points

- Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome, cardiogenic shock, and sudden cardiac death in women of reproductive age who have no traditional risk factors for coronary artery disease.
- A recent review reported that 41% of cases of SCAD occurred in women in the peripartum period, predominantly within 2 weeks after delivery.
- Possible mechanisms of SCAD include rupture of atherosclerotic plaque or vasa vasorum, hemorrhage between the outer media and external lamina with intramedial hematoma expansion, and compression of the vessel lumen.
- Coronary angiography is the gold standard in diagnosing SCAD.
- Management of SCAD includes medical therapy and revascularization procedures using percutaneous intervention and coronary artery bypass grafting.