Coronary Slow Flow Phenomenon and Risk for Sudden Cardiac Death Due to Ventricular Arrhythmias

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ABSTRACT

We report a case of coronary slow flow phenomenon (CSFP) in a patient who underwent coronary angiography due to anginal chest pain, and recurrent syncope with complete normalization of flow after intracoronary adenosine. The patient was noted to have multiple episodes of nonsustained ventricular tachycardia (VT) on holter monitor and increased QTc dispersion on surface electrocardiogram (ECG). He responded very well to oral dipyridamole therapy with complete resolution of his symptoms and no episodes of VT on the event recorder at 3 mo. We reviewed the diagnosis and clinical features of CSFP and its association with increased QTc dispersion, and the role of oral dipyridamole therapy in this condition.

Key words: arrhythmia, syncope, cardiac catheterization, diagnostic interventional electrocardiography, ambulatory electrocardiogram, endothelial function dysfunction

Introduction

The significance of coronary slow flow phenomenon (CSFP) in patients with angina is unclear and what therapy is effective is unknown. Recently CSFP has been found to be associated with increased QTc dispersions, which may be an independent risk factor for ventricular arrhythmias and sudden cardiac death. So far no case report of ventricular arrhythmias in association with CSFP and suppression with dipyridamole therapy has been reported.

Case Report

A 59-y-old Caucasian male presented to the emergency room with a 1 h history of left-sided chest tightness, along with shortness of breath and diaphoresis. He also mentioned that for 3 wk prior to this presentation he had 2 episodes of syncope preceded by palpitations. His past medical history was significant for hyperlipidemia, tobacco abuse, and occasional marijuana abuse. His home medications included aspirin, metoprolol, simvastatin, and nitroglycerin on an as needed basis. He has no family history of syncope, sudden cardiac death, or any seizure disorder. He came to the emergency room with chest pain that responded to sublingual nitroglycerin with complete resolution of his symptoms.

His physical examination was within normal limits. His initial electrocardiogram (ECG) showed normal sinus rhythm with frequent premature ventricular complexes (PVCs) and non specific ST-T changes with normal QTc. Acute myocardial infarction was ruled out with serial cardiac enzymes. His urine drug screen was positive for marijuana but negative for cocaine and any other drugs. His fasting lipid panel showed low-density lipoprotein (LDL) to be 158 and triglycerides (TRG) to be 69, the rest of the blood tests, including electrolytes, were within normal limits. A transthoracic echocardiogram was obtained and was also within normal limits. His carotid duplex scan and computed tomography (CT) scan of the head were within normal limits as well.

The patient was taken to the cardiac catheterization laboratory for coronary angiography that showed no epicardial coronary stenosis. There was slow coronary flow in all 3 coronary arteries. His corrected thrombolysis in myocardial infarction (TIMI) frame count for the left anterior descending artery (LAD) was 82 (normal being 21±2), which improved to 16 with intracoronary adenosine (Figure 1). The TIMI frame count for the right coronary artery (RCA) was 58 and the circumflex artery was 52. The patient was initially treated with oral nitrates, the calcium channel blocker felodepine, and aspirin. He was discharged home with a 48-h Holter monitoring, which showed 2 episodes of nonsustained ventricular tachycardia (VT) (10 beats each) (Figure 2). Further analysis of his ECG showed QTc dispersion of 80 msec (Figure 3). The patient was then seen in the clinic and was started on dipyridamole therapy since his epicardial coronary vessels showed significant improvement in coronary flow with adenosine injection. At 3 mo follow-up, he was asymptomatic with no significant findings on the event recorder.

Discussion

The CSFP was first described in 1972, and remains scantly studied and poorly understood.[1] Beltrame and colleagues suggested that CSFP should be recognized as a separate disease entity.[2] It has been suggested that this phenomenon should be distinguished from occurrence of slow flow in the context of coronary reperfusion therapy, coronary artery spasm, coronary artery ectasia, myocardial

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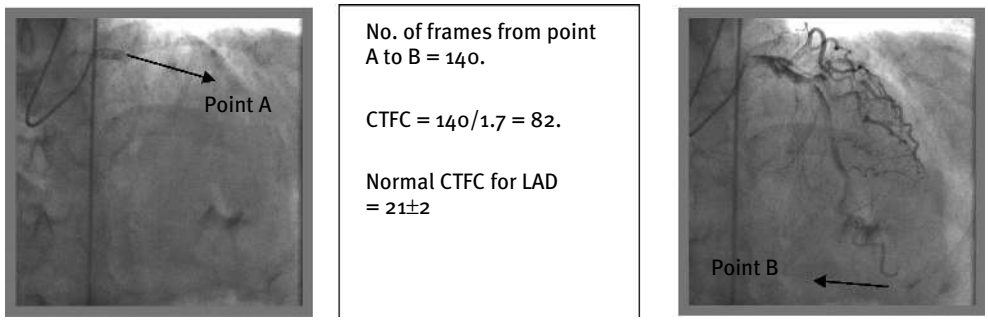

Corrected TIMI frame count using the Gibson's method. Point A = the frame count when the ostium of the vessel gets opacified. Point B = the frame count when the pre-specified most distal vessel segment gets opacified. CTFC = Corrected TIMI frame count. 1.7 is the correction factor used for the LAD due to its longer length.

(A)

Frame count from point A to B = 28. Corrected TIMI frame count for LAD = 28/1.7 = 16. (After intracoronary adenosine)

(B)

Figure 1: (A) Corrected TIMI Frame Count for LAD showing slow coronary flow. (B) The CTFC after intracoronary adenosine of 40 ug in LAD.

dysfunction, valvular heart disease, and certain connective tissue disorders involving coronary microvasculature.[3]

The overall incidence of CSFP has been reported as 1% among patients undergoing coronary angiography, especially in patients presenting with acute coronary syndrome.[3] In the TIMI-IIIA study, the incidence of CSFP was approximately 4% among patients who presented with unstable angina and had no or insignificant epicardial coronary artery disease.[4] The corrected TIMI frame count (CTFC) introduced by Gibson,[5] is a quantitative and reproducible index of coronary artery flow. It represents the number of cine frames required for contrast to reach a prespecified distal coronary artery landmark.[5] Coronary slow flow phenomenon is defined as CTFC greater than 2 standard deviations (SD) from the normal published range, which is 21±3.[5]

Coronary slow flow phenomenon is commonly seen in males who are current smokers.[6] This is in contrast to syndrome X patients, (patients with chest pain and normal coronary arteries), which is predominantly a disorder of postmenopausal females.[6] Compared with other syndrome X patients, those with CSFP present more often with rest pain requiring urgent hospital admission. Both resting ECG abnormalities as well as positive exercise stress tests are more frequent in patients with CSFP as compared with patients having normal coronary flow.[4] Myocardial perfusion scintigraphy shows reversible perfusion abnormalities in 28%–75% of patients with CSFP.[7,8] Over 80% of the patients with CSFP experience recurrent chest pain, and one third of them require readmission for an acute exacerbation.[2,9] Occasionally, patients may present with evidence of acute myocardial infarction.[10] The exact pathophysiological mechanism for CSFP is not known. Different theories have been postulated about the cause of small vessel dysfunction based on observations including microvascular tone dysfunction, endothelial thickening in small vessels,[11] patchy fibrosis in the biopsy specimen taken from the right ventricle,[12] and impaired endothelial release of nitric oxide (NO).[13]

Dipyridamole is an antiplatelet and vasodilator agent used mainly for stroke prevention as an adjunctive agent with aspirin. Dipyridamole has been shown to increase the extracellular adenosine level by inhibiting its re-uptake

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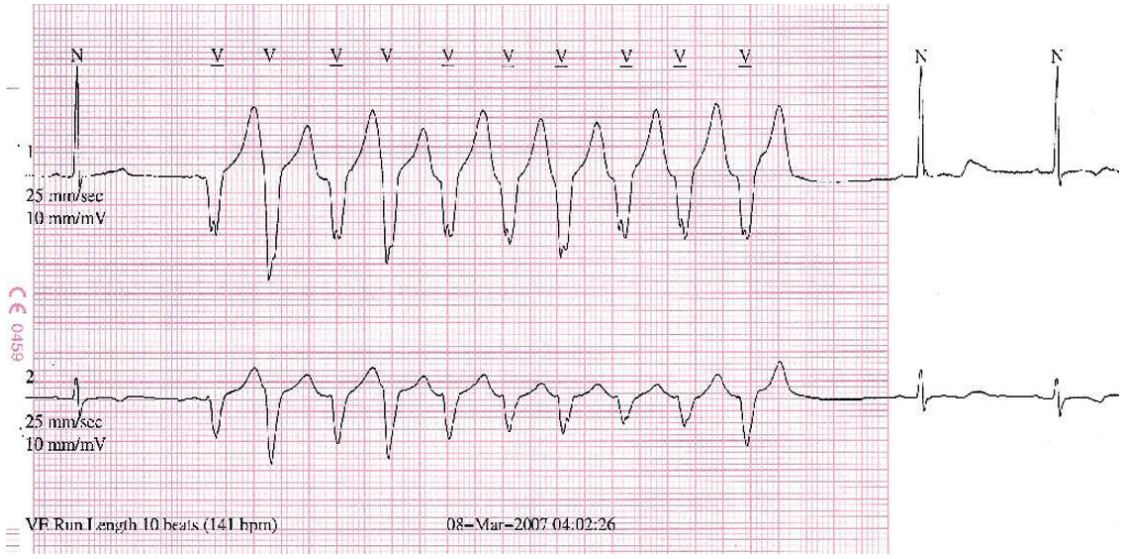

Figure 2: Holter tracing showing 10 beats nonsustained VT.

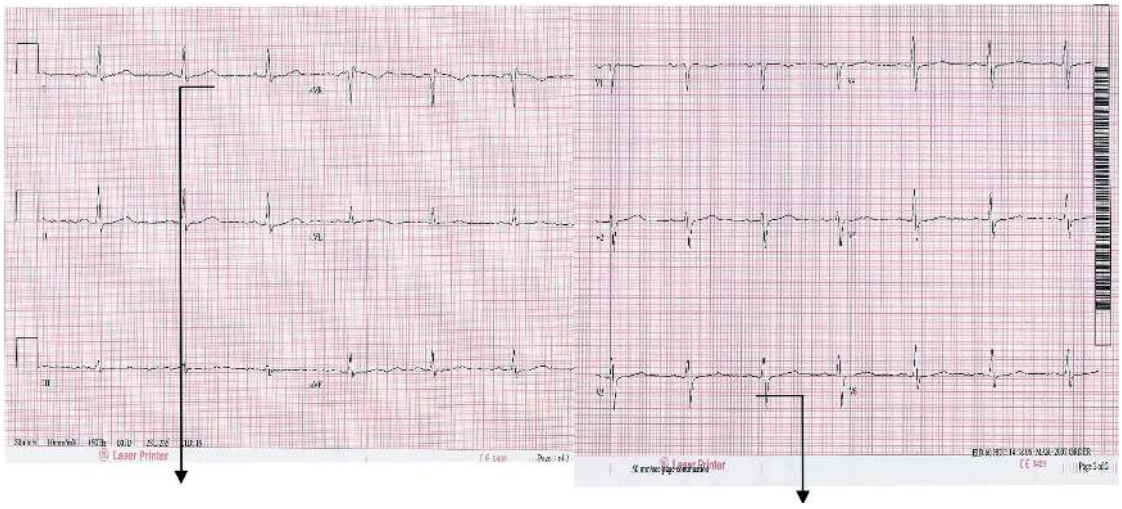

Figure 3: Twelve-Lead ECG at 50 mm/sec speed showing QT dispersion of 60 msec and QTc dispersion of 100 msec.

by erythrocytes and vascular endothelium in the coronary arteries, thus causing coronary arterial dilation.[14,15] Oral dipyridamole therapy has been shown to normalize the flow in patients with CSFP.[16] However, questions have been raised whether the normalization of the coronary flow could in fact be due to the effect of the medicine, or caused by the remission since CTFC improved but did not become normal in patients who had repeat angiography without any treatment, as observed by Beltrame.[9]

The QTc dispersion is defined as the difference between the maximum and minimum QTc interval in a standard 12-lead ECG, which indicates the dispersion of ventricular repolarization. Increased QTc dispersion has been linked to increased incidence of ventricular arrhythmias and has been associated with an adverse prognosis in a variety of patient populations.[17,18] The QTc dispersion of more then 60 msec has been correlated with increased risk for sudden cardiac death in the elderly.[17] In a study of 49 patients, Atak et al.[19] has shown increased QTc dispersion in patients with CSFP raising the concern regarding the association of this syndrome with sudden cardiac death due to ventricular arrhythmia.[18] Aksakal et al.[20] reported a case of apical hypertrophic cardiomyopathy, slow flow in LAD, and ventricular arrhythmias. However, the presence of QTc dispersion was not reported and whether the VT was related to the hypertrophic cardiomyopathy or the CSFP is unclear. Our case supports a possible association between CSFP and ventricular arrhythmias, which needs to be studied further.

Conclusion

This case supports a relationship between the angiographic curiosity of slow coronary flow and clinical manifestations of cardiac disease, including life threatening cardiac arrhythmias, as well as the role of dipyridamole therapy in this condition.

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