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CASE REPORT

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Clinical manifestations of slow coronary flow from acute coronary syndrome to serious arrhythmias

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Abstract

Slow coronary flow is an angiographic phenomenon characterized by delayed opacification of vessels in the absence of any evidence of obstructive epicardial coronary disease. In this article, we present serious clinical manifestations of extremely slow coronary flow in two hypertensive patients with preserved ejection fraction in echocardiographical examination: a 57 year-old woman with acute coronary syndrome and temporary ST elevation; and a 65 year-old man with atrial tachycardia which was leading to sudden arrest of circulation.

The woman was admitted to hospital due to recurrent syncope and chest pain. Because of severe bradycardia, an AAI pacemaker was implanted. Coronary angiography without evident obstructive lesion revealed extremely slow flow of dye through arteries.

The man was admitted to hospital because of heart palpitations (paroxysmal atrial tachycardia, PAT) followed by chest pain. During hospitalization, a sudden arrest of circulation in the course of supraventricular tachycardia of 220/min with atrioventricular conduction of 1:1 occurred. Coronary arteriography did not show any occlusions in the coronary arteries, although extremely slow dye flow was seen. Electrophysiological examination revealed arrhythmia of the left atrial (PAT) (tricuspid valve anulus mapping) without induced ventricular arrhythmia. Because of symptomatic bradyarrhythmia, a VVI heart pacemaker was implanted. Over a 12-month observation, his heart rate remained under control, and the patient did not complain of chest pains or heart palpitations. (Cardiol J 2009; 16, 5: 462–468)

Key words: slow coronary flow, acute coronary syndrome, arrhythmia

Introduction

Slow coronary flow (SCF) is a phenomenon detected by angiographic examination of coronary arteries. It is characterized by slow velocity flow of dye through the coronary artery in the absence of any evident obstructive lesion in it. The phenomenon was first described by Tembe et al. in 1972 [1]. Classic SCF does not include the re-flow and slow re-flow phenomena which are observed during angioplasty, slow flow velocity of dye in ecstatic vessels, cardiomyopathy, connective tissue disorders and other disorders which may have an impact on the flow in microcirculation [2].

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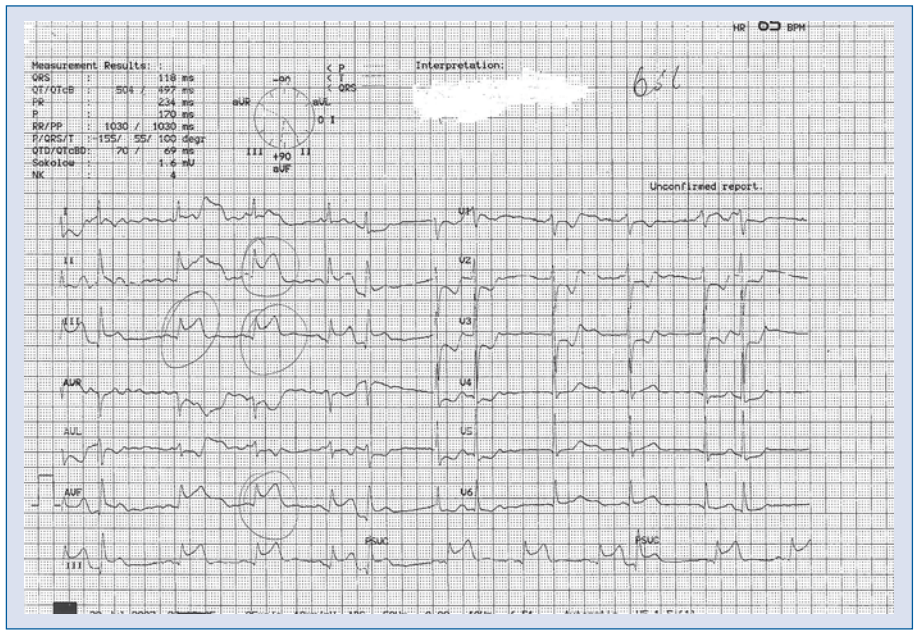

Figure 1. Electrocardiogram in the female patient during chest pain. ST elevation in II, III, avF leads and reciprocal changes of ST segment in the leads: I, AVL and V1–V3 (ST depression to 1.5 mm).

Furthermore, SCF is not a part of the cardiological X syndrome, but constitutes a separate disease entity, although both phenomena show disorders in microcirculation. However, in cardiological X syndrome, there is no slow flow velocity of dye in coronary vessels [2]. Many researchers emphasize the influence of SCF on the electrical disorders of the heart with the tendency for rhythm disorders.

This article presents two cases of patients with extremely slow coronary flow, manifested clinically by acute coronary syndrome with temporary ST segment elevation, and in the second case by atrial tachycardia leading to sudden arrest of circulation.

Case 1

Case 1 is of a 57 year-old woman (registration number 12549/07) suffering from arterial hypertension, alcohol abuse and Parkinson's disease. She has undergone cholecystectomy because of nephrolithiasis. In the past, she suffered from acute pancreatitis and had kidney cysts. She was admitted to hospital due to recurrent syncope, paroxysmal dyspnoea and pain in the chest. Electrocardiography revealed sinus bradycardia of 40 beats/min with no changes in ST segment. Echocardiographic (ECG) examination demonstrated left ventricular muscle hypertrophy of 14 mm, without segmental disorders in contractility, with normal ejection fraction of left ventricle (approximately 59%) and with normal valves. A 24-hour Holter electrocardiography monitoring revealed sinus node dysfunction with symptomatic sinus bradycardia with a rate below 40 beats/min during waking hours. Premature supraventricular beats (2 786/24 h) were registered without atrioventricular conduction disturbances.

Sick sinus syndrome with decreased cerebral blood flow was diagnosed. Indications for permanent atrial pacing were determined and an atrial-inhibited pacing system (AAI) was implanted. Five days after the operation, in the morning, the patient felt an acute 20-minute pain in the chest followed by hypotonia and fainting accompanied by 2 mm ST elevation in ECG above the inferior wall and reciprocal changes of ST segment in the leads: I, AVL and V1–V3 (ST depression to 1.5 mm) (Fig. 1). The coronary arteriography performed immediately did not show any atherosclerotic occlusions. At the same time, however, extremely slow flow of dye through the coronary arteries was detected. TIMI frame count for the left anterior descending coronary artery was 62.4 ± 3.5 frames (reference value 36.2 ± 2.6) and of the right coronary artery 58.8 ± ± 3.1 (reference value 20.4 ± 3) [3]. There was no increase in the serum markers of cardiac damage and no evolution in ST-T segment of the ECG record was observed. Therapy with antiplatelet agents (aspirin and clopidogrel) as well as the angiotension converting enzyme inhibitor, amlodipine and statine was performed. During a 12-month follow-up the patient was well with no complaints. No chest pain or syncope were observed.

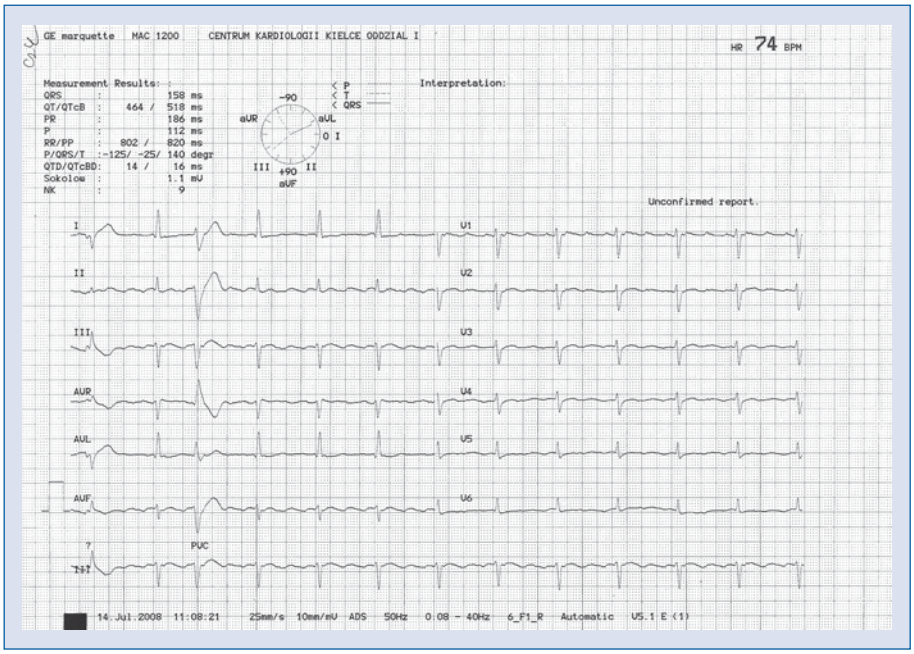

Figure 2. The electrocardiogram record (male patient) with paroxysmal atrial tachycardia 210 beats/min with relationship between P waves and QRS complexes 3:1 and ventricular rate of approximately 70 beats/min.

Case 2

Case 2 is of a 65 year-old man (registration number 12783/08) suffering from arterial hypertension, insulin treated diabetes and the symptoms of obstructive sleep apnea. He was admitted to the Cardiology Department because of heart palpitations followed by exercise-related pain in the chest. The ECG record showed paroxysmal atrial tachycardia (PAT) 210 beats/min with changing relationship (2:1, 3:1, 4:1) between P waves and QRS complexes and average ventricular rate of approximately 70 beats/min (Fig. 2). Laboratory findings showed a minimal increase in troponin T concentration, normal concentration of creatine kinase (CK-MB), dyslipiemia (lower concentration of HDL cholesterol, increased concentration of triglycerides and normal concentration of total cholesterol and LDL cholesterol — the patient was undergoing treatment with statine). The concentration of glycosylated hemoglobin reached the level of 8.4%, which testified to the lack of diabetes control in the last three months. The level of thyrotrophic hormone and inflammatory parameters (blood sedimentation rate and protein level) was normal. A chest X-ray showed symptoms of liquid retention at the bottom of the lungs and revealed enlargement of the heart chambers. Echocardiography examination demonstrated dilatation of the left atrium and right ventricle, and hypertrophy of the left ventricular muscle. Ejection fraction of the left ventricle was about 50% without disorders in segmental myocardial contractility but with impaired diastolic relaxation. The morphology and the function of the valves were normal. The coronary arteriography did not show any occlusions in coronary arteries, although extremely slow dye flow velocity was seen. Thrombolysis in Myocardial Infarction (TIMI) frame count for the left anterior descending coronary artery was 66 ± 2.1 frames (reference value 36.2 ± 2.6) and for the left circumflex coronary artery 44.4 ± 3.7 (reference value 22.2 ± 4.1) [3]. The right artery was recessive. On the fifth day of hospital treatment, a sudden arrest of circulation in the course of supraventricular tachycardia of 220/min with atrioventricular conduction of 1:1 (Fig. 3) occurred, which was brought under control by resuscitation and the use of amiodarone. The patient underwent electrophysiological examination which testified to the arrhythmia of the left atrial (PAT) in the mapping of tricuspid ring without induced ventricular arrhythmia. An ablation of atrioventricular junction was considered. Due to the occurrence of obstructive sleep apnea, the patient underwent spirometrical and polisomnographic examination which testified to the presence of central apnea. The treatment included continuous positive airway pressure and produced satisfactory clinical results. Because of numerous serious hemodynamic tachycardia with rapid increase of the

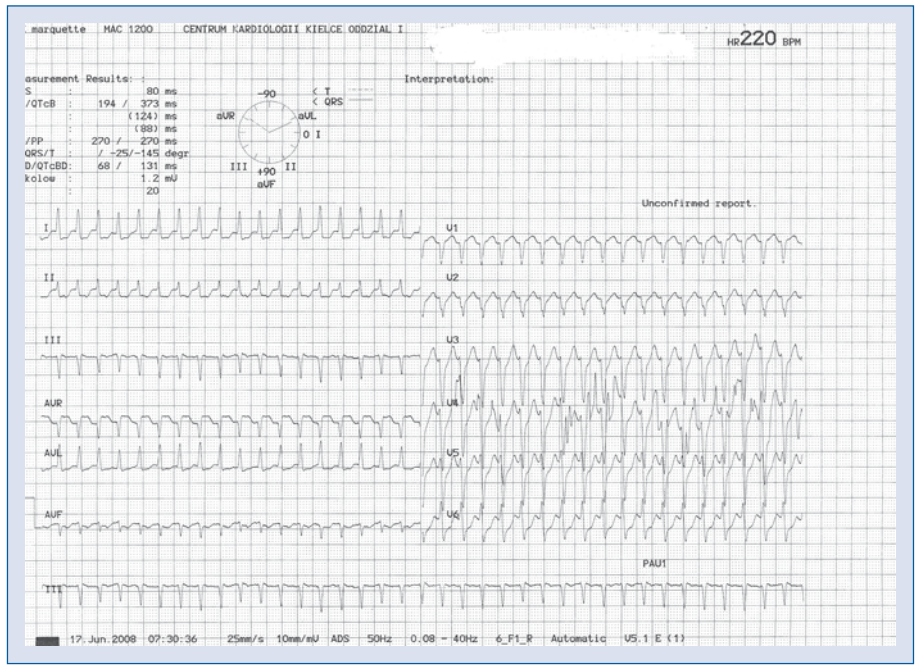

Figure 3. Supraventricular tachycardia of 220/min with atrioventricular conduction of 1:1 with sudden arrest of circulation.

heart rate, caused by slight physical exercise, the treatment included the use of amiodarone and carvedilole. A good control of ventricular rate was observed during the atrial tachycardia, but on the other hand, temporary periods of symptomatic slow heart rate (to 40–50 beats/min) were observed. Because of the need for antiarrhythmic preventive treatment to increase atrioventricular block and decrease the ventricular rate for the patient with the sinus node dysfunction, a VVI heart pacemaker was implanted. Pharmacological treatment included the use of antiplatelet agents, statine, angiotensin converting enzyme inhibitor, carvedilole, verapamile and anticoagulants. During the eight-month observation, a good control of heart rate was observed (during Holter ECG monitoring, the average ventricular rate control during PAT was 71/min, maximum 109//min with frequent periods of ventricular stimulation of 60/min). The ablation of the atrioventricular junction was finally not performed. Good control of blood pressure and glycemia was achieved, and the patient did not complain of chest pains or heart palpitations.

Discussion

Both these cases with their dramatic clinical manifestations have one thing in common. Despite a normal coronary angiogram in patients with typical anginal symptoms, delay of opacification of coronary arteries in coronary angiography was obtained. The etiopathogenesis of SCF is complicated and not yet fully understood. It is believed that some genetic and metabolic factors as well as microcirculation disorders, endothelium dysfunction, disseminated process of atherosclerosis as well as inflammation contribute to its occurrence [4].

Both our patients manifested risk factors connected with the process of arteriosclerosis, the cause of which is endothelial dysfunction. The woman suffered from arterial hypertension, the man from hypertension, diabetes, dyslipidemia and obstructive sleep apnea. Intravascular ultrasound to examine intima-media complex, small atheromatous plaques not detected by angiographic examination, measurement of coronary flow reserve or pressure gradient after adenosine administration, would allow for a more precise examination of the condition of the vessels and exclusion of their pathology. These two patients underwent only coronarography without the above-mentioned examinations, although in the future such examinations may prove extremely valuable in the cases of significantly slow coronary flow.

In examining genetic disorders in patients with SCF, Cakmak et al. [5] concluded that thickening of the intima-media complex of the neck artery occurs with the presence of D allele in the genotype of angiotensin converting enzyme, which, indirectly, testifies to the changes in coronary vessels of

the same character. Meanwhile Nurcalem et al. [6] claims that endothelial nitric oxide synthase gene polymorphism (T-786C) may constitute another risk factor.

Some role in the etiopathogenesis of the phenomenon, as claimed by Beltram et al. [7], may be played by a chronic increase in coronary microcirculation passive tone. Among other causes of SCF, a microvascular spasm detected after the application of contrast may trigger contraction [8]. SCF is also characterized by the increased tendency of platelets to aggregate, examined by test with ristocetin, collagen and ADP [9].

In terms of metabolic disorders in SCF, particular attention is paid to the role played by the thyroid hormones and the level of homocysteine. Thyroid hormones influence the level of plasma concentration of homocysteine as well as causing higher resistance in microcirculation. Research by Evrengul et al. [10] suggests that thyroid hormones and/or the disorders in their metabolism may be responsible for the increase in the level of plasma homocysteine in patients suffering from SCF. Another examination testified to the lower level of folic acid in plasma in patients with increased level of homocysteine [11]. Work by Nurkalem et al. [12] points to the more frequent occurrence of clinically open resistance to insulin in patients with SCF.

Despite the lack of clinical features that would be typical of SCF, common symptoms include paroxysmal angina pectoris and fainting connected with rhythm disorders (e.g. atrial fibrillation or ventricular tachycardia) and conduction disturbances [2, 13]. Our two patients manifested symptoms of angina pectoris and both suffered from sinus node insufficiency which required the implantation of a stimulator. The man suffered from attacks of supraventricular arrhythmia in the form of atrial tachycardia. Most probably, endothelial dysfunction, slow coronary flow with the conduction of 1:1 with atrial tachycardia and fast function of ventricles caused loss of consciousness and sudden circulatory arrest. A usually not life-threatening arrhythmia constituted in this case a direct threat to life.

Among the pathologies of the SCF detected by electrocardiography, particular attention is paid to the longer P-wave duration and a greater difference between maximum and minimum P-wave duration, which may be caused by ischemia in terms of microcirculation and/or changes in the regulation of the vascular system caused by the autonomous nervous system [14, 15]. The same mechanism may be responsible for the increase in dispersion of QT interval which reflects the differences in repolarization time in some areas of the atrium and its electric instability. It has been proved that the dispersion of QT interval changes during myocardial ischemia episodes. It is also claimed that SCF is connected with the prolongation of QT segment or the increase in QT dispersion [16, 17].

Patients with SCF suffer more frequently from paroxysmal atrial fibrillation, changes in ST-T segment and conduction disturbances during resting ECG. Exercise tests in patients with SCF are positive in about 20% of cases [18, 19].

The main diagnostic method for SCF is coronarography. In both our cases, angiography of coronary arteries was performed. The examination was performed immediately, due to the symptoms of acute coronary syndrome or effort angina pectoris. Gibson method was applied to assess SCF and the results testified to significant SCF [20].

A method proposed by Gibson (TIMI frame count) [3] is also useful for detecting SCF. The method counts the number of frames of angiographic record from the moment of the appearance of dye in the artery opening to a given place in a distal section of the vessel. The flow within the vessel is considered slow when the TIMI frame count exceeds the norm twice, i.e. for the anterior coronary artery 41 frames, for the circumflex artery and right coronary artery 27 frames, in the standard angiographic record [3]. Other useful examinations include the measurement of fractional flow reserve and intravascular ultrasound [21–23]. The latter is an examination which detects a very small narrowing, so it can be used to detect small arteriosclerosis focuses not registered by conventional angiographic examination. As we said before, the common angiography examination does not include the above-mentioned examinations, although they prove extremely valuable in the diagnosis of SCF. Cin et al. [24], using FFR and intravascular ultrasound methods, managed to prove the occurrence of scattered narrowings and calcification along the walls of coronary vessels as well as the presence of plaques which do not change the lumen of coronary vessels in coronarography in patients with SCF. Additionally, they claim that the patients have a significant pressure gradient between the initial and final sections of epicardial coronary artery. The authors concluded that SCF may take the form of scattered arteriosclerosis comprising both microcirculation and epicardial arteries [24].

It needs to be stressed that the medicines that stabilized the clinical state and, following lengthy use, resulted in a significant improvement in the female patent, were those from the group of calcium

antagonists, as well as angiotensin convertase inhibitors and statine, whereas in the male patent significant improvement was visible after the administration of continuous positive airway pressure, proper glycemia control, the control of a part of the ventricles by means of carvedilole and, as in the female patient, the administration of calcium antagonists, angiotensin convertase inhibitor and statine. Symptomatic drugs used in coronary arterial disease do not bring significant relief in SCF. Nitroglycerine does not reduce anginal pain because it does not have any impact on the small section vessels and does not improve microcirculation, which is the main cause of SCF [2]. Positive effects are observed after the application of dipyridamole which inhibits reabsorption and decomposition of adenosine, which loosens resistance arterioles [12]. Calcium antagonists (niphedypine) may also be beneficial. Vascular spasm receded after the use of verapamil or adenosine [2]. The use of 40 mg simvastatin for six months led to some improvement regarding myocardium perfusion in patients with SCF [5]. Topal et al. [25] administered 20 mg trimetazidin three times per day for four weeks to patients with slow coronary flow. They observed increased heart rate variability and increased levels of endoteline-1 and nitric oxides and, clinically, a smaller number of angina pectoris episodes. Heart rate variability correlated negatively with the level of endoteline-1 and positively with nitric oxide.

The prognosis for patients with SCF in coronary vessels is generally favourable, although at times the health discomforts may become stronger and occasionally there might be an acute coronary incident. Due to increased QT dispersion, the most serious complication connected with SCF may be sudden death caused by malignant ventricular arrhythmia [13].

An important pathology that has been detected and diagnosed in our patients was SCF. It seems that arterial hypertension separately, or together with diabetes and obstructive sleep apnea, were the factors influencing most strongly endothelial dysfunction, which strengthened the phenomenon of SCF and its consequences. Some authors suggest that microcirculation and endothelial function is impaired in people with SCF [5, 6]. The condition of microcirculation in our two patients was undoubtedly influenced by diseases such as arterial hypertension, diabetes, obstructive sleep apnea or alcohol abuse. The list of symptoms and cardiological complications of obstructive sleep apnea is long. Due to frequent episodes of anoxia, heart rate may increase and there might be disturbances in heart rhythm and conduction as well as episodes of acute coronary incidents, increases in arterial blood pressure, blood stroke or pulmonary hypertension. Circulation complications are the main cause of deaths in the case of obstructive sleep apnea, with men aged 50 and above running the greatest risk [26]. In the case of prolonged apnea, the risk of ventricular and supraventricular rhythm disorders and conduction disturbances is higher. According to Garrigue's register, 68% of patients qualified for continuous stimulation have previously undetected obstructive breathing disorders, and 20% of patients with acute apnea suffer from significant hemodynamic conduction disturbances [27]. Also in patients with the symptoms of angina pectoris, obstructive sleep apnea occurs twice as frequently as in other patients. Recurring significant hypoxemia, acidosis, increased arterial blood pressure and sympathicotonia with recurrent changes in intramural heart pressure and changes inside the chest caused by apnea lead to the dysfunction of the endothelium which is the basis of SCF, and in the long term, to the damage of coronary vessels. It has been proved that treatment which creates positive pressure in air passages lead to fewer rhythm disorders and coronary stabilization [28]. The problem of SCF deserves more attention, especially in patients with no other pathologies which could be responsible for a serious clinical state detected. SCF requires proper diagnosis and treatment.

Conclusions

Slow coronary flow may be associated with serious cardiovascular events and clinically manifests with chest pains, arrhythmia and conductibility disorders. Adequate control of cardiac rhythm, blood pressure, glycemia, any obstructive breathing disorders, treatment with antiplatelet agents, statine, angiotensin converting enzyme inhibitor, all bring relief for the patients and maintain improvement.

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