LETTERS TO EDITOR

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Controversy Surrounding Patients with Chest Pain and Normal Coronary Arteries or Non-Obstructive Coronary Angiogram

Kontrowersje dotyczące chorych z bólem klatki piersiowej i prawidłowymi tętnicami wieńcowymi lub zwężeniami w koronarogramie, niezmniejszającymi przepływu krwi

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The causes of chest pain of cardiac origin, apart from atherosclerotic changes in the coronary vessels, spontaneous angina pectoris, mitral valve prolapse, significant left ventricular hypertrophy, and narrowing of the semilunar valves of the aorta, include syndrome X, which is often referred to as cardiologic syndrome X to differentiate it from the metabolic syndrome. Although some of the symptoms may differ from those of classical angina pectoris due to atheroclerosis of the coronary arteries, it is still not possible to determine unequivocally whether the syndrome constitutes an early stage of the disease or is a separate entity. Syndrome X is characterized by anginal pain occurring both at rest as well as after exertion, accompanied by symptoms of cardiac ischemia on ECG examination, including elevation of the ST segment. On the other hand, angioraphic findings do not present evidence of atherosclerotic changes in the coronary arteries or they present slight parietal changes that do not affect arterial blood flow [1].

Among all patients presenting with symptoms of ischemic heart disease, syndrome X was diagnosed in 6% of men and in 10–20% of women, among whom postmenopausal women constituted 70%. Moreover, it was shown that about 40% of patients suffering from syndrome X are hospitalized several times a year due to recurrent chest pain, and about 30% of patients with this syndrome had successive coronary angiography examinations performed in one to five years' time [2]. The causes of syndrome X are not well understood. It is assumed that in up to 50–60% of women the disease is associated with microcirculatory disturbances caused by impaired release of nitrogen oxide by the vascular endothelium, which not only reduces the relaxation of arterioles in this area, but may also lead to constriction of precapillaries as a result of a disturbed balance between the vasodilating effect of nitrogen oxide and the vasoconstricting effect of endothelin–1 [3]. Patients with syndrome X also reveal an increased neuroticism index [4], increased perception of pain [5], and elevated serum levels of C-reactive protein, which may indicate the participation of inflammatory processes in the etiopathogenesis of the condition [6] as well as estrogen deficiency.

The clinical symptoms of the syndrome include anginal pain at rest as well as after exertion and in stress situations, with the pain threshold changing in the same patient from very high to very low. The pain resembles that experienced by patients suffering from effort angina, but it differs in that it has a higher intensity, prolonged duration (sometimes longer than 30 minutes), radiates to the midline, and presents no or poor response to nitrates. Resting ECG during the attack of pain reveals a depression of the ST segments, which sometimes may be elevated, which may be the reason for a misdiagnosis of myocardial infarction.

The diagnostic value of the electrocardiographic submaximal effort test in patients with syndrome X is low, as the observed changes are similar to those in patients suffering from effort angina but, unlike the latter, the administration of nitrates to patients with syndrome X does not decrease the level of cardiac ischemia, but enhances it. Moreover, it was found that angina patients demon-

strated increased platelet aggregation during the test, while in patients with syndrome X, platelet aggregation was decreased. Echocardiography may be helpful in the differential diagnosis, as it was shown that in cardiac ischemia due to physical effort in patients with syndrome X, administration of dobutamine or dipyridamole was not associated with a regional or global decrease in myocardial contractility. Moreover, the diagnosis of syndrome X may be suggested by a decreased coronary reserve evaluated by means of cardiac vein flow assessment by the thermodilution method, magnetic resonance, or Doppler blood flow through coronary arteries. Coronary angiography did not show evidence of the presence of atherosclerotic changes in coronary arteries in patients with syndrome X, or they were situated near the walls and did not compromise the coronary blood flow. The differential diagnosis of syndrome X from other chest-pain-causing diseases, apart from spontaneous angina pectoris, should take into consideration the following conditions: mitral valve prolapse, narrowing of the semilunar valves of the aorta, as well as such diseases affecting the coronary microcirculation as hypertrophic cardiomyopathy, hypertension, and diabetes mellitus.

The risk of sudden death, myocardial infarction, or coronary failure is, according to some authors, lower that in patients with atherosclerosis of the coronary arteries and is comparable to that of healthy individuals, while other studies demonstrated a 2% risk of myocardial infarction or sudden cardiac death 30 days after diagnosis of the syndrome [1, 2].

The few studies performed so far on the subject showed that the best effects of therapy of the syndrome expressed as a decreased subjective feeling of pain and increased exercise tolerance on stress ECG were achieved after administration of atenolol, verapamil, theophilin, angiotensin-converting enzyme inhibitors, and statins. The two latter drugs have a beneficial effect on syndrome X by reducing the dysfunction of the vascular endothelium. Nitrates do not decrease the frequency of anginal pain or decrease its intensity and they intensify cardiac ischemia on exertion. 17 β-estradiole used in substitutive therapy decreased subjective symptoms, but did not affect physical effort tolerance.

The review of the few studies on the subject leads to the question whether syndrome X is a separate disease or one of the stages of the atherosclerotic process in the arteries. The notion that it is a primary form of coronary atherosclerosis is confirmed by the disturbed function of the vascular endothelium, which precedes the occurrence of atherosclerotic changes in the arteries, and also by the fact that not all the published papers excluded other reasons of chest pain apart from syndrome X. However, the basic symptom of the syndrome, i.e. lack of atherosclerotic changes in the coronary arteries, which means that coronary angiography, unlike intravascular ultrasonography, does not allow detection of small atherosclerotic changes in the coronary arteries, provides evidence against this idea.

References

[1] Crea F, Lanca G: Angina pectoris and normal arteries: cardiac syndrome X. Heart 2004, 90, 457–463.

[2] Bugiardini R, Mertz B: Angina with "normal" coronary arteries. A changing philosophy. JAMA 2005, 293, 477–484.

[3] Chauhan A, Mullins P, Taylor M: Both endothelial-dependent and endothelium-independent function is impaired in patients with angina pectoris and normal coronary angiograms. Eur Heart J 1997, 18, 60–68.

[4] Asbury E, Creed F, Collins P: Distinct psychosocial differences between women with coronary heart disease and cardiac syndrome X. Eur Heart J 2004, 25, 1695–1701.

[5] Pascervi V, Lanza G: Role of abnormal pain sensitivity and behavioral factors determining chest pain in syndrome X. J Am Coll Cardiol 1998, 31, 62–66.

[6] Cosin-Sales J, Pizzi C, Brown S: C-reactive protein, clinical presentation and ischemic activity in patient with chest pain and normal coronary angiograms. J Am Coll Cardiol 2003, 41, 1468–1474.

[7] Asbury E, Creed F, Collins P: Distinct psychosocial differences between women with coronary heart disease and cardiac syndromeX. Eur Heart J 2004, 25, 1695–1001.

[8] Kaski C: Pathophysiology and management of patients with chest pain and normal coronary arteriograms (cardiac syndrome X). Circulation 2004, 109, 568–572.

[9] Doyle A, Fuisz A: The impact of myocardial flow reserve of the detection of coronary artery disease by perfusion imaging method: an NHLBI WISE study. J Cardiovasc Magn Reson 2003, 5, 475–485.

[10] Diver D, Bier J, Ferreira P: Clinical and arteriographic characterization of patients with unstable angina without critical coronary arterial narrowing (TIMI IIIA Trial). Am J Cardiol 1994, 74, 531–537.

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