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MYOCARDIAL INFARCTION IN THE ABSENCE OF OBSTRUCTIVE CORONARY ARTERY DISEASE IN A PATIENT WITH TYPE 2 DIABETES – CASE REPORT

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Myocardial infarction in subjects without obstructive coronary artery disease is an entity defined according to the European Society of Cardiology as the association between acute myocardial infarction criteria, no obstructions on coronary arteries on angiography and no other clear cause for the acute presentation. The prevalence of the condition is estimated at 6% of acute myocardial infarction cases. A 67-years old diabetic Caucasian man was hospitalized at the Institute for Cardiovascular Disease "Prof. Dr. C.C. Iliescu "Bucharest in December 2018 for precordial pain. At the time of admission to the hospital the patient presented a relatively good general condition, blood pressure -160/80 mmHg, ventricular rate-68/min, systolic apical murmur at the apex, grade II/VI. Electrocardiogram performed in emergency highlighted atrial flutter with block 2:1, ventricular rate of 68/min, depression of segment ST of maximum 1 mm in V3-V6. Other paraclinical investigations revealed high blood sugar, high total cholesterol and high sensitivity troponin. The performed coronarography highlighted the permeability of epicardic coronary arteries. The patient presented paroxysmal episodes of atrial flutter and fibrillation for which no anticoagulant therapy was followed. Myocardial infarction was considered to be a consequence of coronary embolism. The association between diabetes and MINOCA is not completely elucidated-some possible mechanisms are investigated. Additional studies focusing on relation between the two conditions and optimal therapies may improve the prognosis for these patients.

Key words: myocardial infarction, non-obstructive coronary artery disease, coronary embolism, diabetes.

INTRODUCTION

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is an entity defined according to the European Society of Cardiology as the association between acute myocardial infarction (AMI) criteria (defined as positive cardiac biomarkers and corroborative clinical evidence of an acute myocardial infarction), lack of obstruction of coronary arteries on angiography (defined as absence of any coronary artery ≥ 50% stenosis) and no other obvious clear cause for the acute presentation[1]. The prevalence of the condition is estimated at 6% of AMI cases and is more common in younger subjects and more frequently in women than in men[2,3]. The pathogenesis of MINOCA involves atherosclerotic (plaque disruption) and non-atherosclerotic (epicardial coronary vasospasm, coronary microvascular dysfunction, coronary embolism/thrombosis, supply-demand mismatch) causes[4]. The plaque disruption includes: plaque rupture or erosion and calcific nodules. Plaque ruptures are defined according to the "*American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology*" guidelines as "*fibrous cap discontinuity leading to a communication between plaque cavity and the coronary lumen*", plaque erosion as "*a thrombus contiguous to the luminal surface of a plaque without signs of rupture*" and calcific nodules based on higher-resolution optical coherence tomography as "*a signal-poor region with poorly delineated borders that protrudes into the arterial lumen*"[4]. Epicardial coronary vasospasm is a common cause of myocardial infarction in the absence of obstructive

coronary artery disease (CAD) and is defined as intense vasoconstriction of an epicardial coronary artery that compromised myocardial vascularization. Standardized criteria for coronary microvascular dysfunction have been proposed by the "*Coronary Vasomotion Disorders International Group*" and include: symptoms suggestive for and objective proof of myocardial ischemia, absence of obstructive coronary artery disease and confirmation of a reduced coronary blood reserve[5]. Coronary embolism or thrombosis can generate non-obstructive angiographic disease. Supply-demand mismatch is a heterogeneous category that includes the pathophysiological mentioned previously and other systemic conditions[4].

CASE REPORT

A 67-year old Caucasian man was hospitalized at the Institute for Cardiovascular Disease "Prof. Dr. C.C. Iliescu" Bucharest in December 2018 for precordial pain. At the time of admission to the hospital the patient presented a relatively good general condition, blood pressure 160/80 mmHg, ventricular rate of 68/min, systolic apical murmur/at the apex, grade II/VI. Electrocardiogram performed in emergency highlighted atrial flutter with block 2:1, ventricular rate of 68/min, depression of ST of maximum 1 mm in V3–V6. Cardiac echography highlighted: left ventricular of normal size with global systolic function preserved, akinesia of the anterior interventricular septum (2/3 basal part), akinesia of apex and hypokinesia of the left ventricular wall(1/3 basal) the left atrium severely dilated, the right ventricular with normal size, without intrapulmonary hypertension criteria. Other paraclinical investigations revealed basal blood glucose 151 mg/dl (normal range: 65–115 mg/dl), total cholesterol 227 mg/dl (normal range: 50–200 mg/dl), high-sensitivity troponin 0.356 ng/ml (reference values: 0.029–0.039 ng/dl). Coronarography performed highlighted the permeability of epicardic coronary arteries. The patient was diagnosed with type 2 diabetes mellitus in 2005, arterial hypertension in 2002 and presented paroxysmal episodes of atrial flutter and fibrillation for which no anticoagulant therapy was followed. Myocardial infarction was considered as a consequence of coronary embolism and the treatment with a combination of perindopril/ indapamide 5/1,25 mg/day, metoprolol 50 mg/day, apixaban 10 mg/day, atorvastatin 80 mg/day was recommended in association with the treatment for diabetes.

DISCUSSION AND CONCLUSION

Coronary emboli may occur in the hypercoagulable states such as atrial fibrillation. The prevalence of coronary tromboembolism in the pathogenesis of MINOCA is low[1] and may be due to inadequate screening of atrial fibrillation or failure of the anticoagulant therapy

There are currently few data on the association between diabetes and MINOCA. In 2009 Djaberi R *and al* published in the *Journal of Nuclear Medicine* one study about the presence of endothelial dysfunction in diabetic subjects with altered myocardial perfusion but without proof of epicardial obstructive CAD. 130 asymptomatic diabetic patients were included in a prospective study. The authors carried out screening for CAD by coronary artery calcium scoring, multi-slice computer tomography, coronary angiography and myocardial perfusion imaging with single-photon emission computed tomography; in addition flow-mediated dilatation of the brachial artery (a validated indicator of endothelial dysfunction) was assessed by ultrasonography. After excluding from the study group patients with obstructive epicardial CAD, abnormal myocardial perfusion was documented in 30 patients. In patients with abnormal myocardial perfusion, flow-mediated dilatation of the brachial artery was significantly lower than in patients with normal myocardial perfusion[6]. Assessment of flow-mediated dilatation of the brachial artery is accepted as the most validated technique of endothelial function[6,7]. The cardiovascular consequence of impaired endothelial function in diabetic patients is not completely elucidated but is suspected to be induced by hyperglycemia and insulin resistance. The two conditions may generate mitochondrial superoxide overproduction[6]. In addition platelet function is altered by increased production of several prothrombotic factors[8]. In nondiabetic patients endothelial dysfunction was related with long-term cardiovascular events[9].

There are currently no strategies regarding the medical management of patients with
MINOCA. Despite the position statement of American Heart Association and European Society of Cardiology some clinicians support that the absence of obstructive coronary artery disease excludes the possibility of an acute myocardial infarction[4,1]. The condition is generated by many pathophysiological causes and it is essential that healthcare professionals identify specific causes in order to target specific therapy. The Scientific

Statement From American Heart Association published in 2019 in Circulation suggests that the management of MINOCA must include:

1. Emergency supportive care,
2. Working diagnosis approach for patient evaluation,
3. Cardioprotective therapies,
4. Cause-targeted therapies[4].

Emergency supportive care may be necessary for treatment of arrhythmias or cardiogenic shock. The diagnosis of condition needs to exclude disorders who mimics an acute myocardial infarction and identify cause responsible for the MINOCA. The conventional cardioprotective medication: dual antiplatet therapy, statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and β-blockers represents the secondary prevention in patients with acute myocardial infarction in the presence of obstructive coronary artery disease[4]. The benefits of cardioprotective therapies in MINOCA has been evaluated in multiple analyses. The "*Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapy*" evaluated the relation between treatment and the all-cause mortality, reinfarction, heart failure or stroke in 9138 patients with MINOCA. After a mean follow-up 4.1years the results indicate "*long-term beneficial effects of treatment with statins and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on outcome in patients with MINOCA, a trend toward a positive effect of β-blocker treatment, and a neutral effect of dual antiplatelet therapy*"[10]. The scientists are waiting for the results of another study – Randomized Evaluation of Beta-Blocker and Angiotensin Converting Enzyme Inhibitor (ACEI)/Angiotensin Receptor Blocker (ARB) Treatment in MINOCA Patients. The primary objective of this randomized clinical trial is to determine all-cause mortality and cardiovascular events at 1 year in estimated 3500 patients with MINOCA enrolled; the study should as well provide information regarding the benefits of cardioprotective therapies in MINOCA patients[4, 11]. Cause-targeted therapies are addressed to patients with identifiable underlying cause.

Studies assessing prognosis in patients with MINOCA were heterogeneous. Some studies have highlighted that MINOCA has a low risk of adverse clinical outcome[12, 13] while other studies report that patients with MINOCA have similar mortality rates like those with myocardial infarction caused by obstructive coronary artery disease[14, 15, 16].

CONCLUSIONS

There are many faces of cardiovascular disease in diabetes and one of them is MINOCA. This association is not completely understood but there is increasing evidence that one possible link is coronary microvascular dysfunction which appears in diabetes. Additional studies focusing on relation between the two conditions and optimal therapies may improve the prognosis for these patients.

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