CASE PRESENTATION

The more you know… the less you understand

Mariana Tarusi[1], Razvan Constantin Serban[2,3], Gabriela Kozma[1], Calin Pop[1,4]

Abstract: Acute coronary syndrome in young people represents a risk condition expected to increase due to nowadays lifestyle. We report the case of a 29-year-old male patient admitted for non ST elevation myocardial infarction. Coronary angiography revealed a non-obstructive thrombus in the proximal segment of the left anterior descending coronary artery, with non-significant stenosis. A multimodality imaging approach was essential for an accurate diagnosis and risk stratification. Intravascular imaging provided important insights regarding the mechanism of non-ST elevation myocardial infarction. Further clinical studies are needed to assess best medical treatment and imaging modalities in myocardial infarction with non-obstructive coronary arteries.

Keywords: coronary thrombus, antithrombotic medication, ventricular ectopic beats

Rezumat: Sindromul coronarian acut la vârstă tânără reprezintă o situație considerată a fi la risc crescut, a cărei incidență va crește probabil în viitor datorită stilului de viață actual. Prezentăm cazul unui pacient în vârstă de 29 de ani, internat cu sindrom coronarian acut fără supradenivelare de segment ST. Angiografia coronariană a evidențiat un tromb non-obstructiv la nivelul segmentului proximal al arterei descendente anterioare, asociat cu stenoză nesemnificativă angiografic. O abordare cu tehnici imagistice multiple a fost esențială atât pentru un diagnostic corect, cât și pentru stratificarea riscului. Tehnicile de imagistică intravasculară au contribuit la stabilirea mecanismului sindromului coronarian acut fără supradenivelare de segment ST. Sunt necesare studii suplimentare pentru a stabili tratamentul și modalitatea imagistică adecvată la pacienții cu afectare coronariană non-obstructivă.

Cuvinte cheie: tromb coronarian, medicație antitrombotică, bătăi ventriculare ectopice

INTRODUCTION

The rate of acute coronary syndromes (ACS) in young patients is much lower than in the older people. Hospital readmissions are more often if the first coronary event occurred at a young age[1-3] and the incidence of ACS in young patients was associated with type 2 diabetes, unhealthy lifestyle such as cocaine abuse, smoking, obesity and low HDL-cholesterol. In rare cases, ACS in young people may be due to anomalous origin of the coronary arteries[4]. Part of the ACS are classified as myocardial infarction with non-obstructive coronary arteries (MINOCA), representing an important challenge in the clinical practice. The most frequent pathophysiological mechanisms for MINOCA are emotional stress, coronary plaque disruption, coronary spasm, embolus or dissection. In a relatively large number of cases the subsequent mechanism is not found even after extensive tests[5].

CASE PRESENTATION

A 29-year-old county policeman presented to the emergency department complaining of two episodes of exertional chest pain, lasted for round five minutes each. He was a professional rugby player several years ago, currently practicing fitness, taking an oral protein nutrition supplement without steroids. He was a smoker, with positive heredity for coronary artery diseases (his father had a myocardial infarction before the age of 50-year-old). The patient was completely asymptomatic before this presentation and remembers having an electrocardiogram (ECG) with an abnormal aspect years ago, but no formal report was available.

[1] Emergency County Clinical Hospital, Baia Mare, Romania
[2] Emergency Institute for Cardiovascular Diseases and Transplantation, Tirgu Mures, Romania
[3] University of Medicine and Pharmacy, Tirgu Mures, Romania
[4] Faculty of Medicine, „Vasile Goldis" Western University, Arad, Romania

Contact address:
Razvan Constantin Serban, MD
Laboratory of Cardiac Catheterization, Angiography and Electrophysiology, Emergency Institute for Cardiovascular Diseases and Transplantation, 50 Gheorghe Marinescu Street, 540136, Tirgu Mures, Romania.
E-mail serbanrazvan1@gmail.com

Clinical examination was unremarkable, blood pressure was 130/80 mmHg, heart rate was 90 bpm, BMI 27 kg/m^2. The ECG on admission showed negative T waves in leads III and avF and no other significant repolarization abnormalities were noted (Figure 1). The laboratory tests revealed an elevation of serum troponin I from 0.02ng/ml to 0.5ng/ml (normal value <0.02ng/ml), slight elevation of creatin kinase and creatin kinase myocardial band, without any inflammatory syndrome nor metabolic disorders. The blood gases were in the normal range and the D-dimer test was negative. The echocardiography was normal; no left ventricular wall motion abnormalities were noted. The coronary angiography performed in the first 24 hours of hospital admission revealed a proximal left anterior descending coronary artery (LAD) non-significant stenosis, before the take-off of the first diagonal branch, with a most probably a non-obstructive thrombus (Figure 2). The right and circumflex coronary arteries were patent. The 24 hours ECG monitoring revealed numerous ventricular ectopic beats, with similar left bundle branch block morphology without any associated symptoms, more pronounced after initiating the beta-blocker therapy.

The patient was started on double antiplatelet therapy with Aspirin and Ticagrelor and unfractionated heparin anticoagulation. A beta-blocker and a high dose of statin was also added to the drug regimen. He was transferred in a University centre for coronary angiogram control, with possibility of intracoronary imaging. An optical coherence tomography examination (OCT) was performed after five days of antithrom-

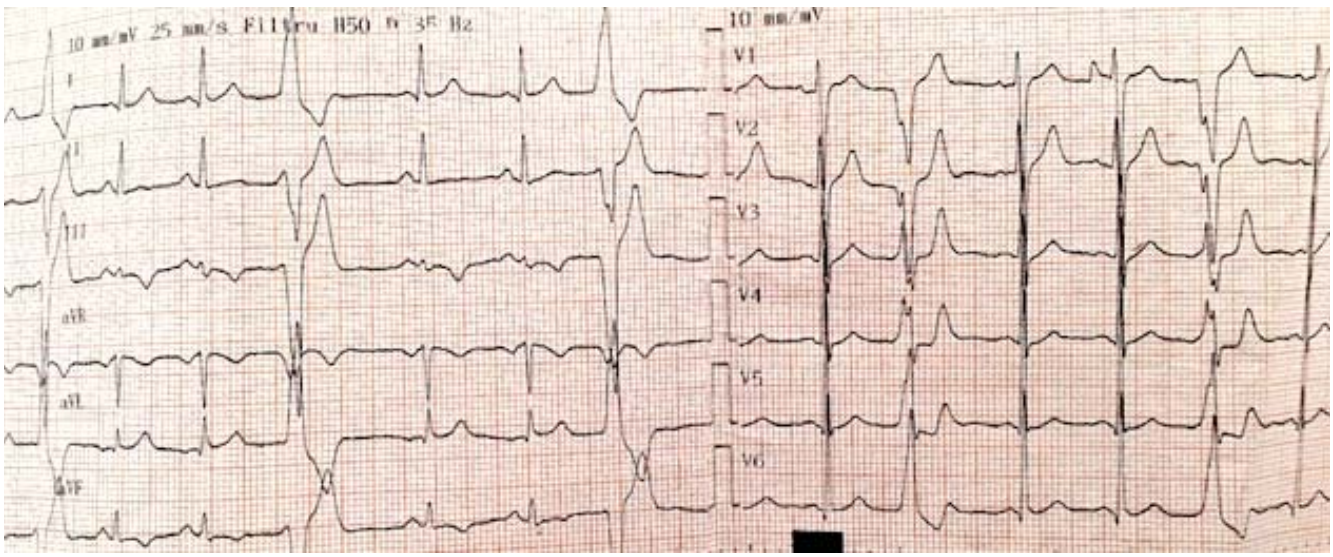

Figure 1. Twelve lead ECG on admission showing normal sinus rhythm, with negative T wave in DIII, avF and isolated ventricular ectopic beats.

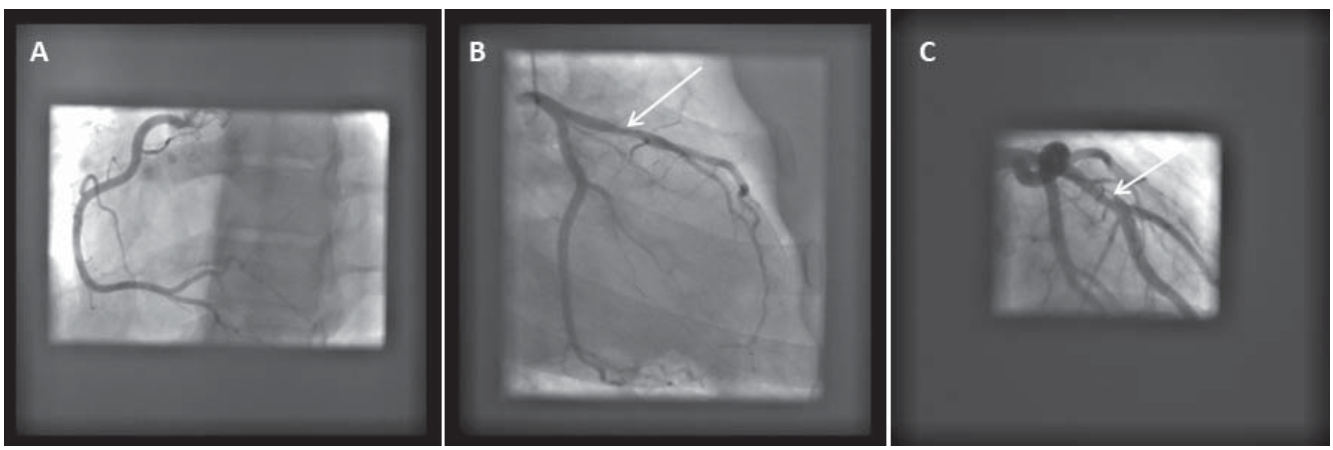

Figure 2. Initial coronary angiogram, showing patent right and circumflex coronary arteries (A, B). Non -obstructive thrombus may be visualised on the proximal segment of the left anterior descending coronary artery in right anterior oblique caudal view (B, white arrow) and right anterior oblique cranial view (C, white arrow).

botic therapy (Figure 3). A residual non-significant stenosis was noted within the mid left anterior descending coronary artery, without thrombus, without intimal tear or rupture, with only mild intimal irregularities. The clinical course was complicated by hepatic cytolysis due to high statin dose with complete resolution after statin cessation. The patient was discharged on Aspirin 75mg od, Ticagrelor 90mg bid, Metoprolol succinate 50mg od, and Ezetimibe 10mg od.

An ambulatory cardiac magnetic resonance (CMR) imaging was performed the first week after his discharge, in order to better assess the myocardium (with a special regard to the right ventricle). There was no myocardial scar, nor right ventricular dysplasia, myocarditis or Takotsubo cardiomyopathy features (Figure 4).

The ECG remained unchanged during the first year, with negative T wave in inferior leads. On beta-blocker

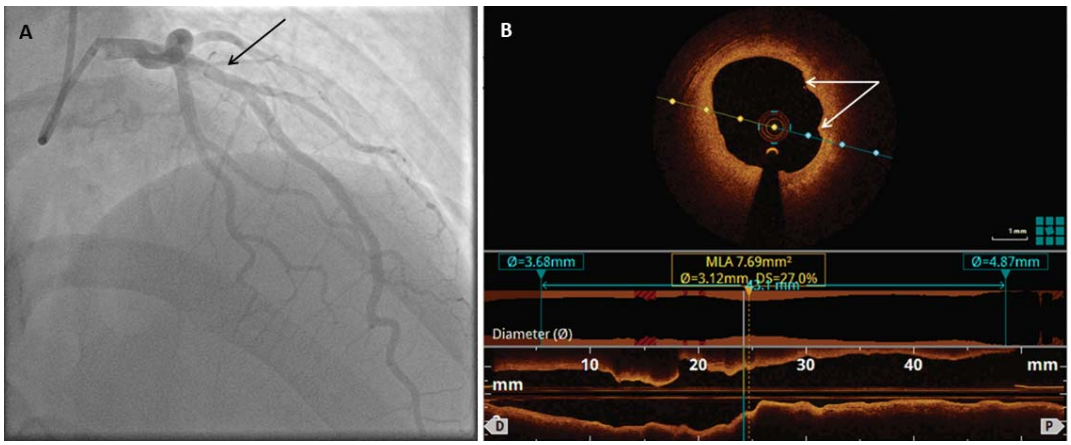

Figure 3. Coronary angiogram performed 5 days later in right anterior oblique cranial view revealing complete resolution of the proximal left anterior descending coronary artery thrombus (A, black arrow). Optical coherence tomography of the proximal left anterior descending coronary artery (B) showing minor intimal irregularities without intimal tear or thrombus.

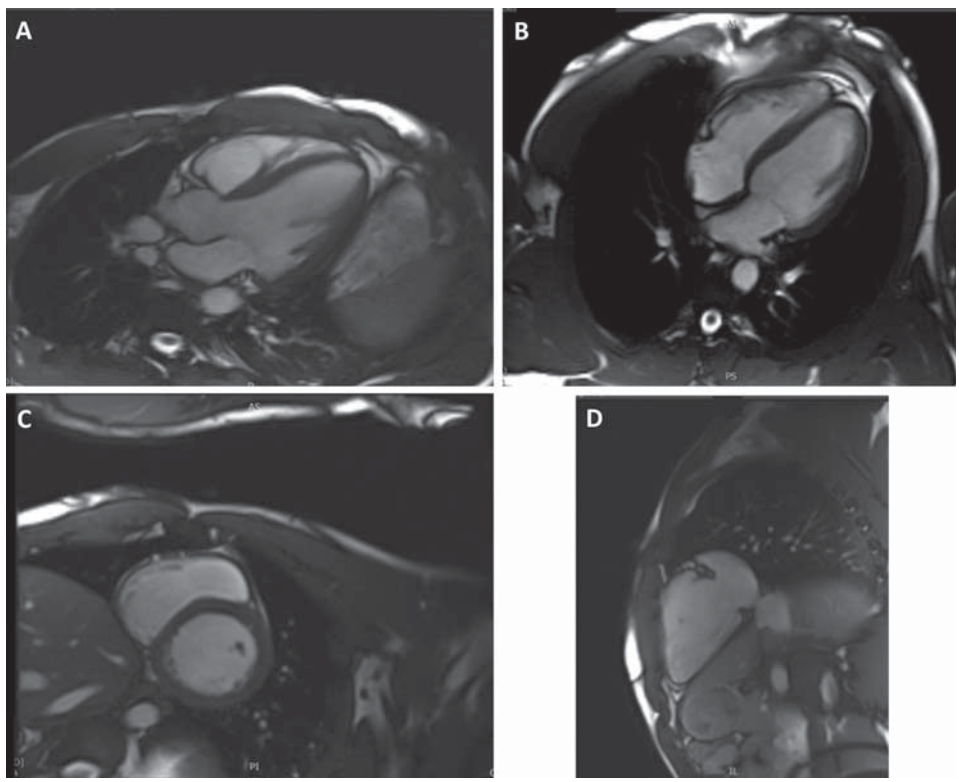

Figure 4. Cardiac Magnetic Resonance Imaging with three chamber (A), four chamber (B) and short axis views showing normal left ventricular function, without late Gadolinium enhancement. The right ventricle view (D) with normal aspect, without scar or criteria for arrhythmogenic dysplasia.

therapy the number of ventricular ectopic beats increased, with a value of 39 500 (34%) per 24 hours (Figure 5, 6). Asymptomatic episodes of non-sustained ventricular tachycardia were noted during the follow-up visits, with the same left bundle branch block QRS morphology. Arrhythmia improved on exertion and restarted in the recovery period of the ECG exercise test. Bradycardia was most probably the arrhythmia trigger. The beta-blocker treatment was ceased and the patient referred for ventricular mapping with a view to ablation therapy. Although the patient was asymptomatic during arrhythmic episodes, his job as a county policeman, with repeated medical visits and subsequent anxiety were the main arguments for referral. A right ventricular septal ectopic pattern was described, with suspicion of a papillary muscle origin. It was decided to continue the medical therapy without ablation due to the increased risk of the procedure. After the electrophysiological study the patient was continued on anti-arrhythmic agent, the medication being well tolerated and the patient continued to be asymptomatic.

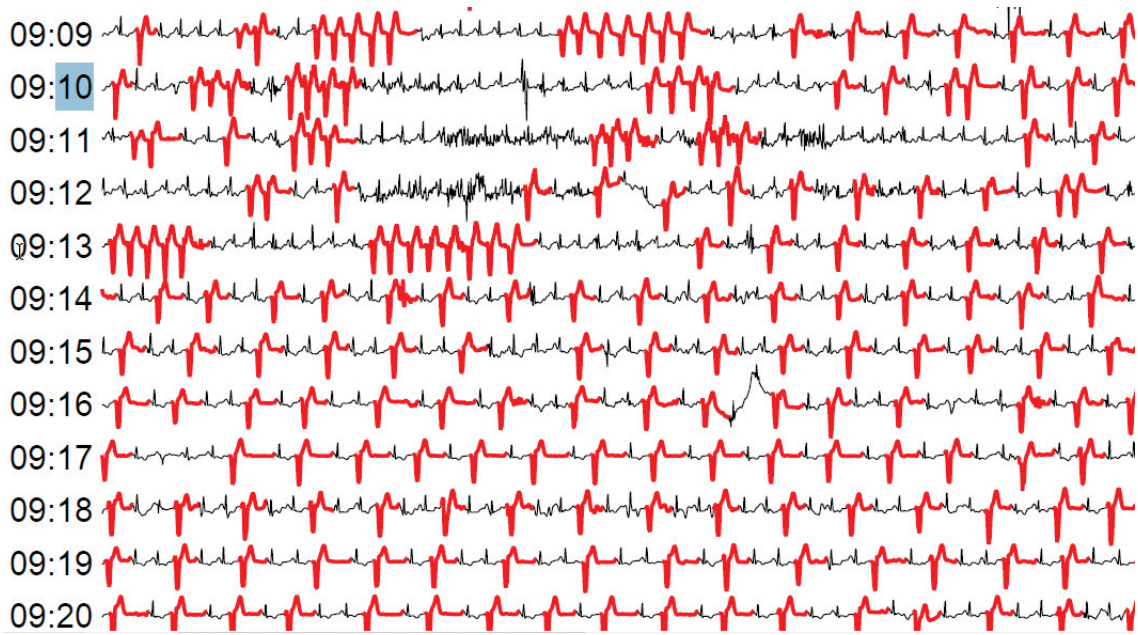

Figure 5. 24 hours ECG showing large number of ventricular ectopic beats and episodes on non-sustained ventricular tachycardia.

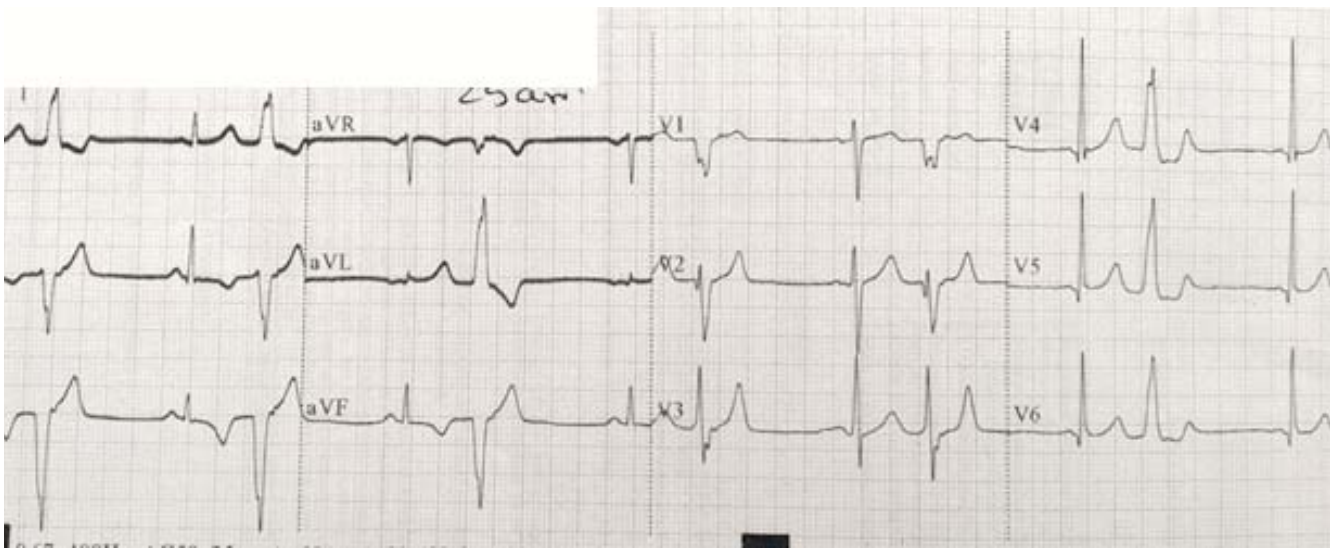

Figure 6. Resting twelve lead ECG during follow up visits showing the persistence of the repolarisation abnormalities and ventricular ectopic beats with the same right side morphology.

DISCUSSIONS

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a heterogeneous entity with a prevalence ranging between 1–14% of all patients with a clinical diagnosis of acute myocardial infarction[6]. It is associated with up to 5% risk of death or recurrent myocardial infarction over 1 year and 25% risk for recurrence of angina . Even if MINOCA associates a better prognosis in terms of in-hospital and twelve months mortality than acute myocardial infarction with obstructive coronary artery disease, early cohort studies suggest that is not as benign as reported before[9,10]. A systematic review published in 2015 reported a 12-month all-cause mortality risk of around 4.7%. The Korean Myocardial Infarction Registry evaluated 12-month all-cause mortality in 8510 myocardial infarction patients, reporting a 3.1% mortality in MINOCA patients[11].

Cardiac magnetic resonance imaging is an important tool in the diagnosis of these patients. Late gadolinium enhancement allows localization of the area of myocardial damage and provides insight into the underlying mechanisms[7,12]. This technique was useful in the evaluation of our patient, to exclude others diseases as well as to evaluate the presence of a possible myocardial scar. Intracoronary imaging with intravascular ultrasound (IVUS) or optical coherence tomography (OCT) are also useful imaging techniques to assess atherosclerotic disease. Further research is needed to understand the potential benefit of routine application of intracoronary imaging at the time of coronary catheterization in patients with MINOCA[7,12,13]. In stable coronary artery disease, OCT is unable to accurately predict physiology when compared with fractional flow reserve (FFR)[14-16]. In acute coronary syndrome OCT has unique features that favor its use. This procedure has 100% sensitivity (vs. 33% sensitivity of IVUS) in detecting intraluminal thrombus when compared with coronary angioscopy[16,17]. The high sensitivity of the method in detecting thrombus can fulfill angiographic limitations in differentiating thrombus from calcium and others etiologies of ambiguous angiographic radiolucency[16]. Intravascular OCT is considered the gold standard method for fibrous cap rupture detection[16,17] for which it has twice the sensitivity of IVUS[16,17]. A great number of reports indicate the ability of the method in discriminating the underlying mechanism of the ACS[18], which can directly impact on the management strategy[16,19,20]. The technique is also used for the detection of non-CAD-related ACS etiology such as spontaneous coronary artery dissection. In this particular clinical setting, OCT-derived information could defer unnecessary stenting. These characteristics make it the ideal method for defining the etiology and anatomic location of the culprit vessel/segment or ruling out ACS[16].

This technique helped us to understand the mechanism of the ACS, to better evaluate the residual non-significant stenosis, confirming the absence of thrombus at this time, as well as absence of any intimal tear or rupture, showing only mild intimal irregularities.

Thrombosis plays a major role in the pathogenesis of MINOCA with plaque disruption[21] and our case supports this hypothesis. Dual antiplatelet therapy is recommended for one year followed by lifetime single antiplatelet therapy for patients with suspected or confirmed plaque disruption and MINOCA[7,22,23]. It is well known that disruption occurs on a background of non-obstructive CAD, statin therapy also being recommended even if only a minor degree of atherosclerosis is found. Unfortunately, our case didn't tolerate statin because of a significant hepatic cytolysis (even on small doses).

It might also be useful to assess the role of long-term anticoagulation and further studies are needed to address this. Long-term administration of the oral direct factor X-a inhibitor Rivaroxaban demonstrated to reduce the expression of pro-inflammatory mediators, enhances thickness of the protective fibrous caps and reduces presence of medial erosions and lateral xanthomas, thus promoting lesion stability in a mice model with advanced atherosclerotic disease[24]. The role of long-term administration of the oral direct factor X-a inhibitor appears to be promising also for atherothrombosis disease in MINOCA patients.

The results from the SwedeHeart registry study (*the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart Disease Evaluated According to Recommended Therapy*)[25] indicated that long-term treatment with statins and renin-angiotensin-aldosterone system blockers (perhaps due to the increase in bradykinin and its vascular benefits) in patients with MINOCA may be more beneficial than beta-blockers and dual antiplatelet therapy[25].

Regarding the ectopic activity, this might have been related to the acute coronary syndrome (with a minimal localized scar, not visualized by echocardiography or CMR) or to a pre-existent non-diagnosed ectopic arrhythmia. It is likely that the ECG abnormality noticed years before was this ectopic activity but no

formal documentation was available. We consider interesting the discrepancy between the localization of the coronary stenosis/thrombus and the ECG abnormalities in two different areas. This could be explained by a large LAD irrigating the postero-inferior part of the apex, but the level of the lesion before the take - off of the first diagonal branch should give another antero-lateral repolarisation abnormality. Taking into account the persistence of the negative T waves in the inferior leads during the follow up visits, we think that this might be a pattern present before the ACS, induced by the pre-existent ectopic arrhythmia.

In the present case, the oral nutrition supplement did not contain any steroid agent nor other component that might have been involved in coronary thrombosis or spasm. It only contained electrolytes and aminoacids which makes it unlikely for the supplement to be the cause of the acute coronary syndrome.

The prognosis of this patient depends largely on secondary preventative measures such as smoking cessation and lifestyle improvement. The medical management for MINOCA patients is still a matter of debate and future research is needed.

CONCLUSIONS

This case suggests the importance of intravascular imaging at the time of coronary catheterization in MINOCA. Optical coherence tomography might help us understand the mechanisms, describe the lesions properly and establish the correct management strategy in these cases. The on-site heart team is of crucial importance in the decision making process, using a comprehensive approach and taking into account not only clinical data, but also social and personal data.

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