



SPECKLE TRACKING ECHOCARDIOGRAPHY ANALYSIS OF GLOBAL AND REGIONAL MYOCARDIAL STRAIN IN DIAGNOSIS AND FOLLOW-UP OF THE PATIENT WITH MYOPERICARDITIS

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ABSTRACT – Myopericarditis is inflammatory disease caused by various, often unidentified, factors. Although considered the gold standard for diagnosis of myocarditis, endomyocardial biopsy in clinical practice is often substituted with clinical, biochemical and imaging parameters. Echocardiography with speckle tracking strain analysis is a valuable tool for diagnosis of myocarditis, estimation of regional and global systolic function showing good correlation with cardiac magnetic resonance imaging (cMRI).

We present the case of a 19-year-old male with chest pain, elevated troponin and ST segment elevation who underwent urgent coronary angiography. Normal angiogram steered diagnosis toward myopericarditis, considering information about recent enterocolitis and vaccination against SARS-CoV-2. Transthoracic echocardiography with speckle tracking analysis showed longitudinal strain reduction in several segments of the left ventricle. Small pericardial effusion alongside those segments was also found supporting our diagnosis. After 3 months of treatment with antiinflammatory drugs, ACE inhibitor and beta blocker, the patient recovered and a repeated echo showed complete recovery of systolic function without pericardial effusion.

We conclude that echocardiography, including global and regional longitudinal strain analysis, is a valuable diagnostic tool in patients with myopericarditis, complementary with not widely available cMRI. It can detect subtle systolic dysfunction not visible with conventional echocardiography, thus having implications on therapy and prognosis.

Key words: *myopericarditis, speckle tracking echocardiography, GLS*

Introduction

Myocarditis is an inflammatory disease of cardiac muscle, caused by infection, unregulated immune response, toxins, and drugs, but, in many cases, the

true cause remains unidentified. It can occur isolated or accompanied by pericardial inflammation hence called myopericarditis¹⁻³. The gold standard and the only method to reach definitive diagnosis is invasive endomyocardial biopsy, but in clinical practice it is seldom conducted and often replaced with combination of clinical, laboratory and imaging criteria²⁻⁴. In that case, patient is diagnosed clinically suspected myocarditis. The European Society for Cardiology position

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paper¹ defines clinically suspected myocarditis if there is ≥ 1 clinical presentation (chest pain, dyspnea, palpitations, signs of heart failure, cardiogenic shock and sudden cardiac death), ≥ 1 diagnostic criteria from different categories - electrocardiographic (ECG) changes, most often ST segment elevation, elevated markers of myocardial necrosis, systolic or diastolic dysfunction detected by echocardiography, angiography or cMRI, and tissue characterization by cMRI showing typical myocarditic pattern. There must be no signs of angiographically significant coronary artery disease (coronary stenosis $\geq 50\%$), known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome. Possibility of myocardial tissue characterization and very high-resolution anatomical and functional imaging, makes cMRI non-invasive the gold-standard method for diagnosis of suspected myocarditis in both acute and chronic settings^{3,5-6}. However, routine implementation in diagnostic algorithm is limited by its low availability. On the other hand, echocardiography is cornerstone of diagnostic imaging in all fields of cardiology due to wide availability, reproducibility and safety. Speckle tracking study of myocardial deformation (particularly longitudinal strain with the greatest body of evidence) is a relatively new method for evaluation of regional and global ventricular systolic function in all major cardiac disorders, including myocarditis and has shown to be powerful

predictor of adverse events in numerous cardiovascular diseases⁷⁻¹⁰. This is especially useful in cases with preserved left ventricle ejection fraction (LVEF) where longitudinal strain can detect subtle changes in systolic function¹¹⁻¹². Following SARS-CoV-2 pandemic and worldwide vaccination campaign, there is a growing awareness of association between mRNA-based vaccines and myocarditis in young subjects. Retrospective studies confirmed mildly increased risk of myocarditis early after vaccination in subjects younger than 40, especially after the second dose of mRNA-based vaccines BNT162b2 (Pfizer-BioNtech) and mRNA-1273 (Moderna)¹³⁻¹⁴.

Clinical case presentation

A 19-year-old man with cerebral palsy came to emergency room complaining of severe retrosternal chest pain augmented with inspiration. Last five days he suffered from fever and diarrhoea and five weeks ago he received the second dose of BNT162b2 (Pfizer-BioNtech) vaccine against SARS-Cov-2 virus. Upon arrival, he was anxious and in pain, but physical examination was otherwise unremarkable. ECG showed ST segment elevation in inferior leads and depression in leads V1, V2 and aVL (Figure 1). Initial high sensitivity troponin values (hs-cTnI) were elevated (11 297 ng/l, normal <14 ng/l), same as inflammatory markers

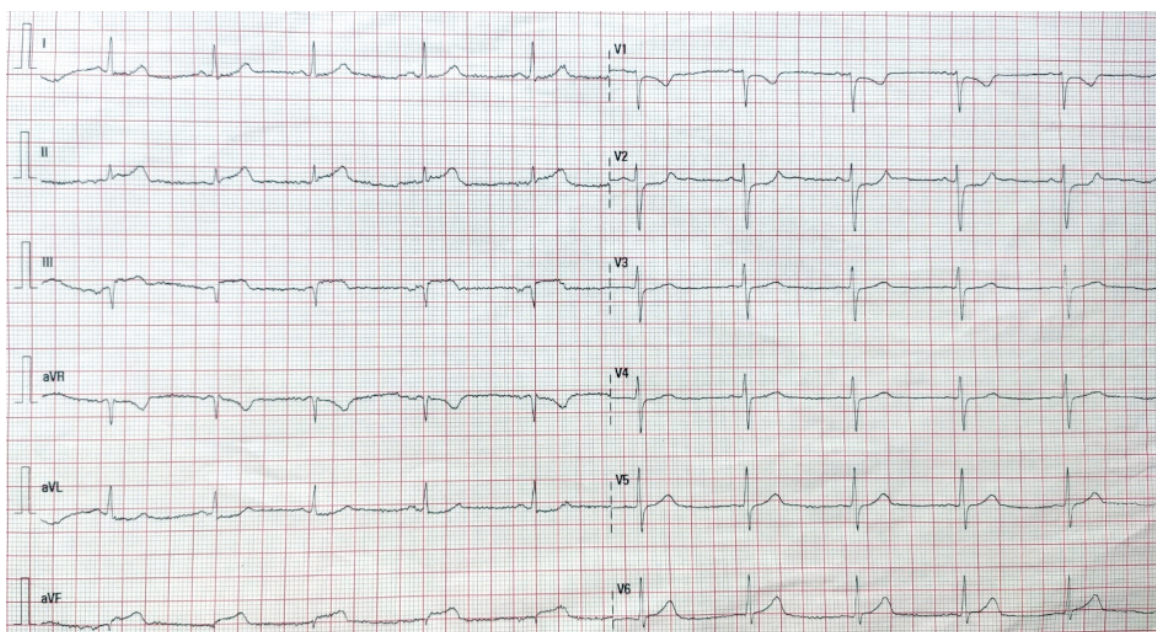


Figure 1. ECG of patient showing sinus rhythm with pseudo infarction pattern in inferior leads.

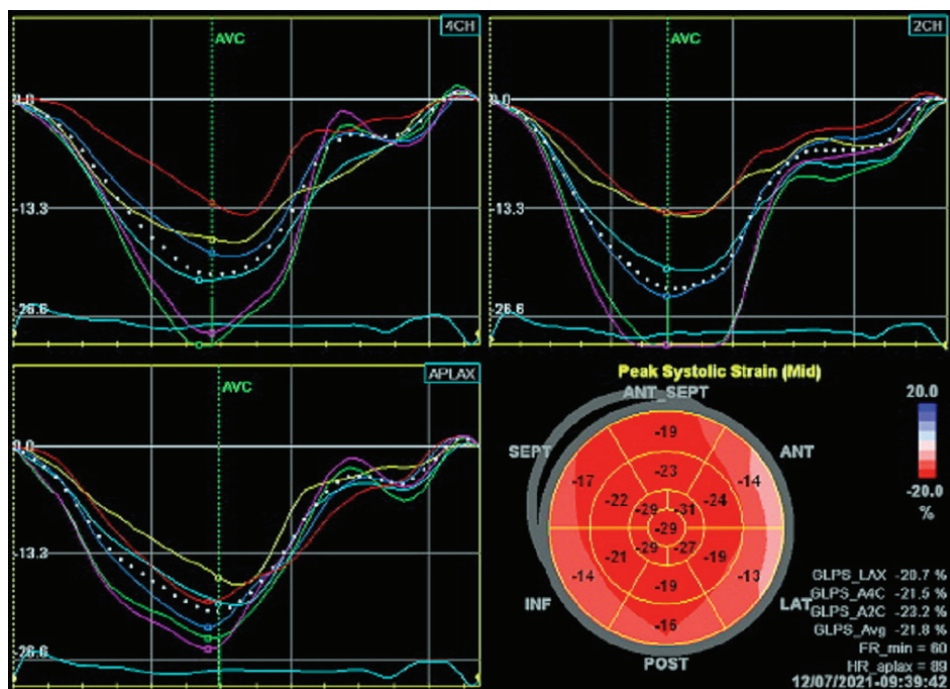


Figure 2. Speckle tracking analysis showing decreased longitudinal strain in basal segments of inferior, posterior (inferolateral), lateral and anterior wall of left ventricle. GLS is on the lower limit of normal for age (-21.8%).

(CRP 53 mg/l; norm <5 mg/l). After loading with dual antiplatelet therapy, the patient was immediately transferred to the local PCI center under working diagnosis of acute coronary syndrome with ST elevation. However, angiography excluded epicardial coronary artery disease, symptoms and ST elevation vanished subsequently and diagnosis of acute pericarditis with myocardial involvement was contemplated. Initial echocardiographic exam revealed a normal-sized left ventricle; there was no wall oedema and discrete hypokinesia of basal inferior, inferolateral and lateral wall was observed. EFLV was estimated at 65% by Simpson biplane method. Longitudinal strain speckle tracking analysis (GE Vivid E95) confirmed systolic dysfunction in abovementioned myocardial segments (Figure 2). Global longitudinal strain (GLS) was preserved (-21.8%) and a small pericardial effusion behind inferior and inferolateral wall was described. The rest of hospital stay was uneventful, pain subsided completely with a non-steroidal anti-inflammatory drug. There were no clinical signs of heart failure (peak nt-proBNP 359 pg/ml, repeated hs-cTnI 75 ng/l) nor significant arrhythmias. The patient was discharged with ibuprofen, colchicin and small doses of ramipril and bisoprolol. Limitation of physical activity was prescribed.

One month later, the patient was doing well, with normal cTnI, nt proBNP and CRP values and no ECG changes. Serology results showed elevated titres of IgG class antibodies to echovirus, adenovirus and Coxsackie. There were no elevated IgM antibodies. Follow-up echocardiography showed complete recovery of regional longitudinal strain and improvement of GLS to -25% (Figure 3). Pericardial effusion regressed completely. During following three months, ibupro-

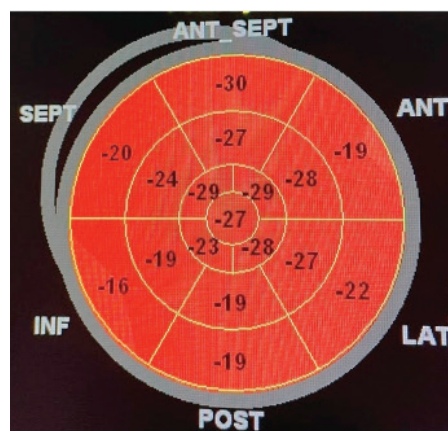


Figure 3. "Bulls eye" representation showing completely normal longitudinal systolic deformation in all myocardial segments.

fen, ACE inhibitor and beta blocker were tapered and finally excluded. Afterwards, the patient resumed his regular physical activities, without any signs or symptoms of recurrence.

Discussion

Myopericarditis can mimic acute coronary syndrome and should be particularly considered in younger patients without risk factors for coronary artery disease and with normal coronary angiograms^{4,15}. Early diagnosis is crucial because it determines further treatment, prognosis and follow-up, obviating the need for potentially harmful diagnostic procedures and therapies (such as antithrombotics). Endomyocardial biopsy still represents the gold standard for the definitive diagnosis of acute myocarditis, but it is seldom used because it is invasive, not widely available and potentially misleading (it can even miss diagnosis if the distribution of myocardial inflammation is regional). Nevertheless, it should be pursued in cases where the exact pathologic diagnosis has therapeutic implications (for instance, gigantocellular myocarditis, sarcoidosis, eosinophilic myocarditis, clinically suspected myocarditis in patients with cardiogenic shock, etc.)²⁻⁴. In most cases, myocarditis is a self-limited disease or presents as a mild heart failure, which can be controlled by medical therapy. In that case, diagnosis is based on clinical, ECG, laboratory and imaging criteria¹⁻². CMRI offers the highest diagnostic accuracy and is considered the non-invasive imaging method of choice^{2,3,6}. However, in most centers, it is not available or cannot be performed in the early phase of the disease. Bearing in mind the necessity to perform cMRI in future course of disease, during acute treatment echocardiography was, besides coronary angiography, the sole used imaging method. Indeed, echocardiography is the main imaging modality in clinical practice, so myocardial deformation study (specifically longitudinal strain analysis) adds value to the echo exam. GLS is a robust, well validated, objective and reproducible technique for the assessment of left ventricle systolic function¹⁰. GLS also has prognostic value, superior to prognostic value to EF for predicting major adverse cardiac events in various clinical scenarios, including myocarditis⁷⁻¹². Degiovanni *et al.* even proposed multiparametric model including GLS, fever and elevated leukocyte count on admission for early diagnosing an acute myocarditis⁸. Our patient had longitudinal strain reduction in basal inferior, inferolateral, lateral

and anterior segments, regions described to be more often affected in myocarditis^{9,11}. GLS was on the lower limit of normal range using age specific cutoffs proposed by Alcidi *et al.*¹⁶. Another differential diagnosis of acute chest pain syndrome with ECG changes, elevated cardiac markers, regional wall motion abnormalities and non-obstructive coronary arteries is focal form of Takotsubo syndrome (TTS)¹⁷. CMRI T2 weighted sequences in TTS show transmural oedema and necrosis while in myocarditis distribution is mainly subepicardial. Echocardiography could also make that distinction with the use of additional systolic deformation parameters, such as circumferential strain and analysis of individual myocardial layers. Bearing in mind that subepicardial layer is composed mostly of circumferential fibers responsible for the rotational motion of the heart, pronounced circumferential strain reduction indicates pathology in that myocardial segment, such as myocarditis¹⁸. Current guidelines recommend institution of heart failure cornerstone therapy only in patients with clinical syndrome of heart failure or evidence of systolic dysfunction (measured by LVEF)¹⁹. Nevertheless, our patient had myocardial necrosis detected by significant hs troponin elevation, regional systolic dysfunction and borderline GLS values, so pharmacological neurohumoral blockade was started to prevent further decline. Follow-up showed complete recovery of regional strain alterations and GLS in normal range for age (-25%). That was another clue to allow the patient to resume usual physical activities relatively early, *i.e.*, 3 months after disease onset, as proposed in recent publications^{3,19}. Exact etiology remains undefined as in most cases of myopericarditis. Post-vaccination myopericarditis after BNT162b2 (Pfizer-Biontech) booster dose was considered, but there is no temporal relationship. Most cases of vaccine caused myocarditis occurred short after exposure (<7 days)¹³ and our patient received his second dose five weeks before symptoms onset. History of recent fever and enterocolitis could indicate underlying viral or other infection not detected by serologic workup.

Conclusion

Global and regional longitudinal strain analysis is a valuable tool for the diagnosis of myopericarditis, complementing not widely available cMRI. It can detect subtle systolic dysfunction not visible with conventional echocardiography, thus having implications on therapy and prognosis of patients. Hence, it should

be part of the routine echo examination in any patient with suspected acute myopericarditis, especially for the patients with preserved LVEF.

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Sažetak

PRIMJENA EHOKARDIOGRAFIJE S ANALIZOM GLOBALNE I REGIONALNE SISTOLIČKE DEFORMACIJE U DIJAGNOZI I PRAĆENJU BOLESNIKA S MIOPERIKARDITISOM

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Mioperikarditis je upalna bolest uzrokovana brojnim, često nepoznatim čimbenicima. Definitivna dijagnoza zahtjeva endomiokardijalnu biopsiju, no u kliničkoj je praksi najčešće zamjenjuju kombinacija kliničkih podataka, nalaza biokemijskih markera i slikovnih pretraga. Ehokardiografija s analizom sistoličke deformacije ("strain") važan je alat u dijagnozi, procjeni regionalne i globalne sistoličke funkcije koja pokazuje dobru korelaciju sa magnetskom rezonancom srca (cMRI).

Predstavljamo slučaj 19-godišnjeg muškarca s bolovima u prsima, povišenim vrijednostima troponina i elevacijom ST spojnice koji je upućen na hitnu koronarografiju. Nakon urednog nalaza koronarografije postavljena je sumnja na mioperikarditis, pogotovo u svjetlu nedavnog enterokolitisa i cijepjenja protiv SARS-CoV-2. Transtorakalnom ehokardiografijom s analizom deformacije miokarda nađeno je oštećenje longitudinalne sistoličke deformacije u više segmenata miokarda lijeve klijetke te prateći mali perikardijalni izljev što se uklapa u dijagnozu. Nakon tri mjeseca terapije protuupalnim lijekovima, ACE inhibitorom i beta blokatorom bolesnik se potpuno oporavio, s normalizacijom sistoličke funkcije i nestankom perikardijalnog izljeva na kontrolnoj ehokardiografiji.

Ehokardiografija s analizom globalne i segmentalne sistoličke deformacije nezamjenjiv je dijagnostički alat u bolesnika s mioperikarditisom, komplementaran s manje dostupnom cMRI. Njome se mogu otkriti znakovi subkliničke sistoličke disfunkcije nedostupni konvencionalnoj ehokardiografiji što utječe na terapiju i prognozu bolesnika.

Ključne riječi: *mioperikarditis, GLS, sistolička deformacija miokarda*