CASE PRESENTATION

Myocarditis or myocardial bridging? Filling the diagnostic gap
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Abstract: We present the case of a 19-year-old patient who was brought to the emergency room of the local hospital during the night for an episode of chest pain that lasted for about 2 hours during the morning, which recurred in the evening, though of lesser intensity and duration. The clinical picture, initial presentation data and paraclinical workup with echocardiography, coronary angiography and cardiac MRI balanced the diagnosis between two possibilities: myocarditis and acute coronary syndrome caused by a myocardial bridge causing severe LAD stenosis. The papers discusses the current literature on both diseases and describes the diagnostic and management algorithm we followed.

Keywords: myocarditis, myocardial bridge, cardiac magnetic resonance

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The ECG at presentation (Figure 1) showed sinus rhythm, R/S >1 in V1, small ST segment elevation and high voltage T waves in leads V2-V5.
The laboratory workup showed elevated troponin (3.26 ng/ml), CK-MB (56.6 ng/ml) and AST (95 U/L); also moderately high levels of C-reactive protein (1.27 mg/L).

The echocardiography (Figure 2) showed normal heart morphology and function, except for a small pericardial effusion (maximum of 3 mm lateral of the left ventricle) (Figure 2A). Moreover, when subclinical LV dysfunction was verified, there was a normal global LV strain without regional dysfunction (Figure 2B).

During his hospital stay he was treated as an acute coronary syndrome with nadroparine, aspirin, beta blocker, NSAIDs and H2-receptor antagonist with good clinical evolution and no recurring chest pain. He was transferred to our clinic for further investigations. At the time of the transfer the necrosis enzyme levels had normalized, the ECG aspect remained the same and no pericardial effusion was visible on the echocardiography.

At local hospital discharge, there remained to determine the final diagnosis with a differential between myocarditis and myocardial infarction in a young patient. There were reasons for and against both of the diagnoses: the acute thoracic pain, high troponin levels and R/S >1 aspect in V1 pleaded for inferior myocardial infarction, while the age of the patient, the pericardial effusion and the inflammatory syndrome were all suggestive for myocarditis.

With the purpose of determining a final diagnosis we decided on a series of investigations:

First, after normal present clinical exam, echocardiographic aspect and laboratory workup, the patient underwent a coronary angiography, which showed no atherosclerotic lesions, but a myocardial bridge on LAD segment II with 80% stenosis during systole (Figure 3). This finding raised the idea that myocardial ischemia was a possible diagnosis.

In order to determine the importance of myocardial ischemia, the patient had an echocardiographic stress test, which was submaximal (max HR=82% of the predicted maximum), but negative clinically, echocardiographically and on the ECG. This development again put doubt on the ischemic hypothesis.

In order to further describe myocardial structural and functional changes, the patient underwent cardiac magnetic resonance (CMR) (Figure 4), which showed normal left ventricle volume and systolic function, with myocardial hypersignal areas in the T2 sequence, with a ratio greater than 2 compared to skeletal muscle, which suggest the presence of edema areas. After the administration of contrast substance, during late enhancement, there was a finding of spotted medioparietal contrast intake with evolution toward the epicardium. It also showed circumferential pericardial effusion of a maximum thickness of 6 mm. The radiologist’s interpretation was that the aspect is highly suggestive for acute myopericarditis, with the location of the lesions being suggestive of infection with B19 parvovirus.

To sum up, this is the case of a young patient with symptoms and paraclinical findings which placed the possible diagnosis between acute coronary syndrome...
and myocarditis. The development of the diagnosis in real-time was very interesting, with data inclining the balance towards each of the two possibilities: after coronary angiography we were highly inclined toward having a final diagnosis of acute coronary syndrome on the basis of a symptomatic myocardial bridge, but after completing the CMR, 2 days later, myocarditis became a certain diagnosis, with the myocardial bridge remaining probably just an incidental finding.

What remained to be determined was the appropriate treatment. For the moment, we considered that there was no treatment needed for the myocarditis, because the episode was thought to be an acute one with no objective or subjective long-term damage, the patient being advised to undergo another CMR investigation in 6 months’ time, to evaluate any progression of the lesions or pericardial effusion. As for the myocardial bridge, the treatment consists of beta-blocker medication, with no interventional or surgical treatment for the present time, the bridge being considered an incidental finding. However, the patient will still need periodic clinical evaluation along with stress echocardiography, to help determine on the opportunity of further treatment, surgical or otherwise.

**DISCUSSION**

The present case reflects in a very practical manner the diagnostic difficulties in acute myocarditis, due to the polymorphic clinical, laboratory and imaging picture.

**MYOCARDITIS**

Myocarditis is defined by WHO/ISFC as an inflammatory disease which envelops histological (Dallas criteria), immunological and immunohistochemical criteria¹. However, most of the patients with clinical manifestations of myocarditis do not undergo endomyocardial biopsy (EMB), exam which can confirm a diagnosis otherwise uncertain for these criteria.

Although in many cases the etiology remains undetermined², the most common cause in developed countries is viral infection³, with the possibility of bacterial, fungal, parasitic, toxic (radiation) and immunologic causes⁴. Even though EMB remains the gold standard, it is not used on clinically stable patients, which is the reason that the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases launched new diagnostic criteria in 2013.

**Figure 4.** Cardiac magnetic resonance: Panels A and B demonstrate good systolic LV function. Panel C shows myocardial hypersignal areas in the T2 sequence. Panels D and E demonstrate diffuse late medioparietal contrast intake.
Clinical manifestations are highly variable, ranging from mild symptoms (fatigue, chest pain) to heart failure and life threatening conditions (ventricular arrhythmias, cardiogenic shock and even sudden death) \(^{2,4-6}\) (Table 1). Myocarditis is more frequent in young people, even though all age groups can be affected.

Because of the large diversity of clinical manifestations, clinical practitioners should have a high level of suspicion with the earliest onset of symptoms and use all the appropriate investigations for quickly determining a correct diagnosis. In all situations of suspected myocarditis, especially in cases of acute coronary syndrome-like symptoms (as is the case with our patient) it is mandatory to exclude coronary artery disease.\(^{3}\)

Sometimes patients with other cardiovascular comorbidities (arterial hypertension, coronary artery disease or cardiomyopathies) can also suffer from myocarditis which means they need more investigations, sometimes including EMB to be able to clarify the diagnosis.

### Imaging in myocarditis

Based on a consensus of experts\(^ {2}\), there are first-line tests recommended for patients whose symptomology is consistent with myocarditis.

The first among these is the ECG, which may be normal or with non-specific abnormalities\(^ {7,8}\). Findings may include ST changes, different types of arrhythmias (atrial and ventricular premature beats, atrial fibrillation, non-sustained ventricular tachycardia, AV block), ST segment elevation in myocarditis is typically concave (while in myocardial infarction it is convex) and diffuse without reciprocal changes. Our patient did not present with evolutive ECG changes, and his ECG pattern was also possibly suggestive of acute ischemia (tall symmetric T waves).

Secondly, echocardiography is a very useful method for detecting impairment of ventricular function\(^ {9,10}\). Other findings include LV dilatation, changes in LV geometry, diastolic dysfunction, wall motion abnormalities and pericardial effusion. Myocarditis can mimic the echographic aspect of different types of cardiomyopathies or coronary artery disease\(^ {11}\). Except for a small pericardial effusion, no changes in conventional echocardiography were found in our patient.

Last but definitely not least, CMR provides the unique ability of non-invasive tissue characterization of the myocardium, which could suggest myocarditis: inflammatory hyperemia and edema, myocyte necrosis and scars, changes in ventricular size and geometry, global and regional wall motion abnormalities, pericardial effusion\(^ {12,13}\). The International Consensus Group on CMR Diagnosis of Myocarditis published a list of recommendations based on preclinical and clinical investigations (Table 2). Specific CMR changes were found in our patient contributing to the final diagnosis of myocarditis.

Finally, radionuclide ventriculography is useful only when echocardiography images are suboptimal and cardiac MRI is unavailable.

### Table 1. Diagnostic criteria for clinically suspected myocarditis (reproduced with permission from \[2\])

<table>
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<th>Clinical presentations^6</th>
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<tr>
<td>Acute chest pain, pericarditic or pseudo-ischemic</td>
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<tr>
<td>New-onset (days up to 3 months) or worsening of: dyspnea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs</td>
</tr>
<tr>
<td>Subacute/ chronic (&gt;3 months) or worsening of: dyspnea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs</td>
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<td>Unexplained cardiogenic shock</td>
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**Diagnostic criteria**

<table>
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<tr>
<th>I. ECG/ Holter/ stress test features</th>
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<td>Newly abnormal 12 lead ECG and/ or Holter and/ or stress testing, any of the following: I to III degree atrioventricular block, ST/ T wave change (ST elevation or non ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supraventricular tachycardia</td>
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<th>II. Myocardiocytolysis markers</th>
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<td>Elevated TnT/ Tnl</td>
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<th>III. Functional and structural abnormalities on cardiac imaging (echo/ angio/ CMR)</th>
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<tr>
<td>New, otherwise unexplained LV and/ or RV structure and function abnormality (including incidental finding in apparently asymptomatic subjects): regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endocavitary thrombi</td>
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<th>IV. Tissue characterization by CMR</th>
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<td>Edema and/ or LGE of classical myocarditic pattern</td>
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Clinically suspected myocarditis if ≥1 clinical presentation and ≥ diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease (coronary stenosis ≥50%); (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome (e.g. valve disease, congenital heart disease, hyperthyroidism, etc. Suspicoin is higher with higher number of fulfilled criteria.

Legend: ‘If the patient is asymptomatic ≥2 diagnostic criteria should be met.'
Even though viruses are the most common cause for myocarditis, viral antibodies as well as serum cardiac autoantibodies have been found to have limited utility in the diagnostic process.

Management of myocarditis

Whenever myocarditis is suspected admission into the hospital is recommended, for unstable patients even in Intensive Care Units with respiratory and cardiopulmonary support capabilities. In cases of fulminating myocarditis, ventricular assist devices or extracorporeal membrane oxygenation could also be necessary as a life-saving measure.

To conclude, in stable patients, CMR is highly recommended, while in patients with life-threatening conditions, EMB should be performed urgently.

Biomarkers in myocarditis

Erythrocyte sedimentation rates and C-reactive protein levels are often increased in myocarditis as a result of inflammation. On the other hand, a normal troponin value does not exclude myocarditis even if troponin levels are sensitive to myocyte injury. It should also be mentioned that in case myocarditis leads to heart failure BNP and NTproBNP are found to be high.
breath to cardiac transplant or to recovery. Treatment for arrhythmias and heart failure are in line with current ESC guidelines. Physical activity should be limited during the acute phase of myocarditis as well as during at least the following 6 months.

One thing to be considered is that immunosuppressive therapy using steroids alone or in combination with azathioprine with or without cyclosporine A should be started only after ruling out active infection. Immunosuppressive therapy should be administered only in proven cases of autoimmune myocarditis without counter indications of immunosuppression. In these cases, an EMB should be repeated to determine the intensity and duration of immunosuppression.

Other less applicable therapeutic methods include: modulatory therapy using antiviral treatment, high doses of intravenous immunoglobulin, and immunoadsorptions.

The prognosis and outcome of myocarditis is variable based on etiology, clinical features, the disease stage, and co-morbidities. Assuming that the majority of cases are resolved in the first 2-4 weeks, approximately 25% will develop persistent cardiac dysfunction and 12-25% may progress and deteriorate into dilated cardiomyopathy or death.

**MYOCARDIAL BRIDGING**

The particularity of the present case consists in the presence of myocardial bridging with severe systolic compression in a young patient with myocarditis.

The major coronary arteries which normally are distributed over the epicardial surface of the heart, occasionally grow intramurally through the myocardium. During the systolic phase the intramural segment is compressed realizing systolic myocardial bridging. Even though, myocardial bridging was first identified as early as 1737, it was first described angiographically in 1960. The estimated frequency of this congenital abnormality has a large variation, ranging between 1.6-16% when assessed by coronary angiography. Even if all major epicardial coronary arteries could be affected, the most prevalent is the LAD. Bridges have been classified as deep or superficial based on the thickness of the overlying myocardium and on the type of myocardial fibers they consist of: ones that only traverse over the coronary segment and ones that encircle it. The hemodynamic impact is influenced by these factors as well as the length of the bridge and the presence of adipose and connective tissue surrounding the segment.

Myocardial bridging is generally a benign condition but it could have complications such as ischemia and acute coronary syndrome, coronary spasms, ventricular septal rupture, arrhythmias, transitory ventricular dysfunction, and even sudden death. Despite it being an inborn condition, symptoms appear usually in the third decade of life. While case presentations are frequent in the literature, no big studies or case-series really reflect the prevalence of associated complications. Myocardial bridging can be suspected in patients with angina without existing risk factors or evidence of ischemia. Myocardial bridging may be associated up to 30% with hypertrophic cardiomyopathy and is a risk factor for cardiac complications in this disease.

The diagnosis can be based on both noninvasive and invasive techniques. Noninvasive imaging has been used for diagnosis and evaluation the ischemic impact: multiple-slice computed tomography shows myocardium surrounding the coronary segment, with recent developments on this method, allows for physiological analysis as well; stress single-photon emission computed tomography can related the ischemic impact to the degree of coronary narrowing; while stress echocardiography is the most readily available noninvasive technique, it is not well validated.

Angiographic diagnosis is based on a change in diameter of more than 70% during systole, creating a significant “milking effect”. In addition to regular angiography, other invasive methods can help with evaluating the impact and pathophysiology of the myocardial bridge. Intravascular ultrasound may show the “half-moon” sign, which is a hyperechogenic area between the coronary segment and the epicardium and can also characterize proximal minimal atherosclerosis, which cannot be detected during angiography. Intracoronary Doppler and pressure measurement (with pharmacological infusion) aids in the evaluation of the endothelial dysfunction, the proximal plaque and the level of vasospasm involved, while stimulating myocardial obstruction.

Myocardial bridging causes coronary artery obstruction only during the systole and it does not significantly influence myocardial perfusion since two thirds of the perfusion occurs during diastole. In situations of persistent narrowing in early diastole (in severe bridging or in tachycardia) myocardial ischemia could be detected.

The relationship between atherosclerosis and myocardial bridging also represents an interesting topic. It has been proven that the intima of tunneled arteries is considerably thinner than the intima of the proximal segment. From a histological point of view the intima beneath the bridge consists only of contractile type...
smooth cells and interstitial collagen without synthetic type smooth cells. These changes indicate protection against atherosclerosis progression, since there is a lack of synthetic type smooth cells which normally proliferate and produce collagen fibrils and elastic fibers. Another notable fact is that at the bridging level there is a decreased expression of vasoactive agents, such as endothelial nitric oxide synthetase (eNOS), endothelin 1, angiotensin converting enzyme. However, using IVUS some researchers have reported increased atherosclerotic plaques proximal of the bridging.

The evaluation of the ischemic impact of myocardial bridging in our patient was performed by echographic stress test, which was negative which suggests that the myocardial bridge does not have a significant functional impact. A study by Escaned et al compared mean diastolic fractional flow reserve (FFR) with and without dobutamin inotropic stimulation in myocardial bridging. The reported data suggested that the functional severity of some myocardial bridges is only established after inotropic stress.

For the treatment of angina produced by myocardial bridging, beta-blockers and nondihydropyridine calcium channel blockers may be valuable options through their action to reduce heart rate and myocardial contractility. Calcium blockers may be more beneficial in patients who associate significant vasospasm (though there are no randomized studies comparing the two). Also worth taking into consideration is the introduction of antiplatelet therapy, because of the increased risk of atherosclerosis and endothelial cell instability right before the start of the bridged segment, especially if subclinical atherosclerosis has been demonstrated through advanced imaging techniques (described above). Nitrates are contraindicated because of their contractility sympathetic stimulation.

Even though preliminary data suggest that stents may normalize coronary distortions and improve clinical symptoms, there are relatively higher rates of target lesions revascularization and complications such as coronary artery perforation or stent fracture. Tsujita et al. in a study on 70 patients with symptomatic myocardial bridging, who had percutaneous angioplasty mostly with drug eluting-stents, showed a need for target-lesion revascularization of 24% in patients with myocardial bridging, compared to 4% in patients with stents for epicardial obstructive lesions. Another study on 11 patients showed that bare-metal stent implantation has a higher risk of intra-stent stenosis, with 4 pts having to undergo revascularization procedures during follow up, which is comparable to lesions of 25 mm length in coronary artery disease.

Surgical therapy with dissection of overlying myocardium is indicated for patients with persistent symptoms despite medical treatment. The optimal surgical treatment is represented by the dissection of the overlying myocardium with the complete exposure of the coronary artery. This is sometimes also accompanied by by-pass graft. A small study showed good clinical results, but also reported serious complications such as ventricular aneurysm and ventricular perforation.

The Schwarz classification for myocardial bridges and treatment suggests no treatment for an incidentally discovered bridge (type A), treatment with beta-blockers or calcium blockers for positive stress tests (type B), and possible invasive treatment (surgical or interventional) for patients with altered intracoronary hemodynamics measured by advanced imaging methods.

For our patient, the preferred treatment was beta-blockers for now even though echographic stress test results were negative for ischemia. This decision was taken because, in a young man with possible interest for exercise and an active life, myocardial ischemia can be exacerbated by the myocardial bridge.

**CONCLUSIONS**

This is a case which reflects very well the diagnostic difficulties which doctors can face. Myocarditis can many times have clinical manifestations and laboratory workup similar to acute coronary syndrome which should always lead to excluding coronary artery disease for a final diagnosis of myocarditis. Even though it is not an uncommon finding, there are no large studies regarding the therapy of myocardial bridging. This paucity of medical data makes it hard to decide on treatment if the bridge provokes severe stenosis and becomesymptomatic.

The case shows the importance of following through with a full set of investigations even after a potential diagnosis is reached, allowing a correct final diagnosis and a proper management.

**Conflict of interest:** none declared.

**References**


Myocarditis or myocardial bridging? Filling the diagnostic gap

Sebastian Militaru et al.


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