ST-segment Elevation: Myocardial Infarction or Simulacrum?

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A rapid diagnosis of ST-segment elevation myocardial infarction (STEMI) is mandatory for optimal treatment of an acute coronary syndrome. However, a small number of patients with suspected STEMI are afflicted with other medical conditions. These medical conditions are rare, but important clinical entities that should be considered when evaluating a STEMI alert. These conditions include coronary vasospasm, Takotsubo cardiomyopathy, coronary arteritis/aneurysm, myopericarditis, Brugada syndrome, left bundle branch block, early repolarization, aortic dissection, infective endocarditis with root abscess, subarachnoid hemorrhage, ventricular aneurysm after transmural myocardial infarction, and hemodynamically significant pulmonary embolism with right ventricular strain. Herein, we present several STEMI mimickers.

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KEY WORDS

ST-segment elevation myocardial infarction • Coronary angiography • Percutaneous coronary intervention • Electrocardiography • Echocardiography • Myocarditis • Coronary vasospasm • Aortic root abscess • Takotsubo cardiomyopathy

A rapid and accurate diagnosis of acute ST-segment elevation myocardial infarction (STEMI) is of crucial importance as early initiation of primary percutaneous coronary intervention (PCI) is beneficial to patients.[1-3] Plaque rupture or erosion with subsequent platelet aggregation and thrombosis development, resulting in an acute occlusion of a coronary artery, are considered

the main mechanisms of STEMI. However, coronary arteries without any stenosis have been reported in 3% of patients with suspected STEMI.[4]

Several conditions may present with an electrocardiographic pattern identical to STEMI in clinical practice.[5] First, transient ST-segment elevation can occur in patients with significant coronary artery stenosis in the absence of total occlusion. Second, noncoronary cardiac entities such as pericarditis and myocarditis can also present with electrocardiogram (ECG) findings that simulate a myocardial infarction (MI).[6,7] A third group of conditions that sometimes have a STEMI-like presentation are of vascular origin, such as pulmonary embolism and aortic dissection.[8,9] Finally, noncardiac conditions such as acute cholecystitis or pancreatitis may also mimic STEMI.[10,11] The clinical implications of recognizing the various diseases that can lead to an ECG manifestation of STEMI allow the appropriate management of these patients. Though first-line administration of antiplatelet and anticoagulation therapy may be pivotal to the management of an acute coronary syndrome (ACS), it is not the appropriate treatment for the rest of the above-named clinical entities and may even be detrimental in some of these clinical scenarios of STEMI mimickers.

Although these disorders simulating STEMI have been described in the medical literature, mostly through individual case reports, the infrequent occurrence of these conditions reduces clinical awareness and mandates a collective discussion of the mimickers of STEMI, such as coronary spasm, aortic dissection/root abscess, Takotsubo cardiomyopathy, myocarditis/pericarditis, coronary embolism, left bundle branch block (LBBB), left ventricular (LV) hypertrophy with repolarization, drugs (eg, cocaine, weight-loss supplements with amphetamine-like properties), pulmonary embolism, ventricular aneurysm, and cardiac contusion. The clinical circumstances surrounding the clinical presentation frequently help distinguish true STEMI from conditions mimicking STEMI. We present seven cases that presented as STEMI alert. These cases reinforce the need for a broad differential diagnosis when a STEMI alert is activated.

The clinical circumstances surrounding the clinical presentation frequently help distinguish true STEMI from conditions mimicking STEMI.

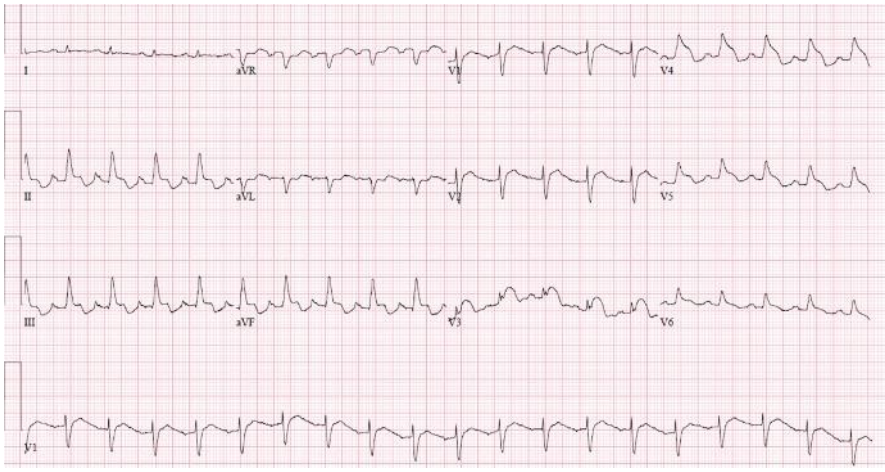
Case 1

Coronary Vasospasm

An obese 35-year-old woman presented to the emergency department (ED) with sudden onset of severe, substernal chest pain that started 30 minutes prior while she was exercising at the gym. Her history was remarkable for phentermine use for weight loss. Initial vital signs were significant for a temperature of 97.3°F, regular heart rate of 75 beats/min, blood pressure of 151/88 mm Hg, and respiration rate of 24 breaths/min. ECG showed ST-segment elevation in the anterior and inferior leads (Figure 1). A STEMI alert was called by the ED physician. While in the ED, she suddenly became unresponsive and cardiopulmonary resuscitation was started. Her rhythm was ventricular fibrillation. She was intubated, given intravenous epinephrine, and defibrillated twice, with the return of spontaneous circulation. She was started on norepinephrine and epinephrine intravenous infusion to maintain her blood pressure, and was taken emergently for cardiac catheterization.

Coronary angiogram revealed a long 99% stenosis in the mid-to-distal segments, suspicious for coronary vasospasm, of a large wraparound left anterior descending artery (LAD) (Figure 2A). The remainder of her coronary arteries was angiographically normal. An intra-aortic balloon counterpulsation pump was inserted to help augment her blood pressure. However, her marginal blood pressure

Figure 1. Electrocardiogram demonstrating ST-segment elevation in the anterior and inferior leads.



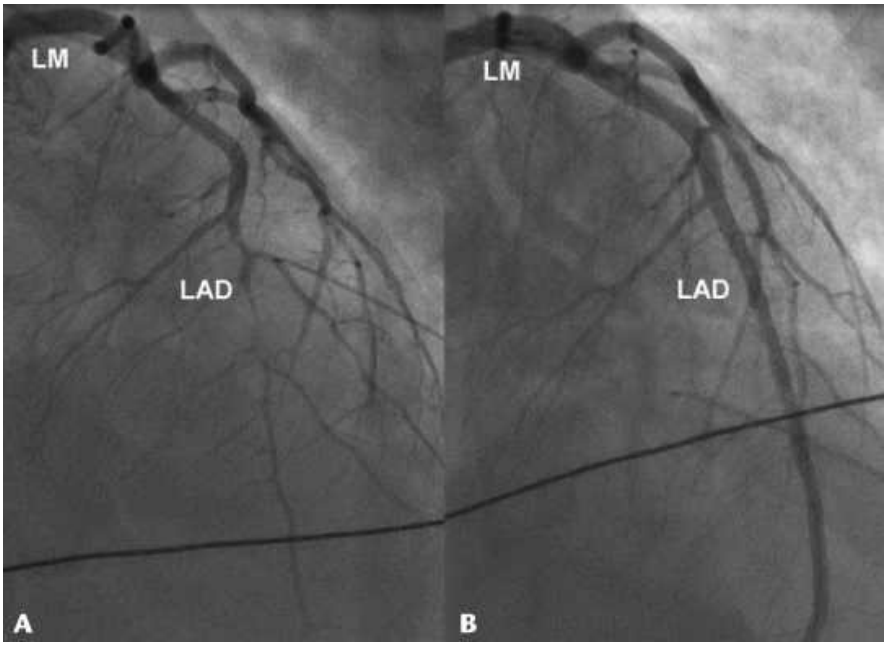


Figure 2. **(A)** Severe LAD spasm. **(B)** After stenting the LAD. LAD, left anterior descending artery; LM, left main artery.

prohibited the use of intracoronary nitroglycerin to relieve the spasm. The stenosis was successfully treated with balloon angioplasty followed by PCI with two overlapping drug-eluting stents and the subsequent return of normal perfusion (Figure 2B).

An ECG after PCI showed sinus tachycardia and resolution of the ST-segment elevation. Transthoracic echocardiogram (TTE) was significant for akinesis of the mid-to-apical septal, anterior and lateral walls, and apex, with an estimated LV ejection fraction (LVEF) of 25% to 30% and apical clot. Her cardiac function recovered; repeat TTE 4 days later showed a normal LVEF of 60% to 65% and normal wall motion and resolution of the apical clot.

The term coronary artery spasm (CAS) refers to a sudden, intense vasoconstriction of an epicardial coronary artery that causes vessel occlusion or near occlusion. Transmural myocardial ischemia caused by occlusive CAS can be complicated by malignant ventricular arrhythmias and may result in acute MI and, potentially, sudden death.[12-14]

CAS results from the interplay of two mechanisms: a localized abnormality of a coronary artery that makes it hyperreactive to vasoconstrictor stimuli, and a vasoconstrictor stimulus, inducing the spasm at the level of the hyperreactive coronary segment. The mechanisms proposed to establish the substrate for susceptibility to CAS include the following: (1) endothelial dysfunction, (2) a primary hyperreactivity of vascular smooth muscle cells (VSMCs), and (3) other clinical factors.

Causes of Coronary VSMC Hyperreactivity

Although local coronary VSMC hyperreactivity appears to constitute the substrate for CAS, the causes of the vascular abnormality in the clinical setting remain largely undefined.

Clinical Risk Factors

Common cardiovascular risk factors do not seem to show a significant association with CAS, with the exception of smoking. Active smokers constitute approximately 75% of patients with variant angina and presumed CAS. Why smoking favors CAS, however, remains unknown. Cigarettes contain several toxic substances, such as nicotine and carbon monoxide, that impact the vascular system as well as proinflammatory substances that might cause spasmogenic alterations in the VSMCs in predisposed subjects.[15,16] It is known that the consumption or abuse of cocaine, amphetamines, marijuana, 5-fluorouracil, capecitabine, and sumatriptan can provoke or favor CAS.[17-20]

Inflammation

The possible role of inflammation in the pathogenesis of CAS was suggested by the detection, in postmortem studies, of inflammatory cells—in particular, mast cells—in coronary vasospastic segments.[20,21] Moreover, higher levels of C-reactive protein have been reported during the active phases of variant angina in comparison with the inactive phases.[22] However, inflammation is highly prevalent in, and most often associated with, atherosclerosis, whereas variant angina is a rare condition.

Genetic Polymorphisms

Several genetic mutations may potentially be involved in the predisposition of patients with variant angina to CAS. They mainly concern the gene encoding for nitric oxide synthase,[23] but polymorphisms have also been described for other proteins able to modulate vascular tone, such as adrenergic and serotoninergic receptors, antioxidant enzymes, angiotensin-converting enzymes, and inflammatory cytokines.[24-28]

Ethnic Influences

When observing the prevalence of vasospastic angina between

Japanese and white populations, there appears to be a difference. In cohort studies of white patients with angina pectoris, the prevalence of variant angina is 1% to 2% only, whereas it is much higher in Japanese cohorts.[29,30] Differences between the two ethnic groups with regard to diet, lifestyle, and cardiovascular risk profiles could also account for the disparity in CAS features, as suggested by the fact that Japanese individuals who live in Western countries develop a pattern of cardiovascular disease similar to that of white people.[31]

Autonomic Nervous System

Among the potential triggers of CAS, the autonomic nervous system has implications in the pathophysiology. The relationship between autonomic nervous system and CAS, however, is complex and dichotomous, because both an increase in either sympathetic or parasympathetic tone can serve as a trigger for CAS. CAS can be induced by catecholamines, or by stimuli such as exercise and cold that increase sympathetic outflow.[32,33] It is known that β-blockers may exacerbate angina attacks in patients with variant angina, likely because of the blockade of vasodilator coronary β_2 receptors, which leaves vasoconstrictor α-adrenergic receptors unopposed.[34-37]

In physiologic conditions, acetylcholine—the neurotransmitter of parasympathetic nerve fibers—causes vasodilation through the endothelial release of nitric oxide, whereas at high doses it may induce vasoconstriction through direct stimulation of VSMC muscarinic receptors. In the clinical setting, some findings suggest a role for vagal activity as a trigger of spasm. In patients with variant angina, attacks often occur during the night, when vagal tone is higher, and the intracoronary administration of acetylcholine is known to induce CAS.[38,39]

Though the underlying pathophysiology of CAS remains elusive and enigmatic, CAS is an important consideration in the differentials for ST-elevation findings on ECG, especially in the appropriate clinical setting.

Case 2

Aortic Abscess Causing Extrinsic Compression of the Coronary Arteries

A 48-year-old woman presented to the ED with sudden-onset crushing chest pain, shortness of breath, and diaphoresis that woke her from sleep. She had a history of bioprosthetic aortic valve replacement and annulus debridement for native aortic valve infective endocarditis 17 days prior. Tissue cultures had grown *Streptococcus agalactiae,* for which she was on intravenous ceftriaxone and gentamycin, with a plan to continue treatment for 6 weeks.

In the ED, her vital signs were significant for a temperature of 98.2°F, a heart rate of 170 beats/min (atrial fibrillation), a blood pressure of 72/48 mm Hg, and a respiration rate of 30 breaths/min. She underwent immediate cardioversion to sinus rhythm without improvement in her symptoms.

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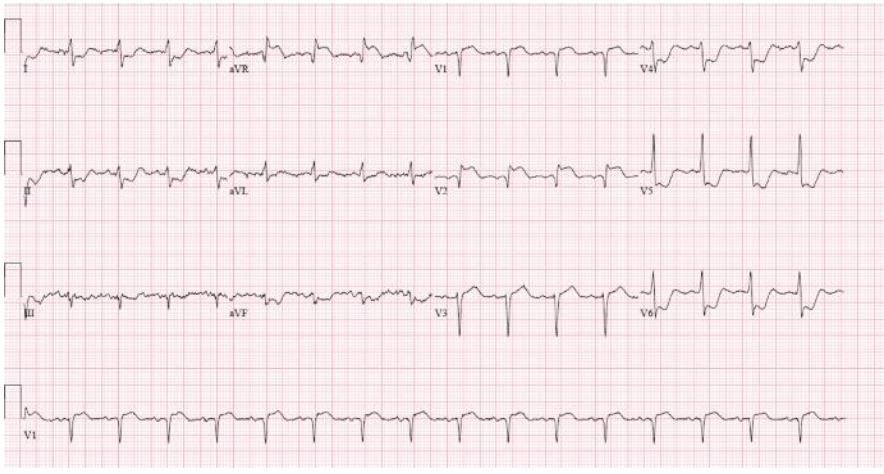
An ECG was performed that showed anterior ST-segment elevation in leads V1-V3 and aVR, with reciprocal inferolateral ST-segment depressions (Figure 3). A STEMI alert was called by the ED physician. She was taken emergently for cardiac catheterization.

Coronary angiogram revealed severe external compression of the left main artery, proximal LAD, and proximal left circumflex coronary artery by an aortic root abscess (Figure 4A). She underwent successful PCI stenting from the left main artery into the LAD and proximal left circumflex

Figure 3. Electrocardiogram showing ST-segment elevation in leads V1-V3 and aVR with reciprocal inferolateral ST-segment depression.



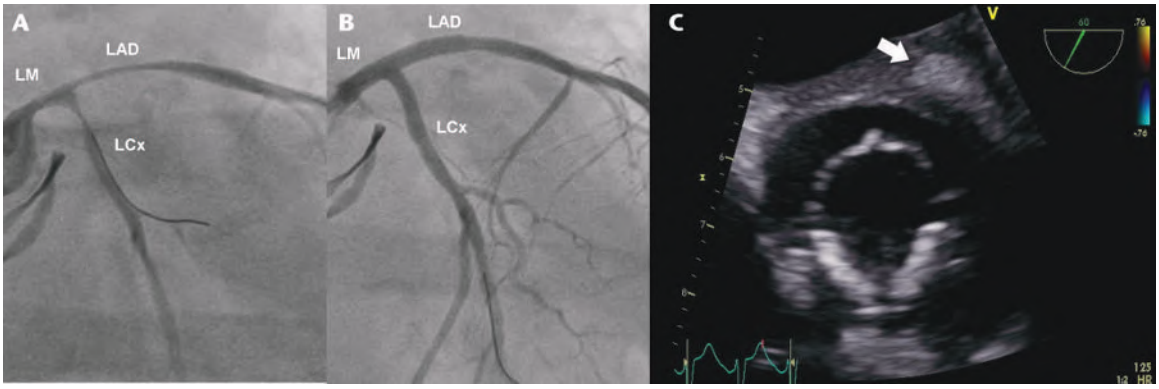


Figure 4. **(A)** Coronary angiogram revealed severe external compression of the left main artery, proximal LAD, and proximal left circumflex coronary artery by an aortic root abscess. **(B)** After PCI stenting from the LM into the LAD and proximal LCx. **(C)** TEE confirming root abscess (*white arrow*) and revealing severe paravalvular aortic regurgitation. LAD, left anterior descending artery; LCx, left circumflex artery; LM, left main artery; PCI, percutaneous coronary angiography; TEE, transesophageal echocardiography.

coronary artery (Figure 4B). Urgent transesophageal echocardiography (TEE) confirmed the root abscess (Figure 4C) and revealed severe paravalvular aortic regurgitation (Figure 4B).

This case highlights the complexity of infective endocarditis (IE) and its erratic and novel clinical manifestations. IE is a clinical entity that leads to serious morbidity and mortality. There are > 15,000 new cases of IE in the United States each year (12.7/100,000 population in 2009).[40]

Cardiac complications occur in 30% to 50% of the cases of IE.[41] Heart failure is the most common cause of death, and most frequent reason for heart surgery in patients with IE. The reported incidence of paravalvular abscess at surgery or autopsy is 30% to 40%.[42] Native valve annular extension of infection is more common in aortic than mitral IE.[43] Paravalvular abscesses may involve the conduction system and are frequently seen with aortic valve IE, especially when the infection involves the valve ring between the right and left cusps. Patients with paravalvular abscesses have higher rates of systemic embolization and fatal outcomes.[44] Infrequent cardiac complications of IE include pericarditis, fistulous cardiac connections between the aorta and atrium or ventricle, and aortic valve dissection.[45]

The diagnosis of IE is based on a characteristic history and a constellation of clinical findings on physical examination. Blood cultures and laboratory results, ECG, chest radiography, and echocardiography all add supportive data to the clinical diagnosis and help identify complications. Individual case recognition of the features of IE is important because underdiagnosis can lead to morbidity and mortality, and overdiagnosis can lead to unnecessary use of antibiotics having potential for drug-related adverse events. The clinical complexity lies in distinguishing IE from an alternative source of infection in a patient with bacteremia and structural heart disease.

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Electrocardiography occasionally reveals diagnostic clues. The presence of ischemia or infarction on ECG may suggest emboli to the coronary circulation. The presence of conduction disturbances may be attributable to an extension of the infectious process to the valvular annulus or adjacent myocardium.

Case 3

Myocarditis

A 19-year-old man with a history of asthma presented with continuous, substernal, sharp, positional chest pain for 3 days. He had an upper respiratory infection 1 week prior. His vital signs were within normal limits. Cardiac auscultation revealed normal S1 and S2 heart sounds without murmurs or rubs. Results of the remainder of his physical examination were also unremarkable. An ECG showed diffuse ST-segment elevation (Figure 5). A STEMI alert was activated by the ED physician. Coronary angiogram was performed and revealed angiographically normal coronary arteries (Figure 6). Laboratory data were significant for a troponin T value of 3.43 ng/mL and an erythrocyte sedimentation rate of 61 mm/h. TTE showed a dilated LV cavity with severe global systolic dysfunction with an estimated LVEF of 25% and a small pericardial effusion. He was started on indomethacin and colchicine for treatment of myopericarditis with improvement in his symptoms. The patient had a transient ischemic episode and a

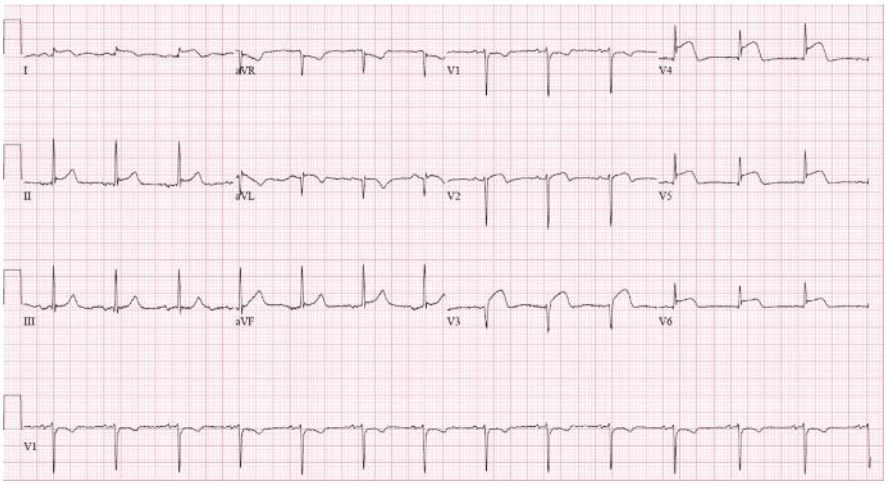

Figure 5. Electrocardiogram showing diffuse ST-segment elevation.

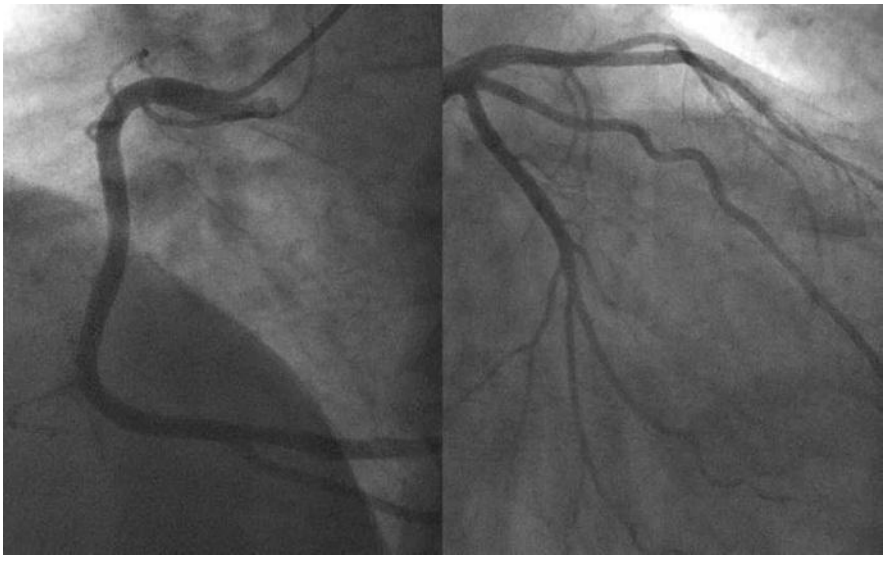

Figure 6. Coronary angiogram revealing normal right (*left panel*) and left (*right panel*) coronary arteries.

TEE was performed to evaluate for apical thrombus. The TEE revealed no evidence of apical clot. LV function remained severely depressed. The pericardial space had fluid and the parietal pericardium was immobile, suggesting an inflamed pericardium.

Myocarditis is a heterogeneous inflammatory disease of myocytes. Clinically and histologically, the disease has a myriad of presentations, ranging from benign to life threatening. Myocarditis has a wide spectrum of clinical manifestations, including subclinical disease, fulminant disease (which can be fatal), or indolent disease, which evolves to dilated cardiomyopathy. Histologic examination may yield focal or diffuse inflammatory involvement of the myocardium, with varying degrees of myocardial necrosis, edema, apoptosis, and cellular infiltration.

The presentation of myocarditis is often perplexing. It can masquerade as diverse disorders such as ACS, heart failure, sudden death, heart block, and myopericarditis when the epimyocardium is involved in the inflammatory process.[46]

The most common causes of myocarditis in Western countries include enteroviruses, adenoviruses, human parvovirus B19, human herpes virus 6, and cytomegalovirus. Bacterial, fungal, and protozoal infections are exceedingly rare in immunocompetent hosts.[47]

Autoimmune disorders such as systemic lupus erythematosus, Wegener granulomatosis, giant cell arteritis, and Takayasu arteritis are often coupled with myocarditis. Drug reactions, including illicit use of cocaine and amphetamines, should always be considered in the differential diagnosis.

Physical examination findings can range from completely normal to physical signs exhibiting cardiac dysfunction with gallop sounds as signs of heart failure, and murmurs associated with valvular regurgitation. Laboratory studies are often unhelpful, although elevated troponin levels reflect myocardial necrosis.

An ECG result can be normal or show abnormal findings such as nonspecific ST changes mimicking that of STEMI. The ischemia associated with myocarditis may be caused by local inflammation of the coronary arteries (coronary arteritis) with associated regional wall motion abnormalities.[5]

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Echocardiography has become a valuable supportive test for the diagnosis of myocarditis. Noninvasive and relatively cost effective, this imaging modality allows for the assessment of segmental wall motion abnormalities,

evaluation of valvular and myocardial function, and detection of thrombus.[48,49]

The 64-slice computed tomographic scan may be useful in evaluating patients because it can assess the coronary arteries, myocardium, and pericardial space, as well as rule out pulmonary embolus and aortic dissection (the triple rule-out). Another helpful and emerging modality in reinforcing the diagnosis of myocarditis is delayed gadolinium-enhanced magnetic resonance imaging. It demonstrates focal or diffuse nodular subepicardial-enhancing lesions in myocarditis and is a supportive test in verifying the clinical diagnosis. Cardiovascular magnetic resonance (CMR) imaging has the potential to predict myocyte recovery and provide insight for the long-term prognosis for patients with viral myocarditis.

The prognostic value of CMR imaging has been evaluated. Five investigators have shown that myocardial enhancement decreases over time in patients with myocarditis. Increased LV size, depressed LV function, and persistent symptoms at 3-year follow-up were observed in patients in whom early enhancement persisted on CMR for 4 weeks after identification of myocarditis. Early- and delayed-perfusion CMR imaging can be used to differentiate acute myocarditis from acute MI. In a study of 55 patients who underwent coronary angiography, 31 had coronary artery disease, and 24 had normal coronary angiogram results. The 24 patients with myocarditis and normal angiogram findings had resolution of symptoms and wall motion abnormalities. First-pass perfusion imaging revealed that 96% of the patients with myocarditis had normal findings, and 100% of the patients with MI had segmental distribution of subendocardial defects. Delayed enhancement revealed that patients with myocarditis had diffuse, patchy distribution in a nonsegmental vascular pattern, whereas patients with MI had segmental vascular distribution.[48]

At present, the definitive diagnosis of myocarditis requires endocardial biopsy. This procedure has a 1 in 250 chance of perforation and a 1 in 1000 chance of death in the hands of experienced operators.[50] The sensitivity of endomyocardial biopsy using Dallas criteria is approximately 10%.[51] Research into the genomic characteristics of myocarditis is yielding hope for noninvasive verification of the clinical diagnosis. Evolving data suggest that genomic studies may be more sensitive than endomyocardial biopsy in identifying myocarditis.[52] Thus, biopsy should be used judiciously and should be limited to patients at high clinical risk for treatable causes of myocarditis.

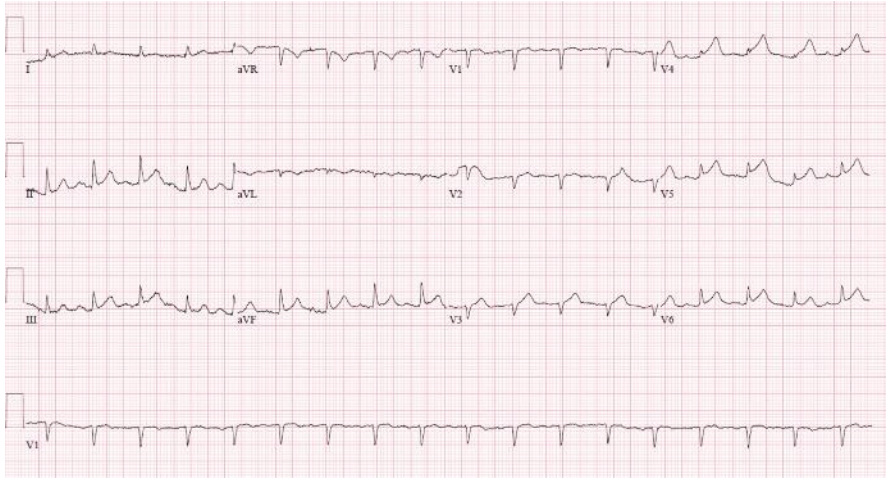
The diagnosis of myocarditis may be elusive; understanding the sensitivity, specificity, and predictive value of laboratory and imaging techniques may support the clinical diagnosis of myocarditis. Treatment of myocarditis is supportive and tailored to the clinical presentation. The natural history of myocarditis is as diverse as the clinical presentation and varies from complete recovery to cardiac transplantation. Patients who require cardiac transplantation have a 1-year mortality of 15% and a 4-year mortality of 50%.[53] Nonspecific therapy includes exercise avoidance, rhythm monitoring, antiarrhythmic therapy, heart failure treatment, and in selected cases, anticoagulation.

Case 4

Takotsubo Cardiomyopathy

Patient 1. A 67-year-old man with hypertension, hyperlipidemia, and type 2 diabetes presented for an outpatient myocardial perfusion imaging stress test ordered by his primary care physician for evaluation of dyspnea on exertion for 1 year. The patient was extremely anxious prior to starting the test. After completion of the rest imaging, intravenous regadenoson was administered as the stressor; 15 minutes after injection and prior to obtaining stress imaging, the patient suddenly complained of substernal chest pain with associated nausea and diaphoresis. An ECG revealed ST-elevation in leads II, III, aVL, and V4-V6 (Figure 7). A STEMI alert was called by the cardiology fellow. Emergent cardiac catheterization revealed angiographically normal coronary

Figure 7. Electrocardiogram revealing ST-elevation in leads II, III, aVL, and V4-V6.



arteries (Figure 8). TTE showed akinesis of the apex with preserved basal function, and an estimated LVEF of 25%.

Patient 2. A 45-year-old white man without any prior medical or cardiac history was admitted to the hospital after a motorcycle accident resulting in a concussion and broken femur. The patient denied use of illicit drugs. Results of his mental status examination were normal with orientation to person, place, and time. His vital signs were within normal limits. His blood pressure was recorded at 130/80 mm Hg and his pulse rate was 90 beats/min. Cardiac auscultation revealed normal S1 and S2 heart sounds without murmurs or rubs. He had chest wall pain on palpation. The remainder of his physical examination was unremarkable. During the course of hospitalization, the patient was anticipating surgery when he developed diffuse ST-segment elevation on the monitor; an ECG revealed findings that led to a STEMI activation (Figure 9). The patient has been having atypical chest pain since being admitted. An urgent coronary angiogram revealed normal coronary arteries (Figure 10). An echocardiogram immediately after catheterization revealed features of the apical ballooning syndrome. A repeat echocardiogram 5 days later revealed near-normal LV function.

Takotsubo cardiomyopathy is a unique form of transient nonischemic cardiomyopathy that typically occurs in a setting provoked by a stressor (physical, emotional, or both), and therefore is also given the nickname of stress-induced cardiomyopathy or "broken heart syndrome." The characteristic clinical syndrome of Takotsubo cardiomyopathy involves acute LV dysfunction with distinctive echocardiographic features of apical to mid-ventricular hypo- to akinesis and sparing of the basal myocardium in the absence of significant obstructive coronary artery disease. These changes resemble a flask with a narrow neck and a round bottom, shaped like the Japanese octopus trap "tako-tsubo," therefore earning the moniker Takotsubo cardiomyopathy. Alternatively, patients may exhibit reverse Takotsubo with basal hypokinesis and hyperkinesia of the apical and mid segments of the left ventricle.[54] Even though the apical ballooning phenotype is the most common and typical presentation, much confusion has resulted from various nomenclatures being used for different presentations of this syndrome. Clinical history, ECG, and diagnostic imaging with coronary angiography and/or CMR imaging that establishes the phenotypic features of the disease and exclude significant obstructive coronary artery disease (CAD) are essential for diagnosis and to differentiate it from an acute MI.

A well-recognized syndrome now, two decades after its first reported case, it is also being reported in populations other than postmenopausal women. The

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Figure 8. Emergent cardiac catheterization revealing angiographically near-normal right (*left panel*) and left (*right panel*) coronary arteries.

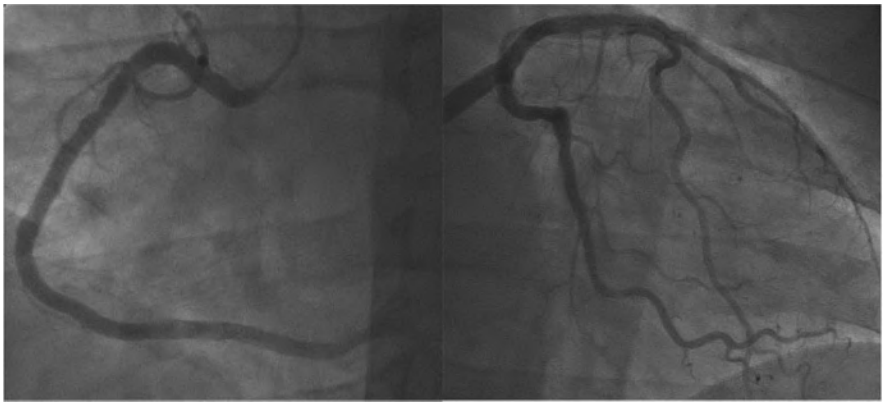
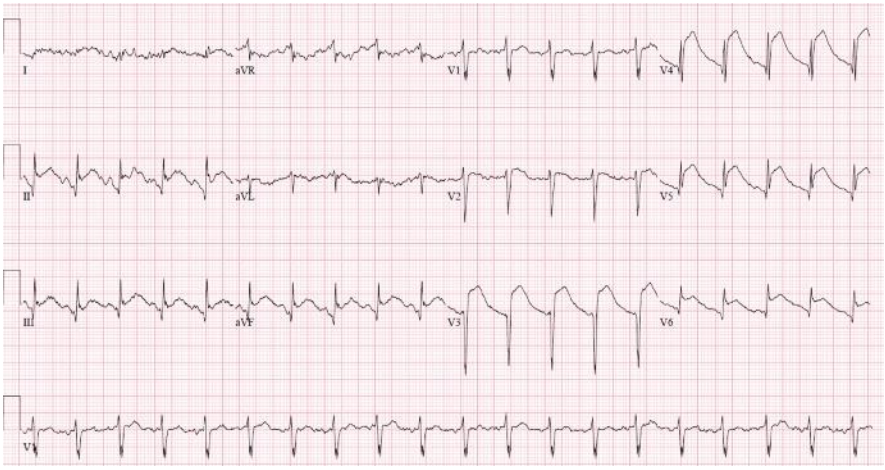


Figure 9. Electrocardiogram demonstrating striking ST-segment elevation in the anterolateral and inferior leads.



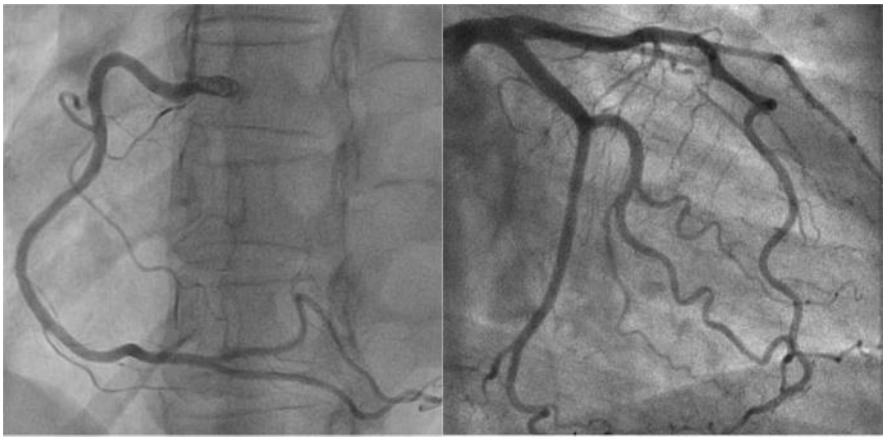


Figure 10. Urgent coronary angiogram revealed normal right (*left panel*) and left (*right panel*) coronary arteries.

underlying mechanism is not fully understood, but could be common and explained by changes in molecular pathways such as stimulus trafficking under supraphysiologic levels of catecholamines, and influenced by hormonal status. More studies are needed to fully understand the underlying mechanisms.

Patients usually present with typical chest pain (70%-90%) and dyspnea (20%); other less common presentations include syncope, pulmonary edema, and cardiac arrest.[55,56] Dynamic electrocardiographic changes and elevated cardiac biomarkers (reflecting acute myocardial injury) are usually present. Coronary angiography, however, does not reveal any evidence of epicardial coronary obstruction. Left ventriculography reveals LV dysfunction and wall motion abnormalities affecting apical, and frequently mid-ventricular, myocardium with sparing of the basal myocardium. Symptoms can be severe and lead to death in 2% of patients.[57] Song and colleagues reported 32% (n = 16) of their patients with Takotsubo cardiomyopathy (n = 50) presented with cardiogenic shock as the initial presentation.[58]

The most common electrocardiographic changes reported in Takotsubo cardiomyopathy are ST-segment elevations in precordial leads on admission (range, 46% to 100% of patients). Subsequent deep symmetrical T-wave inversion in multiple leads and Q-wave formation (range, 6% to 31% of patients) also are frequently found.[55,56] Also present may be QT interval prolongation (range, 450-501 ms).[55,59] The combination of clinical symptoms and electrocardiographic changes at patient's initial presentation makes differentiation of Takotsubo cardiomyopathy from ACS very challenging. Most patients present with elevated cardiac biomarkers and have a modest peak in levels within 24 hours, but levels are markedly lower than would be anticipated on the basis of the extent of wall motion abnormalities and electrocardiogram findings.[60,61]

Echocardiography plays a pivotal role in the diagnosis of Takotsubo cardiomyopathy, given the ability to rapidly perform an echocardiography at bedside. Accurate evaluation by echocardiography, particularly after coronary evaluation by catheterization, can assist in further defining the diagnosis, chiefly when echocardiography repeated after a few days to weeks shows complete normalization of regional wall motion abnormalities and LVEF. Typically, Takotsubo cardiomyopathy mimics an evolving acute anterior wall MI with akinesis of the apex, apical anterior wall, and septum. LV outflow tract obstruction, a transient phenomenon in Takotsubo cardiomyopathy, can also be recognized by echocardiography.

In clinical practice, three-dimensional speckle-tracking echocardiography can be used to assess myocardial mechanical function. It permits the calculation of complex myocardial mechanical parameters such as strain and strain rate, rotation, and torsion, as well as LV volume and ejection fraction in three dimensions within minutes. It has been validated against sonomicrometry and magnetic resonance imaging tagging. Overall, it was found to be more accurate and reproducible than two-dimensional speckle tracking echocardiography. We have observed that the global longitudinal, circumferential, and radial strains are all decreased significantly in acute anterior wall MI and Takotsubo cardiomyopathy in the acute phase. However, regional circumferential and radial strains at the mid and apical left ventricle are significantly lower in Takotsubo cardiomyopathy patients than in acute anterior wall MI.

Management should focus on supportive care in the acute phase, and avoid vasopressor medications. Mortality is low if patients survive the initial critical period and, by definition, they go on to have a full recovery. Recurrence has been reported but is rare. The rates of severe in-hospital complications were similar when comparing patients with Takotsubo cardiomyopathy and patients with true ischemic MI. Takotsubo cardiomyopathy follow-up revealed that the rate of major adverse cardiac and cerebrovascular events was 9.9%

per patient year, and the rate of death was 5.6% per patient year.

Case 5

STEMI

A 28-year-old man presented with substernal chest pressure, occurring multiple times during the day both at rest and exertion, associated with shortness of breath, lasting 30 to 60 minutes, which resolved on its own. He reported that he had been having intermittent chest discomfort for "15 years" that was crescendo in frequency for the past month. His CAD risk factors included tobacco abuse and a family history of premature CAD in his father. His vital signs and results of a physical examination were unremarkable. An ECG showed ST-elevations in the inferior leads and V4-V6 with reciprocal ST-depressions in leads 1 and aVL. A STEMI alert was called by the ED physician (Figure 11). Emergent cardiac catheterization showed a 99% lesion in the proximal LAD, and a 90% ostial lesion in the first diagonal branch of the LAD (D1) (Figure 12). He underwent successful PCI to the proximal LAD lesion, and percutaneous transluminal angioplasty to the D1. His echocardiogram showed an LVEF of 55%. His urine drug screen result was negative. Laboratory tests, including a complete blood count and comprehensive metabolic panel, and measurement of hemoglobin A1C and thyroid-stimulating hormone were normal. His lipid panel showed a total cholesterol of 164 mg/dL, a low high-density lipoprotein (HDL) cholesterol level of 24 mg/dL, a low-density lipoprotein cholesterol level of 109 mg/dL, and a triglyceride level of 149 mg/ dL.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent ECG ST elevation and subsequent release of biomarkers of myocardial necrosis.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent ECG ST elevation and subsequent release of biomarkers of myocardial necrosis. Diagnostic ST elevation in the absence of LV hypertrophy or LBBB is defined as new ST elevation at the J point in at least two contiguous leads of ≥ 2 mm (0.2 mV) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2-V3, and/or of ≥ 1 mm (0.1 mV) in other contiguous chest leads or the limb leads. The majority of patients will evolve ECG evidence of Q-wave infarction. New or presumably new LBBB has been considered a STEMI equivalent.[63]

Most cases of LBBB at presentation are of unknown temporal duration because prior electrocardiograms are not available for comparison. Presumably new LBBB at presentation occurs infrequently, may interfere with ST-elevation analysis, and should not be considered diagnostic of acute MI in isolation.[64] Criteria for ECG diagnosis of acute STEMI in the setting of LBBB have been proposed.

Figure 11. Electrocardiogram showing ST-elevations in the inferior leads and leads V4-V6 with reciprocal ST-depressions in leads 1 and aVL.

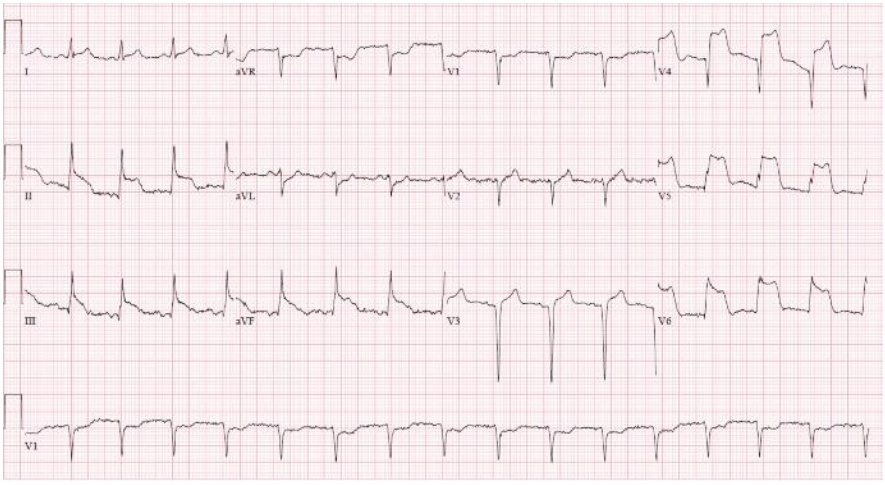
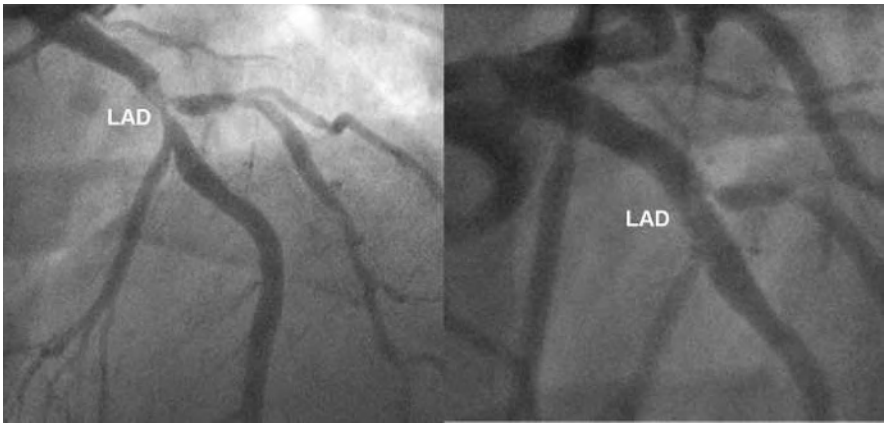


Figure 12. (*Left panel*) Coronary angiogram showing a 99% lesion in the proximal left anterior descending artery (LAD), and a 90% ostial lesion in the first diagonal branch of the LAD. (*Right panel*) LAD after percutaneous intervention.



Baseline ECG abnormalities other than LBBB, such as paced rhythm, LV hypertrophy, and Brugada syndrome may obscure interpretation. In addition, ST depression in ≥ two precordial leads (V1-V4) may indicate transmural posterior injury; multilead ST depression with coexistent ST elevation in lead aVR has been described in patients with left main or proximal LAD occlusion. Rarely, hyperacute T-wave changes may be observed in the very early phase of STEMI, before the development of ST elevation. TTE may provide evidence of focal wall motion abnormalities and facilitate triage in patients with ECG findings that are difficult to interpret. If doubt persists, immediate referral for invasive angiography may be necessary to guide therapy in the appropriate clinical context. Cardiac troponin is the preferred biomarker for diagnosis of MI.[65,66]

Demographics of young patients presenting with STEMI show that they are more likely to be men, obese, and smokers with elevated triglyceride and low HDL cholesterol levels. Other than sex and genetics, the latter risk factors of smoking, obesity, hypertriglyceridemia, and low HDL cholesterol level were important modifiable risk factors in these patients. Therefore, the foci of prevention should be cigarette cessation and reduction of the components of metabolic syndrome.[67]

Case 6

Pulmonary Embolism

A 77-year-old man with a recent history of right hip arthroplasty presented to the ED with acute respiratory distress and subsequent pulseless electrical activity arrest. He was intubated and successfully resuscitated. Physical examination was significant for a heart rate of 121 beats/min and a blood pressure of 76/47 mm Hg. An ECG demonstrated sinus tachycardia and ST elevation inferiorly with reciprocal posterior changes (Figure 13). A STEMI alert was called and emergent cardiac catheterization was performed. The patient had no significant CAD (Figure 14). Urgent two-dimensional TTE showed severe right ventricular (RV) strain with a flat, D-shaped septum, severe RV dilatation, RV free-wall akinesis, and preserved apical contractions. The echocardiographic features were suggestive of McConnell sign. The patient had contraindications to intravenous thrombolytic therapy, and subsequently underwent a pulmonary angiogram with transvenous catheter embolectomy of a massive left pulmonary artery embolism (Figure 15).

Pulmonary embolism (PE) has an incidence of 1 case per 1000 persons each year, and is the third leading cause of cardiovascular death.[68,69] The S1Q3T3 sign (S-wave in lead I, Q-wave and T-wave inversion in lead III) is present in 50% of patients with massive PE.[70] McConnell sign, characterized by RV dysfunction with sparing of the

Figure 13. Electrocardiogram revealing sinus tachycardia and ST-segment elevation inferiorly with reciprocal posterior changes.

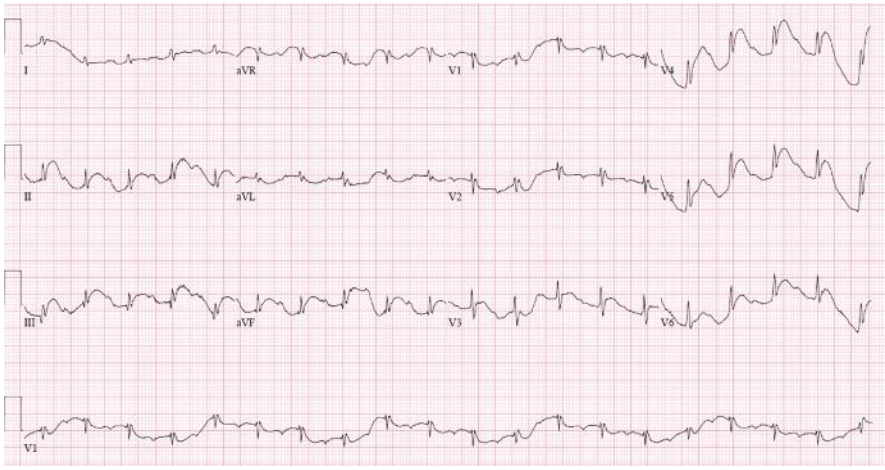
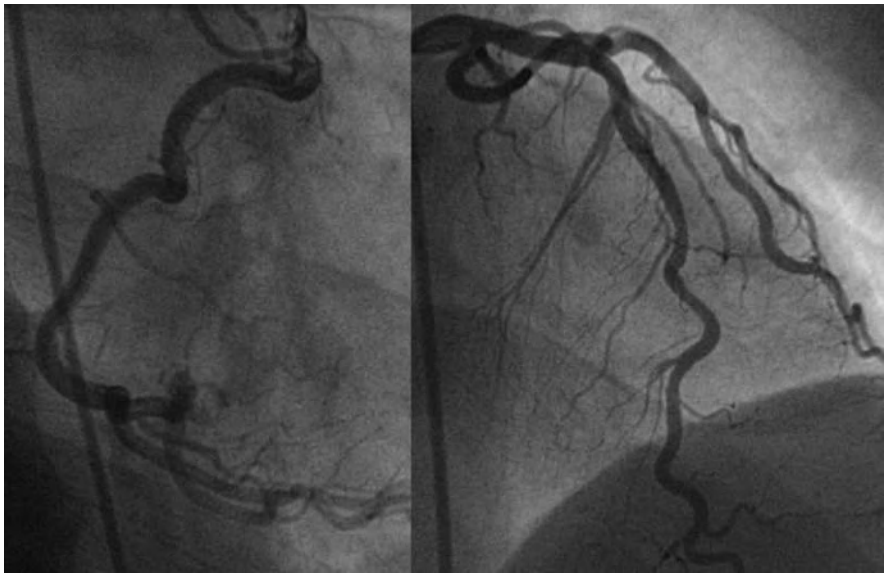


Figure 14. Angiogram showing normal coronary arteries and no significant coronary artery disease. (*Left panel*) Right coronary artery. (*Right panel*) Left coronary system.



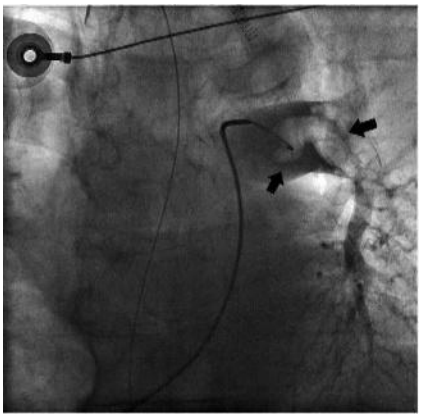


Figure 15. Pulmonary angiogram revealing a massive left pulmonary artery embolism (*black arrows*).

apex, has 77% sensitivity and 94% specificity in diagnosing acute PE.[71] Both are manifestations of acute pressure and volume overload on the right ventricle. ECG and echocardiography can be helpful in diagnosing PE when conventional imaging cannot be utilized.

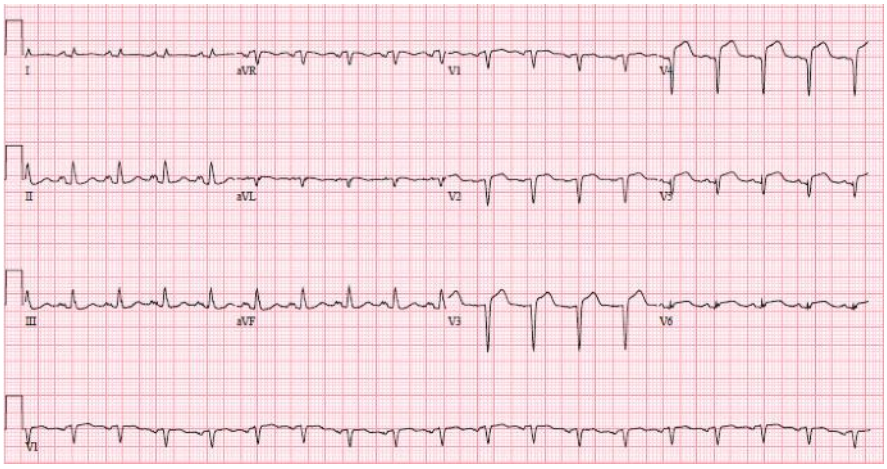
Case 7

Ventricular Aneurysm After Transmural MI

An 80-year-old man was admitted to the hospital for elective spinal lumbar fusion. He had been approved by an outside cardiologist for the operation. He had a history of hypertension, diabetes, and hypercholesterolemia. He denied any cardiac symptoms at his functional capacity. He had normal vital signs and his recorded examination revealed compensated heart function. When he arrived in the operating room, it was noted that the patient had ST elevations (Figure 16). The patient was asymptomatic. A STEMI alert was called. The patient had an occluded proximal LAD (Figure 17). Subsequent echocardiogram revealed an apical aneurysm with pericardial effusion and tethering of the LV apex. The patient also had severe pulmonary hypertension (Figure 18).

Early formation of LV aneurysm occurs frequently after anterior transmural MI and carries a high risk of death within 1 year, independent of LVEF.[72] Ventricular aneurysms predispose patients to ventricular arrhythmias and sudden death, heart failure, mural thrombus, and subsequent embolic events. Electrocardiographic features favoring ventricular aneurysm include absence of dynamic ST segment changes, absence of reciprocal ST depression, well-developed Q waves, and increasing ST elevation in setting of tachycardia. Echocardiography is a gold standard in the evaluation of true STEMI versus ventricular aneurysm formation.

Figure 16. Electrocardiogram demonstrating sinus tachycardia and prior anterior myocardial infarction with ST elevation in leads V2-V6.



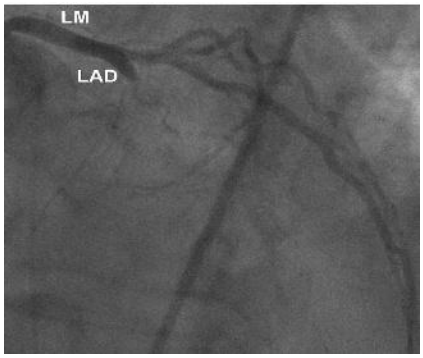


Figure 17. Coronary angiogram demonstrating proximally occluded left anterior descending artery (LAD). LM, left main coronary artery.

Summary

Maintaining a high clinical suspicion of conditions mimicking STEMI is crucial. The advantages of timely intervention in patients with STEMI should be balanced against the possible risks caused by antithrombin and antiplatelet therapy with the delay in treatment of the underlying etiology in case of misdiagnosis. The case presentations highlight the range of condition from true STEMI to mimickers. The clinical circumstances in each case determined the treatment approach.

Case 1 was a 35-year-old obese woman taking the weight-loss medication phentermine. Urine analysis results were positive for amphetamines. The patient's obesity suggested a chronic inflammatory state. The clinical suspicion was the use of dietary supplements in conjunction with her metabolic

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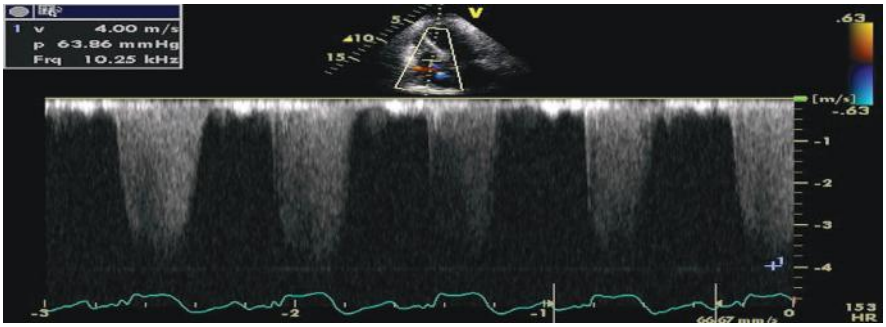

Figure 18. Tricuspid regurgitation envelope on Doppler imaging demonstrating a right ventricle-right atrial gradient of 64 mm Hg.

and autonomic perturbations that resulted in severe coronary vasospasm.

Case 2 highlights the complexity of infective endocarditis. The 48-year-old woman had recent aortic valve replacement for endocarditis. The STEMI ECG demonstrated the potential for aortic root abscess to cause coronary compression and resultant STEMI. TEE demonstrated the abscess. Aortic valve dehiscence resulted in severe paravalvular aortic regurgitation.

Case 3 was a 19-year-old with a clinical history of respiratory infection for several days and a clinical history suggestive of myopericarditis. Laboratory findings supported the clinical presentation. Echocardiographic imaging allowed definitive findings of myopericarditis in the face of clinical and laboratory evidence supporting this diagnosis.

Case 4.1 was a 67-year-old obese man with hypertension, hyperlipidemia, and type 2 diabetes, putting him at high risk for CAD. The patient was extremely anxious prior to starting the stress test. The patient developed STEMI 15 minutes after receiving regadenoson and succumbed to a ventricular arrhythmia death 24 hours later. This case reinforces that stress-induced cardiomyopathy may be associated with high morbidity and mortality in the acute phase.

Case 4.2 represents a dramatic case of apical and mid ventricular Takotsubo cardiomyopathy with classic ECG findings, normal coronaries, and reversibility of the stress-induced cardiomyopathy.

Case 5 demonstrates that true STEMI can occur in patients at a young age, especially if risk factors and metabolic aberrations are present. This young patient had a strong family history of premature CAD, was a heavy smoker, and laboratory analysis revealed severely depressed HDL cholesterol levels. Cigarette smoking, obesity, hypertriglyceridemia, and low HDL cholesterol level are important modifiable risk factors in these patients. Therefore, the foci of prevention should be cigarette cessation and reduction of components of metabolic syndrome.

Case 6 demonstrates that severe RV strain secondary to pulmonary emboli can mimic a true STEMI. This case was an example in which immediate echocardiography could have resulted in an immediate diagnosis, allowing for rapid treatment.

Case 7 demonstrates electrocardiographic features favoring ventricular aneurysm. The ECGs reveal absence of dynamic ST-segment changes, absence of reciprocal ST depression, well-developed Q waves. The patient also had increasing ST elevation in the setting of tachycardia. The echocardiogram revealed the classic features of ventricular aneurysm. The myocardial infarct was several days old, given the inflamed pericardial space with evidence of tethering of the apex on TEE.

Conclusions

Each case represents the complexity and challenges of evaluating STEMI alerts and reinforces the importance of considering the broad differential diagnosis associated with STEMI. The judicious utilization of in-depth analysis of the clinical presentation in conjunction with multimodality diagnostic tools such as ECG, coronary angiography, and echocardiography will typically lead to a rapid diagnosis and appropriate therapy. ■

The authors report no real or apparent conflicts of interest.

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MAIN POINTS

- A rapid diagnosis of ST-segment elevation myocardial infarction (STEMI) is mandatory for optimal treatment of an acute coronary syndrome. A small number of patients with suspected STEMI are afflicted with other medical conditions. These conditions include coronary vasospasm, Takotsubo cardiomyopathy, coronary arteritis/aneurysm, myopericarditis, Brugada syndrome, left bundle branch block, early repolarization, aortic dissection, infective endocarditis with root abscess, subarachnoid hemorrhage, ventricular aneurysm after transmural myocardial infarction, and hemodynamically significant pulmonary embolism with right ventricular strain.
- Although these disorders simulating STEMI have been described in the medical literature, mostly through individual case reports, the infrequent occurrence of these conditions reduces clinical awareness and mandates a collective discussion of the mimickers of STEMI. The clinical circumstances surrounding the clinical presentation frequently help distinguish true STEMI from conditions mimicking STEMI.
- Maintaining a high clinical suspicion of conditions mimicking STEMI is crucial. The advantages of timely intervention in patients with STEMI should be balanced against the possible risks caused by antithrombin and antiplatelet therapy with the delay in treatment of the underlying etiology in case of misdiagnosis.
- The judicious utilization of in-depth analysis of the clinical presentation in conjunction with multimodality diagnostic tools such as electrocardiogram, coronary angiography, and echocardiography will typically lead to a rapid diagnosis and appropriate therapy.

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