Anterolateral Papillary Muscle Rupture Predicted by Post-Infarction Inflammatory Markers

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Patient: Female, 72-year-old
Final Diagnosis: Anterolateral papillary muscle rupture
Symptoms: Discomfort • nausea • sweating
Clinical Procedure: —
Specialty: Cardiology • Genetics

Objective: Rare coexistence of disease or pathology

Background: The incidence of papillary muscle rupture (PMR), a mechanical complication of acute myocardial infarction, has decreased in the reperfusion era; however, its fatality rate remains high. Timely recognition and prompt initiation of treatment for PMR are important to avoid prolonged cardiogenic shock; however, the symptoms of PMR are nonspecific, and early diagnosis is often difficult.

Case Report: A 72-year-old woman with nausea for 2 days presented with ST-segment elevation myocardial infarction with obstruction of the obtuse marginal branch and 75% stenosis of the first diagonal branch. Percutaneous coronary intervention was performed to revascularize the obtuse marginal lesion, which was over thrombolysis in myocardial infarction grade 2 flow. After percutaneous coronary intervention, the patient developed fever, an elevated C-reactive protein level, and an increased neutrophil-to-lymphocyte ratio (NLR). The patient showed no signs of infection but elevated inflammatory marker levels, with C-reactive protein rising to 39.32 mg/dL and NLR to 15. On postoperative day 4, the patient’s clinical condition rapidly deteriorated, resulting in circulatory failure. Transthoracic echocardiography showed anterolateral PMR, and urgent surgical mitral valve replacement was performed. On day 32, the patient was discharged from the hospital, and at the 1-year follow-up, she remained in good health.

Conclusions: When there are multiple lesions, including the obtuse marginal and diagonal branches, anterolateral PMR should be suspected as the cause of cardiogenic shock. Performing point-of-care echocardiography and closely monitoring C-reactive protein levels and NLR can be helpful to detect PMR early.

Keywords: Myocardial Infarction • Papillary Muscles • Neutrophils • Inflammation • Heart Rupture, Post-Infarction

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Background

Papillary muscle rupture (PMR) is a rare, yet life-threatening, mechanical complication of acute myocardial infarction (AMI). Acute PMR often results in acute mitral regurgitation, with subsequent acute heart failure or cardiogenic shock. Generally, PMR can occur 2 to 7 days after ST-segment elevation myocardial infarction (STEMI) [1,2]. Early recognition of AMI and prompt percutaneous coronary intervention (PCI) for the resolution of myocardial ischemia significantly reduce the incidence of PMR [3]. Nevertheless, PMR still occurs in an estimated 1% to 5% of patients with AMI, with a high mortality rate, especially in cases of complete rupture, which is estimated to reach approximately 50% within 24 h, requiring surgical intervention [4,5]. However, early diagnosis remains a challenge because of nonspecific symptoms and signs. Therefore, development of an appropriate strategy for predicting PMR has long been overlooked.

Case Report

A 72-year-old woman presented to the hospital with chest discomfort and cold sweats lasting more than 3 h. She vomited 2 days before presenting to the hospital but had no other symptoms.

The patient had a 20-year history of hypertension and was taking amlodipine 5 mg once daily. There was no history of heart disease. Initial vital signs were as follows: blood pressure, 167/123 mm Hg; heart rate (tachycardia), 147 beats/min; body temperature, 36.5°C; and oxygen saturation, 95% in ambient air. Her physical examination was unremarkable.

Investigations and Treatment

Laboratory studies showed a white blood cell (WBC) count of 16 100/μL (reference: 4000–9000/μL), with 69.0% neutrophils, C-reactive protein (CRP) level 2.3 mg/dL (reference: <0.30 mg/dL), brain natriuretic peptide level (236 pg/mL, reference: <18.4 pg/mL), troponin-I (24 871 pg/mL, reference: <26.2 pg/mL), creatinine kinase (1173 IU/L, reference: 49–189 IU/L), creatinine kinase-MB fraction (125 IU/L, reference: <17 IU/L), aspartate aminotransferase (169 U/L, reference: 7–38 U/L), alanine transaminase (54 U/L, reference: 4–44 U/L), and lactate dehydrogenase (549 U/L, reference: 120–220 U/L). Electrocardiography (ECG) showed atrial fibrillation and ST-segment elevation in the lateral leads, with concomitant reciprocal ST-segment depression in the inferior leads and in leads V4-6 (Figure 1). Chest radiography findings were unremarkable. Transthoracic echocardiography (TTE) revealed severe lateral wall hypokinesis. A tentative diagnosis of STEMI was made. Emergency coronary angiography showed a non-dominant left circumflex artery, with a complete obtuse marginal branch artery obstruction at just the proximal end with no collaterals and 75% stenosis of the first diagonal branch of the left anterior descending artery (Figure 2A, 2B). Subsequent PCI was performed to revascularize the obtuse marginal branch artery, which was over thrombolysis in myocardial infarction grade 2 flow (Figure 2C, 2D).

Outcome and Follow-Up

Serial laboratory tests showed that the value of creatinine kinase peaked within a day of PCI (Figure 3). Echocardiography 1 h after catheterization showed mild mitral regurgitation, with a preserved left ventricular (LV) ejection fraction of 65%.

Figure 1. Electrocardiogram on admission, showing ST elevation in the I and aVL leads (red arrows) and small Q waves and negative T waves in the aVL lead (blue arrow).
On day 2, the patient developed a low-grade fever of 37.5 °C. Laboratory test results showed an elevated WBC count at 24,600/μL, neutrophils at 84.9%, and CRP level of 10.7 mg/dL. Although we initially suspected bacterial infection and initiated intravenous empiric antimicrobial therapy with ceftriaxone (2 g/day) and vancomycin (0.5 g/day), repeated blood cultures remained negative. Follow-up laboratory test results on day 4 showed exacerbation of inflammatory response (WBC, 26,300/μL and CRP, 39.32 mg/dL) with a high neutrophil-to-lymphocyte ratio (NLR) of 15, raising concerns about the possibility of secondary mechanical complications (Figure 3). No appreciable cardiac murmur or leg edema was observed. Follow-up chest radiography revealed flush pulmonary edema, without increased cardiac silhouette. TTE showed hyperkinetic LV contraction with massive mitral regurgitation caused by anterolateral PMR. The rupture resulted in flail anterior mitral valve leaflet and severe mitral regurgitation. (Figure 4C, 4D; Videos 3, 4). Based on these findings, a final diagnosis of acute mitral regurgitation secondary to PMR was made. The patient’s clinical condition rapidly deteriorated, resulting in cardiogenic shock requiring infusions of dopamine (7 μg/kg/min) and noradrenaline (0.3 μg/kg/min) and intra-aortic balloon pump support.
Figure 3. Changes in plasma myocardial and inflammatory biomarker levels during admission. Day 1 denotes percutaneous coronary intervention performed at 9:00 a.m. Day 4 denotes the diagnosis of papillary muscle rupture, for which surgical mitral valve replacement was performed (black arrow). CK – creatinine kinase; CKMB – creatinine kinase-MB fraction; CRP – C-reactive protein; NLR – neutrophil-to-lymphocyte ratio.

Figure 4. Serial Transthoracic echocardiography (TTE). (A, B) TTE 1 h after the catheterization shows mild mitral regurgitation. (C) TTE 4 days after the admission shows the head portion of the anterolateral papillary muscle swinging into the left atrium during systole (arrow). (D) TTE 4 days after the admission shows severe mitral regurgitation with a posterior jet caused by frail anterior mitral valve leaflet. LA – left atrium; LV – left ventricle; TTE – transthoracic echocardiography.
Subsequent emergency surgical mitral valve replacement with an Epic bioprosthetic mitral valve of 25 mm (St Jude Medical, Inc, St Paul, MN, USA) was performed to confirm the complete and total rupture of the single main papillary trunk, with almost normal valve leaflets and chordae (Figure 5A, 5B). The postoperative course was uneventful. Adenosine-induced stress myocardial perfusion single-photon emission computed tomography (SPECT) confirmed a complete perfusion defect in the anterolateral wall (Figure 6A, 6B). She was discharged on day 32 and remained healthy, with a normally functioning prosthetic mitral valve and minimal regurgitation at the 1-year follow-up TTE.

**Discussion**

Herein, we report a case of complete anterolateral PMR following STEMI due to an anterolateral ischemia, which was successfully treated with surgical mitral valve replacement. Our case provides several important clinical insights.
First, total occlusion of the obtuse marginal branch artery and stenosis of the first diagonal branch caused complete PMR in our case.

It is well known that anterolateral PMR occurs less frequently than posteromedial PMR. This is owing to the difference in the blood supply to the papillary muscle. The anterior papillary muscle is often perfused by the first diagonal and obtuse marginal branches. In our case, obstruction of the obtuse marginal and stenosis in the first diagonal branch led to insufficient blood flow to the papillary muscles, which could have caused PMR. Therefore, even a small area of myocardial infarction due to anterolateral ischemia can cause PMR. The exact pathogenesis of PMR is yet to be elucidated, but it is considered to be multifactorial. As in our case, most cases of PMR had preserved LV function concurrent with small areas of ischemia, corresponding to less than a quarter of the LV [6]. Thus, it is believed that the tear is presumably the result of high shear stress from hyperkinetic LV contraction applied to the vulnerable ischemic papillary muscle. Therefore, the key to preventing PMR is to salvage myocardial ischemia as quickly as possible. According to the ACCF/AHA/SCAI guideline, patients with STEMI and ischemic symptoms for less than 12 h should undergo PCI to enhance their chances of survival (class I, level of evidence A) [7]. However, our patient had the following 2
concerns regarding delayed PCI. First, the patient did not have typical chest pain at the initial presentation. If nausea were the chief symptom of STEMI, the onset of STEMI may have started the day before admission. A second concern is that ECG findings on admission showed ST-segment elevation as well as the onset of small Q waves and negative T waves in the aVL lead, suggesting that the patient might have already passed the hyperacute phase. Based on these findings, the patient might have undergone delayed PCI of more than 12 h after the onset of STEMI. Myocardial perfusion SPECT scan following cardiac surgery confirmed irreversible myocardial necrosis, supporting this notion. Thus, our case illustrates the difficulty in predicting the exact time of STEMI onset and the importance of suspecting PMR as a cause of acute heart failure in patients with STEMI and anterolateral ischemia.

Second, the CRP level and NLR were useful in predicting the development of PMR in our case.

Primary PCI has remarkably improved the prognosis of patients with AMI. The incidence of mechanical complications has significantly decreased to approximately 1% with PCI [8]. However, once a mechanical complication occurs, the in-hospital mortality rate for patients with STEMI remains high (42.4%). The American Heart Association recommends that proper diagnosis and treatment is necessary to shorten the duration of cardiogenic shock and reduce the possibility of death. Additionally, it is important to distinguish post-infarction mechanical complications from other causes of heart failure or non-cardiogenic shock [9]. However, early diagnosis of PMR remains extremely challenging because it presents similar findings, such as elevated jugular venous pressure and pulmonary congestion. PMR often results in hemodynamically unstable acute mitral regurgitation. Rapid and severe regurgitation causes a rapid increase in atrial pressure. The subsequent pressure gradient between the left atrium and left ventricle can often be equalized early, explaining why new murmurs were not audible in our case. In addition, various noises caused by pulmonary edema and rapid breathing can obscure the cardiac murmurs. Silent mitral regurgitation is observed in approximately 30% of patients with ischemic mitral regurgitation, which supports this notion [10]. TTE is used as an initial diagnostic tool to identify acute PMR. The pathognomonic echocardiographic finding of acute PMR is the prolapse of the ruptured papillary muscle head attachment to the flail mitral leaflet into the left atrium. However, TTE may be not informative in patients with partial PMR or ruptured heads that do not prolapse into the left atrium (up to 35% of cases with acute PMR), which could be mistaken for a valvular tumor, thrombus, or vegetation [11]. TTE has a diagnostic sensitivity of 65% to 85% [12]. Transesophageal echocardiography is an alternative diagnostic modality for such cases, with a high diagnostic sensitivity of 95% to 100% [13]. Prompt medical therapy and emergency surgery are often required for acute PMR, and all mechanical complications after AMI generally have a poor prognosis; however, among them, PMR has a relatively good prognosis, and early diagnosis and surgery can improve the prognosis [14]. Therefore, the development of a predictive index for the incidence of post-infarction PMR has long been awaited. Previous studies have shown a correlation between increased levels of inflammatory markers and cardiac rupture [3,15]. CRP is an acute-phase response protein that is synthesized in the liver during the acute phase of AMI or infection and is mainly induced by cytokines, such as interleukin 6 [16]. The CRP levels reflect the degree of inflammation and tissue necrosis, and cardiac rupture following AMI induces higher levels of CRP. The peak serum CRP levels of >20 mg/dL can be a good predictor of cardiac rupture, with 89% sensitivity and 96% specificity. Elevated CRP levels are also present in cases of extensive myocardial infarction; however, a study has shown that levels in these cases are significantly lower than those found in the rupture group [15].

Furthermore, CRP levels can be a biomarker not only for free-wall cardiac rupture but also for other mechanical complications, such as PMR and ventricular septal defect [3]. Based on previous studies, the pathological images of PMR show findings of tissue necrosis and inflammatory cell infiltration, which can reflect elevated CRP levels [17]. Simultaneously, cortisol release in response to the extent of tissue necrosis caused by myocardial infarction leads to a decrease in lymphocyte levels [18]. Therefore, the combination of high CRP levels and low relative lymphocyte counts can be a marker for a wide range of myocardial tissue necrosis and rupture [3]. NLR has also been reported to be associated with post-PCI mechanical complications [19,20]. Based on these findings, NLR can be a good indicator of mechanical complications following AMI, similar to the CRP level. High levels of inflammatory markers were also useful in predicting the development of PMR in our case. The CRP level increased rapidly 2 days after admission, peaked on day 4, and remained high (39.32 mg/dL) until the day of the rupture. Simultaneously, NLR increased significantly the day after admission (Figure 3). In this case, the NLR recorded the day after admission was 11, notably higher than the reported average NLR of 4.5 within the first 24 h following AMI [21]. As PCI can also cause an inflammatory response, a marked increase in CRP level and NLR on the day after revascularization can be a good indicator of the early detection of mechanical complications [22].

Generally, prediction of PMR occurrence is difficult, even in the presence of conventional risk factors for mechanical complications of AMI, as in our case. A discrepancy between significantly increased inflammatory markers and hyperkinetic LV contraction or less elevated CK levels can be a red flag for PMR following AMI, as per our case [23].
However, because elevated CRP levels and leukocytosis are also observed in septic shock or infective endocarditis, it is necessary to simultaneously perform serial echocardiographs to identify other foci that can cause fever. Further research and accumulation of data on the relationship between PMR development and time course of inflammatory marker expression are warranted.

This case highlights the importance of careful monitoring with biomarkers to predict post-infarction mechanical complications, even after successful primary PCI, in patients with STEMI.

Conclusions

We report a case of STEMI caused by obtuse marginal branch and diagonal branch ischemia resulting in complete anterolateral PMR that was successfully treated with surgical mitral valve replacement.

Early detection and prompt surgical treatment are directly associated with patient prognosis.

This case highlights the effectiveness of point-of-care echocardiography and close monitoring of CRP and NLR for early detection of PMR.

Ethical Approval

The authorization for the use of case information and materials was obtained from the Institutional Review Board of Shonan Fujisawa Tokushukai Hospital.

Declaration of Figures’ Authenticity

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