

CASE REPORT

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## Successful Medical Management of a Left Ventricular Thrombus and Aneurysm Following Failed Thrombolysis in Myocardial Infarction

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**Abstract:** We report the case of a patient with an extensive anterior myocardial infarction complicated by left ventricular systolic dysfunction, left ventricular apical thrombus and an apical left ventricular aneurysm following failed thrombolysis. We obtained serial two-dimensional echocardiograms at short intervals in the acute phase and also during the months of recovery and follow up. The patient was successfully and exclusively medically managed.

**Keywords:** myocardial infarction, failed thrombolysis, aneurysm, thrombus, successful medical management

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## Background

The precise definition of the incidence of failed thrombolysis is difficult, but, however defined, failed thrombolysis is associated with a much higher chance of early death and left ventricular dysfunction. The benefit of primary percutaneous coronary intervention (PCI) over fibrinolysis is greatest in high-risk patients. Alternatively, low risk patients have similar outcomes with fibrinolysis and primary PCI. This report reviews the literature and examines the outcome in an exclusively medically managed patient who had failed thrombolysis following myocardial infarction.

## Case presentation

We report the case of a 50-year old hypertensive male and non-smoker who presented to the emergency room because of recurrent sudden-onset crushing central chest pain occurring at rest. The patient had a similar unreported episode 24 hours prior to presentation. The current episode was associated with palpitations and sweating.

Examination revealed an anxious man who was diaphoretic and dyspneic at rest. He was overweight with a body mass index of 29 kg/m<sup>2</sup> and a waist circumference of 112 cm. He had a resting tachycardia of 104 beats per minute and blood pressure of 190/110 mmHg. Cardiac auscultation revealed fourth, first and second heart sounds. The lung fields were clear.

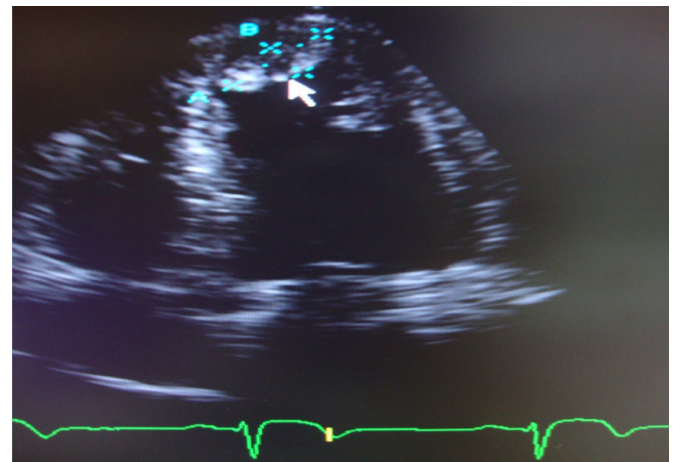
An urgent 12-lead electrocardiogram (ECG) showed marked ST segment elevation (convex upwards) with T wave inversion in leads V1-V5. The T waves were inverted in the inferior leads and there were pathological Q waves in leads V1-V5. Cardiac enzymes obtained 12 hours from symptom onset were elevated. Troponin T was 0.71 (<0.03 ng/mL), troponin I was 9.24 (<0.07), CK-MB was 7 ng/mL (0.6–6.3 ng/mL). The serum creatinine was marginally elevated at 124 µmol/L (<115 µmol/L) as was the LDL cholesterol at 3.45 mmol/L (<3.36 mmol/L). Complete blood count, fasting blood sugar, electrolytes and remaining cholesterol fractions were all within normal limits. Chest radiograph demonstrated cardiomegaly, in keeping with hypertensive heart disease. Our diagnosis was of a fully evolved anterior acute myocardial infarction (AMI).

Preliminary two-dimensional (2D) echocardiography performed on the fifth day post-infarction revealed extensive regional wall motion abnormalities (RWMA).

The left ventricular (LV) ejection fraction was estimated at 30%–35% with a dyskinetic apex, inferior wall hypokinesia, anterolateral wall akinesia, grade one LV diastolic dysfunction and central mitral regurgitation (1+). A 2.5 cm × 1.2 cm apical, protruding, but relatively immobile, left ventricular thrombus (LVT) was detected (Fig. 1). In view of the extensive RWMA, the culprit lesion was suspected to be multi-vessel in nature.

During the acute phase, after intravenous access was secured, the following treatments were given: 5–6 liters of oxygen by face mask, chewable aspirin (300 mg stat) and intravenous morphine (10 mg stat). Two doses of isosorbide mononitrate spray (400 µg) were given sub-lingually. Thrombolysis with tenecteplase was instituted 63 minutes after symptom onset as an alternative to emergency percutaneous coronary intervention (PCI), which was not readily available. The patient immediately commenced adjunct therapy consisting of lisinopril (20 mg daily) and atorvastatin (40 mg daily). Carvedilol was initiated later at 3.125 mg BD and titrated to 12.5 mg BD. There was a good response to the above management, with significant resolution of pain and satisfactory vital sign readings. Initial hypotension caused by lisinopril was addressed by brief discontinuation. We administered subcutaneous clexane (40 mg BD) for 1 week. Oral warfarin was commenced at 5 mg daily, four days prior to discontinuing clexane. The dose was titrated to achieve an international normalized ratio (INR) of 2.5 for one year.

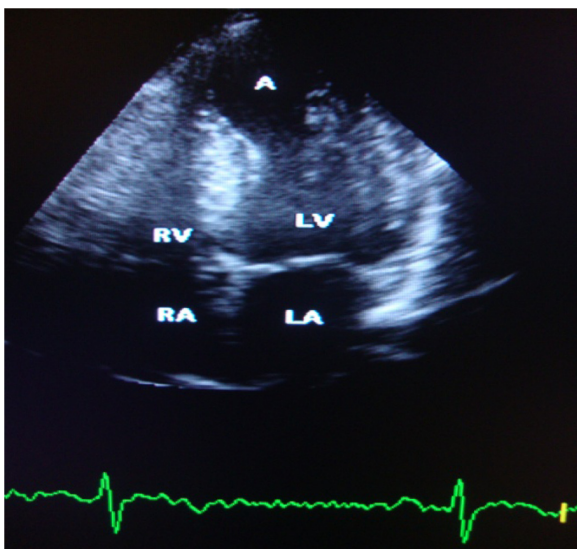
Serial echocardiograms were done on days 7, 14, 28, 60 and 120 post-infarction. The 120-day scan



**Figure 1.** Apical four chamber view showing the thrombus (arrow) in the apex of the left ventricle.

revealed a frankly large dyskinetic and aneurismal left ventricular apex devoid of obvious thrombus (Fig. 2). Repeat ECG had been acquired at 90-minutes and 180-minutes post-admission, and then daily for three weeks after initiation of thrombolysis. The lead with maximum ST elevation in the initial recording was used for comparison and it showed persistent ST segment elevation in the anterior walls (V1–V5). The basal and mid (lateral and anterior) walls remained akinetic on 2D echocardiography. The left ventricular segments contiguous with the thrombus were akinetic and remained so after the thrombus resolved, as seen in Figure 2. Regression of the thrombus was not associated with clinically evident embolic events. During follow-up, the presence of the large aneurysm did not prevent thrombus regression. The left ventricular ejection fraction (LVEF) had improved significantly to 55% (bi-plane method).

Diagnostic catheterization (Fig. 3) was only accessible after one week of admission and it revealed a 30% distal stenosis of the left main coronary artery, as well as significant occlusion of the left anterior descending (LAD) coronary artery in the mid segment with collaterals from the right coronary artery. The left circumflex coronary artery was normal and non-dominant while the right coronary artery (RCA) was normal and dominant. Left ventriculography was not done in view of the LV apical thrombus. The renal arteries were normal and bilateral. In summary, the angiogram showed significant single vessel coronary



**Figure 2.** Apical four chamber view demonstrating the apical aneurysm (A).



**Figure 3.** Coronary angiogram showing an occluded mid left anterior descending artery.

artery disease (CAD) with an occluded mid LAD coronary artery.

There was good post-infarction recovery and we proceeded to commence cardiac rehabilitation with self-paced exercise testing (6- and 12-minute walk test). A sub-maximal exercise stress test and echocardiography were performed four weeks post-infarction; this revealed a good exercise capacity of 8.1 metabolic equivalents (METs). Post-stress images demonstrated improved contractile function in the anterior wall with increased systolic function. At discharge, the patient received information regarding resumption of normal activity.

## Discussion

Guidelines from the European Society of Cardiology now recommend angioplasty rather than thrombolysis, provided that it can be delivered within 90-minutes of first medical contact.<sup>1</sup> The goals for the treatment of ST-Elevation Myocardial Infarction (STEMI) include achieving a time to reperfusion (measured from first medical contact) of 90-minutes for primary percutaneous coronary intervention (PCI) and 30-minutes for fibrinolysis.<sup>2,3</sup> In the past, reperfusion was commonly assessed in terms of coronary blood flow, with achievement of TIMI 3 flow being a favorable sign,<sup>4</sup> however, this angiographic index is not a reliable indicator of myocardial reperfusion, which is prognostically more relevant than coronary reperfusion.<sup>5</sup>

We opted for thrombolysis because this was the intervention that was readily accessible.



Thrombolytic therapy for an AMI reduces case fatality and improves clinical outcomes.<sup>6,7</sup> In up to 60% of patients, however, treatment does not restore perfusion in the myocardium at risk<sup>8</sup> and such failure indicates a worse prognosis.<sup>9</sup> Successful thrombolysis has been defined as >50% resolution of the worst ST segment at 180 minutes.<sup>10</sup> ST-segment resolution (STR) 90–180 minutes after thrombolysis is an excellent marker of successful myocardial reperfusion<sup>11</sup> and a strong predictor of survival and preservation of LV function.<sup>12</sup> We demonstrated significantly elevated ST segments until three weeks after the initial presentation, hence our diagnosis of failed thrombolysis. The LV function also remained impaired for up to three weeks after presentation. The management of lytic failures and slow reperfusers has been described as a dilemma facing physicians working in coronary care units. The clinical features predisposing to failure of thrombolysis have been identified, but the precise mechanisms are not well established. Patients with failure of thrombolysis are generally older, more likely to have had a previous infarct, non-smokers, and have a greater delay to lytic treatment.<sup>13,14</sup> The last three characteristics were applicable to our patient who had ignored a similar chest pain about 24 hours prior to eventual presentation.

The incidence of failed thrombolysis is difficult to establish precisely since it is dependent on multiple factors, including the timing and method of evaluation of efficacy and the definition of success and failure.<sup>8</sup> Generally, thrombolytics fail to achieve patency in at least 15%–40% of patients and fail to achieve normal perfusion in 60%–75%.<sup>15–17</sup> However defined, failed thrombolysis is associated with a much higher chance of early death and greater LV dysfunction.<sup>13</sup> We documented LV dysfunction characterized by an impaired ejection fraction (EF) of 30%–35%. The ideal method of diagnosing failure of thrombolysis would be some test of myocardial perfusion—possible tests include positron emission tomography (PET) and contrast echocardiography.<sup>8</sup> These are, however, not readily available in all countries. In many coronary care units, failed thrombolysis is either not detected, or alternative treatments are not considered. Even if the early response to thrombolysis is poor, many, just as we did, hope that given more time, the thrombolytic agent will be effective.

An incomplete (<50%) STR is a recognized marker of failed thrombolysis and is a suitable recruitment criterion for rescue angioplasty.<sup>18</sup> The current management options for failed thrombolysis are repeat thrombolysis, rescue angioplasty, stenting, and the use of glycoprotein IIb/IIIa inhibitors.<sup>19–21</sup> Older trials have shown that rescue angioplasty was not better than conservative management in terms of subsequent death.<sup>22</sup> Similarly, the Middlesbrough Early Revascularization to Limit Infarction (MERLIN) trial in which 307 patients with failed thrombolysis were randomized to PCI or conservative management showed no advantage for the rescue therapy in terms of either 30-day mortality or LV function. Furthermore, rescue therapy was associated with more strokes and major haemorrhage.<sup>23</sup> The major drawback of glycoprotein IIb/IIIa inhibitors is the risk of bleeding complications.<sup>24,25</sup> In dealing with the dilemma of choosing the best option, we adopted a conservative approach. In this case, the outcome was favorable as evidenced by an improvement in the LV systolic function and regression of the thrombus. However, follow-up echocardiogram showed persistence of the aneurysm. In patients with a first acute transmural anterior myocardial infarction and isolated anterior descending artery disease, left ventricular aneurysm often results from a large infarct caused by total occlusion of the proximal LAD artery without collateral supply to the infarct region.<sup>26</sup> Greater than 80% of left ventricular aneurysms involve the anterior wall and/or apex and are associated with high-grade stenosis or complete occlusion of the proximal or mid-LAD coronary artery.<sup>27–29</sup>

Although our patient had collaterals from the RCA, the risk factors for aneurysm formation are similar to previously described risk factors, including a large infarct and high-grade stenosis of the mid LAD artery. It is likely that the presence of collaterals contributed to survival in this patient. In patients with aneurysm, the state of the left anterior descending artery obstruction and collaterals are independent predictors of mortality.<sup>26</sup> In relatively small aneurysms, survival is influenced by symptoms at presentation; symptomatic patients have a survival in 55%–59% range.<sup>27</sup> Medical treatment can extend the 50% survival rate to 6.5 years with angiotensin-converting enzyme inhibitors (ACEI), 7.5 years with beta blockers and 8.5 years with spironolactone. We managed the aneurysm conservatively with immediate



commencement of ACEI and beta blockers. In general, the risk of thromboembolism is low for patients with aneurysms (0.35% per patient-year).<sup>30</sup> The role of long-term anticoagulation remains arguable. We acknowledge that our immediate commencement of lisinopril at 20 mg was overenthusiastic, as evidenced by the initial hypotension the patient suffered. The recommendation for ACEI therapy is titration to target. The 2004 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Management of Patients With STEMI recommend the use of oral anticoagulation, targeted to an INR of 2.0–3.0 for at least 3 months (class I, level of evidence B) and perhaps indefinitely in patients without an increased risk of bleeding (class I, level of evidence C) who are post-STEMI with documented LVT.<sup>31</sup> This recommendation is based primarily on observational studies demonstrating that patients with LVT treated with heparin and warfarin had better outcomes and fewer cerebral emboli.

In this setting of a LVT within the aneurysm, we commenced both oral and parenteral anticoagulation and followed-up with long-term oral anticoagulation. 2D echocardiography has demonstrated that LV thrombi are common in patients with acute anterior MI (30%–43% of patients)<sup>32,33</sup> and most (>75%) develop in the first week after infarction.<sup>34,35</sup> Mortality is increased in patients with LVT, especially when these develop within 48-hours.<sup>36,37</sup> Although we did not acquire the first echocardiogram till after 48-hours of admission, considering the favorable outcome, we presume the thrombus formed after 48-hours of infarction.

The incidence of embolic events is low in protruding but relatively immobile thrombi.<sup>37</sup> The thrombus demonstrated in this case had similar characteristics and this may have contributed to its stability till it finally regressed.

In determining the optimal treatment strategy for LVT, the perceived risk of embolism as estimated by the 2D echo should be used as a guide. First, a course of intravenous heparin followed by oral anticoagulants is appropriate.<sup>38</sup> Concomitant platelet inhibition by aspirin should be considered. We followed this management plan with an impressive outcome in this case. Our patient was maintained on warfarin for one year with evidence of resolution of thrombus after the 6th month. Thrombolysis of ventricular thrombi

has been attempted but increased mobility of apical clot has been documented together with sometimes fatal embolic phenomena; thus, the safety of this approach appears questionable.<sup>39</sup> Finally, surgical removal may be indicated in patients sustaining embolic events, especially when these events are recurrent.<sup>40</sup> Spontaneous regression of LVT in patients with myocardial infarction who are not treated with anticoagulants has been reported.<sup>33,37</sup>

There is now evidence supporting a regimen of secondary prevention for acute MI survivors that typically includes antiplatelet agents, statins, beta blockers, and ACE-inhibitors.<sup>41</sup> These were all initiated from the onset of management. The benefits of beta blockers are greatest in high risk anterior infarction and LV dysfunction. Many centers now perform some form of risk stratification testing before discharge and higher risk patients are considered for revascularization to improve their prognosis. Post-infarction exercise capacity of our patient was 8.1 METs. A sub-maximal exercise testing protocol has been developed to provide risk stratification information to determine the prognosis for post MI patients.<sup>42</sup> Failure to achieve 5 METs during treadmill exercise is a commonly used marker for increased risk.<sup>43</sup>

## Conclusions

Failed thrombolysis after acute myocardial infarction is a common finding and can be associated with early development of a LV aneurysm. In the absence of severe heart failure, refractory ventricular arrhythmias, or recurrent thromboembolism, a conservative approach is usually adequate. Development of LVMT occurring in the setting of LV aneurysm can be managed conservatively with resultant reduction in the associated risk of embolization. Although our experience is limited to one patient, we believe that in the absence of compelling indications for intervention, a conservative approach is likely to yield good results despite lytic failure.

## Author Contributions

ATO was involved in the conception of the report, clinical care of the patient and initial drafting of the manuscript. CL was involved in revising the manuscript critically for important intellectual content, OOO was involved in revising the literature and manuscript drafting, and OJA and AAA were involved



in editing and revising the manuscript. All authors reviewed and approved of the final manuscript.

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## Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. The external blind peer reviewers report no conflicts of interest. The patient has given his consent for the case report to be published.

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