Intra-pericardial thrombin injection for post-infarction left ventricular free wall rupture

European Heart Journal: Acute Cardiovascular Care
1(4) 337–340

© The European Society of Cardiology 2012

Reprints and permission:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/2048872612460966

acc.sagepub.com

Joe-Kin-Tong Lee, Kin-Lam Tsui, Kwok-Keung Chan and Shu-Kin Li

Abstract

Left ventricular free wall rupture (LVFWR) is a fatal complication of acute myocardial infarction. Different modalities of treatment were previously described, including surgical intervention and medical treatment. We report a case treated with intra-pericardial thrombin injection that gave a favourable outcome for a patient who presented with LVFWR and cardiac tamponade, following acute myocardial infarction.

Keywords

Acute myocardial infarction, cardiac tamponade, case report, fibrin glue, left ventricular free wall rupture, thrombin

Received: 30 June 2012; accepted: 21 August 2012

Introduction

Left ventricular free wall rupture (LVFWR) is a well-known, fatal complication following acute myocardial infarction. Open-heart surgical repair is the definitive and standard treatment. Surgical series published in recent years show promising hospital survival rates, ranging from 64–88%, with more favourable outcome in the oozing type than in the blow-out type of LVFWR.^{1,2} Still, in clinical practice, the patients in moribund condition are often considered too ill and are excluded from surgical intervention. Medical treatment for LVFWR by prolonged bedrest and blood pressure control is highlighted.³ For the patient with cardiac tamponade, an urgent pericardiocentesis is deemed necessary as the initial measure to correct haemodynamic instability. Intra-pericardial fibrin-glue injection after pericardiocentesis is described as a way to promote haemostasis and sealing of the ruptured myocardium;^{4–7} however, such an approach has not been widely adopted. Moreover, to our knowledge there is no report on the use of intra-pericardial thrombin in post-infarction LVFWR: The use of thrombin may have both advantages and disadvantages over fibrin-glue. We report a case of LVFWR and cardiac tamponade after myocardial infarction that was successfully stabilized by an urgent pericardiocentesis and intra-pericardial thrombin injection.

Case report

An 84 year-old woman with a past medical history of hypertension with good blood pressure control presented to us, complaining of shortness of breath for several days. She did not recall any chest pain event. On admission, her blood pressure was stable at 135/92 mmHg and her oxygen saturation was 94%, without supplementary oxygen. Physical examination revealed signs of congestive heart failure, including elevated jugular venous pressure, pitting ankle oedema and crepitation over the lung bases. Chest X-ray examination revealed cardiomegaly and upper lobe venous diversion. Electrocardiogram showed a sinus rhythm. Q-wave and 2 mm convex-shaped ST elevation were found over the chest leads. Her serum troponin-I level was grossly elevated to 6.88 ng/mL (reference < 0.03 ng/ml), while her creatine kinase level was within the normal range. Her clinical diagnosis was recent silent anterior myocardial

Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong Special Administrative Region, China

Corresponding author:

Joe-Kin-Tong Lee, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan, Hong Kong Special Administrative Region, China.

Email: jklee@gmail.com

Figure 1. Transthoracic echocardiogram. (a) The patient had a large amount of circumferential pericardial effusion with a layer of echogenicity in the pericardial space on the subcostal view; and (b), as seen by the parasternal view.

infarction, complicated with mild congestive heart failure. The patient was put on medical treatment, including aspirin, clopidogrel, subcutaneous enoxaparin, and simvastatin. She was started on heart failure medications, including lisinopril and metoprolol. The patient stabilized with treatment.

On the sixth day of hospitalization, the patient developed shock, exhibiting a rapid fall in blood pressure to 60/40 mmHg and a sinus tachycardia of 140 beats per minute (bpm). Clinical deterioration in her heart failure status required treatment with high levels of oxygen. Repeated electrocardiograms showed no remarkable serial changes, when compared with her admission electrocardiogram. An urgent transthoracic echocardiogram showed large amount of circumferential pericardial effusion, with a layer of echogenicity in the pericardial space, which was an indicator of haemopericardium with clot formation (Figure 1). Her right atrium and right ventricle collapsed during diastole. The anterior left ventricular wall was akinetic, resulting in impaired left ventricular systolic function. The deteriorated clinical condition and echo findings were compatible with LVFWR, complicated by cardiac tamponade. The condition was further complicated by acute pulmonary oedema, as confirmed by chest X-ray, and acute renal failure with creatinine levels up to 422 $\mu\text{mol/L}$ (reference, 60–90 $\mu\text{mol/L}$).

In view of her advanced age and critical clinical condition, the patient was considered to be at very high risk for any open-heart repair of the ruptured myocardium; therefore, a more conservative treatment strategy was adopted: The patient was treated with high-dose dopamine for haemodynamic support; an urgent pericardiocentesis was performed, via the subcostal approach, and a 5F sheath was inserted into the pericardial space. By aspiration from this sheath, we obtained 450ml of heavily blood-stained pericardial fluid. Following the aspiration of all pericardial fluid, as confirmed by echocardiogram, we injected 5000 units of bovine thrombin (THROMBIN-JMI®, GenTrac Inc, Wisconsin, US) reconstituted with 20 ml normal saline (i.e.

250 units/ml) into the pericardial space, through the sheath, with the aim of promoting haemostasis at the oozing myocardium and preventing the re-accumulation of pericardial effusion. After a brief period of ‘thrombin rinsing’ in the pericardial space by the patient’s heart beating, we inserted a pigtail catheter and connected it to a suction bottle, for drainage. Her blood pressure improved immediately, to 106/77 mmHg, after the pericardiocentesis. In the next few days, her haemodynamic status remained stable and we were able to gradually tail off the patient’s inotropic support. The patient’s renal function also normalized over this period. Only minimal pericardial fluid drained out since the initial aspiration and another echocardiogram showed no evidence of fluid re-accumulation. After seven days of drainage, we removed the drain. The patient showed good progress in the rehabilitation programme, so she was discharged on the 37th day of hospitalization. This patient continued to remain well, up to and including the writing of this case report, which is nine months after her initial presentation.

Discussion

The use of intra-pericardial fibrin-glue injection to enhance haemostasis in post-infarction LVFWR was first described in 1995.⁴ Fibrin-glue is a 2-component topical haemostat, comprised of a tissue adhesive component (human fibrinogen-aptinin and blood coagulation factor XIII) and thrombin. The mixture of these two solutions, applied topically, exerts a local haemostatic and sealant effect. Fibrin-glue is widely used in the surgical field as a haemostat, adhesive and sealant, in various surgical procedures.⁸ Intra-pericardial fibrin-glue injection for LVFWR was reported in several case reports and case series, with a finding of reasonable short and medium-term clinical outcomes.^{5–7} Despite an initial concern about uncontrolled pericardium adhesion after fibrin-glue application, studies using serial echocardiographic follow-up do not show development of left ventricular restriction.^{6,7} The role of fibrin-glue in

promoting haemostasis and myocardial healing, as well as the convenient regression of fibrin sealant after the initial healing process, are described in histological and pharmacokinetic animal studies.⁹ Nevertheless, the use of intra-pericardial fibrin-glue injection for alternative treatment of LVFWR has not been widely adopted.

In this report, we describe the use of intra-pericardial thrombin injection as an alternative sealant. Local thrombin injection is used in treating arterial aneurysms, as well as oesophageal and gastric varices.^{10–12} From the perspective of interventional cardiologists, thrombin is also used in post-catheterization femoral pseudoaneurysms.^{13–16} Thrombin injection into a pseudoaneurysm promotes thrombosis, therefore healing. Using the same pharmacological rationale, we believe that thrombin injection could also be applied to the situation of post-infarction LVFWR. In the pericardial space, the concentrated thrombin acts locally at the ruptured site, promoting fibrinogen to convert to fibrin, enhancing the haemostasis process. A thrombin preparation lacks the fibrinogen substrate component present in fibrin-glue, so theoretically it may perform less well than fibrin-glue for haemostasis. The superiority of fibrin-glue over thrombin is demonstrated in promoting puncture closure after dialysis graft intervention.¹⁷ On the other hand, the haemostatic effect of thrombin appears to be comparable to fibrin-glue in treating peripheral pseudoaneurysms by percutaneous injection.¹⁸ An advantage of thrombin preparations over fibrin-glue is that the tissue adhesive component in certain fibrin-glue commercial preparations, for example: Beriplast-P (CSL Behring) & Tisseel (Baxter) consist of a bovine aprotinin solution. The bovine component poses a risk of allergic reaction and possibly of transmission of the human form of bovine spongiform encephalopathy. A human thrombin preparation, therefore, at least eliminates the risk of bovine product-related complications. Moreover, a single agent injection of thrombin can provide simplicity over the use of multi-vial fibrin-glue, in terms of drug preparation and administration. Also, concerning cost and availability, a single unit of fibrin-glue preparation is 2–4 times more expensive than thrombin. For some institutions, like our own, thrombin may be more readily available as a stock item available in preparation for use in treating femoral pseudoaneurysms.

Another safety issue regarding intra-pericardial thrombin injection is that thrombin may leak into the systemic circulation, leading to embolism, with there being a particular concern over the possibility of cerebral vascular insufficiency. No such complication is reported from the use of intra-pericardial fibrin-glue injection; however, this complication may be under-reported, as fibrin-glue use in LVFWR is only reported in studies involving a low number of subjects.^{4–7}

From the experience in treating femoral pseudoaneurysms by percutaneous thrombin injection, the risk of a distal embolic event to a lower limb is approximately 2%, although

sometimes that condition can be severe.^{15,16,19} Nevertheless, most of the thromboembolic events that actually occurred are believed to be asymptomatic, as the thrombin leaked into the systemic circulation becomes instantaneously diluted, while the formed fibrin and clots are lysed by fibrinolytic factors that are abundant in the systemic circulation. It is uncertain whether the high pressure gradient seen between the left ventricle and the pericardial space could affect the chance of thrombin leakage and embolic events.

In this patient, we could not ascertain the diagnosis of LVFWR without operative or histological findings, although this diagnosis was supported by the clinical presentation and echocardiographic appearance of blood clots in the pericardium. Post-infarction pericarditis with haemorrhagic transformation precipitated by enoxaparine could also give rise to a similar clinical picture. Such patients often do well with pericardiocentesis alone; nevertheless, the haemostatic property of thrombin may also be applicable in the treatment of haemorrhagic pericarditis. Thus, this case illustrated that, for critically ill patients having a clinical diagnosis of LVFWR, even with the differential diagnosis of haemorrhagic transformation of post-infarction pericarditis, an intra-pericardial thrombin injection does appear to be a reasonable treatment modality, as the last resort.

Conclusion

LVFWR is a fatal complication of acute myocardial infarction. Open-heart surgical repair is the standard treatment, but few of these patients are truly suitable for surgical treatment. We demonstrated the use and feasibility of an intra-pericardial thrombin injection to act as a haemostat and sealing agent, for treatment of post-infarction LVFWR.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

None declared.

References

1. Sakaguchi G, Komiya T, Tamura N, et al. Surgical treatment for postinfarction left ventricular free wall rupture. *Ann Thorac Surg* 2008; 85: 1344–1346.
2. Haddadin S, Milano AD, Faggian G, et al. Surgical treatment of postinfarction left ventricular free wall rupture. *J Card Surg* 2009; 24: 624–631.
3. Figueras J, Cortadellas J, Evangelista A, et al. Medical management of selected patients with left ventricular free wall rupture during acute myocardial infarction. *J Am Coll Cardiol* 1997; 29: 512–518.
4. Ogiwara M, Kyo S, Yokote Y, et al. Clinical result of left ventricular free wall rupture resulting from acute myocardial infarction. *Kyobu Geka* 1995; 48: 286–289.

5. Murata H, Masuo M, Yoshimoto H, et al. Oozing type cardiac rupture repaired with percutaneous injection of fibrin-glue into the pericardial space: Case report. *Jpn Circ J* 2000; 64: 312–315.
6. Joho S, Asanoi H, Sakabe M, et al. Long-term usefulness of percutaneous intrapericardial fibrin-glue fixation therapy for oozing type of left ventricular free wall rupture: A case report. *Circ J* 2002; 66: 705–6.
7. Terashima M, Fujiwara S, Yaginuma GY, et al. Outcome of percutaneous intrapericardial fibrin-glue injection therapy for left ventricular free wall rupture secondary to acute myocardial infarction. *Am J Cardiol* 2008; 101: 419–421.
8. Spotnitz WD. Fibrin sealant: Past, present, and future: A brief review. *World J Surg* 2010; 34: 632–634.
9. Hattori R, Otani H, Omiya H, et al. Fate of fibrin sealant in pericardial space. *Ann Thorac Surg* 2000; 70: 2132–2136.
10. Cope C and Zeit R. Coagulation of aneurysms by direct percutaneous thrombin injection. *Am J Roentgenol* 1986; 147: 383–387.
11. Nakamura R, Bucci LA, Sugawa C, et al. Sclerotherapy of bleeding esophageal varices using a thrombogenic cocktail. *Am Surg* 1991; 57: 226–230.
12. Williams SG, Peters RA and Westaby D. Thrombin – An effective treatment for gastric variceal haemorrhage. *Gut* 1994; 35: 1287–1289.
13. Liao CS, Ho FM, Chen MF, et al. Treatment of iatrogenic femoral artery pseudoaneurysm with percutaneous thrombin injection. *J Vasc Surg* 1997; 26: 18–23.
14. Kang SS, Labropoulos N, Mansour MA, et al. Percutaneous ultrasound guided thrombin injection: A new method for treating postcatheterization femoral pseudoaneurysms. *J Vasc Surg* 1998; 27: 1032–1038.
15. Paulson EK, Nelson RC, Mayes CE, et al. Sonographically guided thrombin injection of iatrogenic femoral pseudoaneurysms: Further experience of a single institution. *Am J Roentgenol* 2001; 177: 309–316.
16. Khoury M, Rebecca A, Greene K, et al. Duplex scanning-guided thrombin injection for the treatment of iatrogenic pseudoaneurysms. *J Vasc Surg* 2002; 35: 517–521.
17. St. George J, Murphy KD and Kwon OJ. A comparison of fibrin glue and thrombin as agents to facilitate puncture closure following dialysis graft intervention. *J Vasc Interv Radiol* 2001; 12: S30.
18. Owen RJ, Haslam PJ, Elliott ST, et al. Percutaneous ablation of peripheral pseudoaneurysms using thrombin: A simple and effective solution. *Cardiovasc Intervent Radiol* 2000; 23: 441–446.
19. Friedman SG, Pellerito JS, Scher L, et al. Ultrasound-guided thrombin injection is the treatment of choice for femoral pseudoaneurysms. *Arch Surg* 2002; 137: 462–464.