

Use of Intracoronary Thrombolysis for Huge Thrombus Burden in an Ectatic Right Coronary Artery

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الحقن المباشر لمواقع التخثر داخل شريان تاجي أيمن مترهل و مسدود بكميات غزيرة من الخثرة التاجية في مريض مصاب باحتشاء قلبي حاد

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ABSTRACT: Managing a high intracoronary (IC) thrombus burden is a major challenge in patients with ectatic coronary arteries who present with an ST-elevation myocardial infarction (STEMI). We report a 45-year-old male patient who presented to the Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman, in 2017 with an inferior STEMI. Coronary angiography revealed ectatic coronary arteries with an occluded right coronary artery (RCA). The RCA had a massive thrombus burden that did not resolve with aspiration thrombectomy or balloon angioplasty. Subsequently, IC thrombolysis was administered resulting in significant reperfusion. During the course of his treatment, the patient suffered from intracranial bleeding as a complication; however, he recovered completely with no residual neurological sequelae. This case report demonstrates that IC thrombolysis is a valid option in patients with a massive thrombus burden in the setting of a STEMI, albeit with an increased risk of major bleeding.

Keywords: Ectasia; Mechanical Thrombolysis; Myocardial Infarction; Case Report; Oman.

المخلص: تعتبر معالجة وتفتيت كميات هائلة من الخثرة التاجية أحد التحديات الكبيرة التي تعوق علاج مريض القلب المصاب باحتشاء قلبي حاد وخصوصا في شرايين تاجية متوسعة ومترهلة. نعرض هنا حالة لمريض في سن الخامسة والأربعين من عمره تلقى علاجه في 2017 بمستشفى جامعة السلطان قابوس لنوبة قلبية مفاجئة من جراء انسداد كامل وحاد في الشريان التاجي الرئيسي الأيمن. كشف تصوير الأشعة عن طريق قسطرة القلب ترهلا وتمددا ملحوظا غير طبيعي في الشريان التاجي الأيمن مع وجود خثرة تاجية ضخمة لم تستجب لمحاولات استئصالها بالشفط التداخلي أو تفتيتها بالبالون. تم علاج الحالة بنجاح عن طريق الحقن المباشر لمواقع الخثرة في الشريان المنسد، الأمر الذي أدى إلى تحلل الخثرة واسترجاع تروية الدم إلى الجزء المتأثر من عضلة القلب. للأسف أصيب المريض بنزيف دماغي مؤقت و تعافى منه بشكل كامل بدون أي آثار متبقية. يوضح هذا التقرير أن الحقن المباشر لمواقع التخثر في الشرايين التاجية خيار بديل فعال في علاج حالات احتشاء عضلة القلب الحادة والتي يستعصي علاجها بالأساليب الاعتيادية بسبب ضخامة الخثرة المسببة للنوبة القلبية.

الكلمات المفتاحية: توسع الشرايين؛ تحليل الخثرة الميكانيكي؛ احتشاء عضلة القلب؛ تقرير حالة؛ عُمان.

CORONARY ARTERY ECTASIA IS A RELATIVELY uncommon abnormality with a reported incidence of around 0.3–5.3% of patients undergoing coronary angiography.¹ Due to the abnormal flow dynamics, these vessels are prone to thrombus formation and occlusion presenting as an acute ST-elevation myocardial infarction (STEMI). The management of these patients is often challenging due to the high thrombus burden, with the use of various available modalities such as manual thrombus aspiration often being inadequate.² Presence of a large amount of thrombus has been shown to be associated with poor long-term prognosis and is also often associated with complications such as stent thrombosis, no reflow phenomenon and distal embolisation.^{3,4}

Intracoronary (IC) lysis is an option that is not considered often either due to lack of clear practice protocols or a high perceived bleeding risk.² In addition, the 2017 European guidelines on management of STEMI do not clearly state how these patients should be managed besides the usual procedures, such as aspiration thrombectomy and balloon angioplasty.⁵ In this report, we present a case of an occluded ectatic right coronary artery (RCA) presenting as a STEMI which was successfully treated with IC fibrinolysis.

Case Report

A 45-year-old male patient presented to the Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman, in 2017 with a central chest

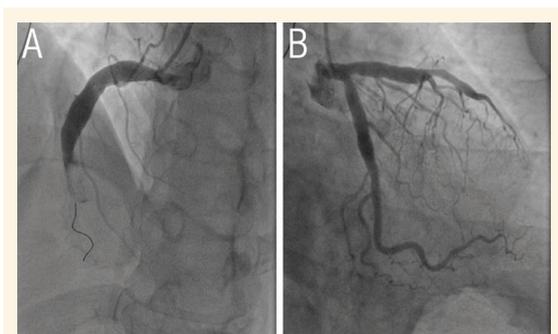


Figure 1: Initial angiogram of a 45-year-old male patient who presented to Sultan Qaboos University Hospital, Muscat, Oman showing (A) an occluded right coronary artery and (B) ectatic left coronary arteries.

pain lasting for two hours. He was not known to be diabetic or hypertensive. On examination, he was in pain with a blood pressure of 140/80 mmHg and heart rate of 80 beats per minute, which was regular. His electrocardiogram (ECG) showed ST-segment elevation in the inferior leads. He was immediately transferred for primary percutaneous coronary intervention (PCI).

His angiogram showed that all the coronary arteries were ectatic. The RCA was occluded at the junction of the proximal and mid-third with a heavy thrombus burden [Figure 1]. A balance middle weight universal II wire (Cordis Ltd, Santa Clara, California, USA) easily passed into the distal vessel. After predilatations were performed, manual thrombus aspiration was performed with an Export™ aspiration catheter (Medtronic Ltd, Minneapolis, Minnesota, USA) as per standard protocol. The thrombus was only slightly resolved, requiring further aspirations directly through the guide catheter deeply engaged in the vessel and also through a Guideliner™ (Teleflex Ltd, Morrisville, USA) passed deep into the vessel. A *bolus* dose of weight-adjusted IC eptifibatide was also administered. At the end of the procedure, there was significant, although not complete, thrombus resolution with thrombolysis in myocardial infarction (TIMI) grade two flow into the distal vessel [Figure



Figure 2: The right coronary artery of a 45-year-old male patient at the end of the first aspirations procedure.

2]. The ST-segment elevation in the patient's ECG had resolved and he was free of chest pain. At this point, it was decided to stop the procedure and start intravenous eptifibatide infusion with the intention to check again with another angiogram after 48 hours. However, the next day the patient developed chest pain with ST-segment elevation in the inferior leads once again.

The patient underwent an emergency coronary angiogram where the RCA was found to be occluded again, but in a more proximal location to the previous occlusion [Figure 3A]. Further aspiration was performed, but with no significant reduction in the thrombus burden. Therefore, it was decided to administer IC fibrinolysis. This was done using alteplase in aliquots of 5 mg over 10 minutes. This was given four times (total dose of 20 mg at 10 minute intervals) due to incomplete resolution of the thrombus. A Spider FX device (Medtronic Ltd) was used to prevent distal embolisation during thrombolysis. At the end of the procedure, there was TIMI grade three flow in the RCA [Figure 3B]. The patient was then started on eptifibatide and heparin infusion.

He remained well from a cardiac point of view with no further chest pains and normalisation of the ECG changes; however, he developed ataxia 24 hours

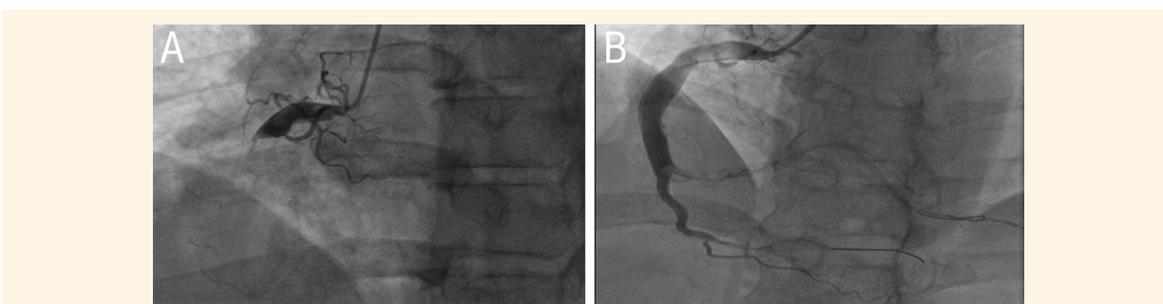


Figure 3: The right coronary artery of a 45-year-old male patient at the (A) beginning and (B) end of the second aspirations procedure.

later. A head computed tomography (CT) revealed a small intracerebellar bleed secondary to an existing previously undiagnosed arterio-venous malformation. The eptifibatid and heparin infusions were stopped but he was continued on dual antiplatelet agents. He subsequently had a full neurological recovery.

At three months, he remained free of chest pain with no new ECG abnormalities and no neurological deficits. He was not willing to undergo another coronary angiogram but instead underwent a cardiac CT which showed that the RCA remained widely patent.

Discussion

Percutaneous management of acute coronary occlusion presenting as an acute STEMI focuses on restoration of normal flow in the infarct-related epicardial artery. In addition, the operator also aims to restore coronary perfusion at the microcirculatory level using a combination of mechanical measures (e.g. aspiration thrombectomy) and pharmacological agents (e.g. glycoprotein [GP] IIb/IIIa inhibitors). Impaired coronary flow results in reperfusion injury and microvascular impairment which leads to arrhythmias, irreversible myocardial damage and permanent ventricular contractile dysfunction, heart failure and increased mortality.^{6,7}

Thrombus management is the cornerstone of PCI in acute STEMI. The level of thrombus burden predicts slow-flow, no-reflow phenomenon, which is a predictor of poor outcome.⁴ The presence of a large amount of thrombus is also associated with a higher incidence of stent thrombosis and reinfarctions. The thrombus may also embolise distally and obstruct the microcirculation, impairing tissue perfusion which may manifest as incomplete resolution of the ST-segment on the ECG or persistent wall motion abnormalities on the echocardiogram.⁴ Therefore, many strategies have been described to tackle the problem of large IC thrombus.² The thrombus can be disrupted with local balloon dilatation or treated with thrombectomy devices such as aspiration catheters or mechanical rheolytic thrombectomy.⁸ Injectable antiplatelets, such as GP IIb/IIIa inhibitors, are also used to help reduce thrombus burden and prevent complications.

Thrombectomy may be performed using standard aspiration catheters such as the Export™ (Medtronic Ltd), Diver™ (Invatec, Thurgau, Switzerland) or Pronto® (Vascular Solutions Inc., Maple Grove, Minnesota, USA) catheters, which are advanced into the vessel and manual aspiration with a syringe is performed. Specialised thrombectomy devices

such as the Angiojet™ (Medrad Inc., Warrendale, Pennsylvania, USA), X-sizer™ (Covidien, Dublin, Ireland) systems are motorised devices that can also be used in situations with high thrombus burden.⁹ These latter devices, although more successful in aspirating thrombus are cumbersome to use and are associated with more complications and have fallen out of favour by the interventionalists. Although routine thrombectomy is discouraged due to an unacceptably high risk of cerebral embolism and disabling strokes, it is still performed if there is a high level of thrombus present in the infarct related artery.¹⁰

Massive thrombus burden is not uncommon and is encountered in nearly 16–17% of acute coronary syndromes (ACS) undergoing coronary angiography.¹⁰ They are also unlikely to respond to conventional thrombus dissolution strategies whether mechanical (thrombus aspiration) or potent anticoagulant and antiplatelet agents, with studies showing persistent significant amount of thrombus in 8% of patients despite employing various measures to resolve it.¹¹

Systemic fibrinolysis is recommended in the management of acute STEMI where facilities for primary PCI are limited.⁵ However, the evidence for its use via the IC route for the treatment of large IC thrombus is not clear. The most commonly used agent for this indication is alteplase or tenecteplase (TNK). Streptokinase (one of the first thrombolytic agents to be used in STEMI) is not used routinely anymore due to various side effects and the availability of more potent and fibrin-specific agents. Alteplase is administered in a 5–10 mg aliquots given IC over five minutes.¹¹ This allows for a more controlled delivery of the agent locally, especially in a patient heavily pre-treated with antiplatelet agents, anticoagulation and GP IIb/IIIa inhibitors.

Kelly *et al.* studied 34 patients treated with IC thrombolysis for various indications (22 for acute STEMI, four for rescue PCI, six for non-STEMI and two for *in situ* thrombosis during elective PCI).¹² They found that IC administration of tenecteplase was proven to be both safe and effective with clot dissolution documented in 91% of treated patients. IC thrombolysis has also been shown to improve measures of microvascular function including coronary flow reserve, microvascular resistance, collateral flow, diastolic deceleration time as well as corrected TIMI frame count.¹³ Boscarelli *et al.* showed that low dose IC thrombolysis is both safe and effective in restoring epicardial flow and myocardial reperfusion.¹¹

Jayagopal Basha recently published a series of nine cases where IC tenecteplase was used successfully in patients with very high thrombus burden.¹⁴ In the series, TNK was given IC at one fifth the systemic dose

and the remaining four fifths were given systemically along with intravenous unfractionated heparin. All the patients had prompt and complete ST resolution and improvement in their TIMI myocardial blush grade with no patients having any significant bleeding.

The delivery of thrombolytics before thrombectomy in patients with STEMI undergoing primary PCI (DISSOLUTION) randomised trial compared IC urokinase with IC saline control group prior to aspiration thrombectomy in patients with large thrombus.¹⁵ This trial showed that patients with IC thrombolytic upfront had better angiographic findings (higher rate of TIMI3 flow and higher myocardial blush grade) as well as a significantly lower major adverse cardiovascular event rate at six months—driven mainly by a lower rate of rehospitalisation for heart failure. There was no increase in bleeding. Although the sample size was small (N = 102), it does suggest that IC thrombolysis may be useful.

In the current patient, the first attempt at percutaneous revascularisation with manual aspiration thrombectomy and balloon angioplasty resulted in modest restoration of epicardial flow to the distal vessel. However, two days later, the vessel had re-occluded and had no improvement with aspiration. Therefore, IC thrombolysis was performed. Using thrombolytic therapy, major bleeding is a not an uncommon complication. Due to an underlying previously undiagnosed arteriovenous malformation, the current patient developed intracranial bleed that was precipitated by the GP IIb/IIIa inhibitor infusion and heparin infusion. Fortunately, the patient recovered completely with no neurological sequelae. Therefore, efforts to open an infarct related artery with large thrombus burden should be done with caution as it exposes the patient to a higher risk of severe potentially fatal bleeding complications, including intracranial haemorrhage.

Conclusion

Occluded ectatic coronary vessels often present a therapeutic dilemma due to the huge thrombus burden that does not respond well to routine management. IC thrombolysis is a viable option in these patients with good resolution of thrombus but with a higher risk of major bleeding.

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