CASE STUDY

Platelet IIb/IIIa antagonists followed by delayed stent implantation. A new treatment for vein graft lesions containing massive thrombus

N Robinson, K Barakat, D Dymond

Abstract

The percutaneous treatment of saphenous vein graft lesions containing angiographically massive thrombus is associated with a high risk of distal embolisation and no-reflow. The optimal management for these lesions remains unclear and a challenge to the interventional cardiologist. Five cases are described in whom the risks of percutaneous angioplasty were felt to be excessive owing to a high thrombus load. Each case was treated with a bolus and infusion of abciximab (ReoPro; Eli Lilly—a platelet glycoprotein IIb/IIIa receptor antagonist) at least 24 hours before further angiography. Repeat angiography of the culprit vein graft, following treatment with abciximab alone, demonstrated a major reduction in the thrombus score and the presence of TIMI 3 flow in each case. Immediately following repeat angiography, angioplasty with stent insertion was performed successfully with no distal embolisation or no-reflow phenomenon. This staged approach, with abciximab used alone to reduce thrombus load, is a new treatment for vein graft lesions containing massive thrombus.

Keywords: thrombus; abciximab; glycoprotein IIb/IIIa receptor antagonists; interventional cardiology; angioplasty

Percutaneous transluminal coronary angioplasty (PTCA) in the clinical settings of unstable angina and acute myocardial infarction is performed at increased risk of acute coronary occlusion. One of the mechanisms underlying this increased risk is the presence of lesions containing thrombus. Angiographically identifiable thrombus has been shown to be associated with an increased risk of abrupt closure, distal embolisation, and no-reflow phenomenon.

The risk of distal embolisation is increased further following angioplasty of coronary bypass vein grafts with no-reflow reported after 10–15% of percutaneous interventions. The angiographic presence of thrombus associated with a vein graft lesion is an important predictor of distal embolisation. The optimal treatment for vein graft lesions containing thrombus remains unclear.

The platelet glycoprotein IIb/IIIa receptor antagonist abciximab (ReoPro; Eli Lilly, Basingstoke, Hants, UK) has been shown to reduce the complications of PTCA when given prophylactically to patients presenting with unstable angina and acute myocardial infarction. This new treatment for vein graft lesions containing massive thrombus is a promising alternative to traditional methods of treatment.

Figure 1 (A) Stenosis in the saphenous vein graft with long filling defect indicating thrombus. (B) Resolution of thrombus following treatment with abciximab.
unstable angina or complex lesion morphology.\(^7\)\(^8\) However, the possible role of glycoprotein IIb/IIIa antagonists alone before PTCA has not been assessed for the treatment of thrombus associated with vein graft lesions. We investigated whether abciximab alone would promote dissolution of massive thrombus thereby pacifying high risk vein graft lesions and allowing delayed PTCA to be performed at lower risk.

Patients
The five patients in this case study presented over a six month period. All patients had previous coronary artery bypass grafts and presented to their referral hospital with unstable angina (table 1). On transfer for angiography each patient was on treatment with intravenous heparin and had been pain free for the previous 24 hours.

In each case, angiography demonstrated multiple vessel coronary artery disease including a culprit saphenous vein graft stenosis with associated massive thrombus (fig 1). Angiographically assessed flow in the vein graft was TIMI 0–1 in two cases and TIMI 2 in three cases. After angiography each patient was treated with intravenous abciximab with the aim of performing angioplasty the following day. The decision to delay PTCA was because the thrombus burden was felt to be too great to allow immediate angioplasty as the risks of distal embolisation were excessive. A bolus of 0.25 mg/kg body weight abciximab was given followed by a 12 hour infusion at 10 µg/min. No further heparin was given until the angioplasty procedure. All patients remained pain free until returning to the cardiac catheter laboratory a mean of 28 hours later. Repeat angiography of the culprit vein graft showed a dramatic reduction in the thrombus score\(^9\) with TIMI grade 3 flow in each case (table 2). Two patients had complete resolution of thrombus.

Table 1 Patient demographics (n = 5)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Mean age (years)</td>
<td>65</td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>1</td>
</tr>
<tr>
<td>Previous MI</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>2</td>
</tr>
<tr>
<td>Family history</td>
<td>4</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1</td>
</tr>
</tbody>
</table>

PTCA, percutaneous transluminal coronary angioplasty; MI, myocardial infarction.

Table 2 Effect of abciximab

<table>
<thead>
<tr>
<th></th>
<th>Before abciximab</th>
<th>After abciximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean thrombus length (mm)</td>
<td>12.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Mean thrombus score*</td>
<td>3.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean TIMI flow</td>
<td>1.6</td>
<td>3</td>
</tr>
</tbody>
</table>

*0, no thrombus; 1, haziness; 2, definite thrombus < ½ vessel diameter; 3, definite thrombus ½ to 2 vessel diameters; 4, definite thrombus > 2 vessel diameters.\(^9\)
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More recently Muhlstein preventing the development of thrombus.

increased flow will have assisted abciximab in treatment with reduction of stenosis and
cally at the onset of balloon angioplasty. Lesion these studies abciximab was given prophylacti-
ction or no-reflow phenomenon. Each patient was subsequently mobilised and discharged pain free.

Discussion
Currently the optimal treatment for intracoronary thrombus associated with a target lesion is not clearly defined. Routine balloon angioplasty with stent insertion was performed successfully in each case with no distal embolisa-
ion or no-reflow phenomenon in up to 73% of cases, distal embolisation in up to 31% of
cases, and no-reflow phenomenon in up to 7% of cases.10 Angioscopic studies have demon-
strated lesion associated thrombus in 40–90% of patients presenting with acute ischae-
mic syndromes.11 Initial guidelines for the use of intracoronary stents considered lesions con-
taining thrombus as an absolute contraindication12 but stents are now being used effectively in acute coronary syndromes.13 14 Intracoronary thrombolytic agents have also been used without clear benefit15 and will not prevent further platelet aggregation.16 Mechanical approaches to the dissolution of thrombus17 are being evaluated but are again unlikely to reduce platelet activa-
tion or prevent platelet aggregation.

This preliminary report demonstrates that platelet glycoprotein IIb/IIIa receptor antago-
nists may have a role in pacifying coronary lesions that are heavily thrombus laden, thereby presumably reducing the risk of ischaemic complications following subsequent PTCA. In each of the cases in this report treat-
ment with abciximab predicted to a reduction in the thrombus load seen at angiography. The thrombus score improved from 3.6 before abciximab to 0.8 a mean of 28 hours after ini-
tiation of abciximab (table 2). Dissolution of friable thrombus before any attempt to cross a lesion with a wire or balloon will theoretically reduce the risk of distal embolisation and its associated ischaemic complications. For this reason, the objective of this study was to evalu-
ate thrombus load after treatment with intra-
venous abciximab and before any mechanical coronary intervention. This approach contrasts with the selective use of glycoprotein IIb/IIIa receptor antagonists during PTCA.

The ability of abciximab to prevent throm-
rosis during high risk angioplasty1 and in some lower risk patients1 has been documented. In these studies abciximab was given prophylacti-
cally at the onset of balloon angioplasty. Lesion treatment with reduction of stenosis and increased flow will have assisted abciximab in preventing the development of thrombus. More recently Muhlstein et al reported the “rescue” use of abciximab for the treatment of coronary thrombus developing as a complica-
tion of PTCA.18 Again in this study mechanical factors will have assisted thrombus resolution as each case was treated with one or more repeat balloon inflations after abciximab ad-
mistration. Gold et al assessed the effects of an intravenous administration of abciximab in 13 cases of TIMI grade 0 or 1 coronary flow.19 They reassessed coronary flow 10 minutes after the start of abciximab administration immediately before PTCA. They noted an improve-
ment in TIMI grade flow from a mean (SD) of 0.31 (0.5) to 1.54 (0.8). In contrast to our report they proceeded directly to PTCA in the presence of angiographically documented thrombus. Our report provides the first clinical evidence to support the role of abciximab alone to promote dissolution of intracoronary throm-
bis. This reduction in thrombus load allowed subsequent intracoronary stent insertion to be performed effectively. We do not know if this pretreatment with abciximab rather than treatment during PTCA offers better longer term outcome.

Several potential mechanisms exist whereby platelet glycoprotein IIb/IIIa inhibitors may lead to dissolution of thrombus. Coronary thrombosis is dynamic with platelet and fibrin deposition coexisting with partial lysis.20 Abciximab may displace fibrinogen from glyco-
protein IIb/IIIa receptors as the affinity con-
stant for the binding of abciximab to the IIb/IIIa receptor is significantly greater than that for fibrinogen binding.15 In vitro studies have also suggested that abciximab may accel-
erate endothelium based fibrinolysis by inhibit-
ing the action of plasminogen activator inhibitor.21 More recently, in vitro thrombin generation by tissue factor has been shown to be reduced by abciximab.22 The contribution made by these mechanisms to the resolution of thrombus seen in our patients remains unclear.

Current clinical practice in the UK does not include administration of abciximab to all patient groups considered in the EPIC (evaluation of 7E3 for the prevention of ischemic complications)7 and EPILOG (evaluation in PTCA to improve long term outcome with abciximab GP IIb/IIIa blockade)8 studies. The prophylactic use of abciximab for all patients comparable to those in EPIC7 and EPILOG8 would create a significant cost burden.23 Most departments are rationing the use of abciximab to patients with angiographically visible throm-
bis, a commonly accepted indication for its use. The best time to perform balloon angioplasty once thrombus has been demon-
strated angiographically is unclear. If there is ongoing ischaemia at the time of angiography, immediate PTCA may be necessary. Our preliminary report suggests that for patients with no ongoing ischaemia, pacifying the vessel wall with a reduction in thrombus load is pos-
sible following administration of abciximab. A delay before PTCA will allow time for the endogenous fibrinolytic system to reduce thrombus load and may therefore reduce the risks of subsequent intervention.

This study of five cases draws attention to a new role for glycoprotein IIb/IIIa receptor inhibitors in the treatment of lesions associated with massive thrombus. Further evaluation is required with randomised clinical trials. Coronary thrombus formation is equally an
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integral part of the pathogenesis of unstable angina in patients who do not yet have access to coronary angiography. Platelet glycoprotein IIb/IIIa inhibitors may therefore have a role in the treatment of patients with unstable angina before consideration for angiography. Alleviating the clinical syndrome would perhaps allow angiography to be performed electively and may reduce the ischaemic complications of PTCA if subsequently required.

Thanks are given to Dr Hogan and Dr Rothman for inclusion of their patients.

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