

Is conventional antiplatelet therapy for the prevention of coronary stent thrombosis always safe? A case report of a patient with polycythemia vera

Dennis Zavalloni, Federica Marsico, Francesco Milone, Patrizia Presbitero

Division of Interventional Cardiology, Istituto Clinico Humanitas, Rozzano (MI), Italy

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A 63-year-old male patient with both polycythemia vera and unstable angina underwent an angioplasty with the deployment of a stent. Conventional antiplatelet therapy failed to prevent stent thrombosis and an association with chronic anticoagulation seemed to be the only safe treatment. Moreover, after the late withdrawal of warfarin, stent thrombosis recurred.

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Address:

Dr. Dennis Zavalloni
U.O. di Emodinamica
e Cardiologia Invasiva
Istituto Clinico Humanitas
Via Manzoni, 56
20089 Rozzano (MI)
E-mail:
patrizia.presbitero@
humanitas.it

Introduction

Acute or subacute in-stent thrombosis in a coronary artery is nowadays a rare event¹. The use of high inflation pressures and the shifting from anticoagulation to a double antiplatelet regimen (aspirin and ticlopidine) have played a key role in achieving this result. Nevertheless, previous case reports have described how with polycythemia vera (PV) a percutaneous coronary intervention (PCI) may be complicated by recurrent in-stent thrombosis². We report a case of a patient with PV in whom this complication was prevented by the use of anticoagulant therapy.

Case report

A 63-year-old male patient was admitted to our hospital because of unstable angina. In his clinical history, a previous myocardial infarction and an event-free PCI with stenting had been carried out 3 years earlier on both the proximal left anterior descending (LAD) and the left circumflex coronary arteries. The only cardiovascular risk factor was a smoking habit (10 cigarettes/day). A few months earlier PV had been diagnosed and treated with phlebotomies. At admission, the hemoglobin level was 12 g/dl, with a 42% hematocrit, and a platelet count of $500 \times 10^3/l$.

Coronary angiography showed a complex stenosis of the mid LAD (Fig. 1A).

The lesion was distal to the previously treated segment and involved the ostium of a large diagonal branch. Both lesions were treated with a PCI including the deployment of a carbofilm-coated stent on each vessel. Aspirin and ticlopidine had been started 48 hours previously.

Procedural details. After a bolus of 10 000 IU of heparin (activated clotting time > 300 s), the PCI was performed on both the diagonal branch and the LAD. In the former, two stents (3.5×12 mm + 3.5×9 mm) were implanted, while in the latter, one stent (3.5×19 mm) was deployed. High pressures were used (15 atm) and finally, a "kissing balloon" technique was performed with an optimal angiographic result (Fig. 1B).

The patient was discharged 2 days later on 100 mg of aspirin daily and 250 mg bid of ticlopidine. After 4 days, the patient presented with sudden-onset precordial pain and acute dyspnea. Physical signs of left ventricular dysfunction were present and the ECG showed ST-segment elevation in the anterior and lateral precordial leads. The patient underwent an urgent coronary angiography which revealed an in-stent subacute thrombosis of the LAD-diagonal bifurcation (Fig. 2A). Total vessel patency was achieved by means of a repeat PCI performed 5 hours after the onset of symptoms.

Abciximab (0.25 mg/kg bolus followed by a $0.125 \mu\text{g}/\text{kg}/\text{min}$ 12-hour infusion)

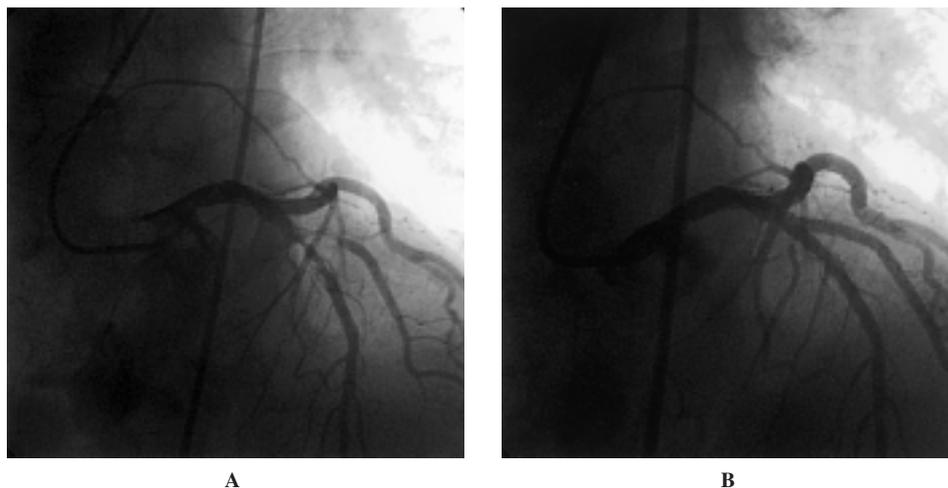


Figure 1.

was administered and a balloon angioplasty performed on both the LAD and the first diagonal (using a 3.5 mm diameter balloon on the LAD at 14 atm and a 3.0 mm balloon on the diagonal branch at 8 atm, with a final “kissing balloon” technique at 8 atm). A further stent (Bx Velocity 3.0 × 13 mm) had to be implanted on the diagonal branch because of a residual distal dissection after prolonged balloon inflation. An optimal angiographic result with TIMI 3 flow was obtained (Fig. 2B).

The hemodynamic profile improved immediately after reperfusion; the creatine kinase peak was 2208 U/l with a creatine kinase-MB peak of 193 U/l. The blood count did not differ from previous values. A complete screening for prothrombotic diathesis revealed heterozygosis for the enzyme methylenetetrahydrofolate with mild hyperhomocysteinemia (fasting level 14 μmol/l; post-load level 50 μmol/l). Treatment with both folate and vitamin B12 was started even though

the concomitant mild hyperhomocysteinemia does not seem to increase the risk of thrombosis in PV³.

An echocardiogram showed akinesis of the lateral wall and of the inferoposterior wall (previous myocardial infarction); it also showed hypokinesis of both the anterior wall and the apex, with an ejection fraction of 35%.

Anticoagulation (with warfarin maintaining an INR of 2.5-3.5) was administered indefinitely, together with ticlopidine (250 mg bid) for the first month. The patient was discharged 1 week after PCI.

Five months later, the patient was free from angina and an echocardiogram revealed an improvement in the anterolateral wall motion with an ejection fraction of 48%.

A control angiography was planned and, 1 week before hospitalization, the patient’s family doctor replaced warfarin with low doses of low molecular weight heparin (nadroparin 4000 U/day-60 U/kg).



Figure 2.

A relapse of the in-stent thrombosis with asymptomatic occlusion of the LAD (Fig. 3) was detected. Left ventriculography showed anterolateral and apical akinesis with severe worsening of the ejection fraction (30%).

Therefore, the patient underwent a coronary artery bypass with the left internal thoracic artery on the LAD and a saphenous vein graft on the first diagonal branch. The postoperative period was free of complications and the patient was discharged 6 days later on both warfarin and ticlopidine indefinitely.

After 6 months the patient was asymptomatic with an ejection fraction stabilized at 30-35%.

Discussion

PV is a rare (4-16:1 000 000) myeloproliferative disease associated with a high proportion of vascular complications⁴. The platelet quantitative and qualitative changes observed in PV⁵ may lead either to bleeding or to a thrombosis diatheses but, when the platelet count is between $400 \times 10^3/l$ and $1000 \times 10^3/l$, thrombotic events are more frequent^{4,6}.

Among all the thrombotic events reported in PV, up to 50% have been myocardial infarctions (accounting for 14% of the mortal outcomes in these patients)⁴. Therefore, when both PV and coronary artery disease are present, the use of aspirin has been proposed as a prophylactic measure for thrombotic events⁴. Nevertheless, when the cyclo-oxygenase pathway is not the only mechanism involved in platelet activation, an adjunctive and/or alternative therapy should be considered. In particular, anticoagulation has been recommended in those patients who have experienced thrombotic events despite the use of aspirin⁴. Since our patient had an acute coronary syndrome associated with a coagulation disease, an underlying predisposition toward recurrent thrombosis should have been strongly suspected⁷. Moreover, coronary angioplasty with stent

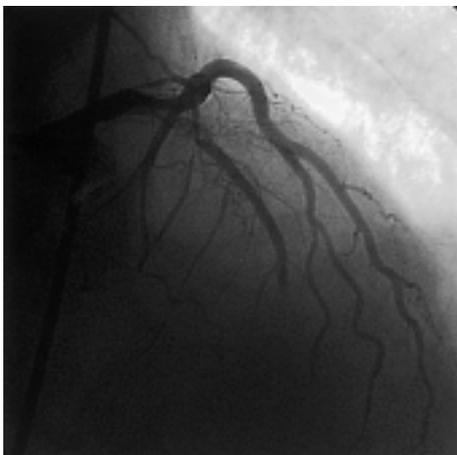


Figure 3.

implantation has to be considered as a further trigger for coronary thrombosis.

In previous case reports, a favorable outcome for invasive treatment in patients with both PV and coronary artery disease has been related only to balloon angioplasty, whereas a high rate of recurrent thrombosis has been observed after stent implantation^{2,8,9}. For this reason, we decided to use one of a new generation of carbofilm-coated stents which had been successfully deployed in a series of patients with a high risk of thrombosis^{10,11}. Although an optimal angiographic result was achieved and a stent with claimed antithrombotic properties was used, the conventional antiplatelet therapy (aspirin plus ticlopidine) was not sufficient to neutralize the prothrombotic stimulus. Only the association with anticoagulation seemed to be successful in preventing recurrent thrombosis.

The shifting from anticoagulation to a double antiplatelet therapy has significantly reduced the rate of both acute and subacute in-stent thrombosis (from 10 to 0.5-1%)¹². This reduction¹³⁻¹⁷ has occurred despite a warning some 30% unapposition of stent struts on the artery wall has been still observed in studies on stent deployment under intravascular ultrasound guidance¹⁸. In our case report, despite the use of high pressures and a final kissing balloon technique, inadequate apposition of the stent struts cannot be excluded as a cause of in-stent thrombosis, because of the lack of intravascular ultrasound data.

The problem of the optimal management of a patient with PV and acute coronary syndromes is further complicated by the fact that antithrombotic therapy administered to such patients has been associated with both severe bleeding and the enhancement of thrombosis^{4,6}. For this reason, we avoided administering glycoprotein IIb/IIIa inhibitors in the first instance, despite the treatment of a difficult bifurcation.

In conclusion, the current data on PCI in patients with PV derive only from case reports; the optimal antithrombotic therapy can be inferred from data reported in studies enrolling patients without PV, and data on the rate of in-stent restenosis in this condition are lacking. Retrospectively, in our patient with PV and a large area of myocardium at risk, a coronary artery bypass would have probably been the best treatment since the beginning, especially with the use of arterial grafts. Conversely, when planning a PCI, the deployment of a stent should probably be limited to "bailout" conditions. Although double antiplatelet therapy must be considered the "gold standard" for the prevention of in-stent thrombosis, in patients with both coronary artery disease and PV it might not be able to prevent this adverse event, and the association with chronic anticoagulation should be considered. In addition, the risk of bleeding due to the concomitant use of other antithrombotic drugs, such as glycoprotein IIb/IIIa inhibitors, must be taken into consideration, even though adverse hemorrhagic events did not occur in our patient.

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