Concomitant Use of Glycoprotein IIb/IIIa Inhibitor and Streptokinase after Unsuccessful Rescue Angioplasty

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A 38-year-old man with acute myocardial infarction in the lower wall affecting the right ventricle underwent thrombolytic treatment with streptokinase. Approximately 2 hours after the thrombolytic treatment started, he presented with signs of coronary reocclusion. He underwent emergency cineangiocoronariography that revealed that his right coronary artery was completely occluded by a clot. He unsuccessfully underwent angioplasty and stent implantation. After the concomitant use of glycoprotein IIb/IIIa inhibitor, coronary TIMI III flow was achieved without additional dilations, and he was discharged from the hospital 5 days later with no further complications.

Antiplatelet therapy for acute coronary syndrome is widely established [1]. As for acute myocardial infarction, the data from the ISIS 2 study showed clearly that acetylsalicylic acid, alone and/or combined with thrombolytic therapy with streptokinase, plays a role in the reduction of mortality [2]. Over the last few years, important progress has been made in this field as new and stronger antiplatelet drugs, such as the glycoprotein IIb/IIIa inhibitors, have been discovered. However, the role of these new medications as a primary support therapy in acute myocardial infarction still needs to be better understood.

Case Report

A 38-year-old male patient, smoker, previously in good health, came to the emergency department complaining of a 4-hour-long oppressive retrosternal pain that had started during intense exercise, irradiating to the left upper limb, accompanied by dyspnea, sweating and vomiting, which improved slightly after sublingual nitrate and aspirin administration.

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On admission, he was tachypneic, with a blood pressure of 130x80mmHg and a heart rate of 80 bpm, normal pulmonary auscultation, and a regular heart pace of three beats at the 4th sound, without murmurs. Pulses were symmetrical, and no jugular stasis was present. The electrocardiogram showed an AV dissociation, an overunlevelling of 8mm of the ST portion at D_2, D_3, and the VF and of 4 mm at V_2 to V_6, V_3R, V_4R, V_7, and V_8, and an underunlevelling at D_1, VL, and VR (fig. 1).

An acute myocardial infarction was diagnosed, and 20 minutes later thrombolysis with 1,500,000 U of endovenous streptokinase was administered for 40 minutes. The patient reported moderate pain relief and had a slight reduction in the overunlevelling of the ST portion, while the AV dissociation persisted. Approximately 2 hours later, he developed recurrent pain, without any change in the initial electrocardiographic alterations. After the introduction of low-dose endovenous nitroglycerin, he experienced a slight improvement, but about an hour later, he again felt intense pain, which persisted even with nitroglycerin use, so an emergency heart catheterization was performed. Prior to this test, with persistent pain, the patient developed significant hypotension accompanied by jugular stasis and slight stertors at the lung bases, requiring dobutamine, even after adequate volemic repositioning. The procedure was started approximately 10 hours after the infarction began to develop.

The left coronariography showed no atherosclerotic lesions. The right coronariography showed a dominant, gross-caliber right coronary artery to be totally occluded at its proximal third (fig. 2). A guiding lead was threaded to the distal third of the right coronary artery without any difficulty. Then, insufflation with a 3.5x20mm balloon was performed for 2 minutes. The control coronariography (fig. 3) showed a TIMI II flow and a type B dissection at the balloon insufflation site. It was then decided to implant a 4.0x15mm NIR stent, which was done with no difficulty. Afterwards, a control coronariography was performed that showed the right coronary artery to be totally occluded where the stent had been placed (fig. 4). The patient was still hypotensive, slightly dyspneic, tachy-

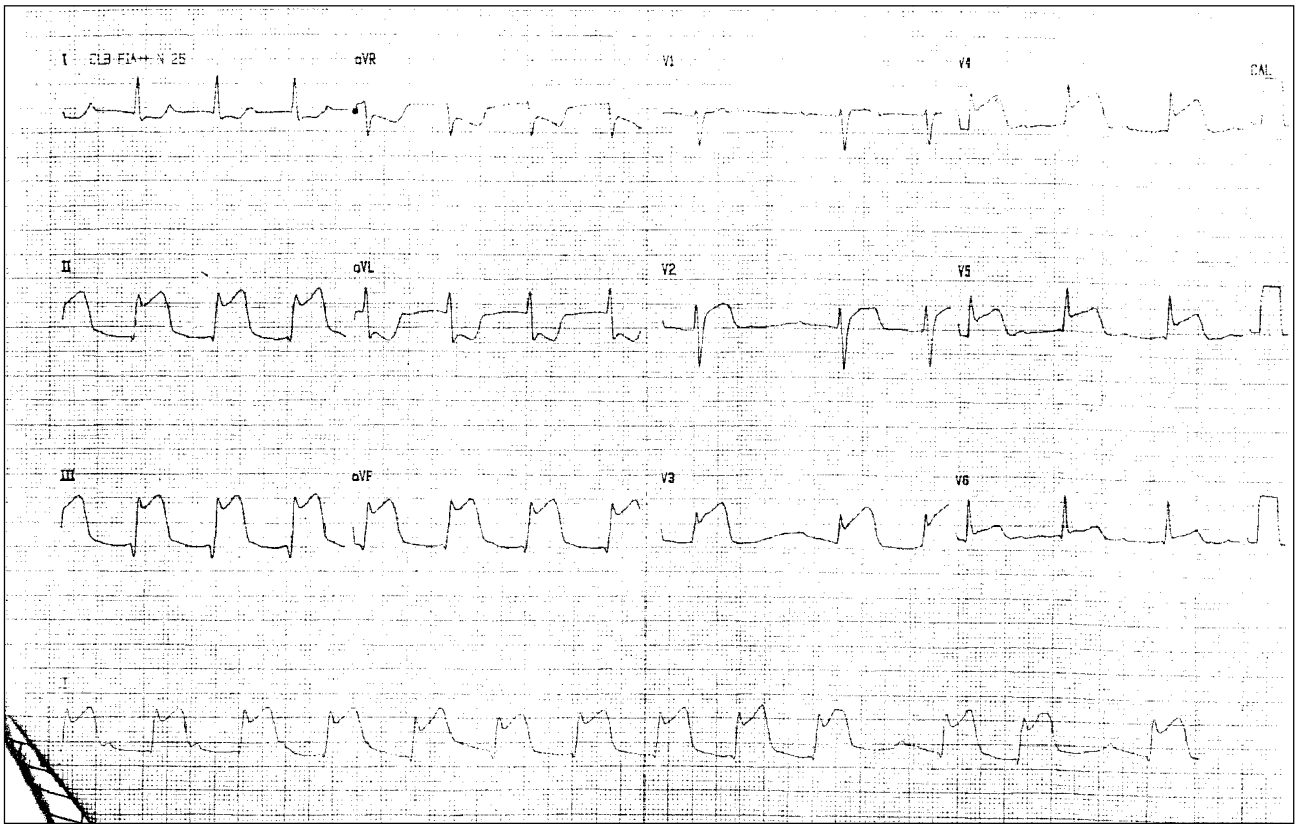

Fig. 1 – Patient's electrocardiogram on admission, showing overunlevelling of the ST segment at D_2, D_3, and the VF, V_2 to V_6, V_3R, V_4R, V_7 and V_8, and underunlevelling at D_1, VL, and VR.

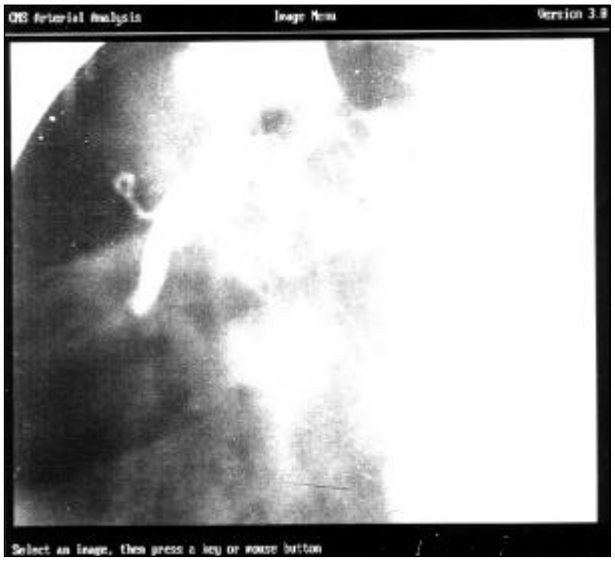

Fig. 2 – Completely occluded right coronary artery after thrombolysis by streptokinase.

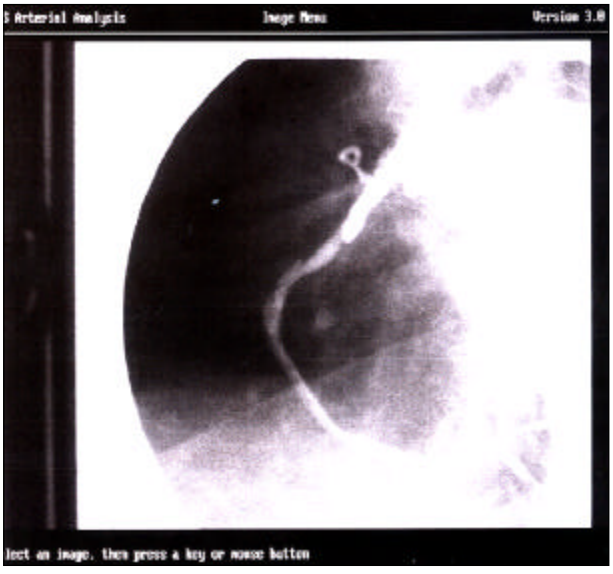

Fig. 3 – Right coronary artery after balloon insufflation, showing type B dissection at its medium third.

cardic, and with precordial pain. We chose to perform further dilations at several places, with pressure of up to 18 atm, at the stent site, but were unsuccessful. At this point, activating cloting time (ACT) was 300 s, and we decided to use abciximab, in the usual dose. Ten minutes after the bolus, the flow was re-established, but with a clot at the medium and distal thirds of the right coronary (fig. 5), and 30 minutes after continuous infusion, the vessel had a TIMI 3 flow, but clots were still present (fig. 6). After 90 minutes, TIMI 3 flow returned and no signs of dissection or clot (fig. 7) were present. After the introduction of abciximab, no additional insufflation was performed.

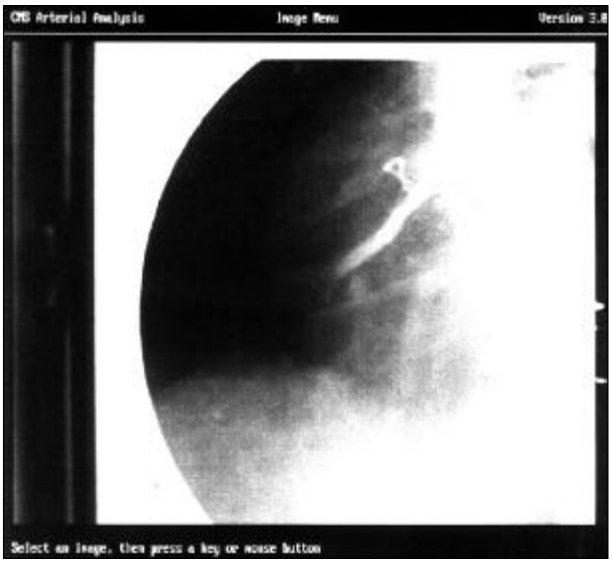

Fig. 4 – Completely occluded right coronary artery after stent implantation.

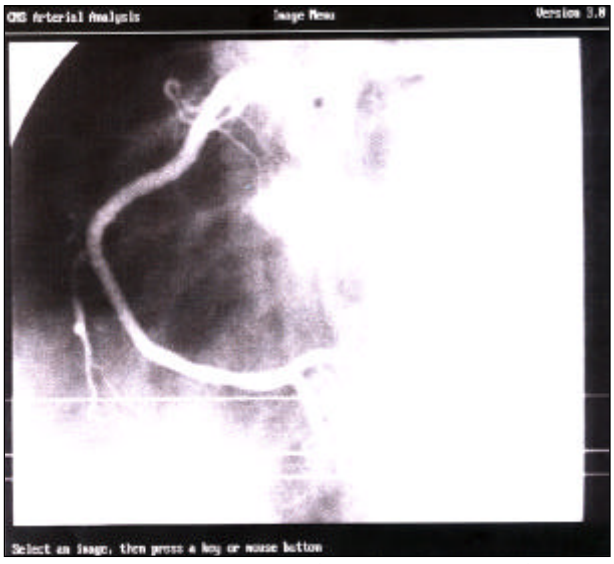

Fig. 6 – Right coronary artery 30 minutes after continuous abciximab infusion, showing TIMI III flow, but still with a clot.

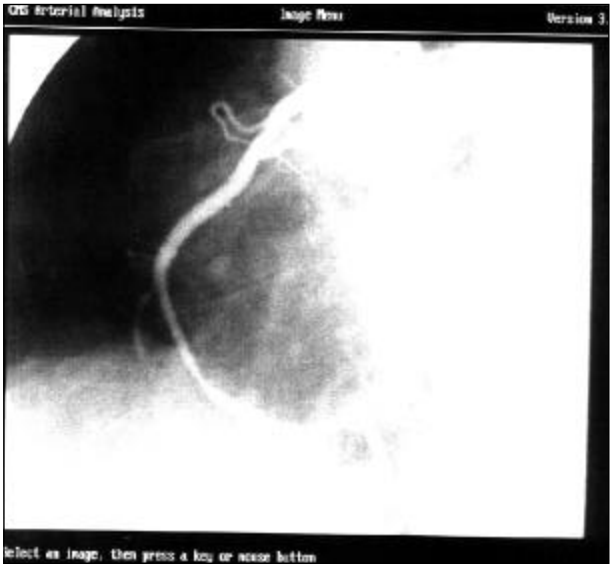

Fig. 5 – Right coronary artery 10 minutes after the abciximab bolus, with re-established flow and an intraluminal clot.

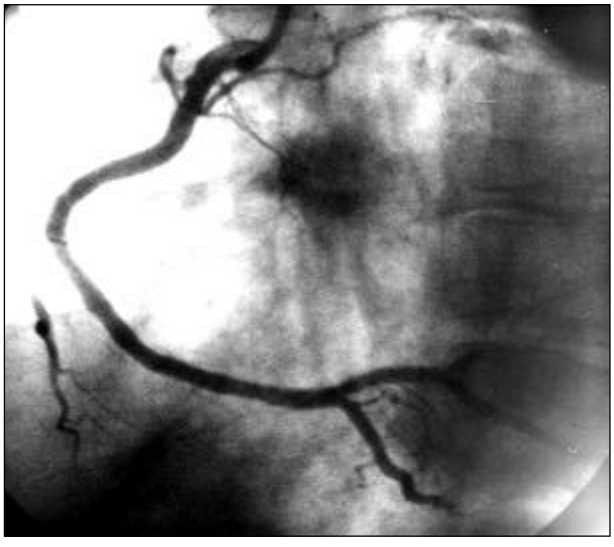

Fig. 7 – Right coronary artery 90 minutes after continuous abciximab infusion, with TIMI III flow, without an intraluminal clot.

The patient's pain resolved and he was transferred to the coronary unit, where he stayed on continuous abciximab infusion for another 12 hours, being discharged from the hospital 5 days later, with no symptom recurrence.

Discussion

Ever since the results of the GISSI [1] study with streptokinase and the ASSET [2] study with r-TPA were published, the reduction in mortality by thrombolytic therapy in cases of acute myocardial infarction with overunlevelling of the ST segment has been established. However, depending on the thrombolytic agent used, the patency of the vessel, defined as TIMI II and III flows, varies in 60% to 80% of the treated patients [3,4]. When the full flow of the vessel responsible for the infarction (TIMI III flow) is considered, this goal is achieved in no more than 30% to 50% of the treated patients [4]. Even after successful thrombolytic therapy, about 5% to 10% of the patients have their reperfused vessel reoccluded, and, as a consequence, reinfarction and an increase in morbidity and mortality occur [5,6].

In our case, after successful thrombolytic therapy with streptokinase, the patient again showed signs of reocclusion, confirmed by cineangiocoronariography.

After this confirmation, the patient underwent rescue angioplasty with implantation of a stent and additional dilations, which were unsuccessful. Because coronary rethrombosis occurred, despite full anticoagulation with heparin and systemic fibrinolysis produced by streptokinase, the glycoprotein IIb/IIIa inhibitor was then successfully used. In such circumstances, rapid decision making is crucial, and basically 2 options are possible: the surgical one, with all

the risks inherent to systemic fibrinolysis determined by streptokinase, and the use of a glycoprotein IIb/IIIa inhibitor, being equally aware of the risks possible with this combination. As the patient had only one severely injured artery, the latter option was chosen.

Therapy with glycoprotein IIb/IIIa inhibitors was analyzed in different clinical situations, and its benefits (reduction in ischemic events) were proven in high- and low-risk percutaneous therapeutic procedures, resistant unstable angina and in cases of acute myocardial infarction primarily treated by angioplasty.

Until now, only the endovenously given GPIIb/IIIa inhibitors have proved effective in reducing major cardiac events. Studies that analyzed the GPIIb/IIIa inhibitors given orally in acute myocardial infarction without the Q-wave and in unstable angina and in invasive therapeutic procedures showed negative results with regard to its benefits [7,8].

Some phase II studies analyzed, as a primary treatment for acute myocardial infarction, associated with thrombolytic therapy, the use of Integrilin with r-TPA (IMPACT-AMI) [9], lamifiban with streptokinase or r-TPA (PARADIGM), and abciximab with r-TPA or streptokinase (TIMI 14) [10]. However, in dose analysis studies, such as TIMI 14, where 14 therapeutic regimes were studied, it was shown that, in the group that used 50mg TPA with the usual dose of abciximab, the TIMI III flow was reached in 72% of cases after 60 minutes. In the group whose thrombolytic regime was a full dose of streptokinase, the incidence of hemorrhage was prohibitive, only 5 patients being included 4 of whom had significant bleeding, and 2 died. In our case, the patient was in an unfavorable hemodynamic condition, abciximab therapy was chosen in spite of the risk of bleeding, and the result of the procedure was successful, with full flow resumed in the artery responsible for the infarction, without any additional dilation after the start of the GPIIb/IIIa inhibitor.

Sakharov and Rijken [11] demonstrated that continuous activation of plasminogen may be necessary if complete reperfusion is the goal. But this occurs more markedly with streptokinase than with the other thrombolytic drugs, thus increasing the risks of this therapy. Coronary thrombosis simultaneously involves deposition and lysis of fibrin and platelets, causing intermittent occlusions. According to the results of the recently published SPEED [12] study, the association of small doses of a thrombolytic agent with a strong platelet inhibitor appears to enhance fibrin and platelet lysis, producing more adequate reperfusion. Since TIMI 14, it has become clear that a high incidence of severe bleeding occurs when the combination of streptokinase and abciximab is used, which makes this combination basically prohibitive. In spite of a very interesting result, the risks should not be forgotten, so extreme practices should only be adopted in very special situations. The ongoing GUSTO 4 phase III study will bring us a final answer concerning the use of this combination for treatment during the acute period of acute myocardial infarction.

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