

ACUTE MYOCARDIAL INFARCTION IN A PATIENT WITH ESSENTIAL THROMBOCYTHEMIA TREATED WITH PRIMARY CORONARY ANGIOPLASTY

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Esansiyal trombostemili ve trombosit sayısı 1.428.000mm³ olan, 53 yaşında akut öndüvar miyokard infarktüsü ile başvuran ve primer koroner anjiyoplasti bir olgu sunduk.

Hastaya işlem sonrası 48 saat süreyle glikoprotein IIb/IIIa reseptör antagonisti verildi ve hasta daha sonra hasta komplikasyonsuz olarak takip edildi. Hastaya taburuluk öncesi tromboferes tedavisi birkaç kez uygulandı.

Hasta Aspirin, klopidogrel, hydroxyurea, enalapril, metoprolol tedavisi ile 3. günden sonra taburcu edildi.

Anahtar kelimeler: Akut miyokard infarktüsü, Trombostemi, Primer koroner anjiyoplasti

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INTRODUCTION

A 53-year-old male with no previous cardiac history presented with recurrent episodes of chest pain lasting about fifteen minutes at rest during the last two days. His past medical history was significant for a high platelet count which was detected fifteen days prior to his admission. He was taking aspirin and denied any episode of bleeding or thrombotic events. He was a non-smoker and did not have hypertension, diabetes mellitus or family history of coronary artery disease. Physical examination at presentation revealed a blood pressure of 110/70 mmHg and a heart rate of 65 bpm. His lungs were clear to auscultation and cardiac examination revealed normal first and second heart sounds. There were no murmurs or clicks. No hepatosplenomegaly or lymphadenopathy was appreciated. The electrocardiogram showed biphasic T wave changes in leads V4-V6. Results of a complete blood count were significant for a platelet count of 1,428,000/mm³. Hemoglobin was 14.2 gr/dl and white blood cell count was 9900/mm³. Cardiac enzymes were not elevated at initial evaluation. Total serum cholesterol level was 120 mg/dl, and HDL was 34 mg/dl. Liver function tests, electrolytes and creatinine were in

normal range. His chest roentgenogram was normal. After his admission he developed recurrent brief episodes of epigastric pain radiating to his neck. Electrocardiographic examination revealed development of pathological Q waves and ST-segment elevation in V1-V4. Emergent platelet pheresis was performed before coronary angiography. Severe left ventricular anterolateral and apical hypokinesis was seen at cardiac catheterization. There was 99% obstruction of left anterior descending coronary artery (LAD) after the take-off of the first diagonal branch (Figure 1). The left main, left circumflex, and right coronary arteries were angiographically normal. During right oblique projections total occlusion of LAD developed after first septal branch (Figure 2). A filling defect was seen at the site of total occlusion probably reflecting platelet rich thrombus. As soon as this view was detected a GP IIb/IIIa receptor antagonist tirofiban (Aggrastat, MSD) was administered. Since platelet count was significantly elevated, the dose of tirofiban was higher than previous recommendations (15 g/kg over 3 minutes as a bolus, followed by 0.25 g/kg/min 48 hours). After administration of 10.000 IU of intravenous heparin and 600 mg clopidogrel the diagnostic catheter was exchanged for an 8 Fr JL4 guiding catheter (Boston Scientific, Weisse guide, USA), and the left main coronary artery was engaged. The proximal LAD lesion was crossed with a 0.014 in 182 cm Choice floppy wire

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Figure 1: Left coronary angiogram (LAO lateral). Severe obstruction of left anterior descending coronary artery (LAD) after the take-off of the first diagonal branch. A filling defect is seen at the first septal branch

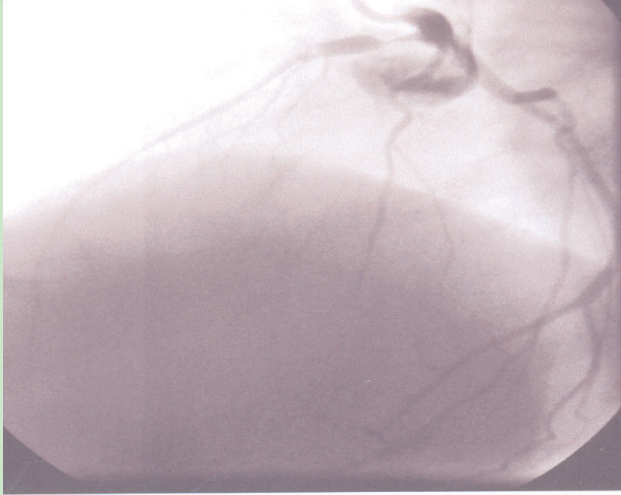
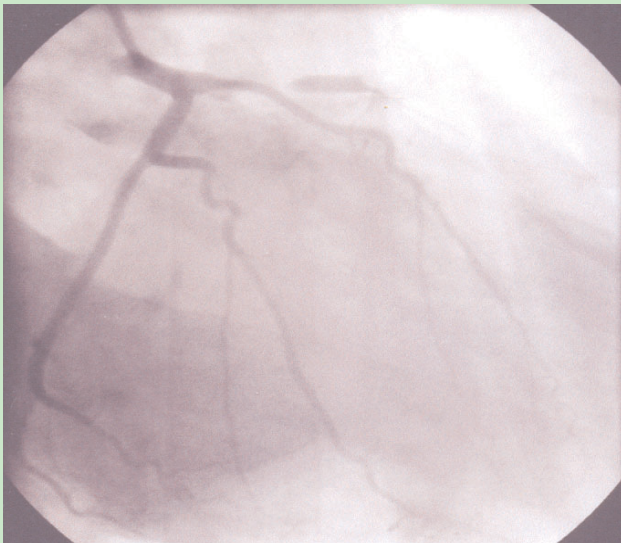


Figure 2: Left coronary angiogram (RAO caudal). Total occlusion of LAD developed after first septal branch



(Boston Scientific, USA). As soon as floppy wire was crossed TIMI II flow was established distal to the second occlusion site. Angioplasty was performed with a 3.0 × 20 mm Viva Balloon (Boston Scientific, USA) at 6 atm. Due to suboptimal balloon angioplasty results, a 3.5 × 16 mm Direct stent was deployed to the LAD at 10 atm. Repeat angiogram revealed TIMI III flow with less than 10% residual stenosis in LAD (Figure 3).

The patient was started on medical therapy with acetylsalicylic acid (ASA), clopidogrel, metoprolol, heparin, enalapril, tirofiban (Aggrastat, MSD) and

hydroxyurea. Platelet pheresis performed before coronary angiography was able to achieve a platelet count of 700.000/mm³. A peripheral blood smear was remarkable for thrombocytosis and presence of large dysmorphic platelets. The patient's subsequent hospital course was uncomplicated. Cardiac troponin-T level was elevated to 1.7 ng/ml and CK-MB level to 40.48 ng/ml. On the second day of his hospitalization his platelet count was found to be 1.095.000 /mm³ and platelet pheresis was performed for the second time. During the hospitalization period the patient did not have any bleeding or recurrent chest discomfort. He was discharged on clopidogrel, ASA, hydroxyurea and enalapril three days later and was asymptomatic on 30.day follow-up control

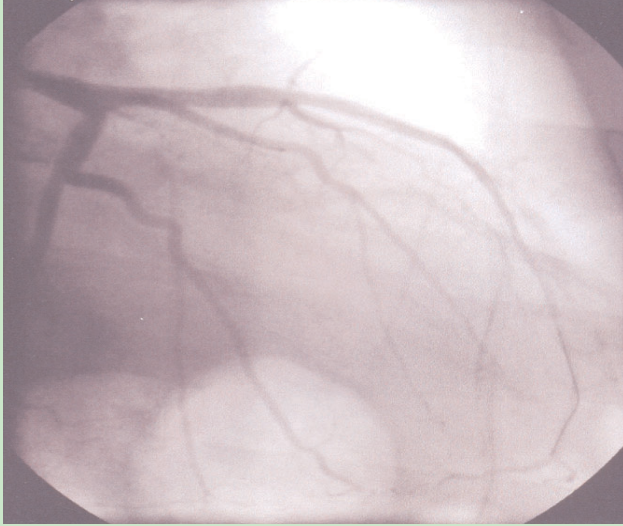
DISCUSSION

Essential thrombocythemia (ET) is a myeloproliferative disorder characterized by abnormal proliferation of megakaryocytes and resulting thrombocytosis¹. The disease is a clonal disorder originating from multipotent stem cells in which an excessive number of morphologically and functionally abnormal platelets are produced². This disease group also includes polycythemia vera, chronic myelogenous leukemia, and myelofibrosis with myeloid metaplasia.

The disease is generally diagnosed in the sixth and seventh decades of life with an incidence of approximately seven per million year³. Occasionally, ET presents with hemorrhagic complications, but more often with arterial and/or venous thrombosis. Approximately 10% of patients with ET, and in some studies up to 75% of such patients manifest thrombotic events⁴. Vascular thrombosis can involve either large vessels and/or microcirculation, causing increased morbidity and mortality⁴. The most common thrombotic manifestations are deep venous thrombosis and pulmonary embolism⁵. A higher incidence of thrombosis does not appear to correlate with the platelet count⁶. Arterial thrombi, in contrast to venous thrombi, contain a high number of activated platelets and platelet rich thrombi resistant to lysis⁷. Arterial thrombosis, particularly in the microcirculation, is associated with erythromelalgia, digital ischemia, and gangrene/neurologic disturbances in patients with ET⁸.

Although ET may cause vascular thrombosis and tissue ischemia, the involvement of coronary arteries with consequent myocardial infarction (MI) is a rare finding. Of the reported cases, occlusion of the LAD artery is the most frequently involved⁹⁻¹³. In ET, interestingly, the pathophysiology of events leading to thrombosis in coronary arteries seems to be different. In these patients, atherosclerosis may not necessarily be present and acute coronary thrombosis can

Figure 3: Left coronary angiogram (RAO caudal). The occlusion has successfully been recanalized, and a Direct stent has been placed.



develop without any signs of a vessel damage. Safitz et al¹². reported a 22-year-old man with fatal congestive heart failure after a large MI with thrombocytosis. His necropsy findings showed platelet-fibrin thromboemboli in multiple small intramural coronary vessels. Histologic examination of the coronary arteries were free of foam cells, cholesterol clefts or calcific deposits.

In patients with ET recurrent myocardial infarction is also seen. Douste-Blazy et al¹³ reported a patient with ET who experienced recurrence of MI after his discontinuation of hydroxyurea. One month after each event coronary angiogram demonstrated normal coronary arteries. Kaya et al¹⁴ reported a 61-year-old patient with ET with recurrent MI. Coronary angiography 10 days after the infarction was normal. Simultaneous involvement of the coronary arteries is also a recognized finding in patients with ET. Hamada et al¹⁵ reported a 59-year-old woman who was admitted with an inferior wall MI. Coronary angiogram showed total occlusion of the right coronary artery and a thrombus like filling defect in the LAD.

Treatment modalities for this group of patients are not clearly defined, but there are reports of angioplasty and intracoronary thrombolytic therapy, and coronary artery bypass surgery. Turgut et al¹⁶ reported a patient with ET who presented with an acute anterior myocardial infarction. Emergent coronary angiogram revealed a total occlusion of the LAD after first septal perforator. The patient was treated with primary coronary angioplasty and stenting. However, bleeding from his femoral puncture site caused the

discontinuation of ticlopidine and heparin therapy. After 48 hours the patient experienced recurrent anterior wall MI and repeat coronary angiogram revealed total occlusion of mid-LAD at the previous stent. Angioplasty and thromboectomy was performed. A second stent was deployed inside the previous stent. In our case after stent deployment we administered tirofiban infusion with low dose heparin and postangioplasty course was uncomplicated without any sign of bleeding from the puncture site or recurrent ischemic events.

Michaels et al¹⁷ reported a 50-year-old man who presented with an acute inferior wall myocardial infarction. Coronary angiogram revealed a total occlusion of the right coronary artery and a heavy thrombus burden in left main coronary artery. The patient was treated with GP IIb/IIIa receptor antagonist abciximab followed by primary angioplasty of the right coronary artery. The patient's post-angioplasty course was uncomplicated.

The GP IIb/IIIa receptor is abundant on the platelet surface. When platelets are activated, this receptor undergoes a change in configuration that increases its affinity for binding to fibrinogen and other ligands. The binding of molecules of fibrinogen to receptors on different platelets results in platelet aggregation. This mechanism is independent of the stimulus for platelet aggregation and represents the final and obligatory pathway for platelet aggregation¹⁸. The platelet GP IIb/IIIa receptor antagonists act by occupying the receptors, preventing fibrinogen binding, and thereby preventing platelet aggregation. Tirofiban is a potent synthetic GP IIb/IIIa receptor antagonist that has been studied in acute coronary syndromes¹⁹⁻²¹ and in percutaneous interventions^{22,23}. In the case of ST segment elevation MI abciximab, a monoclonal antibody GP IIb/IIIa receptor antagonist has been studied in two large clinical trials as an adjunct to coronary stenting^{24,25}. In CADILLAC trial abciximab didnot offer clinical benefit, nor was the post-procedural TIMI grade 3 flow improved with abciximab²⁴. On the other hand, ADMIRAL study demonstrated that abciximab reduced combined end-point of death, MI, or urgent target vessel revascularization from 14% to 6.0% (p=0.001).

To our knowledge, this is the first report of use of primary angioplasty and stenting along with glycoprotein IIb/IIIa receptor antagonist tirofiban for acute MI in a patient ET. An uncomplicated postangioplasty course of our patient is most likely due to the effect of GP IIb/IIIa blockade.

CONCLUSION

Ischemic symptoms in a patient without known

risk factors should prompt the clinician toward further evaluation for unusual causes of acute coronary syndromes. Essential thrombocythemia, a myeloproliferative disorder characterized by abnormal proliferation of dysfunctional platelets is one of those rare causes in which thrombi formation may lead to acute coronary occlusion and MI. Glycoprotein IIb/IIIa receptor antagonists may prevent further complications following percutaneous coronary intervention.

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