Hemorrhagic Pericarditis as a Complication of Combined Thrombolytic, Antiplatelet and Anticoagulant Treatment

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We report a case of cardiac tamponade as a result of hemorrhagic pericarditis in a patient who received combination therapy of thrombolytic, antiplatelet and anticoagulant agents. This was a patient who underwent programmed percutaneous coronary artery angioplasty for single vessel disease and developed acute vessel occlusion with subsequent anterior myocardial infarction after stent placement. Although such combination therapies might be effective for the prevention and treatment of adverse events of coronary artery interventions and acute myocardial infarction, they should be carefully monitored as they may be associated with an excessive risk of hemorrhagic complications.

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Co-administration of thrombolytic, antiplatelet and anticoagulant treatment may be effective in patients with acute myocardial infarction, however, there is a potential risk for serious hemorrhagic complications. We describe a case of a patient with cardiac tamponade after administration of these agents.

Case report

A 61- year old man on chronic aspirin treatment with unstable angina was admitted to our hospital to undergo programmed percutaneous coronary artery angioplasty. A balloon angioplasty (with a 3.5 mm diameter balloon) to a type B lesion in the proximal LAD was performed, and a stent (4.0 x 16mm stent) was implanted because of a dissection producing acute vessel occlusion. During the procedure 5000 IU of heparin was administered as a bolus. However, after the stent placement, haziness and a slow flow distally to the lesion was observed, TIMI scale 1 to 2[1], suggestive of coronary thrombus, and a bolus of 0.25 mg/kg body weight of the glycoprotein IIb/IIIa antagonist abciximab was given

followed by infusion of 10 μg/min. Unfortunately, a short time later the chest pain recurred with concomitant ST elevation in all precordial leads. An anterior-lateral myocardial infarction evolved, and at that time thrombolytic treatment with a total of 10 U of reteplase was administered intravenously. Reteplase was administered as 2 boluses, 5+5 IU, with half an hour interval in between. The pain abated and the patient remained stable for 4 hours after which he became hypotensive and developed shortness of breath. The clinical manifestations of jugular veins distension, hypotension and pulsus paradoxus were strongly suggestive of cardiac tamponade (Fig. 1). This was further confirmed by cardiac echocardiography that revealed a large pericardial effusion surrounding the right and left ventricles and the right and left atria. Diastolic compression of the right ventricle and right atrium and severe hypokinesia of the apical part of the interventricular septum and the cardiac apex were present. Careful examination of the heart, especially in the severely hypokinetic segments of the apex, showed no evidence of cardiac rupture. A
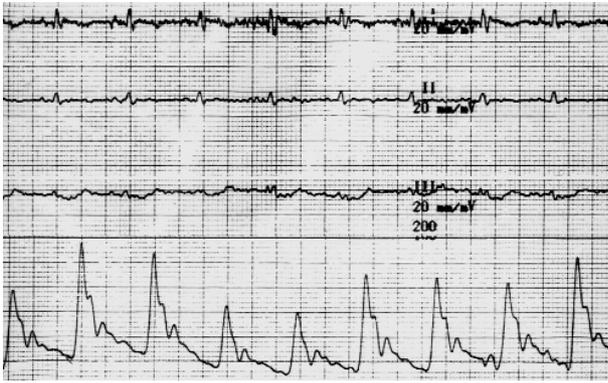
Figure 1. Arterial pressure tracing before pericardiocentesis. There is marked inspiratory reduction of pressure more than 20 mm Hg, indicating pulsus paradoxus. The pressure scale is 100 mm Hg and systolic blood pressure ranges between 95-70 mmHg.
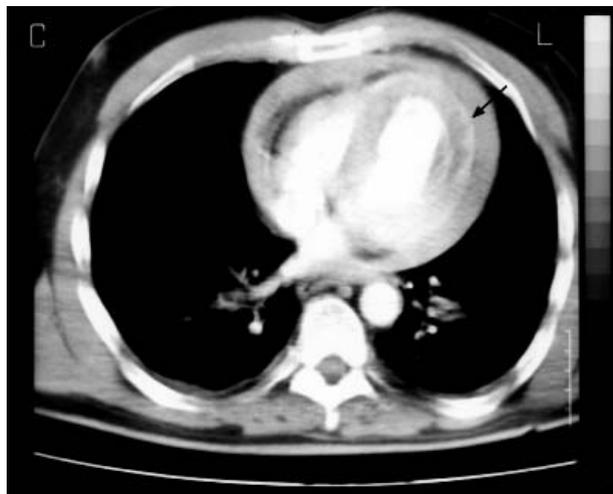
contrast enhanced cardiac CT scan also revealed a large pericardial effusion surrounding the heart with no evidence of continuity between the contrast enhanced ventricular chambers and the pericardial space, that would suggest cardiac rupture (Fig. 2). Because the patients' condition was severely compromised he underwent urgent pericardiocentesis under fluoroscopic guidance with hemodynamic and electrocardiographic monitoring. The initial aspiration of 100ml hemorrhagic fluid led to a striking reduction in intrapericardial pressure, marked improvement of arterial pressure and abolition of pulsus paradoxus. Laboratory examination of the pericardial fluid demonstrated hematocrit value of 43 per cent, almost the same as in the peripheral vein blood. A pigtail catheter was left in the pericardial space for fluid accumulation monitoring and drainage. The amount of hemorrhagic fluid that was drained each of the following 4 days was 60-100 ml. The patient's condition was markedly improved immediately after pericardiocentesis, aspirin was discontinued for a week and his clinical course remained uneventful. The cardiac enzymes curve was typical for an acute infarction, with a late (>12 h) peak CK value 5.044 U/L and peak CK-MB 381 U/L. The pre-discharge cardiac echocardiogram revealed severe hypokinesia of the antero-apical part of the intraventricular septum and the apex, with moderate left ventricular impairment. A tiny amount of pericardial fluid was localized behind the left atrium at the coronary sinus level. The electrocardiogram demonstrated QS in lead V_2 and qR in

leads I, aVL. All the above, indicate that thrombolysis was unsuccessful.

Discussion

There are three main reasons that could possibly explain the development of cardiac tamponade and myocardial infarction in our patient after percutaneous coronary angioplasty: coronary artery perforation, cardiac rupture and hemorrhagic pericarditis. The incidence of coronary artery perforation during balloon angioplasty is very low, compared with the new device revascularization techniques, and usually results from guide wire trauma and balloon oversizing[2,3]. Our patient had no angiographic appearance of perforation, that is no extraluminal crater, extravasation or contrast streaming into the pericardium or anatomic cavity chamber.[2] Some small type 1 perforations, with an extraluminal crater without extravasation, may be impossible to distinguish angiographically from localized dissections, however they rarely develop tamponade. It has been described that tamponade due to perforation may occur up to 24 hours after the angioplasty procedure,[2] but the absence of any obvious sign of coronary perforation in our case make this diagnosis very unlikely.

Cardiac rupture leads to hemopericardium, but usually occurs 1 to 3 days following myocardial infarction[4-6], something that was not the case in our patient. The diagnosis can usually be made by two-dimensional echocardiography. Fluid in the peri-

Figure 2. Contrast enhanced cardiac CT scan. Notice the pericardial effusion surrounding the heart (arrow), and the contrast enhanced ventricular chambers.

cardial space can be also reliably detected by computed tomography.[7] Contrast enhanced computed tomography was particularly helpful in our patient to rule out the possibility of cardiac rupture, by providing information about the density of pericardial fluid and the absence of contrast medium out of the cardiac chambers and into the pericardial space.

Pericardial effusion during the course of myocardial infarction is a quite common echocardiographic finding[8-10], but only a few cases of tamponade attributed to thrombolysis-associated hemorrhagic pericarditis have been reported in the literature[11,12]. Utilization of abciximab as a rescue treatment for the dissolution of coronary thrombus developing during angioplasty has been used, [13,14] however in our case this treatment failed to restore adequate coronary flow rate and therefore we decided to give additional thrombolytic therapy. The glycoprotein IIb/IIIa receptor inhibitors as an adjunctive therapy along with thrombolytics have been used in experimental and clinical trials of acute myocardial infarction and this was associated with excess bleeding complications[15-19]. Most bleeding complications were mild and related to the angiographic access site, however some major intracranial bleedings have also been reported[19,20]. In our case the combination of abciximab with reteplase without adjusting the dose of the thrombolytic agent was probably the cause of hemorrhagic pericarditis that led to tamponade. Indeed, the activated partial thromboplastin time (aPTT) level was very prolonged (> 120 sec) and this has been shown to confer an increased risk of bleeding in patients receiving thrombolytic therapy. It should be noted however that during the first 12 hours following thrombolytic therapy the aPTT may be elevated from the thrombolytic agent alone, making it difficult to interpret the patient's coagulation status. Heparin was administered after thrombolysis in the usual dose, 15IU/ kg/ h, with no initial bolus. In the TIMI 14 study, administration of abciximab along with reteplase and 3 different doses of heparin, (the usual dose 15 IU/ kg/ h, low dose 7 IU/ kg/ h, and very low dose 4 IU/ kg/ h), led to a significantly lower rate of hemorrhagic complications in the low and very low heparin groups[18]. It seems therefore that adjustment of heparin dosage is mandatory when fibrinolytics are co-administered with the newer anti-platelet drugs.

Because the pressure volume curve of the pericardium is steep, initial aspiration of 50-100 ml of pericardial fluid leads to rapid improvement of the clinical condition and is a life-saving intervention in the severely ill patient with cardiac tamponade after myocardial infarction. We think that combination therapies of glycoprotein IIb/IIIa receptor inhibitors and thrombolytics should be carefully monitored regarding the coagulation status and hemorrhagic complications, and that is much safer to adjust the dosage of the drugs given. This may be particularly helpful especially in view of the increasing number of patients who receive such combination therapies for coronary artery interventions or acute myocardial infarction.

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