

Near simultaneous atherothrombotic occlusion of two coronary arteries challenges the theory of the single vulnerable plaque

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Received April 12, 2007, accepted after revision July 11, 2007

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Nahezu simultaner atherothrombotischer Verschluss zweier Koronargefäße stellt die Theorie des einzelnen vulnerablen Plaques in Frage

Zusammenfassung. *Hintergrund:* Die Auslösung eines akuten Myokardinfarkt infolge eines fast gleichzeitigen proximalen atherothrombotischen Verschlusses der rechten Koronararterie und des Ramus interventricularis anterior der linken Koronararterie als Resultat einer durch mechanischen Stress bedingten Plaqueruptur ist unwahrscheinlich.

Akutes Management: Durch eine sofortige interventionelle Therapie konnten beide Gefäße rekanalisiert und jeweils ein TIMI-III-Fluss wiederhergestellt werden. Es wurde eine Bolusinjektion sowie anschließend eine kontinuierliche Infusion mit Abciximab verabreicht, um die Myokardperfusion zu optimieren.

Diagnostik: Bei Aufnahme waren die Leukozytenzahl stark und das C-reaktive Protein mäßig erhöht. Nach der katheterinterventionellen Rekanalisation erhöhte sich das C-reaktive Protein weiter deutlich, bevor es schließlich nach zwei Tagen abfiel.

Verlauf: Dreißig Tage nach dem Ereignis war der Patient beschwerdefrei und hatte sich vollständig erholt. Echokardiographisch wurde eine gering- bis mittelgradige globale Hypokinesie nachgewiesen.

Schlussfolgerung: Eine generalisierte Entzündung vergesellschaftet mit einer multifokalen Plaqueruptur und nachfolgendem Zweigefäßinfarkt ist wegen der Wahrscheinlichkeit des plötzlichen Herztodes selten zu beobachten und zeigt andererseits, dass zumindest diese Infarktereignisse nicht durch die weithin akzeptierte Theorie des einzelnen und mechanisch alterierten vulnerablen Plaques erklärt werden können.

Summary. *Background:* It is unlikely that mechanical stress altering a single vulnerable plaque leads to myocardial infarction from almost simultaneous proximal atherothrombotic closure of the right coronary artery and the left anterior descending coronary artery.

Acute management: Immediate catheter diagnosis and revascularization including stent deployment restored

TIMI III flow in both coronary arteries. After an initial bolus, abciximab was continuously infused to optimize myocardial perfusion.

Laboratory tests on admission: The patient's white blood cell count was markedly elevated and the level of C-reactive protein slightly so. After interventional recanalization, C-reactive protein rose steeply before falling again after two days.

Follow-up: Thirty days after acute myocardial infarction, the patient was fully recovered and asymptomatic. Echocardiography revealed only mild-to-moderate global left ventricular hypokinesia.

Conclusion: Widespread inflammation associated with multifocal plaque rupture and subsequent two-vessel acute myocardial infarction is a rare phenomenon, usually associated with sudden cardiac death. Widespread inflammation is one of the reasons why the widely accepted theory of the single vulnerable plaque for such events can be contradicted.

Key words: Acute myocardial infarction, vulnerable plaque, coronary inflammation.

The theory of mechanical alteration of a single vulnerable plaque leading to acute coronary syndrome (ACS) [1–3] has been repeatedly challenged in laboratory studies [4, 5] and post-mortem findings [6]. Studies have revealed fresh thrombi [7] or multiple fissured, thrombosed and healed plaques [6, 8] in coronary arteries remote from the vessels harboring the culprit lesion. Multifocal plaque rupture and subsequent two-vessel acute myocardial infarction is commonly associated with sudden cardiac death, therefore these phenomena are only rarely detected clinically. The following case report raises the question of whether this phenomenon can be explained by the widely accepted theory of the single vulnerable plaque or if an alternative concept such as general inflammation appears to be the more likely pathogenetic mechanism. To our knowledge, only two clearly proven cases of myocardial infarction caused by the occlusion of two major coronary arteries have been published [9].

The case

A 61-year-old male sustained an acute myocardial infarction. The electrocardiogram suggested involvement of the posterior wall (Fig. 1). Within 50 minutes after onset of symptoms, the patient was transferred to the University Clinic Innsbruck and received standard prehospital care (intravenous aspirin, heparin, analgesics and β -blocker) but no thrombolytic agents. Shortly after the initial electrocardiogram, ventricular fibrillation occurred. After immediate defibrillation, the patient arrived in the catheterization laboratory in stable condition and without any further support, but still complaining of chest pain.

In view of what appeared to be a common posterior myocardial infarction, we first performed angiography of the left coronary artery to detect any non-culprit lesion. To our surprise, the left anterior descending coronary artery was proximally occluded (Fig. 2). In addition, cineangiography of the right coronary artery confirmed the expected vessel closure (Fig. 3). Immediate guide-wire passage through the closure site of the thrombosed right coronary artery led to recanalization of the vessel. We administered an abciximab bolus, performed balloon angioplasty and stent deployment, restoring TIMI III flow. A second electrocardiogram (Fig. 4) now showed ST-segment elevation in leads V3 to V6, whereas the previous ST-segment elevation in leads II, III, aVF and V1

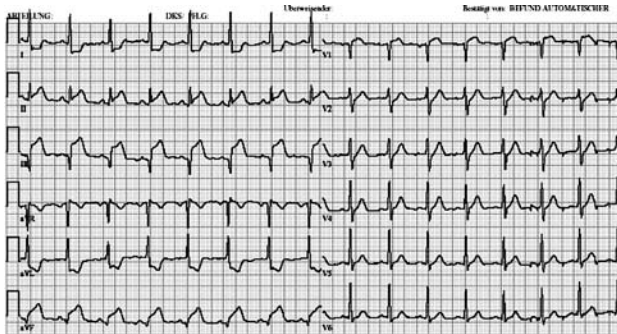


Fig. 1. The initial electrocardiogram shows acute posterior myocardial infarction but no anterior wall involvement



Fig. 2. Unexpected proximal closure of the left anterior descending (LAD) coronary artery demonstrated by use of a 7 F catheter

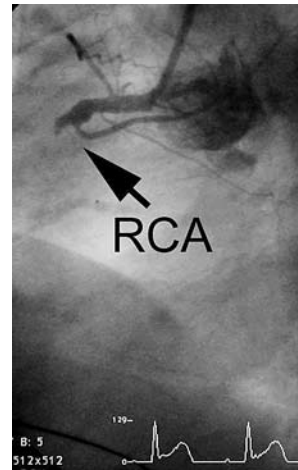


Fig. 3. Proximal closure of the right coronary artery (RCA) (7 F catheter) expected from the first electrocardiogram

decreased. Subsequently, the left anterior descending coronary artery was reopened in the same manner and with the same result as the right coronary artery. In both coronary vessels, effortless passage of the guide wire was indicative of sudden thrombotic closure. Control coronary angiography immediately after recanalization and before balloon angioplasty suggested that plaque rupture had caused atherothrombotic closure of both the left anterior descending and the right coronary artery. With the patient completely stable and free of complaints, the interventional procedure was finished 90 minutes after onset of symptoms (Fig. 5). Weight-adapted continuous infusion of abciximab was subsequently started. On admission, the patient's white blood cell count was markedly increased to 14.6 G/l (reference range 4.0–10.0 G/l) and the C-reactive protein level exceeded the upper threshold (2.44 mg/dl). Laboratory follow-up revealed signs of increasing systemic inflammation in addition to evidence of only moderate myocardial damage (Fig. 6). The following blood clotting anomalies were ruled out: deficiency of antithrombin, protein S and protein C; presence of phospholipid antibodies and lupus anticoagulants; mutation of coagulation factor V; and resistance against activated protein C. Thirty days after myocardial infarction, transthoracic echocardiography revealed a left ventricular ejection fraction of approximately 40% associated

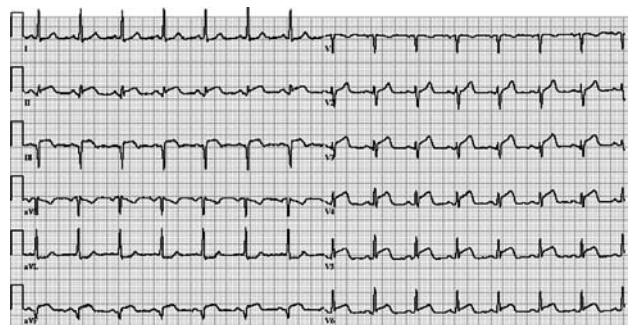


Fig. 4. The second electrocardiogram recorded after right coronary artery revascularization demonstrates anterior myocardial infarction and diminishing signs of posterior myocardial infarction

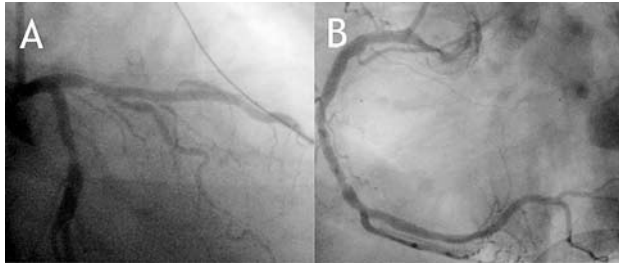


Fig. 5. Angiogram of both coronary vessels after successful catheter intervention: **A** left coronary artery; **B** right coronary artery

with only mild-to-moderate anterior, lateral and posterior hypokinesia and grade I diastolic dysfunction [10].

Discussion

According to the clinical and diagnostic findings, primary atherothrombotic closure of the right coronary artery was directly followed by proximal occlusion of the left anterior descending coronary artery which became clinically manifest as ventricular fibrillation. This case shows that even a myocardial infarction caused by two-vessel occlusion is survivable if rapid recanalization is achieved; left ventricular function can be restored to acceptable levels. Presumably, multifocal plaque rupture does occur on occasion, but it is prone to fatal outcome and thus

remains undetected in many cases. Nevertheless, this patient's presentation with elevated circulating inflammatory markers raises the question of whether systemic signs of inflammation are mostly a reflection of ongoing atherothrombosis or indicative of primary inflammatory mechanisms directly responsible for recurrent coronary instability [11] and thus, for the development of an ACS.

The hypothesis that atherothrombotic closure develops almost simultaneously at different sites merely as a result of mechanical stress appears quite improbable, although this is the only explanation consistent with the widely accepted theory that a single vulnerable plaque is responsible. It seems sensible to consider a more general underlying mechanism. As previously reported, widespread inflammation in patients with ACS has been shown to be associated with activated neutrophils traversing the coronary circulation (not only the perfusion bed of the artery with the culprit lesion) [4]. This needs to be considered in the context of our findings. Widespread endothelial inflammation is thought to shift the properties of the interface between blood and vessel wall from anticoagulant to prothrombotic, while simultaneously activating metalloproteases and collagenases which cause lysis of the fibrous capsule of the plaque [4].

The observation that relief of the culprit artery stenosis by interventional therapy restores culprit artery flow to the level of flow in the nonculprit artery, but that both flows are 45% slower than normal [12], supports the hypothesis of an underlying common etiologic mechanism. Our report concurs with another investigation which

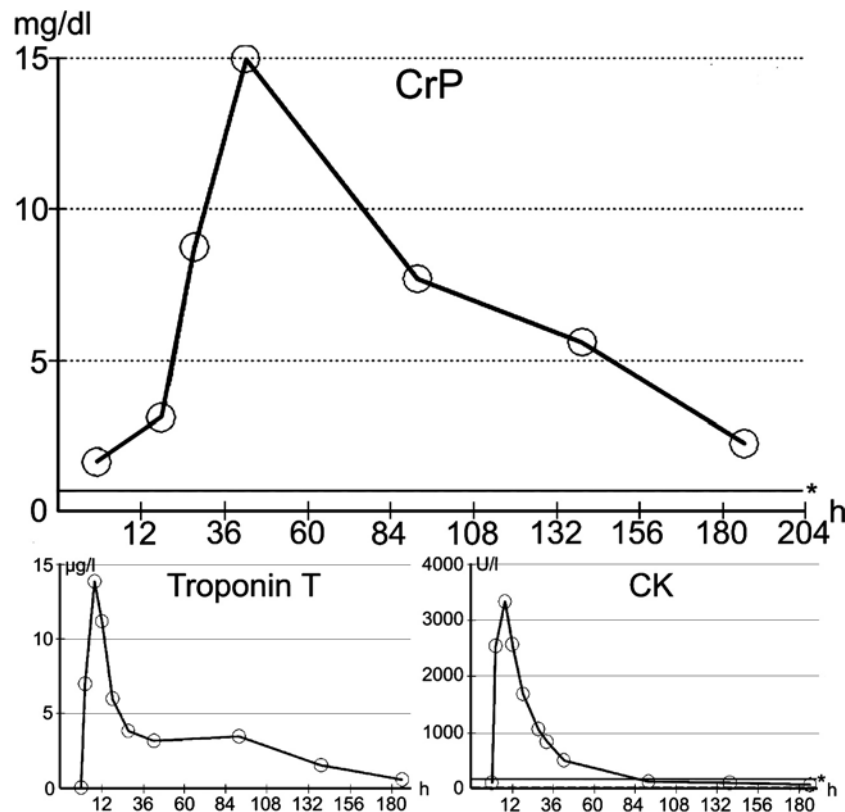


Fig. 6. Courses of laboratory parameters: Upper graph, C-reactive protein; left lower graph, troponin T (upper threshold value 0.03 µg/l); right lower graph, creatinine kinase. * upper threshold value; CK creatinine kinase; CrP C-reactive protein

showed that elevation of C-reactive protein at the time of hospital admission predicts severe ACS and may be indicative of inflammation in the pathogenesis of this condition [13]. Furthermore, it is not likely that atherothrombosis by itself can account for the elevated inflammatory markers that characterize patients with ACS [14, 15]. The discrepancy between atherosclerotic burden and extent of inflammation makes atherosclerosis without inflammation an unlikely cause of ACS [14]. Moreover, inflammation has been described to be an atherosclerosis-inherent characteristic [16]. Intravascular ultrasound has proven underlying overall coronary instability in association with ACS [17]. That plaque rupture could not be explicitly proven by intravascular ultrasound must be considered a limitation. Nevertheless, closure of two coronary vessels required prompt recanalization.

The systemic inflammatory syndrome preceding myocardial infarction and the involvement of the left and right coronary perfusion beds suggest a temporal link between inflammation causing pancoronary plaque vulnerability [18] and plaque rupture. Therefore, almost simultaneous atherothrombotic closure of two coronary arteries might be considered a result of a pancoronary condition related to the presence of multiple plaques, the vulnerability of which seems to be triggered by widespread coronary inflammation. The rare clinical observation of a two-vessel myocardial infarction associated with general inflammation raises two questions: (1) could one expect a second plaque rupture with consecutive closure of another coronary vessel at any time in acute myocardial infarction combined with systemic inflammation, and (2) should new therapeutic strategies to adequately respond to systemic inflammation as an underlying mechanism in ACS be investigated?

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