Dipyridamole-Atropine-Induced Myocardial Infarction in a Patient with Patent Epicardial Coronary Arteries

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Background: The diagnostic accuracy of the physical and pharmacological stress echocardiography tests is higher than routine exercise electrocardiography. They have an acceptable safety profile and have been rarely associated with severe adverse effects.
Case Report: We present a case of acute anterior myocardial reinfarction immediately after exercise and pharmacological (dipyridamole-atropine) stress echocardiography testing 1 month after successful stent implantation in LAD. Our patient was a 43-year-old man with a history of heavy smoking and hypertension. Remarkably, the stress echocardiogram was non-diagnostic few hours before the infarction occurred. Angiography performed 4 months after the reinfarction revealed neither a culprit lesion nor stent thrombosis.
Conclusion: Aggressive "last generation" pharmacological stress testing may provide optimal diagnostic accuracy, but as in our case, complications may occur, even after negative stress testing. To our knowledge, this is the first reported case of an acute myocardial infarction as a severe complication of stress testing, which developed in a patient after stent implantation.

Key Words: Atropine · Dipyridamole · Infarction · Stress test

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Dipyridamol-Atropin-induzierter Myokardinfarkt ohne Verschluss der Koronargefäße

Hintergrund: Die diagnostische Wertigkeit der Belastungs- und pharmakologischen Stressechokardiographie ist besser als ein Routine-Belastungs-EKG. Die Stressechokardiographie hat eine niedrige Komplikationsrate und selten Nebenwirkungen.
Kasuistik: Wir berichten über einen Patienten mit akutem Vorderwandreinfarkt am selben Tag nach einer für eine Ischämie negativen Stressechokardiographie (kombinierte Belastungs- und Dipyridamol-Atropin-Stressechokardiographie), 1 Monat nach der erfolgreichen Stentimplantation im RIVA. Der Patient war 43 Jahre alt, starker Raucher und eingestellter Hypertoniker. Bei der Herzkatheteruntersuchung 4 Monate nach der Reinfarzierung konnte ein offenes Koronargefäß ohne relevante Stenose oder Stentthrombose nachgewiesen werden.
Schlussfolgerung: Der aggressive, kombinierte, pharmakologische Stresstest hat eine optimale diagnostische Wertigkeit für die Diagnose der koronaren Herzkrankheit. Er kann aber auch nach unauffälligem Testergebnis Komplikationen verursachen, wie in diesem Fall gezeigt werden konnte. Unseres Wissens ist das der erste beschriebene Fall eines Myokardinfarkts nach Stressechokardiographie bei Zustand nach erfolgreicher Stentimplantation.

Schlüsselwörter: Atropin · Dipyridamol · Myokardinfarkt · Stresstest

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Introduction

Physical and pharmacological stress echocardiography tests are established methods for the functional assessment of patients after angioplasty [1]. The diagnostic accuracy appears higher than routine exercise electrocardiography [1]. They have an acceptable safety profile and have been rarely associated with severe adverse effects [1–4].

We present a patient who developed an acute myocardial infarction immediately after exercise and pharmacological (dipyridamole-atropine) stress echocardiography testing 1 month after successful stent implantation. To our knowledge, this is the first reported case of an acute myocardial infarction as a severe complication of stress testing, which developed in a patient after stent implantation.

Case Report

This 43-year-old man with a history of angina pectoris suffered an acute anterior myocardial infarction one month before he was admitted to our hospital for diagnostic heart catheterization. He had family history of coronary artery disease and was a heavy cigarette smoker (30 cigarettes/day). He was treated for hypertension for several years.

His physical examination, chest radiography, and routine laboratory tests were normal. His resting electrocardiogram (ECG) showed sinus rhythm, with QS in leads V1–4 and negative T waves in leads V1–5 and aVL (Figure 1). Coronary arteriography revealed a significant tubular coronary artery stenosis of the medial part of the left anterior descending artery suitable for angioplasty (Figure 2a). Left ventricular angiography and echocardiography showed a moderate hypokinesia of the anteroseptal region of the left ventricle. Treadmill exercise echocardiography stress test was non-diagnostic for myocardial ischemia, but the patient could not reach the submaximal predicted heart rate, while a high-dose dipyridamole stress echocardiography test was positive for myocardial ischemia by worsening of the pre-existing anteroseptal hypokinesia.

A balloon angioplasty procedure was performed in standard manner, but a long dissection of the left anterior descending artery developed, and was treated successfully with the implantation of two serial 3.0 mm Palmaz-Schatz stents (each 1.5 cm long). Routine follow-up arteriography was performed on the next day, and showed an excellent short-term result (Figure 2b). Furthermore, combined dipyridamole-atropine stress

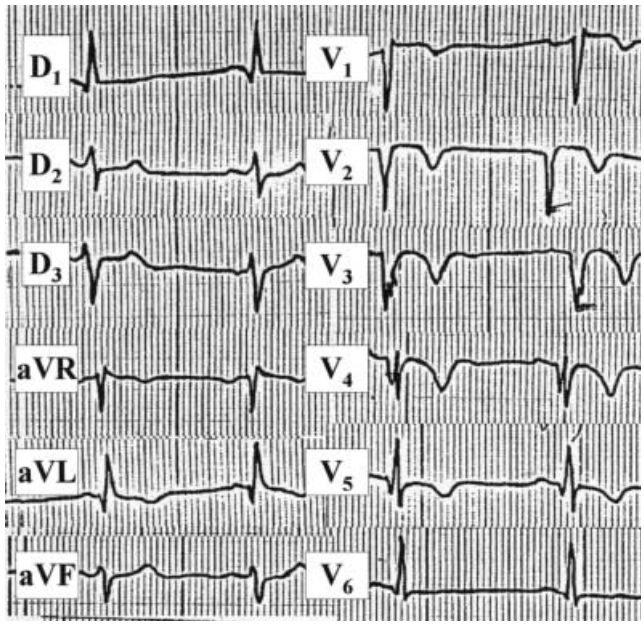

Figure 1. ECG on admission to the hospital showing signs of previous anterior myocardial infarction (before the stress echocardiography).

Abbildung 1. Aufnahme-EKG mit Zeichen des alten Vorderwandinfarkts (vor der Stressechokardiographie).

echocardiography test was also negative. The patient was discharged on ticlopidine (250 mg bid), aspirin (500 mg), mononitrates (20 mg bid), and nifedipine (20 mg bid).

1 month later, the patient was readmitted for revaluation of recurrent resting chest pain, relieved by nitrates. The maximal Bruce treadmill exercise echocardiography test (maximal reached heart rate: 170 beats/min) was negative for ECG and left ventricular wall motion changes, but the patient complained of atypical chest pain. Therefore, 1 hour later dipyridamole-atropine echocardiography test was also performed (0.84 mg/kg over 10 minutes dipyridamole infusion, followed with 1 mg of atropine in four divided doses of 0.25 mg, in 1-minute intervals). It did not demonstrate any deterioration in segmental left ventricular contraction, but again some non-characteristic chest pain was noted. On the basis of the negative physical and pharmacological stress echocardiography tests he was discharged from our hospital.

A few hours later the patient, however, was readmitted for persistent chest pain with ST elevation in lead aVL, ST depression in D2, D3 and aVF, and mild ST elevation in leads V2–4, suggestive of acute myocardial reinfarction (Figure 3).

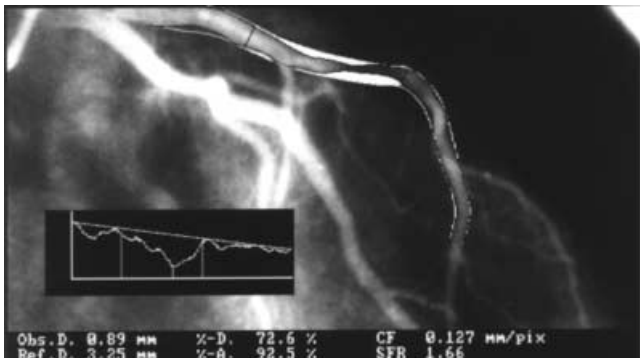

Figure 2a – Abbildung 2a

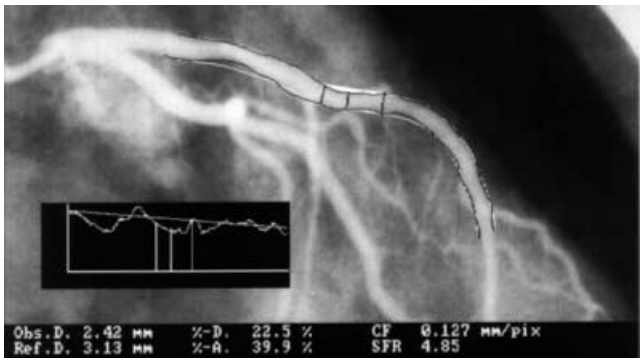

Figure 2b – Abbildung 2b

Figures 2a and 2b. a) LAD stenosis before the stent implantation. b) Successful stent implantation in LAD.

Abbildungen 2a und 2b. a) RIA-Stenose vor der Stentimplantation. b) Erfolgreiche Stentimplantation in RIA.

The patient was monitored in the ICU and treated with heparin, aspirin, nitrates, and beta blockers. Laboratory examination showed an elevation of plasma creatine kinase activity (peak 482 U/l) with gradual fall over next days (12 hours: 460 U/l; 24 hours: 359 U/l; 2nd day: 205 U/l; 3rd day: 121 U/l; 4th day: 91 U/l; 5th day: 59 U/l). During his hospitalization the patient complained of recurrent chest pain relieved by sublingual nitrates, but without ECG evidence of myocardial ischemia. Also, ECG showed development of negative T waves in leads D1, aVL and V1–V5, with normalization of ST segment in leads D2, D3 and aVF (Figure 4). At

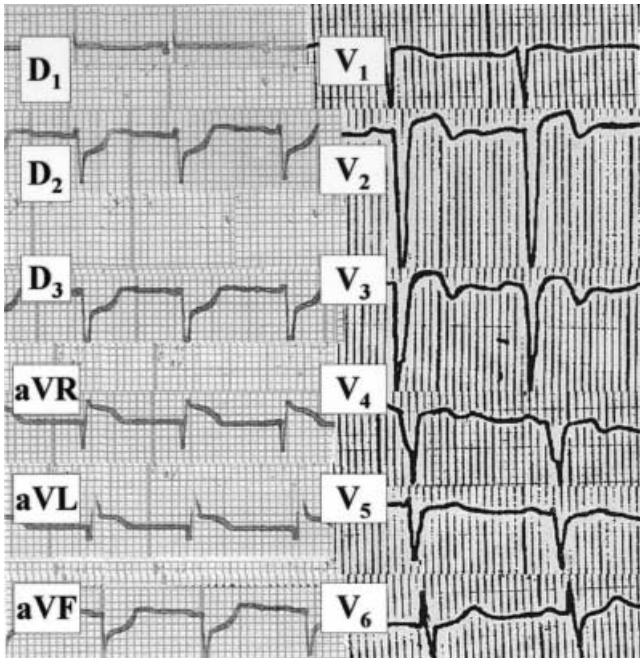

Figure 3. ECG on readmission to the hospital for persistent chest pain showing ST elevation in lead aVL, ST depression in leads D2, D3 and aVF, and mild ST elevation in leads V2–4.

Abbildung 3. Das zweite Aufnahme-EKG bei prolongierter Angina pectoris einige Stunden nach der Stressechokardiographie: ST-Hebung in Ableitung aVL, ST-Senkung in D2, D3 und aVF und minimale ST-Hebung in V2–V4.

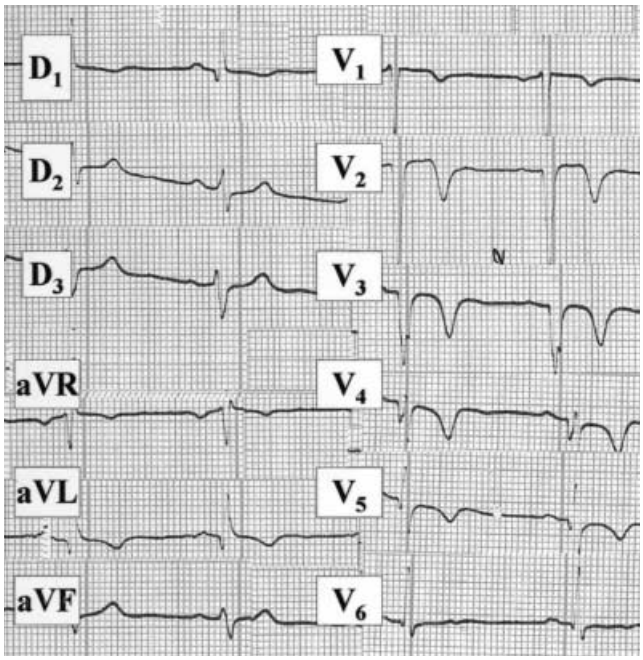

Figure 4. ECG, 2 days after acute coronary event, showing negative T wave in leads D1, aVL and V1–V5, and normalization of ST segment in leads D2, D3 and aVF.

Abbildung 4. EKG 2 Tage nach dem Infarkt: negative T-Wellen in D1, aVL und V1–V5. ST-Segment-Normalisation in D2, D3, aVF.

that time, the patient was unwilling to perform coronary arteriography.

The patient was free of angina on discharge. Exercise stress echocardiography test, monthly performed, was negative. 4 months later, control coronary arteriography showed an excellent result at the site of stent implantation without new and significant changes in the other coronary arteries.

Discussion

Picano et al [4] have shown that only seven out of more than 10,000 (0.07%) dipyridamole stress echocardiography tests were accompanied by serious adverse affects including myocardial infarction in three patients. Also, the addition of atropine to dipyridamole for stress echocardiography in negative patients increases the sensitivity without loss in specificity and without deterioration of safety profile [5].

Several potential mechanisms may underlie the occurrence of ST segment elevation during stress testing. Coronary vasospasm has been described to occur at the end of dipyridamole testing in patients with variant angina [6]. In addition, platelet activation has been described minutes and hours after stress testing, probably as a result of catecholamine surge [7]. Finally, in a patient with stent implantation, thrombus formation, with or without coronary spasm, and/or microembolization may occur from the site of stent implantation following vigorous physical and pharmacological stress testing.

In the present case report, the mechanisms inducing occlusion of a vessel are complex and largely speculative. Independent of the underlying pathophysiology, it is interesting that myocardial infarction can occur in spite of a patent coronary artery at the site of stent implantation.

The second lesson of this case is that complications may occur even hours after a negative stress testing. This is in accordance with the multicenter dipyridamole safety study in more than 70,000 patients [8], suggesting that in five out of 13 patients myocardial infarction occurred several hours after a dipyridamole stress test.

Conclusion

Aggressive "last generation" pharmacological stress testing may provide optimal diagnostic accuracy, but complications may occur, even relatively late after negative stress testing. Sometimes complications can occur outside the "protected" environment of stress echocardiography laboratory.

References

1. Flachskampf FA, Hoffmann R, von Dahl J, Lethen H, Hanrath P. Functional assessment of PTCA results by stress echocardiography: when and how to test. Eur Heart J 1995;16:Suppl J:31–4.
2. Stuart R, Ellestad MH. National survey of exercise stress testing facilities. Chest 1980;77:94–100.
3. Fletcher GF, Froelicher VF, Heartley H, Haskell W, Pollock ML. Exercise standards: A statement for health professionals from the American Heart Association. Circulation 1990:82:2286–315.
4. Picano E, Marini C, Pirelli S, et al., on behalf of the Echo-Persantine International Cooperative Study Group. Safety of intravenous high-dose dipyridamole echocardiography. Am J Cardiol 1992;70:252–8.
5. Picano E, Pingitore A, Conti U, Kozakova M, Boem A, Cabani E, Ciuti M, Distante A, L'Abbate A. Enhanced sensitivity for detection of coronary artery disease by addition of atropine to dipyridamole echocardiography. Eur Heart J 1993;14:1216–22.
6. Picano E, Lattanzi F, Masini M, Distante A, L'Abbate A. Aminophylline termination of dipyridamole stress as a trigger of coronary vasospasm in variant angina. Am J Cardiol 1988;62:694–7.
7. Schoming A. Catecholamines in myocardial ischemia. Systemic and cardiac release. Circulation 1990;82:Suppl II:II-13–22.
8. Lette J, Tatum J, Fraser S, et al. for the Multicenter Dipyridamole Safety Study Investigators. Safety of dipyridamole testing in 73,806 patients: The Multicenter Dipyridamole Safety Study. J Nucl Cardiol 1995;2:3–17.

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