Coronary Spasm after Administration of Propranolol During Dobutamine Stress Echocardiography

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Dobutamine stress echocardiography, a highly useful and safe challenge test for myocardial ischemia, is being used increasingly. We report the case of a 37-year-old man with rest angina, repolarization abnormalities in precordial leads and normal coronary arteries who was referred for dobutamine-atropine stress echocardiography, which was negative for ischemia. However, after testing, upon injection of propranolol, the patient suffered chest pain associated with ST elevation and severe regional systolic abnormalities. After intravenous nitroglycerin administration, chest pain and electrocardiographic abnormalities disappeared quickly, and systolic motion became normal. This complication was interpreted as a coronary spasm. We discuss the causes for the spasm and the role that might have been played by the drugs employed.

Key words: *Vasospasm. Echocardiography. Dobutamine. Propranolol.*

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Espasmo coronario tras infusión de propranolol durante un ecocardiograma de estrés con dobutamina

La ecocardiografía de estrés con dobutamina es una prueba muy útil y segura para el diagnóstico de isquemia miocárdica, cuyo uso está cada vez más extendido. Presentamos el caso de un varón de 37 años con angina de reposo, alteraciones de la repolarización en las derivaciones precordiales y arterias coronarias normales al que se le realizó un ecocardiograma con dobutamina-atropina que fue negativo. Una vez finalizada la prueba, y coincidiendo con la inyección de propranolol intravenoso, el paciente presentó dolor torácico acompañado de elevación del segmento ST y alteraciones severas de la contractilidad segmentaria. La clínica y los cambios electrocardiográficos desaparecieron rápidamente tras la administración de nitroglicerina intravenosa, con normalización de la contractilidad segmentaria. Esta complicación fue interpretada como espasmo coronario. Se discute su mecanismo de producción y cuál de los fármacos empleados pudo haber sido el desencadenante.

Palabras clave: *Vasoespasmo. Ecocardiografía. Dobutamina. Propranolol.*

INTRODUCTION

Given its high diagnostic and prognostic value, the use of stress echocardiography has been extended exponentially to patients with a previous or suspected diagnosis of heart disease.

Stress echocardiography with dobutamine (SED) is based on an increase in the myocardial consumption of oxygen induced by the inotropic and chronotropic capacity of dobutamine. The rate of serious complications for this test is low, and similar to that described with conventional stress tests. The complications that usually present during the performance of SED tend to be related to ischemia or arrythmias induced by dobutamine.[1,2]

We present the case of a patient on whom a stress echocardiogram with dobutamine-atropine was performed. After the study was finished, without ischemic changes occurring, propranolol was administered. The injection of the beta-blocker triggered angina, ST segment elevation, and contractility anomalies related to coronary spasm, which are rarely associated with this diagnostic test.[3]

CLINICAL CASE

A 37-year-old man, 2-pack a day smoker, and with a moderate habitual consumption of alcohol, without other significant antecedents.

For 2 or 3 weeks prior to his admission he experienced episodes of oppressive pain located in the lower

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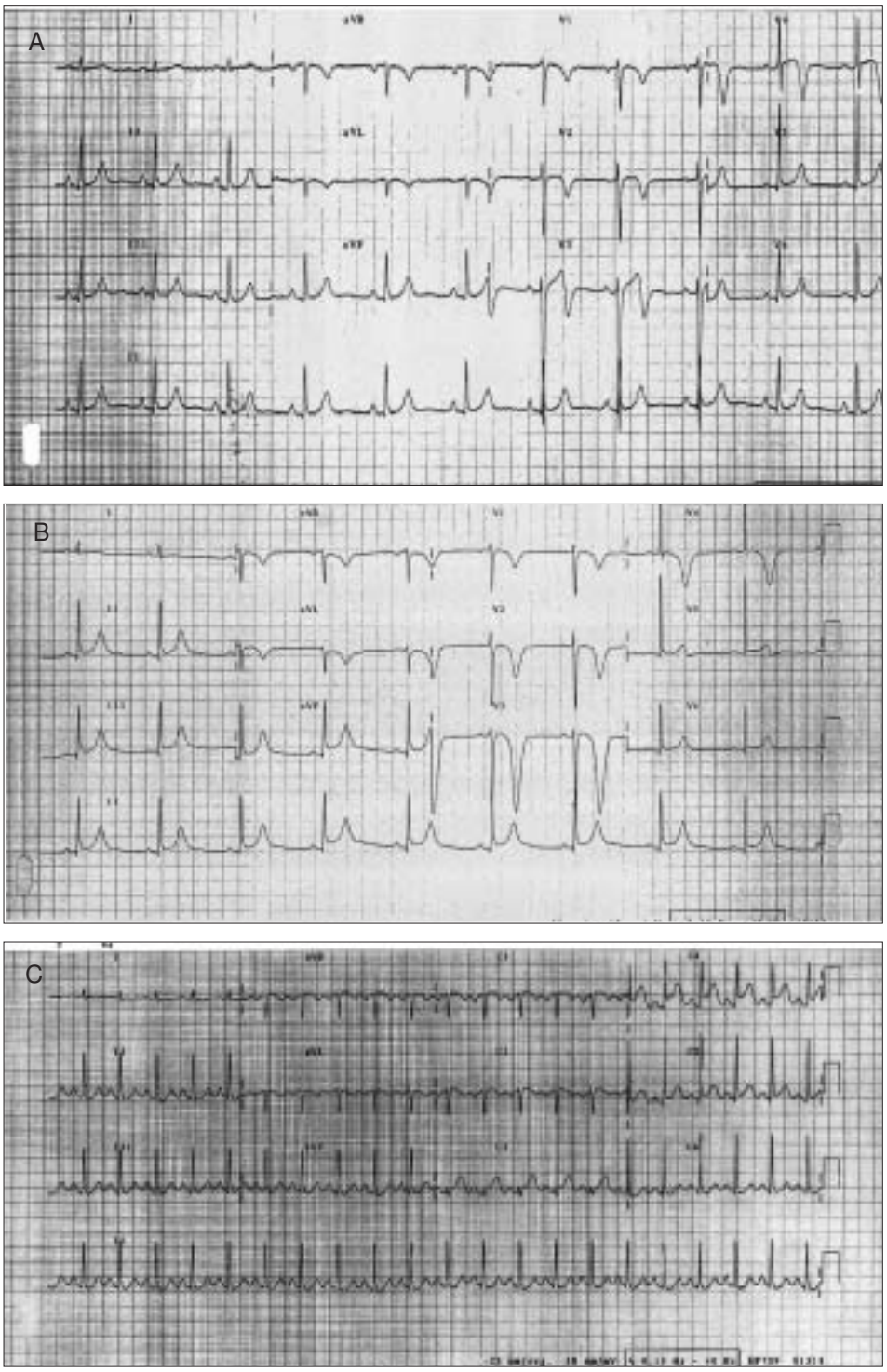

Fig. 1. A: Electrocardiogram performed upon the patient´s arrival at the emergency room, already without chest pain, in which a subepicardial lesion and ischemia on the anterior face were observed. B: Electrocardiogram 24 hours later. The patient remained asymptomatic, with normalization of the ST segment and development of deep negative T-waves. C: Electrocardiogram during an SED after the end of the dobutamine infusion, immediately after the administration of IV propranolol. The image of the subepicardial lesion on electrocardiogram coincides with the appearance of angina and echocardiographic changes that were immediately reversed with the administration of intravenous ni-

chest lasting about 5 minutes, not effort-related, that resolved spontaneously. On the day of admission, he went to the hospital because of a similar episode, but of longer duration. Upon his arrival at the emergency room he was already asymptomatic on physical evaluation, and analytical and X-ray studies were normal. Electrocardiogram revealed a sinus rhythm of 60 beats/minute with depression of the ST segment in V3-V4 and negative T-waves from V1 to V4 (Figure 1A).

During the following 24 hours the patient did not have any new pain episodes, being treated with aspirin and but not anti-angina medications or anticoagulants. An electrocardiogram revealed progressive normalization of the ST segment, with persistent negative T-wa-

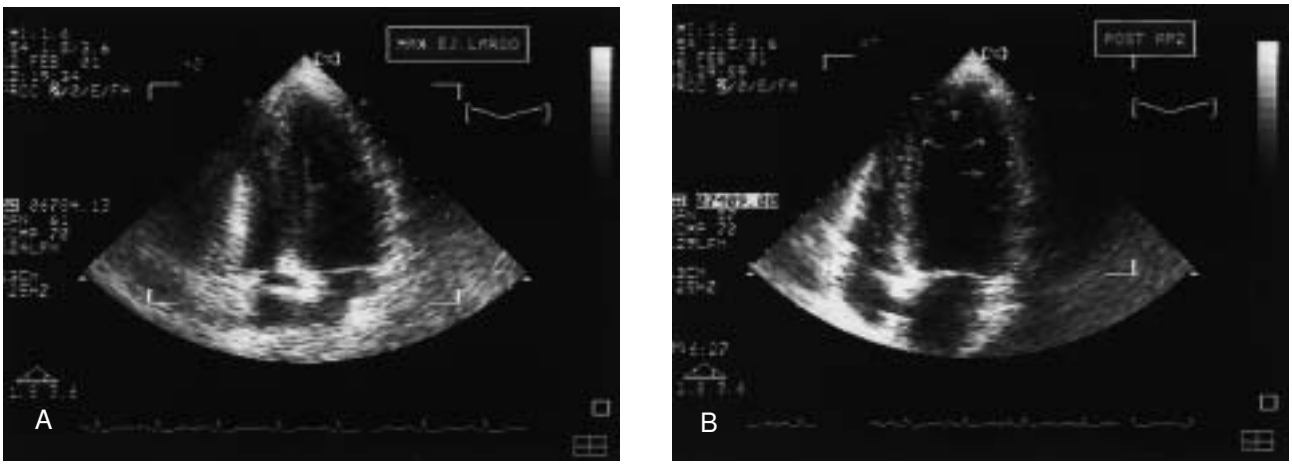

Fig. 2. A: Echocardiogram after the infusion of dobutamine-atropine, where there are no ventricular anomalies. B: echocardiogram after the infusion of propranolol where a narrowing of the septo-latero-inferoapical can be seen.

ves that became progressively deeper (Figure 1B). Serial tests of cardiac enzymes and troponin I were always within normal limits. Echocardiogram did not show evidence of an anomaly. Coronary angiography was performed and revealed normal coronary arteries on angiography with a questionable image of the intramyocardial trajectory in the descending anterior artery. Faced with the possibility that this last finding was the cause of the patient´s clinical findings, we decided to perform an SED. We used a protocol of an intravenous infusion of increasing dobutamine doses every 3 minutes from 10 to 40 µg/kg/minute. After the infusion of 40 µg/kg/minute for 6 minutes 85% of the maximum frequency foreseen was not achieved, and 0.6 mg of atropine were administered; a heart rate of 180 bests/minute was reached, and the test was finalized.

Up until that time, the clinical, electrical, and echocardiographic findings were negative (Figure 2A). When the heart rate persisted for more than 1 minute at 180 beats/minute, 1 mg of intravenous propranolol was administered. One minute after the injection of the propranolol bolus (approximately 2 minutes after finishing the dobutamine infusion, the patient experienced chest pain similar to that which motivated his admission, accompanied by an elevation of the ST segment >2 mm in V4 to V5 (Figure 1C). On echocardiography, there was severe septoapical, lateroapical, and inferoapical hypokinesia (Figure 2B). Intravenous nitroglycerine (0.25 mg)was administered, the angina disappeared, and the electrocardiography and echocardiography changes normalized in less than a minute.

DISCUSSION

SED provokes changes in myocardial contractility in the majority of patients with significant coronary lesions. In the case we presented, chest pain and electrocardiographic and echocardiographic changes appear once the SED is finalized, tests that until the end of the test were negative. The administration of the beta-blocker probably provoked a coronary spasm that triggered the subsequent ischemic cascade, with the characteristic ST segment elevation on electrocardiogram. Propranolol is a non-cardioselective beta-blocker that can trigger coronary spasm by predominance of the α stimulus by blocking the β receptors.[4]

Nevertheless, the fact that dobutamine may have contributed in part to the pathogenesis of the patient´s clinical picture cannot be totally discarded, cases of vasospasm associated with dobutamine infusion have been described.[5-7] Dobutamine is a synthetic catecholamine with a predominantly inotropic effect by stimulation of the β1 myocardial receptors, but also by chronotropic and dromotropic action. In the blood vessels, it modulates the vasomotor tone by stimulating α2 (vasoconstriction) and β2 (vasodilatation). The normal action of dobutamine on the coronary arteries is an increase in coronary flow.[8] At high doses (20 µg/kg/min), nevertheless, there is a predominance of the β2 effect. In patients with endothelial dysfunction, this vasodilator predominance is lost in favor of a vasoconstrictor response. This may be due to a change in the vasomotor function mediated by the endothelium (liberation of vasodilator substances)[9] and to an increase in the α stimulus. This would explain the relationship between vasospastic angina and, for example, tobacco, a factor known to be related to endothelial dysfunction.[10] A recent study analyzed the response to a dobutamine infusion in patients with coronary arteries without angiographic lesions but with endothelial dysfunction. In 13% of these patients, angina with ST segment elevation appeared, preceded by changes in contractility on echocardiogram due to vasospasm by dobutamina.[7]

In the case we present, we believe what occurred in our patient was a spasm triggered principally by propranolol, rather than the administration of dobutamine and atropine, or both, supporting the narrow temporal relationship between the appearance of ischemia and the infusion of the beta blocker and knowing, in addition that up until that time the test was clinically, electrically, and echocardiographically negative. On the other hand, the rapid response to the administration of nitroglycerine reaffirms this hypothesis.[11] Nevertheless, we cannot completely discard the idea that dobutamine may have contributed to the provocation of coronary spasm. Finally, the sequence of events described does not support the idea that the intramyocardial trajectory of the descending anterior artery could have been the determining factor in the patient´s symptomatology.

The patient was discharged with the diagnosis of vasospastic angina was to continue treatment with nifedipine and nitrates. At 2-month follow-up, the patient was asymptomatic, having not had any new episodes of angina and with a normal electrocardiogram.

In summary, the case shows how, after finishing a dobutamine stress test, which was negative, the administration of propranolol to antagonize the effects of the dobutamine and atropine can trigger, although in only a few cases, an ischemic phenomenon related to coronary spasm.

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