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'SILENT' PRINZMETAL'S ST ELEVATION RELATED TO ATENOLOL OVERDOSE

Daniel Petrov, MD, FESC, Svetlozar Sardowski, MD, FESC, and Margarita Gesheva, MD

Department of Emergency Cardiology and Acute Internal Diseases, "Pirogov" Emergency Hospital, Sofia, Bulgaria
Reprint Address: Daniel Petrov, MD, FESC, Department of Emergency Cardiology and Acute Internal Diseases, "Pirogov" Emergency Hospital, 21 Macedonia Ave., Sofia 1606, Bulgaria

□ **Abstract—Prinzmetal's angina is a condition characterized by chest pain, transient ST elevation, and negative biochemical markers of myocardial cell necrosis. We describe a case of chemically-induced "silent" ST segment elevation related to Atenolol overdose in a patient without coronary artery stenosis. We conclude that the cause for the transient myocardial ischemia is coronary vasospasm, precipitated by beta-blocker overdose.** © 2007 Elsevier Inc.

□ **Keywords—Prinzmetal's angina; beta-blocker overdose; chemically induced**

INTRODUCTION

Beta-adrenoreceptor antagonists (β-blockers) are responsible for life-threatening poisonings that commonly manifest as hypotension, bradycardia, sinus nodal suppression, junctional rhythms, atrioventricular block, idioventricular rhythm, congestive heart failure, and cardiac asystole (1). According to the Toxic Exposure Surveillance System (TESS) of the American Association of Poison Control Centers, United States (US) poison centers were contacted regarding ingestion of beta-blockers by 15,350 patients in 2003, including 3766 patients (25%) under 6 years of age. A review of all intentional and unintentional fatalities reported by US poison centers for the years 1985–2002 revealed 41 deaths in which a β-blocker was the only ingested drug, and the age range of this beta-blocker-only fatality cohort was 14 to 80 years (2).

In our article, a case of massive Atenolol ingestion leading to hypotension and bradycardia in association with painless ST segment elevation on the electrocardiogram is presented. Transient ST elevation in a patient with chest pain (and negative biochemical markers of myocardial necrosis) is a sign of ischemia, and is usually seen in vasospastic (variant or Prinzmetal's) angina. We describe a patient with non-significant coronary artery disease who experienced 'silent' Prinzmetal's ST elevation after Atenolol overdose. We conclude that coronary artery spasm as a result of beta-blocker overdose is the cause of the ischemia.

CASE REPORT

A 57-year-old man, previously diagnosed with bipolar disorder, presented to the Emergency Department (ED) after an overdose of Atenolol as a result of attempted suicide. The patient had a large single acute ingestion of Atenolol 500 mg. The time of his arrival at the hospital was approximately 2 h after the intentional ingestion, according to the history the patient provided. On admission the patient denied chest pain, and clinical findings were consistent with hypotension and bradycardia. Vital signs on his arrival at the ED were: temperature 36.9°C (98.4°F) axillary, pulse 53 beats/min, blood pressure 90/50 mm Hg, respiratory rate 19 breaths/min. The heart and lungs were normal on auscultation, and peripheral vascular examinations were unremarkable. Routine laboratory studies were normal, including cardiac enzymes and

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electrolytes. Blood chemistries revealed normal liver and renal function. There was no family history of ischemic heart disease, and the lipid profile was within normal limits. The chest radiograph delineated a normal cardiothoracic ratio, and no focal lung lesions. The electrocardiogram (EKG) showed sinus bradycardia (53 beats/min) and ST segment elevation in inferior leads (II, III, αVF), with no Q wave (Figure 1), which returned to normal about 20 min after admission (Figure 2). Transthoracic echocardiography performed to evaluate left ventricular function was normal, with no evidence of regional wall motion abnormalities.

The patient was placed on a cardiac monitor, intravenous access was obtained, and a urinary catheter was placed to follow urine output. Initial treatment included activated charcoal 1 g/kg, oxygen administered, intravenous fluids to correct hypovolemia, and dopamine as a pressor agent. Blood pressure improved within 90 min from the start of the treatment, and the infusion of catecholamines was reduced and stopped over the next few hours. After hemodynamic improvement, the patient was treated with felodipine 10 mg daily. Over the next few days, Holter monitoring did not record any new ischemic attacks. Coronary angiography revealed irregularities of the middle portion of the right coronary artery, without significant stenosis, as well as normal left ventricular function. The patient was discharged 8 days later. At follow-up, a month later, the patient's condition was good, and no EKG abnormalities were detected.

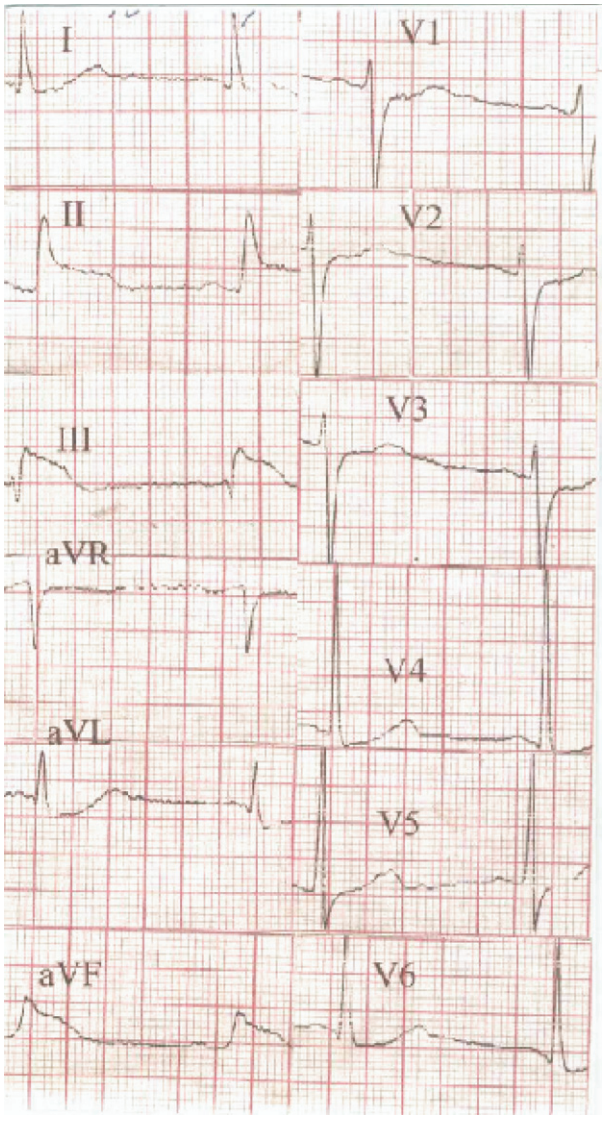

Figure 1. Initial EKG shows ST elevation in inferior leads (II, III, αVF).

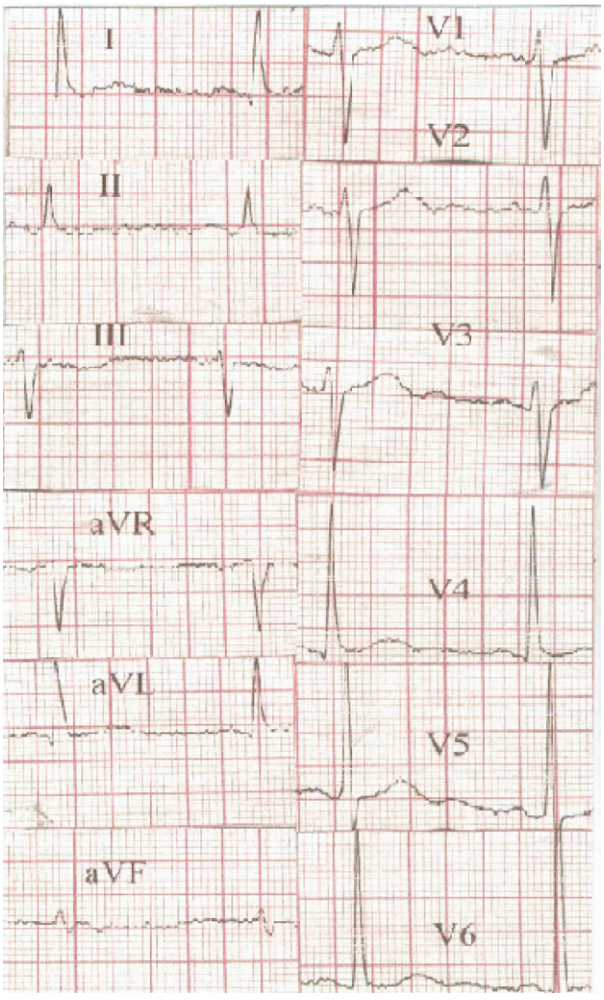

Figure 2. 20 minutes later: EKG shows complete resolution of the ST elevation.

DISCUSSION

Beta-blockers are commonly administered in cardiology for coronary heart disease, dysrhythmias, hypertension,

and chronic heart failure. However, they present a heterogeneous group of medications with differing channel selectivities, lipophilicity, protein binding, bioavailability, metabolism, membrane stabilizing activity, and intrinsic sympathomimetic activity. Beta-blockers possessing membrane-stabilizing activity are associated with the largest proportion of beta-blocker overdoses (3). Love et al. found that the single most important factor associated with the development of cardiovascular morbidity in beta-blocker ingestion is a history of a cardioactive coingestant: a primary calcium channel blocker, cyclic antidepressants, and neuroleptics. In the absence of such coingestion, exposure to a beta-blocker with membrane-stabilizing activity is associated with an increased risk of cardiovascular morbidity (4). Beta-adrenergic blockers produce toxicity through bradycardia and depression of cardiac contractility (negative inotropy), and treatment is oriented toward reversing the negative intropy, which is the primary cause of the hypotension (5). Beta-blockers are routinely used in all forms of ischemic heart disease except Prinzmetal's angina. This condition is a rare entity and angina-like symptoms tend to occur at rest, mostly at a specific hour in the early morning, together with transient ST elevation (6). Prinzmetal's angina, often referred to as variant angina, is a temporary increase in coronary vascular tone (vasospasm), causing a marked but transient reduction in the luminal diameter. This coronary vasospasm is usually focal at a single site, and can occur in either a normal or diseased vessel (7). Endothelial dysfunction, a strong thrombotic tendency, an increased platelet aggregation, together with changes in autonomic tone, can trigger coronary vasospasms (6). Alpha-adrenergic activation enhances coronary vascular tone; beta-blockade leaves alpha-adrenergic vasoconstriction unopposed.

The present report describes an unusual case of 'silent,' chemically induced Prinzmental's ST elevation after Atenolol overdose in a patient without history of variant angina, and without coronary artery stenosis. The patient experienced transient myocardial ischemia during which EKG changes occurred, and resolved in the absence of biochemical evidence of myocardial cell necrosis. In their study, Love et al. characterize EKG changes with symptomatic beta-blocker overdose (8). First-degree heart block ($>$ 200 ms) is the most common EKG finding (10/12) and also has the greatest likelihood ratio (5.3) when comparing those with symptomatic exposures to asymptomatic exposures. The authors conclude that the majority of clinically significant beta-blocker intoxications demonstrate negative dromotropic effects on EKG tracings.

In our case, we suggest coronary artery spasm as the most probable cause of ischemia, and it is, in fact, well described that beta-blockers may exacerbate coronary vasospasm by increasing alpha-adrenergic activity (9). This can occur with the use of beta-blockers to treat cocaine toxicity. Cocaine's principal effects on the cardiovascular system are mediated via alpha-adrenergic stimulation, and include an increase in the determinants of myocardial oxygen demand (heart rate and systemic arterial pressure), and a concomitant decrease in myocardial oxygen supply (caused by vasoconstriction of the epicardial coronary arteries). Beta-adrenergic blocking agents may exacerbate cocaine-induced coronary arterial vasoconstriction, thereby increasing the magnitude of myocardial ischemia (10).

After hemodynamic improvement, the patient was treated with felodipine and ischemic episodes were no longer recorded. There are a number of cardiovascular conditions in which calcium channel antagonists are accepted as first-line therapy, including Prinzmetal's angina. Calcium antagonists have multiple mechanisms whereby they are able to protect against myocardial ischemia, and these agents remain useful in Prinzmetal's angina, a condition in which there are no long-term comparative outcome studies (11). In their study, Ardissino et al. report that treatment with felodipine once daily provides 24-h anti-ischemic protection (12).

Our case findings are also consistent with those of Lin et al., who claim that coronary arterial spasm can be induced by beta-blockers, not only in patients with variant angina but also in normal persons (13).

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