

Case Report

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Unusual Side Effect of Adenosine Infusion

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Abstract

We report the case of 22-year-old man who showed adenosine induced sinus tachycardia during the transesophageal electrophysiological evaluation for suspect accessory pathway.

Learning objective: Our case is the first report of sinus tachycardia induced by intravenous adenosine infusion without previous bradycardia. We are aware that the relation between adenosine infusion and sinus tachycardia is anecdotal, but we believe that all possible and unexpected pro-arrhythmic effects should be known when we use in clinical practice this drug.

Keywords: Sinus tachycardia; Adenosine; Proarrhythmic effect

Case Report

A 22 year old man was referred to our observation for recurrent palpitations at rest which subside after few minutes. The medical history was negative for familiar sudden death, dizziness or syncope. His body weight was 75 kg and his height was 170 cm. Physical examination revealed a blood pressure of 130/70 mmHg, clear lungs and normal heart sounds. Hematological examination, urinary analysis and thyroid function were all normal. He had no past medical history and denied taking alcohol, tobacco or any medications. Electrocardiographic (ECG) examination showed sinus rhythm of 75 beats/minute, normal atrioventricular conduction (PR: 120 ms), mild slurred QRS upstroke in leads V3-V4, no ST segment or T wave changes (Figure 1). Neither chest x-ray or color-doppler echocardiography revealed any cardiac structural or functional abnormalities. 24 hours ECG Holter monitoring and treadmill stress test did not show arrhythmias. He underwent transesophageal electrophysiological evaluation: the atrioventricular node refractory period was 240 msec. During the test it was not used any anesthesia. The patient was conscious during the entire test and its O₂ saturation, measured at pulse oximeter, was consistently 98-99%. Programmed atrial stimulation up to two extrastimuli did not induce supraventricular arrhythmias. Intravenous adenosine (12 mg) was performed for slowing of AV conduction and unmasking unapparent pathways. After a single-bolus, rapidly followed by saline flush, a sinus tachycardia at a frequency of 145 beats/min was induced. It was self-terminated in approximately 50 seconds, without change in QRS morphology (Figure 2). At the second adenosine bolus, carried out about 5 minutes later, similar effect was induced. Patient remained conscious and asymptomatic during the tachycardia.

Discussion

Adenosine is an endogenous nucleoside whose actions were first investigated by Drury and Szent-Gyorgyi [1]. They described a slowing of sinus rate and a reduction of conduction through the atrioventricular node in the hearts of laboratory mammals. The adenosine test seems to have good sensitivity for unmasking pre-excitation about 76-100% in small series [2,3], because it extends the atrioventricular node refractory period favoring anterograde conduction through an accessory pathway. The electrophysiologic effects of adenosine on a specific AV bypass tract depend on the type of cell that the tract consists: nodal type cells (with decremental conduction) or atrial myocytes. In sinoatrial nodal cells, the activation of a potassium outward current results in a reduced rate of phase IV depolarization, thereby slowing sinoatrial node automaticity.

In the AV node, adenosine prolongs postrepolarization refractoriness and suppresses excitability of cells in the N region of the node, resulting in AV nodal conduction block of variable degrees.

Some authors reported serious adverse events related to the adenosine infusion, including supraventricular and life threatening ventricular arrhythmias [4,5]. To date, while the association between adenosine infusion and ventricular arrhythmias is well known [6-9], little is still known about the adenosine induced supraventricular arrhythmias. The possible mechanisms underlying proarrhythmic effect of adenosine are summarized in Figure 3.

The most common proarrhythmic effect of adenosine is the induction of atrial fibrillation (AF). This is probably owing to the shortening of atrial refractoriness, which is a favorable condition for the induction of reentrant arrhythmias. Because the signal transduction pathways activated by adenosine and acetylcholine converge on the same potassium channels to produce similar electrophysiologic effects in the atrial myocardium, adenosine induced and vagus nerve-dependent AF are mechanistically similar. Both adenosine and vagus nerve activation cause spatially and temporally heterogeneous shortening of atrial refractoriness [10].

Some authors reported also a dangerous increase of the ventricular rate in atrial flutter patients following the administration of adenosine, with conduction increasing from 2:1 to 1:1 after a brief period of high grade atrioventricular block [11-13]. Three of these five reported cases required electrical cardioversion. The secondary enhancement of atrioventricular (AV) nodal conduction following initial AV block was thought to be related to sympathetic activation, which was then perpetuated by the onset of 1:1 conduction.

Garratt et al. [14] reported supraventricular proarrhythmic effects in three patients: a rapid pre-excited atrial fibrillation, terminated by

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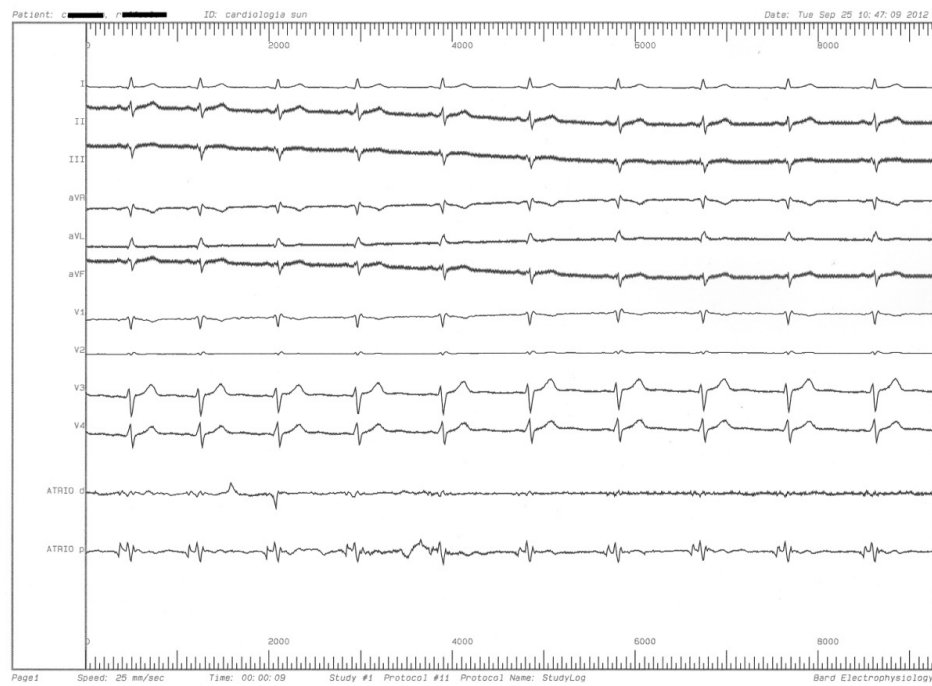


Figure 1: Baseline ECG.

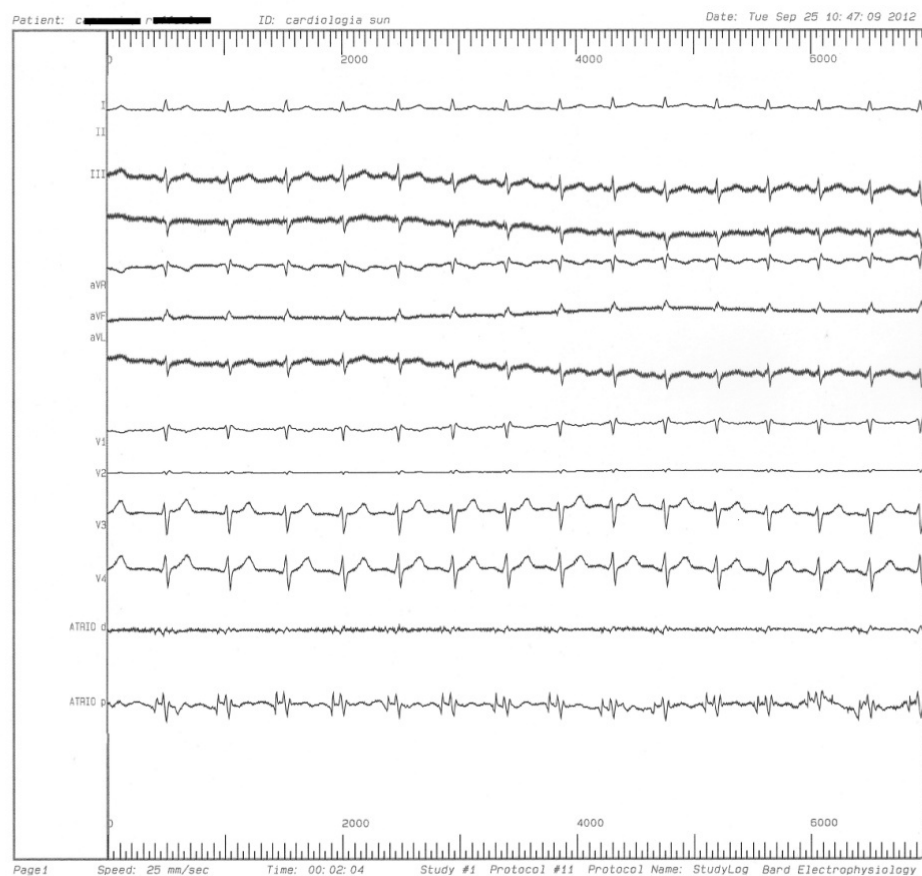


Figure 2: Adenosine induced sinus tachycardia.

Type of arrhythmia	Underlying mechanisms
Atrial fibrillation/atrial flutter	-Shortening of atrial refractoriness -Sympathetic activation
Rapidly conducted atrial flutter /atrial fibrillation	-Sympathetic activation
Orthodromic atrioventricular reentry tachycardia	-Critical prolongation of antero-grade AV nodal and retrograde activation of the atrium via an accessory pathway
Pre-excited atrial fibrillation/atrial flutter	-Critical prolongation of antero-grade AV nodal and activation of the ventricle via an accessory pathway
Sinus tachycardia/atrial tachycardia	-Reflex sympathetic discharge -Direct sympathetic activation by stimulation in the carotid body chemoreceptors

Figure 3: Possible mechanisms underlying adenosine induced supraventricular tachyarrhythmias.

intravenous flecainide, a pronounced acceleration of AV re-entrant tachycardia, and a rapid pre-excited atrial tachycardia that required atrial pacing for termination. None of these arrhythmias had occurred previously, and all resulted in severe haemodynamic compromise. Jaeggi et al. [15] observed three instances of adenosine-induced atrial proarrhythmia (two atrial fibrillation and one atrial flutter) in children with manifest or concealed Wolff-Parkinson-White syndrome. Dougherty et al. [16] reported an orthodromic atrioventricular re-entry tachycardia, during intravenous adenosine administration, in patient with intermittent pre-excitation and only retrograde accessory pathway conduction documented at the time of invasive electrophysiological study. Probably a critical prolongation of anterograde AV nodal conduction was thought to have allowed retrograde activation of the atrium via an accessory pathway and thus the emergence of the reciprocating tachycardia [17].

Rapid ventricular rate after adenosine has been reported also in the absence of an accessory pathway. Orebaugh and Handy [18] described two patients with a narrow QRS complex tachycardia in whom adenosine (6 mg followed by 12 mg) caused an increase in heart rate. In both these patients, there was no evidence for preexcitation.

Previous case series [19,20] showed two episodes of 'mild sinus tachycardia' following the brief period of bradycardia related to the adenosine infusion. This effect was probably determined by an increase in sympathetic discharge in response to the bradycardia and to the transient atrioventricular nodal block induced by adenosine infusion.

Our case, instead, is the first report of sinus tachycardia induced by intravenous adenosine infusion without previous bradycardia, supporting the hypothesis of Biaggioni et al. [21] that the adenosine may be responsible of a direct increase in circulating catecholamine levels and sympathetic nerve traffic by sympathetic stimulation in the carotid body chemoreceptors. The transesophageal electrophysiological evaluation was performed under continuous ECG monitoring and was not recorded any bradycardia during the entire test. We are aware

that the relation between adenosine infusion and sinus tachycardia is anecdotal, but we believe that all possible and unexpected proarrhythmic effects should be considered when we use in clinical practice antiarrhythmic drugs.

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