Intraoperative Ventricular Tachycardia Responsive to Adenosine

Stephen R. Wagner IV, MD, Scott S. Johnson, MD, and Roger D. White, MD
Department of Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, Minnesota

The safety and efficacy of adenosine in treating atrioventricular (AV) nodal reentrant and AV reciprocating tachycardias are well established (1). Adenosine depresses the upstroke of the action potential of AV nodal cells ("N" cells). Although the ionic mechanism for this depression is unknown, it is the most likely cause of adenosine-induced impairment of AV nodal conduction (2). The short half-life of adenosine (<6-10 s) primarily accounts for its safety (3,4). Because of both its safety and efficacy, adenosine has become the drug of choice in the treatment of paroxysmal supraventricular tachycardia.

Less well appreciated is a form of ventricular tachycardia (VT) which, because of its mechanism of initiation, is sensitive to adenosine. It has been most frequently observed in patients with structurally normal hearts and in whom the VT was exercise induced (5). The proposed mechanism of initiation involves afterdepolarizations triggered by the preceding action potential (triggered activity) (6). Catecholamines have been demonstrated experimentally to induce triggered activity, and the initiation of this form of VT is believed to be caused by intracellular calcium (Ca\(^{2+}\)) overload mediated by elevation of intracellular cyclic adenosine monophosphate (cAMP) (7). Therefore, catecholamines appear to play a pivotal role in the initiation of this type of VT. We describe a patient undergoing hypothermic cardiopulmonary bypass for coronary artery bypass grafting (CABG) who was observed to be hyperdynamic during rewarming and who developed a wide-complex tachycardia sensitive to adenosine.

Case Report

A 67-yr-old man with a history of progressive shortness of breath and dyspnea on exertion was admitted to the hospital for CABG. He was taking aspirin 325 mg daily and diltiazem 90 mg twice a day. Past medical history was unremarkable except for degenerative joint disease and reflux esophagitis.

Left ventricular and coronary angiography revealed mild to moderate hypokinesia in the posterobasal and posterolateral segments, respectively, left ventricular end diastolic pressure 14 to 29 mm Hg, and an ejection fraction of 0.68. The major arteriographic findings were 80% obstruction of the proximal left anterior descending coronary artery, 70% obstruction of the first diagonal, 100% occlusion of the proximal circumflex, and 90% obstruction of the proximal right coronary artery.

During exercise radionuclide angiography, which was positive for ischemia, the electrocardiogram (ECG) showed >2 mm ST segment depression, "T wave inversion, supraventricular tachycardia, and complex ventricular ectopy," with the heart rate reaching 150 bpm. Arterial blood pressure increased from 132/70 mm Hg at rest to 220/100 mm Hg at peak exercise. The test was stopped at 7.0 min because of dyspnea.

The patient was brought to the operating room, and anesthesia was induced with 250 µg sufentanil and 4.5 mg midazolam intravenously (IV). Endotracheal intubation was facilitated by administration of 6 mg of pancuronium bromide and 6 mg of vecuronium IV. Monitoring included five-lead electrocardiography, systemic blood pressure with a left radial arterial catheter, pulse oximetry, nasopharyngeal temperature, and capnography. Additionally, a pulmonary artery catheter was placed via the right internal jugular vein for purposes of pulmonary artery and pulmonary artery occlusion pressure monitoring and for thermodilution measurement of cardiac output. Anesthesia was maintained with sufentanil and midazolam, nitrous oxide, oxygen, and air. Supplemental relaxation was accomplished with 2 mg incremental pancuronium bromide.

The pre–cardiopulmonary bypass (CPB) course was uneventful. A total dose of 1500 µg sufentanil (15 µg/kg) was administered prior to CPB. Saphenous vein grafts were inserted into the diagonal, circumflex, and posterior descending coronary arteries, and the left internal mammary artery was anastomosed to the left anterior descending coronary artery. Bypass and aortic cross-clamp times were 113 and 57 min, respectively. Ten minutes after removal of the aortic cross-clamp, a wide-complex tachycardia occurred (Fig. 1). The tachycardia persisted despite three successive attempts at electrical defibrillation (20 J, 20 J, 30 J) and 100 µg IV lidocaine. The Pao\(_2\) was 315 mm Hg, Paco\(_2\) 48 mm Hg, pH 7.35, bicarbonate 27 mEq/L, base deficit +2 mEq/L, and potassium 4.5 mEq/L. Core temperature was 37°C. There was no ECG evidence of an acute ischemic event or of difficulty with internal mammary artery or vein graft function.

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Address correspondence and reprint requests to Roger D. White, MD, Department of Anesthesiology, Mayo Clinic, 200 First St. S.W., Rochester, MN 55905.

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Discussion
We describe a patient undergoing a CABG operation who developed an adenosine-sensitive VT. Over the past 15 years, evidence has been accumulating for the presence of at least three mechanically distinct forms of VT: reentrant, automatic, and triggered. Reentrant VT is more common in patients with structural heart disease, such as coronary artery disease and myocardial infarction (8-10). It can be initiated by programmed stimulation and is characterized by an excitable gap, similar to a Schmitt-Erlanger entrainment circle, thought to be involved in the majority of paroxysmal supraventricular tachycardias (11,12). Automatic VT can be induced by isoproterenol or exercise, cannot be initiated or terminated by programmed stimulation, and can be suppressed with propranolol (6). This form of VT often occurs in diseased ventricular myocardium and probably involves abnormally low resting membrane potentials resulting in myocyte hyperexcitability (6). Triggered VT generally occurs in younger patients without organic heart disease. It is catecholamine- and exercise-induced and can be initiated by programmed stimulation (5,7). The focus for such triggered activity is frequently near the right ventricular outflow tract (13), and the ECG often displays a left bundle branch block morphology. The mechanism is believed to involve increased levels of Ca^{2+} that depolarize the myocyte and result in a lower resting membrane potential (1,6,7,14). This state of hyperexcitability makes it more likely that the cell will reach its firing threshold when exposed to a delayed afterdepolarization.

Adenosine terminates AV nodal reentrant tachyarrhythmias by a cAMP-independent effect on the conduction system (1,14,15). More recently, adenosine has been demonstrated to terminate triggered VT, and this mechanism is proposed to involve alterations in intracellular cAMP concentrations (7). Specifically, adenosine attenuates the catecholamine-stimulated calcium inward current, also called the slow inward, L-type calcium current, and the transient inward current, both of which have been implicated in the genesis of afterdepolarizations (15). Adenosine binds to the A1 receptor and stimulates a guanine nucleotide-binding protein that in turn inhibits intracellular adenylate cyclase. This decreases intracellular cAMP, attenuating the calcium inward current and the transient inward current, and thereby lowers Ca_{i}^{2+} levels (1,5,15). This mechanism for adenosine mimics the actions of acetylcholine, which binds to a muscarinic cholinergic receptor on the outside of the myocyte and thereby activates the same inhibitory guanine nucleotide-binding protein acted on by adenosine (7).

It follows from the above discussion that adenosine would be effective only in triggered activity due to stimulation of cAMP production, and indeed this is probably the case. For instance, adenosine is ineffective in ouabain-induced and in digitalis-induced triggered activity (16). In these cases, Ca_{i}^{2+} overload is mediated by inhibition of Na,K-ATPase and not by increases in intracellular cAMP levels.

The effect of adenosine on Ca_{i}^{2+} levels is more pronounced in the presence of exercise or catecholamine stimulation (1,5,14,15). This is consistent with the known stimulatory effects of β-receptor activation on adenylate cyclase. In effect, β-receptor stimulation (e.g., exercise, hyperdynamic conditions) and adenosine have opposite effects on adenylate cyclase, cAMP, and consequently, Ca_{i}^{2+} levels. Thus, in the presence of catecholamine stimulation, adenosine will appear to have an enhanced effect, explaining adenosine’s effectiveness in rapidly terminating catecholamine-induced VT.

Adenosine has been shown to stimulate ventilatory drive (4,17). Since increases in ventilatory drive attenuate sympathetic nerve activity by activating thoracic...
stretch receptors (18,19), some authors suggest that
termination of VT by adenosine could be related to
reactive withdrawal of sympathetic nerve traffic (7),
although verification of this in the literature is lacking
and the application of this concept to patients under
controlled ventilation is problematic.

Perhaps the antiadrenergic actions of adenosine are
due to modulation of β-adrenoreceptor affinity to ago-
nists, although these findings are highly variable by
species (20). Finally, probably the most important in-
fuence that causes subthreshold delayed afterdepo-
larizations to reach threshold is a decrease in the cycle
length at which action potentials occur. This decrease
in cycle results in an accumulation of Ca2+ and thus
cellular depolarization. Therefore, arrhythmias trig-
gerred by delayed afterdepolarizations, such as trig-
gered VT, can be expected to be initiated by a spon-
taneous increase in the heart rate, as would occur in a
hyperdynamic state (6).

While these remain possibilities, it is more likely
that adenosine terminates VT through its known ac-
ction at the cardiac A1 receptor, leading to decreased
intracellular cAMP. In particular, there is in vitro evi-
dence that adenosine attenuates catecholamine-
induced activation of adenylate cyclase via A1 recep-
tors by decreasing the ability of β-adrenergic agonists
to promote the formation of a high-affinity complex
composed of the β-agonist, receptor, and stimulatory
guanine nucleotide-binding protein (20).

While the patient we describe here had coronary
heart disease, both the hyperdynamic response clic-
ited during exercise testing and the rapid termination
of the VT by adenosine implicates a catecholamine-
mediated, triggered mechanism for the arrhythmia.
This is the first reported case of intraoperative
adenosine-sensitive VT.

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