Acute Cardiogenic Shock after Isoproterenol Infusion for Induction of Atrial Tachycardia

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ABSTRACT. The differential diagnosis of acute and reversible cardiomyopathy is limited and includes stress-induced, metabolic, infectious, iatrogenic, and ischemic etiologies. Herein, we present a potential cause of an increasingly recognized clinical syndrome. An otherwise healthy 38-year-old woman was referred to our institution for evaluation of paroxysmal episodes of narrow-complex tachycardia, refractory to high-dose oral β-blockers. Despite a normal resting electrocardiogram (ECG), an ECG obtained during an episode of tachycardia showed inverted P-waves in leads II, III, and aVF, suggestive of ectopic atrial tachycardia. Isoproterenol infusion was used for induction and mapping an ectopic focus originating from the crista terminalis. The focus was successfully radiofrequency ablated. Post procedure, she was in sinus tachycardia. She received IV metoprolol and became severely hypotensive. Pulseless electrical activity ensued, and cardiopulmonary resuscitation was performed. Epinephrine and phenylephrine were administered; a perfusing rhythm was noted after 2 min. An echocardiogram showed left ventricular systolic dysfunction (ejection fraction (EF) 10–15%), with preservation of wall motion at the base. No pericardial effusion noted. Coronary angiography was normal. Wedge pressure was elevated with reduced cardiac output. She was given inotropic and pressor support. Over the next 24 h, blood pressure and cardiac output significantly improved. An echocardiogram 4 days later showed significant recovery of the mid and apical segments. Causality is difficult to demonstrate experimentally; however, biologic plausibility and reversibility are integral to the recognition of novel clinical associations. Through non-selective β-receptor stimulation, continuous isoproterenol infusion could theoretically induce a catecholamine-mediated cardiomyopathy with prompt resolution following discontinuation.

KEYWORDS. cardiogenic shock, isoproterenol, stress-induced cardiomyopathy.

Introduction
Stress-induced cardiomyopathy (SIC), also known as Takotsubo cardiomyopathy, is a clinical entity characterized by the acute and reversible onset of left ventricular systolic dysfunction often with ischemic-appearing electrocardiogram (ECG) findings in the absence of obstructive coronary artery disease. There have been multiple accounts of SIC occurring in tandem with severe psychologic, physical, and iatrogenic stressors.1,2 Herein, we present a potentially novel cause of SIC resulting from prolonged isoproterenol infusion.

Case
An otherwise healthy 38-year-old woman was referred to our institution for evaluation of a 1-year history of symptomatic paroxysmal episodes of narrow-complex tachycardia, refractory to high-dose oral β-blockers. Her resting ECG showed no abnormalities; however, an ECG obtained during an episode of long RP tachycardia showed inverted P-waves in leads II, III, and aVF, indicating possible atrial tachycardia. A baseline transthoracic echocardiogram (TTE) 6 weeks prior to presentation showed normal left and right ventricular function with a left ventricular ejection fraction (LVEF) of 60%. Imaging and
biomarker studies were obtained and negative for a catecholamine-secreting tumor. She subsequently underwent an electrophysiologic study with isoproterenol infusion for induction and mapping which identified an ectopic focus originating from the crista terminalis (Figure 1). The isoproterenol dose used was intermittently titrated up to 8 µg/min, and the total duration of isoproterenol use was 90 min including post-ablation testing. This focus was successfully treated with radiofrequency ablation and there were no procedural complications. Post procedure, she was noted to be in sinus tachycardia (120 bpm) and received 5 mg of IV metoprolol. She subsequently became severely hypotensive and her condition deteriorated rapidly into pulseless electrical arrest. Cardiopulmonary resuscitation (CPR) was initiated and administration of epinephrine and phenylephrine resulted in restoration of a perfusing rhythm after 2 min. An emergent bedside TTE showed left ventricular systolic dysfunction (LVEF) of 10%, with preservation of wall motion at the base (Figure 2) and no evidence of a pericardial effusion. Emergent coronary angiography revealed normal coronary arteries. Hemodynamic monitoring confirmed reduced cardiac output (2.83 l/min), elevated pulmonary capillary wedge pressure (23 mmHg), and a pulmonary vascular resistance of 99 dynes·sec/cm². She was continued on inotropic support along with an intra-aortic balloon pump. Over the ensuing 24 h, blood pressure and cardiac output significantly improved. A repeat TTE on post-procedural day 4 showed significant recovery of her left ventricular function with an estimated LVEF of 42% (Table 1). A follow-up TTE 4 months after her ablation showed complete resolution of the mid and apical wall motion abnormalities. LVEF was quantitated at 65%.

Discussion
A full discussion of the etiology, pathophysiology, and diagnostic criteria of SIC is beyond the scope of this report.
and the reader is referred to a recent review article for further reading. The pathophysiologic mechanisms leading to SIC are not fully understood but catecholamine toxicity has been implicated. Consistent with this hypothesis, catecholamine levels have been shown to be higher among individuals with SIC than those presenting with myocardial infarction. There have been multiple reports of SIC following exposure to a variety of medications. A 2011 review of the literature identified 58 possible cases of SIC in which epinephrine was thought to be a major cause (33% of the cases), followed by dobutamine (15.5% of cases). Two reports implicated both isoproterenol and epinephrine in the development of SIC. Isoproterenol is a non-selective β-agonist with sympathomimetic activity and is commonly used to induce arrhythmias during electrophysiologic studies for the identification of ectopic foci. It is possible that prolonged infusion of this medication was responsible for the development of SIC in our patient. Causality is difficult to demonstrate experimentally; however, biologic plausibility and reversibility are integral to the recognition of novel clinical associations. Through non-selective β-receptor stimulation, continuous isoproterenol infusion could theoretically induce a catecholamine-mediated cardiomyopathy with prompt resolution following discontinuation. Appreciation of this potentially under-recognized phenomenon is important in the management of cardiogenic shock in patients undergoing invasive electrophysiology procedures.

Table 1: Echocardiographic parameters at baseline, at cardiac arrest, and before and after discharge

<table>
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<tr>
<th></th>
<th>Baseline</th>
<th>At the time of cardiac arrest</th>
<th>Prior to discharge</th>
<th>5 Weeks after discharge</th>
<th>4 Months after discharge</th>
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<tbody>
<tr>
<td>Ejection fraction (EF)</td>
<td>60%</td>
<td>10%</td>
<td>42%</td>
<td>58%</td>
<td>65%</td>
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<td>LV dimensions</td>
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<td>Dimension (d) (mm)</td>
<td>48</td>
<td>49</td>
<td>50</td>
<td>50</td>
<td>48</td>
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<tr>
<td>Dimension (s) (mm)</td>
<td>32</td>
<td>46</td>
<td>38</td>
<td>34</td>
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References