Trazodone overdose–induced Prinzmetal’s angina pectoris

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ABSTRACT

A 29-year-old man presented to the emergency department with chest pain after ingestion of 25 tablets of 50 mg trazodone. Initial electrocardiography revealed a 3-mm ST-segment elevation in leads II, III, and aVF along with reciprocal ST-segment depression in anterior wall leads. Cardiac catheterization showed normal epicardial coronary arteries. His subsequent electrocardiograms showed resolution of ST-segment changes with uneventful recovery.

KEYWORDS Electrocardiography; Prinzmetal’s angina; ST-segment elevation; trazodone; vasospastic angina

Vasospastic angina pectoris is a syndrome of chest pain caused by myocardial ischemia secondary to reversible coronary artery vasospasm. It is characterized by transient ischemic changes on the electrocardiogram (ECG) in the presence of angiographically normal coronary arteries. Although tricyclic antidepressants have been previously associated with coronary vasospasm, trazodone’s association has been seldom reported.¹

CASE DESCRIPTION

A 29-year-old man with recently diagnosed depression and a family history of coronary artery disease was brought to the emergency room after consuming 25 tablets of 50 mg trazodone with suicidal intention. He complained of substernal and left-sided chest pain that began shortly after the overdose. The pain was stabbing in nature, 8/10 in intensity. It radiated to the left arm with no noted aggravating or relieving factor. He also had nausea, with one episode of vomiting. He denied any palpitations, dyspnea, or lightheadedness. He smoked a half pack of cigarettes per day for 5 years and consumed alcohol on weekends but denied use of illicit substances, including cocaine. He was drowsy and diaphoretic, with stable vital signs other than the heart rate, which showed sinus tachycardia (116 beats/min). His drowsiness gradually worsened, and he became unresponsive during his emergency stay.

The initial 12-lead ECG showed a 3-mm ST-segment elevation in leads II, III, and aVF with concomitant ST-

segment depression in leads V1 through V3 and leads I and aVL (*Figure 1a*). The corrected QT interval was 401 ms. Markers of myocardial injury through troponin I and creatine kinase muscle-brain were negative. Emergent 2D echocardiography at the bedside revealed normal global right and left ventricular function with no regional wall motion abnormality or apical ballooning. The left ventricular ejection fraction was about 55%. Coronary angiography revealed normal epicardial coronary arteries (*Figure 2*). Repeat ECG obtained 1 hour after catheterization revealed resolution of ST-segment elevation and reciprocal changes (*Figure 1b*). The corrected QT interval was 557 ms, and serum creatinine, glycated hemoglobin, and lipid profile were within normal limits. A comprehensive urinary drug screen was negative.

Given the ongoing chest pain in view of acute ST-segment elevation myocardial infarction, our patient was treated briefly with nitroglycerin and heparin infusion, aspirin (325 mg), clopidogrel (300 mg), and atorvastatin (80 mg). Endotracheal intubation was performed. He was later treated with oral nifedipine, atorvastatin, and sublingual nitroglycerin as required. The QT interval was monitored with serial ECGs every 6 hours. The maximum recorded corrected QT interval was 564 ms, which resolved to baseline over 2 days. During the 4-day hospital course, the patient did not develop any other serotonergic signs or features of autonomic instability and had an uneventful recovery.

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Received July 26, 2019; Revised August 15, 2019; Accepted August 21, 2019.

Figure 1. Electrocardiograms. (a) ST-segment elevation in leads II, III, and aVF (marked by arrow). (b) Resolution of ST-segment elevation after the resolution of angina.

Figure 2. Coronary angiography of the left and right coronary arteries with no luminal irregularity: (a) left coronary artery and (b) right coronary artery.

DISCUSSION

The typical presentation along with supportive ECG findings in our patient raised a high suspicion of acute ST-segment elevation myocardial infarction. However, he was young and did not have atherosclerotic risk factors other than smoking. Further, his Thrombolysis in Myocardial Infarction score was 1, and his Global Registry of Acute Coronary Events score was 66. Thus, we considered the possibility of nonatherosclerotic causes. Urinary drug screen was negative for vasoactive substances. Given the history of newly diagnosed depression and ongoing history of emotional stress, the possibility of takotsubo cardiomyopathy was considered. However, normal cardiac enzymes and the absence of transient left ventricular systolic dysfunction (hypokinesis, akinesis, or dyskinesis) in 2D echocardiography made it unlikely.^{2,3} Benign early repolarization was a possibility given his young age; however, the ECG did not show J point elevation, and the ST-segment elevation followed a specific vascular territory. Because the repeat ECG revealed resolution of ST-segment elevation, the possible cause was a reversible process, likely vasospasm of the epicardial coronary artery.

Multiple vasoconstrictors such as acetylcholine, serotonin, histamine, noradrenaline, and dopamine have been used to produce coronary vasospasm, suggesting that a single receptor pathway cannot explain this phenomenon.^{4,5} In addition to neurotransmitters and vasoconstrictor stimuli, endothelial dysfunction and microvascular dysfunction have been associated with coronary vasospasm.^{6,7}

Deficits in neurotransmitters like serotonin, norepinephrine, and dopamine are attributed to the pathophysiology of depression. Further, these abnormalities are involved in the stiffening and narrowing of arteries as well as increased endothelial reactivity seen in the different types of coronary artery

disease.⁸ Thus, we believe that this patient had some underlying endothelial dysfunction considering his history of smoking, depression, and alteration in neurotransmitters. We assume that the vasospastic angina seen in our patient was induced by the action of serotonin in the coronary artery in the setting of some preexisting endothelial dysfunction. Serotonin mediates vasoconstriction, and trazodone has been shown to possess some constrictor activity in an experimental study.⁹

Trazodone, a serotonin modulator antidepressant, acts by antagonism of 5-hydroxy-tryptamine 2A and 5-hydroxy-tryptamine 2C receptors and also causes serotonin reuptake inhibition. Its exact mechanism of action in treating depression is not known but is thought to involve increased serotonin at select neurologic synapses. Interestingly, priapism has been described as a side effect, which is the result of “low flow” (as opposed to “high flow” following trauma). Although there is a well-established association of trazodone with cardiac arrhythmia, including impaired atrioventricular conduction and QT prolongation, Prinzmetal’s angina pectoris needs to be further explored.¹⁰

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