Clinical Case Report

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Takotsubo cardiomyopathy associated with serotonin syndrome in a patient with stroke

A case report

Sung Ho Jang, MD[a], Jong-Ho Nam, MD[b], Jun Lee, MD[c], Min Cheol Chang, MD[d,*]

Abstract

Rationale: Takotsubo cardiomyopathy (TC) is characterized by transient left ventricular dysfunction. We describe a patient with stroke who presented with TC caused by serotonin syndrome (SS) following the administration of serotonergic and dopaminergic agents.

Patient concerns: A 55-year-old man with stroke was administered venlafaxine, tianeptine, ropinirole, carbidopa/levodopa, bromocriptine, and methylphenidate during rehabilitation. The patient presented with clinical features of SS (mental confusion, agitation, hyperhidrosis, chills, rigidity, and tachycardia), which persisted over 24 hours. The day after his SS symptoms disappeared, the patient's blood pressure decreased, and he developed tachycardia.

Diagnoses: Echocardiography revealed an extensively akinetic apical segment and a severely hypokinetic midventricular segment of the left ventricle with basal hyperkinesia. The ejection fraction was reduced to 38%, and he was diagnosed with TC by the cardiologist.

Interventions: He was administered oxygen at 8 to 10 L/minutes via a Venturi mask, and norepinephrine bitartrate was administered intravenously. Hydration was maintained with normal saline infusion.

Outcomes: Following appropriate management of TC, the patient was hemodynamically stable with significant recovery of his left ventricular wall motion.

Lessons: Prognosis of TC is usually favorable; however, it could be fatal in some cases. Clinicians should be aware of the potential development of TC in patients with stroke presenting with SS following the administration of serotonergic and dopaminergic agents.

Abbreviations: ICH = intracranial hemorrhage, MRC = Medical Research Council, SS = serotonin syndrome, TC = Takotsubo cardiomyopathy.

Keywords: dopaminergic agent, serotonergic agent, serotonin syndrome, stoke, takotsubo cardiomyopathy

1. Introduction

Takotsubo cardiomyopathy (TC), also known as stress-induced cardiomyopathy, is characterized by transient left ventricular dysfunction induced by emotional or physical stress without coronary disease.[1] Although the pathomechanism for this condition remains unclear, myocardial stunning caused by catecholamine excess is the most common theory that explains its occurrence.[2,3] Stressful events and factors contributing to physical stress including pheochromocytoma, subarachnoid hemorrhage, and the exogenous administration of norepinephrine or medications causing elevated plasma norepinephrine levels are known triggers for TC.[4]

Serotonin syndrome (SS), a potentially life-threatening condition increases serotonergic activity in the central nervous system.[5] Patients with SS present with a combination of various symptoms including mental status changes, autonomic instability, and neuromuscular hyperactivity.[5] Antidepressants (serotonergic), dopaminergic agents, opioids, and antiemetics are known to induce SS.[6] SS can lead to a hyperadrenergic state, and previous studies have reported SS-induced TC.[7,8]

Serotonergic and dopaminergic agents are known to effectively manage depressed mood and improve cognitive, executive, language, and motor function in patients with stroke; therefore, these agents are commonly prescribed for patients with stroke during rehabilitation.[9,10] However, the use of these agents in patients with stroke may precipitate SS.[11] We report the case of a patient with stroke who presented with SS-induced TC after the administration of serotonergic and dopaminergic agents during rehabilitation.

2. Case report

A 55-year-old man underwent conservative treatment at the Neurosurgery Department of a University Hospital for a spontaneous intracranial hemorrhage (ICH) involving the right

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[a] Department of Physical Medicine and Rehabilitation, [b] Division of Cardiology, Department of Internal Medicine, [c] Department of Neurology, Daegu, [d] Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Daemyungdong, Namku, Taegu, Republic of Korea.

[*] Correspondence: Min Cheol Chang, Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, 317-1, Daemyungdong, Namku, Taegu 705-717, Republic of Korea (e-mail: wheel633@gmail.com).

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frontoparietal lobe. Three days after the ICH, he was admitted to the Rehabilitation Department of our University Hospital for rehabilitative management. He presented with complete weakness of the left upper extremity (Medical Research Council [MRC] score 0/5) and severe weakness of the left lower extremity (MRC score 2/5). His Mini-Mental State Examination score was 22. Serotonergic and dopaminergic agents were administered to improve functional impairment. These agents were initiated at a low dosage and gradually increased to the following daily dosages on the 60th day of admission: venlafaxine 75 mg, tianeptine sodium 37.5 mg, ropinirole 1.5 mg, carbidopa/levodopa 75/750 mg, bromocriptine mesylate 7.5 mg, and methylphenidate 7.5 mg. On the 60th day of admission, the patient developed mental confusion, agitation, hyperhidrosis, chills, rigidity, and tachycardia (heart rate 130 beats/minutes). His body temperature (36.8°C) and blood pressure (120/80 mm Hg) were within normal ranges. The patient's symptoms fulfilled 4 major and 2 minor symptoms of the Radomski criteria for SS[12]; thus, he was diagnosed with SS. The patient was hydrated with normal saline infusion. The serotonergic and dopaminergic agents administered to the patient were gradually tapered over 3 days and then discontinued. Approximately 24 hours after initiating treatment for SS, SS-related symptoms nearly completely disappeared. However, the day following the disappearance of his symptoms, the patient suddenly complained of dyspnea. His blood pressure was observed to be 70/40 mm Hg, heart rate was 180 beats/minutes, and partial pressure of arterial oxygen was 56.3 mm Hg. Blood tests revealed elevated levels of troponin I (3.54 ng/ml), creatine kinase-MB (23.5 ng/ml), and N-terminal prohormone of brain natriuretic peptide (4443 pg/ml). Electrocardiography showed sinus tachycardia at a rate of 167/minutes with QT prolongation at 620 ms. No ST-segment changes or T-wave inversion were observed. Echocardiography revealed an extensively akinetic apical segment and severely hypokinetic midventricular segment of the left ventricle with basal hyperkinesia. The ejection fraction was reduced to 38%. Chest radiography was within normal limits. Also, the coronary angiogram showed normal coronary arteries without any obstruction. Based on the Gothenburg criteria,[13] he was diagnosed with TC and administered oxygen at 8 to 10 L/minutes via a Venturi mask, and norepinephrine bitartrate was administered intravenously. Hydration was maintained with normal saline infusion. The patient was hemodynamically stable 3 days after the onset of TC-related symptoms. Although echocardiography performed on the 10th day of admission continued to show reduced wall motion, the wall-motion abnormality showed significant improvement compared with previous examination. The ejection fraction showed improvement to 53%. Three months after the onset of TC, echocardiography showed complete normalization of wall-motion abnormalities with an ejection fraction of 61%. Also, the QT interval was normalized. Written informed consent was obtained from the patient for publication for this case report. The study was approved by the local Institutional Review Board of our hospital (YUH-2018-09-007).

3. Discussion

We describe a patient with SS-induced TC that developed after serotonergic and dopaminergic agents were administered to improve functional impairment that occurred after ICH.

Among the various hypotheses that explain the pathophysiological mechanism of TC, catecholamine excess is the most convincing.[2,3] The human myocardium contains both, B1- and B2-adrenoreceptors,[14] and B2-adrenoreceptors are more sensitive to changes in epinephrine levels.[3,14] Paur et al[3] reported that the gradient of B2-adrenoreceptors increases from the basal to the apical segment of the heart, which explains the typical pattern of myocardial dysfunction observed in TC (transient akinesia or hypokinesia of the apical and midventricular segments with basal hyperkinesia).[1,4] Simultaneous multivessel coronary spasm of an epicardial artery could be another possible mechanism for TC.[4] Echocardiographic findings in our patient were consistent with the typical pattern of TC-associated myocardial dysfunction. Additionally, the cardiac dysfunction was transient, and the patient's ejection fraction recovered from 38% to 53% 10 days after the onset of TC. Therefore, we could confirm that our patient had developed TC.

We diagnosed our patient with SS based on the Radomski criteria,[12] which require the presence of at least 4 major symptoms or 3 major symptoms with 2 minor symptoms (major symptoms: confusion, elevated mood, coma or semi-coma, fever, hyperhidrosis, myoclonus, tremors, chills, rigidity, and hyperreflexia; minor symptoms: agitation, insomnia, tachycardia, tachypnea, diarrhea, low or high blood pressure, impaired coordination, mydriasis, and akathisia). Our patient's symptoms fulfilled 4 major and 2 minor symptoms of the Radomski criteria; thus, we could confirm that our patient showed SS-related symptoms. The patient was administered several serotonergic and dopaminergic agents; therefore, we could not accurately determine which specific drug induced SS. All the serotonergic and dopaminergic agents we used (venlafaxine, tianeptine sodium, ropinirole, carbidopa/levodopa, bromocriptine mesylate, and methylphenidate) can cause hyperactivation of the serotonergic system and precipitate SS.[11] SS causes a hyperadrenergic state leading to physiological stress[7,8] and consequent stress-induced cardiomyopathy. Additionally, the elevated serotonin level following the administration of serotonergic agents can directly overstimulate serotonin receptors in the heart, which might have contributed, at least in part, to TC observed in our patient.[4]

To date, 2 studies have reported SS-induced TC.[7,8] In 2011, Mehta et al[7] reported a case of SS-induced TC in a patient with major depressive disorder. They reported that the co-administration of monoamine oxidase inhibitors (isocarboxazid) and lithium precipitated SS in their patient. In 2012, Sasaki et al[8] reported a case of a patient with SS-induced TC in whom SS occurred following the administration of tetracyclic antidepressant (maprotiline) for the management of major depressive disorder. Therefore, to our knowledge, this is the first report describing SS-induced TC in a patient with stroke.

Notably, serotonergic and dopaminergic agents are widely prescribed during the rehabilitation of patients with stroke to control a depressed mood and to enhance rehabilitation outcomes.[10,11] Usually, the prognosis of TC is favorable when managed appropriately; however, cardiogenic shock is reported to occur in 4.2% of patients with TC, and the mortality rate is 1.1%.[15] Therefore, clinicians should be aware of the possibility of SS-induced TC in patients with stroke following the administration of serotonergic and dopaminergic agents.

Author contributions

Conceptualization: Sung Ho Jang, Jun Lee, Min Cheol Chang.
Data curation: Jong-Ho Nam, Min Cheol Chang.
Investigation: Sung Ho Jang.
Methodology: Jong-Ho Nam, Min Cheol Chang.

Writing – original draft: Min Cheol Chang.
Writing – review & editing: Min Cheol Chang.

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