

Takotsubo cardiomyopathy in a patient with oral cancer

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A patient with squamous cell carcinoma on the left mandible presented with symptoms similar to acute coronary syndrome just after surgery. The exact etiology was unclear, but following transthoracic echocardiogram, takotsubo cardiomyopathy was diagnosed. This is a rare, acute, and reversible form of heart failure, and the patient recovered completely within weeks. Related risk factors are believed to include extended surgery times and extended time under general anesthesia. Early recognition, followed by postoperative control of pain and anxiety are crucial to patient recovery.

Key Words: Oral cancer; Takotsubo cardiomyopathy; Transthoracic echocardiogram.

Takotsubo cardiomyopathy (TTC), also known as stress-induced cardiomyopathy, is a rare, acute and reversible form of heart failure [1]. We report a case of TTC in a patient with oral cancer. Following tumor ablation and reconstructive surgery, the patient presented with symptoms similar to acute coronary syndrome. After appropriate treatment, the patient made a complete recovery.

CASE REPORT

A 74-year-old male patient (height: 157.6 cm, weight: 50.7kg) was hospitalized to undergo wide excision of squamous cell carcinoma (cT2N2bM0, stage IVA) on the left mandible. One month prior to hospitalization, he received neoadjuvant chemotherapy twice. He underwent marginal mandibulectomy, left supraomohyoid neck dissection, and reconstruction with reconstruction plate

and right radial forearm free flap under general anesthesia. He had no medical morbidities including hypertension or diabetes. Preoperative laboratory findings and chest radiograph were normal. The electrocardiogram (ECG) finding was sinus arrhythmia with low voltage in frontal leads and ST elevation, but a transthoracic echocardiogram (TTE) was normal. He remained hemodynamically stable throughout the perioperative time. After surgery, the patient was transported to the intensive care unit (ICU) for postoperative care. During transport, a nasotracheal tube (NTT) remained in his airway, and ventilation was assisted with Ambu bagging (oxygen: 7 L/min) and 100% peripheral oxygen saturation (SpO₂). On arrival at the ICU, the patient's vital signs were taken. Both his blood pressure (BP) and heart rate (HR) were elevated. He complained of pain and analgesics were administered followed by opioids. BP remained high (259/115 mmHg) while HR surged (168 beats/min). He complained of persistent pain with agitating. For sedation

and pain control, dexmedetomidine was administered. Under sedation, respiratory rate and SpO₂ dropped to 7 breaths/min and 89% respectively. Because of sedatives, BP was dropped. ST elevation was showed in ECG monitor, so further evaluation, serial ECGs was checked and revealed ST elevation in the anterior and lateral leads. The cardiac markers were elevated. Myoglobin measurements surged to 1275.8 ng/ml; Troponin I measurements rose to 6.32 ng/ml; serum creatine kinase MB peaked at 55.6 ng/ml.

For further evaluation, the patient was referred to the cardiology department. Cardiologists performed TTE, although it was limited by the patient's fixed supine position and the presence of a ventilator. Results showed a dilated left ventricular (LV) with normal LV wall thickness. Akinesia of apical lateral, inferior wall and

mid-cavity with severe systolic dysfunction were observed (Fig. 1). LV ventriculogram showed an estimated ejection fraction (EF) of 25%. The features showed ischemic insult of multivessel territory and stress-induced cardiomyopathy was suspected.

The patient was transferred to a medical ICU where he was managed conservatively with inotropics, chronotropics and diuretics with hemodynamic monitoring. Dopamine 5 μ g/kg/min, dobutamine 5 μ g/kg/min, norepinephrine 0.1 μ g/kg/min were administered. He experienced a rapid clinical improvement. By the third postoperative day, previous ST-segment elevations were normalized. He was extubated on the fifth postoperative day and transferred to a general ward in the dental hospital. Troponin I levels normalized, and all laboratory test values were within normal ranges. One month later, TTE showed no evidence of cardiac ischemia and a left ventricular EF of 63%, a result similar to his preoperative result. No clinical signs of heart failure were found.

Following surgery, the patient received consolidation radiotherapy (total dose: 5040 cGy). Currently the patient is in good condition. Oral cavity lesions were healing well. Complete dentures are being prepared to provide him with masticatory function. For this case presentation, we received consent from the patient.

DISCUSSION

TTC is a rare form of reversible heart failure. The name of the syndrome comes from the shape of a Japanese octopus fishing pot, which resembles the unusual appearance of the left ventricle with hyperkinetic base and akinetic apex [2]. It is also called apical ballooning syndrome.

A diagnosis of TTC is made when all four of the Mayo Clinic Criteria are met: (i) transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid-segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always



Fig. 1. Four-and-two chamber echocardiographic views demonstrating the typical apical and mid-ventricular left ventricular wall-motion abnormalities of a patient.

present; (ii) absence of obstructive coronary artery disease or angiographic evidence of acute plaque rupture; (iii) new electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion) or modest elevation in cardiac troponin; and (iv) absence of pheochromocytoma and myocarditis [3,4].

The clinical symptoms of TTC are often identical to those of acute myocardial infarction. They include angina, dyspnea, ischemic changes on ECG, and elevated cardiac markers. Most myocardial infarctions (MIs) are the result of thrombosis or luminal stenosis and obstruction of the coronary arteries. However, coronary angiography on most patients with TTC reveals patent coronary arteries [5-7]. In this case, an invasive coronary angiography could not be performed due to the presence of the mechanical ventilator. Lacking an angiography, making a definitive diagnosis was difficult. Because the patient's preoperative echocardiogram was normal, he received supportive care only. TTC is a reversible and transient form of heart failure, while MI is irreversible. This patient recovered after a few weeks and all clinical symptoms disappeared. Cardiac markers, ECG and echocardiogram normalized. There were no abnormal findings in periodic follow-up observation.

The etiology of TTC is poorly understood, but stress is considered a risk factor [1,8-10]. It is often associated with an acute emotional event or physical stress preceding presentation [11]. Japanese investigators have found that the mental stress associated with events such as the loss of a family member or divorce contributes to the development of left ventricular apical ballooning [12,13]. Other cases have been associated with physiologic stress such as non-cardiac medical surgery, sepsis, and subarachnoid hemorrhage [13,14]. Extended operation times can cause stress in a patient. In this case, mandibulectomy, neck dissection and free flap surgery took place over a 14 hours period. Medication used for general anesthesia can also cause physical stress. During surgery, this patient's vital signs were well-maintained. However, his BP and HR were elevated on arrival in the ICU. Surgical site pain and discomfort from NTT could have been the cause.

Hypertension and tachycardia are tremendous stressors to the heart. Analgesics and sedatives were administered but vital signs were not stabilized quickly. Earlier and more aggressive interventions to control pain and anxiety would have been more appropriate.

TTC occurs most commonly in postmenopausal women aged 58-75 years [4,7]. One recent study found that physical stress was a more frequent trigger in men compared to women [15]. The present patient was a 74-year-old man. Surgery could have been a stressful experience and compared to younger patients, patients of advanced age may be more vulnerable to such stresses. The patient underwent surgery in December. He was transferred from the dental hospital to the medical hospital ICU in a process that took about 10 min. The temperature in the bridge between the two hospitals was colder than both the operating room and the ICU. Usually, patients who undergo lengthy surgeries require intensive care and are moved to an ICU adjacent to the operating room, and experience no room temperature changes. The patient may have required more energy to maintain his body temperature, which could have induced stress. Stress in various forms is considered a cause of TCC.

In conclusion, the present study report a case of TTC in a patient following surgery for oral cancer. The exact etiology of TTC was unclear in this patient, but early recognition and proper postoperative care are crucial in assuring positive outcomes.

REFERENCES

1. Gangadhar TC, Von der Lohe E, Sawada SG, Helft PR. Takotsubo cardiomyopathy in a patient with esophageal cancer: a case report. *J Med Case Rep* 2008; 2: 379.
2. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Koike H, Sasaka K. The clinical features of takotsubo cardiomyopathy. *Qjm* 2003; 96: 563-73.
3. Akashi YJ, Goldstein DS, Barbaro G, Ueyama T. Takotsubo cardiomyopathy: a new form of acute, reversible heart failure. *Circulation* 2008; 118: 2754-62.

4. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J* 2008; 155: 408-17.
5. Pavin D, Le Breton H, Daubert C. Human stress cardiomyopathy mimicking acute myocardial syndrome. *Heart* 1997; 78: 509-11.
6. Sharkey SW, Shear W, Hodges M, Herzog CA. Reversible myocardial contraction abnormalities in patients with an acute noncardiac illness. *Chest* 1998; 114: 98-105.
7. Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol* 2001; 38: 11-8.
8. Ueyama T, Kasamatsu K, Hano T, Yamamoto K, Tsuruo Y, Nishio I. Emotional stress induces transient left ventricular hypocontraction in the rat via activation of cardiac adrenoceptors: a possible animal model of 'tako-tsubo' cardiomyopathy. *Circ J* 2002; 66: 712-3.
9. Ueyama T, Senba E, Kasamatsu K, Hano T, Yamamoto K, Nishio I, et al. Molecular mechanism of emotional stress-induced and catecholamine-induced heart attack. *J Cardiovasc Pharmacol* 2003; 41(1 Suppl): 115-18.
10. Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J* 2006; 27: 1523-9.
11. Steptoe A, Kivimaki M. Stress and cardiovascular disease: an update on current knowledge. *Annu Rev Public Health* 2013; 34: 337-54.
12. Kawai S, Suzuki H, Yamaguchi H, Tanaka K, Sawada H, Aizawa T, et al. Ampulla cardiomyopathy ('Takotsubo' cardiomyopathy)--reversible left ventricular dysfunction: with ST segment elevation. *Jpn Circ J* 2000; 64: 156-9.
13. Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005; 111: 472-9.
14. Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. *J Am Coll Cardiol* 1994; 24: 636-40.
15. Schneider B, Athanasiadis A, Stollberger C, Pistner W, Schwab J, Gottwald U, et al. Gender differences in the manifestation of tako-tsubo cardiomyopathy. *Int J Cardiol* 2013; 166: 584-8.