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Anesthesia-induced Takotsubo cardiomyopathy in trigeminal neuralgia: illustrative case

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BACKGROUND Takotsubo syndrome (TS) represents a form of nonischemic cardiomyopathy characterized by sudden and temporary weakening of the myocardium. Many data suggest a primary role for sympathetic overstimulation in its pathogenesis. Nevertheless, these correlates are less easily identified during anesthesia.

OBSERVATIONS A 50-year-old female patient with a 4-year history of drug-resistant left trigeminal neuralgia. She was scheduled for surgical microvascular decompression. In the operating room, after induction of general anesthesia and oral intubation, the electrocardiogram revealed a significant ST segment elevation along with a sudden decrease in systolic blood pressure and heart rate. Administration of atropine caused a conversion into ventricular tachycardia. The advanced cardiac life support protocols were applied with prompt defibrillation and rapid recovery at sinus rhythm. A transthoracic echocardiogram revealed apical akinesia with ballooning of the left ventricle with a reduction of systolic function. An emergency coronary arteriography was performed, showing normal epicardial coronary vessels. After 4 days, echocardiography revealed normalization of the left ventricular function with improvement of the ejection fraction.

LESSONS In patients affected by trigeminal neuralgia, chronic pain can lead to a state of adrenergic hyperactivation, which can promote TS during the induction of general anesthesia, probably through the trigeminocardiac reflex.

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KEYWORDS anesthesia-induced; catecholamine; myocardial stunning; Takotsubo cardiomyopathy; trigeminal neuralgia; trigeminocardiac reflex

Takotsubo syndrome (TS) was first described in the 1990s in Japan. "Takotsubo" refers to the Japanese ceramic pot for catching octopuses, which is similar to the typical echocardiographic shape of the left ventricle found in TS. Typical manifestations of TS are apical akinesia and basal hyperkinesia at the echocardiogram, chest pain, ST segment elevation on the electrocardiogram (EKG), and normal or mildly elevated cardiac blood biomarkers of ischemia.[1] The angiographic alterations are transient and reversible and always without evidence of obstructive coronary artery disease.[2,3]

Multiple etiopathogenetic theories have been proposed. Among the most discussed theories, one concentrates on the excessive tide of catecholamines under emotional or physical stress, which activates beta- and alpha-adrenergic receptors and leads to microvascular spasms resulting in myocyte damage.[4] Moreover, a combination of sudden pain stimuli may trigger a catecholamine surge in Takotsubo cardiomyopathy.[5] Although the relevance of catecholamine excess is frequently observed in awake patients, these correlates are less easily identified during anesthesia. Nevertheless, it may be argued that inadequate control of the stress response during surgery may provoke a catecholamine excess that, in turn, may induce acute left ventricle ballooning.

Takotsubo cardiomyopathy has also been described in patients with cerebrovascular accidents, epileptic attacks, bronchial asthma exacerbations, electrophysiological studies, and during surgical

ABBREVIATIONS EKG = electrocardiogram; MVD = microvascular decompression; TCI = target controlled infusion; TCR = trigeminocardiac reflex; TS = Takotsubo syndrome.

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noncardiac procedures. However, the exact relationship with anesthesia has never been elucidated.[6] Consistent with the proposed pathophysiological mechanism, trigeminal neuralgia is linked with sudden pain and prolonged suffering that may provoke a physical and psychological stress response.

In this paper, we present a case of TS that manifested during induction of anesthesia to perform a surgical microvascular decompression (MVD) of the left trigeminal nerve in a patient with trigeminal neuralgia. We expose the peculiar clinical picture and discuss the possible underlying pathophysiological mechanisms.

Illustrative Case

We present a case of a 50-year-old female patient scheduled for an MVD who presented immediately after induction of general anesthesia with EKG and echocardiographic alterations resembling acute TS. At admission, the patient complained about a 4-year history of drug-resistant left trigeminal neuralgia. She reported no relevant comorbidities. Magnetic resonance imaging of the brain with constructive interference steady state sequences revealed a neurovascular conflict between the superior cerebellar artery and the root entry zone of the left fifth cranial nerve in its cisternal portion. MVD was indicated. An EKG showed a sinus rhythm (78 beats per minute) at preoperative evaluation. On physical examination, no signs of cardiac or respiratory impairment were observed. The patient's body mass index was 24 kg/m^2. Her American Society of Anesthesiologists physical status classification system score was I.

Thirty minutes before transfer to the operating room, premedication was administered (4 mg diazepam orally). Upon arriving in the operating room, standard monitoring commenced (EKG, oxygen saturation, noninvasive blood pressure), and all parameters were in the normal range. The patient was calm and did not report any anxiety. The placement of the peripheral venous catheter was uncomplicated and did not cause any relevant painful reaction. According to our standard protocol, induction of anesthesia is provided with a slow infusion of propofol and remifentanil, managed through target-controlled infusion (TCI). This minimizes the painful stimulation connected with propofol injection. Induction was obtained with incremental concentration steps up to a propofol TCI Schneider effect site concentration target of 4 and a remifentanil TCI Minto effect site concentration target of 2. After the complete loss of consciousness, cisatracurium (0.1 mg/kg) was administered. The procedure was painless. Oral intubation was rapidly and uneventfully performed with a GlideScope video laryngoscope. EKG revealed a significant ST segment elevation along with a sudden decrease in systolic blood pressure and heart rate. The administration of atropine (0.5 mg) caused a conversion into ventricular tachycardia. Advanced cardiac life support protocols were applied with prompt defibrillation (200 J) and rapid recovery at sinus rhythm. Hemodynamic stability was maintained with an infusion of epinephrine (0.07 mcg/kg/min). A transthoracic echocardiogram revealed apical akinesia with ballooning of the left ventricle with a reduction of ejection fraction (30%). Surgery was postponed, and the patient was successfully transferred to intensive cardiological care. Emergency coronary arteriography was performed, showing normal epicardial coronary vessels (Fig. 1). After 4 days, echocardiography revealed normalization of the left ventricular function with an improvement in the ejection fraction. The patient was transferred to the normal ward and, after 15 days, was discharged from the hospital with a diagnosis of TS with transient apical ballooning without coronary lesions.

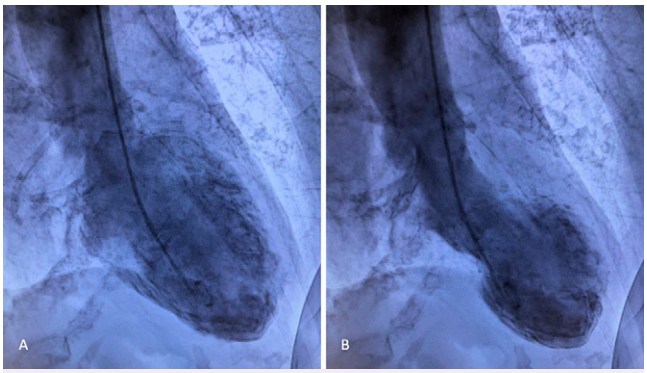

FIG. 1. Images of cardiac ventriculography. **A:** Diastole. **B:** Apical akinesia with ballooning of the left ventricle during systole.

Discussion

Observations

Takotsubo cardiomyopathy, also named "transient apical ballooning syndrome" or "stress-induced cardiomyopathy," represents a form of nonischemic cardiomyopathy characterized by sudden and transient weakening of the myocardium. The onset resembles an acute myocardial infarction. The most common manifestations are chest pain, dyspnea, syncope, and shock.[7] The EKG features ST segment elevations, particularly in anterior precordial leads, deep T-wave inversions, or anomalous Q-waves.[4]

In one of the most accepted pathogenic theories, elevated circulating levels of catecholamines may cause microvascular spasms with subsequent myocardial dysfunction and stunning.[8] Therefore, the presence of a sudden pain stimulus may trigger a catecholamine surge in TS.[5]

Concordantly, Sanai et al.,[9] in a case of transient midventricular ballooning syndrome precipitated by trigeminal neuralgia, hypothesized that catecholamine-mediated myocardial stunning was the responsible mechanism. They suggested that an episode of "*tic douloureux*" ironically led to a pain in the heart, a "*coeur douloureux*."[9]

Strittmatter et al.[10] measured catecholamine plasma levels at four different times of day in patients with trigeminal neuralgia and found a significant increase in daily mean values that correlated with the intensity and frequency of attacks and the duration of the disease. Nevertheless, the time of sampling and the time of the painful attacks often did not correspond, corroborating the hypothesis of a state of tonic catecholamine excess in trigeminal neuralgia.[10]

One plausible explanation for TS in patients with trigeminal neuralgia undergoing anesthesia could be the trigeminocardiac reflex (TCR). Indeed, intubation may cause a strong, painful stimulation of the face and mouth area and trigger painful shocks in trigeminal neuralgia.

The trigeminal nerve is the greatest of all cranial nerves and gives sensory supply to the face, scalp, mucosa of the nose and mouth, and most of the dura mater.[11] Stimulation of these territories has been linked to the activation of the TCR.[12,13] The TCR represents an important interaction between the central nervous system and heart, thus providing a deeper understanding of mechanisms related to cardiac changes during cranial surgery.[14,15]

The TCR is defined as the sudden onset of bradycardia, arterial hypotension, apnea, or gastric hypermotility during stimulation of

any of the sensory branches of the trigeminal nerve.[11] The fifth cranial nerve transmits neural impulses through the Gasserian ganglion to the sensory nucleus of the trigeminal nerve, constituting the afferent route of the reflex.[11,16] This pathway runs through the short interneuronal nerve fibers in the reticular formation of the pons, where it connects with the efferent branch in the dorsal motor nucleus of the vagus nerve (Fig. 2).[11] Experimental evidence shows that trigeminal-induced cardiovascular reflexes may originate in the trigeminal nucleus caudalis and the parabrachial nucleus, the rostral ventrolateral medulla oblongata, the dorsal medullary reticular field, and the paratrigeminal nucleus.[16,17]

TCR may occur during peripheral and central manipulation of the trigeminal nerve and Gasserian ganglion. In a retrospective study, Schaller et al.[18] demonstrated the incidence of TCR under MVD for trigeminal neuralgia. Clinical signs of TCR activation are a reduction in heart rate and blood pressure, asystole, ventricular tachycardia, fibrillation, ST-T wave alterations, and other patterns of arrhythmias.[18,19] Risk factors already known to increase the incidence of TCR include hypercapnia, hypoxemia, light general anesthesia, age (more pronounced in children), and drugs (sufentanil, alfentanil, and calcium channel blockers).

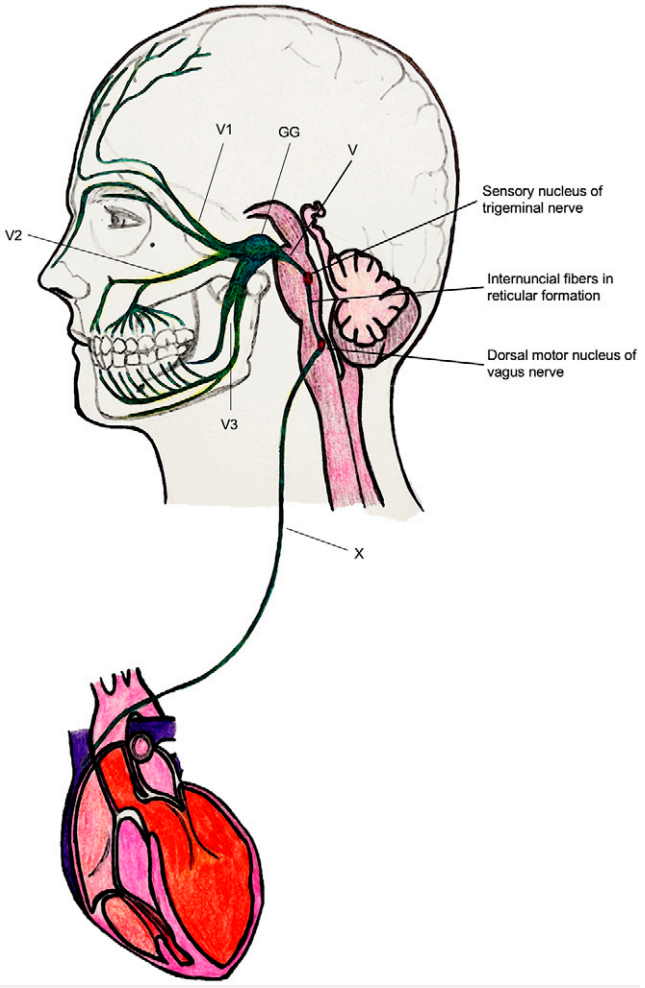

FIG. 2. Schematic representation of the trigeminocardiac reflex. The afferent branch of the reflex consists of the trigeminal nerve, which reaches the sensory nucleus from its three branches via the Gasserian ganglion. This pathway runs through the short interneuronal nerve fibers in the reticular formation of the pons, where it connects with the efferent branch in the dorsal motor nucleus of the vagus nerve. GG = Gasserian ganglion; V = trigeminal nerve; V1 = ophthalmic nerve; V2 = maxillary nerve; V3 = mandibular nerve; X = vagus nerve.

Therefore, we speculate that in our patient with trigeminal neuralgia, on a background of tonic excess of catecholamines, a TCR was triggered at the induction of anesthesia by a combination of mechanical stimulation and pain in the face and oral mucosa during intubation plus a contribution from the medication for general anesthesia.

We suggest that potential prophylaxis in these patients vulnerable to TS during anesthesia may be the administration of a low dose of propranolol, which proved to lead to a short-term reduction in heart rate, blood dosages of epinephrine, norepinephrine, cortisol, and clinical pain responses.[20] Nevertheless, this does not affect blood pressure, cardiac output, and total vascular resistance.[20]

Lessons

TS is a rare disorder that is probably often misdiagnosed. Its pathogenesis and prevalence remain unclear, despite the clear role of acute stress-induced myocardial dysfunction. In patients affected by trigeminal neuralgia, chronic pain can lead to a state of adrenergic hyperactivation, which can generate TS during the induction of general anesthesia, probably through the TCR. Considering these observations, acute treatment with low-dose beta-blockers could be indicated in these patients.

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References

1. Aizawa K, Suzuki T. Takotsubo cardiomyopathy: Japanese perspective. *Heart Fail Clin.* 2013;9(2):243–247.
2. Sato H, Tateishi H, Dote K, et al. Tako-tsubo like left ventricular dysfunction due to multivessel coronary spasm. In: Kodama K, Haze K, Hori M, eds. *Clinical Aspects of Myocardial Injury: From Ischemia to Heart Failure.* Tokio Kagakuhyoronsha; 1990:56–64.
3. Liu S, Dhamee MS. Perioperative transient left ventricular apical ballooning syndrome: Takotsubo cardiomyopathy: a review. *J Clin Anesth.* 2010;22(1):64–70.
4. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med.* 2005;352(6):539–548.
5. Kilbourn KJ, Ching G, Silverman DI, McCullough L, Brown RJ. Clinical outcomes after neurogenic stress induced cardiomyopathy in aneurysmal sub-arachnoid hemorrhage: a prospective cohort study. *Clin Neurol Neurosurg.* 2015;128:4–9.
6. Consales G, Campiglia L, Michelagnoli G, et al. Acute left ventricular dysfunction due to Tako-tsubo syndrome after induction of general anesthesia. *Minerva Anestesiol.* 2007;73(12):655–658.
7. Madhavan M, Borlaug BA, Lerman A, Rihal CS, Prasad A. Stress hormone and circulating biomarker profile of apical ballooning syndrome (Takotsubo cardiomyopathy): insights into the clinical significance of B-type natriuretic peptide and troponin levels. *Heart.* 2009;95(17):1436–1441.
8. Artukoglu F, Owen A, Hemmerling TM. Tako-tsubo syndrome in an anaesthetised patient undergoing arthroscopic knee surgery. *Ann Card Anaesth.* 2008;11(1):38–41.

9. Sanai R, Mazhari R, Zeman RK, Choi BG. Coeur douloureux: transient midventricular ballooning syndrome precipitated by trigeminal neuralgia. *J Am Coll Cardiol.* 2009;54(15):1478.
10. Strittmatter M, Grauer MT, Fischer C, et al. Autonomic nervous system and neuroendocrine changes in patients with idiopathic trigeminal neuralgia. *Cephalalgia.* 1996;16(7):476–480.
11. Schaller B, Probst R, Strebel S, Gratzl O. Trigeminocardiac reflex during surgery in the cerebellopontine angle. *J Neurosurg.* 1999;90(2):215–220.
12. Chowdhury T, Sandu N, Meuwly C, Cappellani RB, Schaller B. Trigeminocardiac reflex: differential behaviour and risk factors in the course of the trigeminal nerve. *Future Neurol.* 2014;9:41–47.
13. Chowdhury T, Sandu N, Schaller B, Meuwly C. Peripheral trigeminocardiac reflex. *Am J Otolaryngol.* 2013;34(5):616.
14. Chowdhury T, Sandu N, Sadr-Eshkevari P, Meuwly C, Schaller B. Trigeminocardiac reflex: current trends. *Expert Rev Cardiovasc Ther.* 2014;12(1):9–11.
15. Chowdhury T, Meuwly C, Sandu N, Cappellani RB, Schaller B. Coronary spasm in neurosurgical patients and role of trigeminocardiac reflex. *Neurol Res Int.* 2014;2014:974930.
16. Schaller BJ, Buchfelder M. Trigemino-cardiac reflex in skull base surgery: from a better understanding to a better outcome? *Acta Neurochir (Wien).* 2006;148(10):1029–1031.
17. Ohshita N, Nakajo N, Takemura M. Characteristics of the trigeminal depressor response in cats. *J Neurosci Res.* 2004;76(6):891–901.
18. Schaller B. Trigemino-cardiac reflex during microvascular trigeminal decompression in cases of trigeminal neuralgia. *J Neurosurg Anesthesiol.* 2005;17(1):45–48.
19. Cornelius JF, Sadr-Eshkevari P, Arasho BD, et al. The trigeminocardiac reflex in adults: own experience. *Expert Rev Cardiovasc Ther.* 2010;8(7):895–898.
20. Light KC, Bragdon EE, Grewen KM, Brownley KA, Girdler SS, Maixner W. Adrenergic dysregulation and pain with and without acute beta-blockade in women with fibromyalgia and temporomandibular disorder. *J Pain.* 2009;10(5):542–552.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Bonomo, Mazzaglia, Rubiu, Murabito, Amato, Ferroli. Acquisition of data: Bonomo, Murabito. Analysis and interpretation of data: Bonomo, Ferroli, Gemma. Drafting the article: Bonomo, Mazzaglia, Murabito, Amato. Critically revising the article: Bonomo, Mazzaglia, Murabito, Amato, Ferroli, Gemma. Reviewed submitted version of manuscript: Bonomo, Mazzaglia, Murabito, Amato. Approved the final version of the manuscript on behalf of all authors: Bonomo. Administrative/technical/material support: Bonomo. Study supervision: Ferroli, Gemma.

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