Takotsubo following Severe Anaphylactic Reaction During Anesthesia Induction

ABSTRACT

Introduction: Takotsubo cardiomyopathy (apical ballooning or broken heart syndrome) is a reversible left ventricular dysfunction due to apical asynergy that occurs typically after sudden emotional stress in a subject without coronary disease. Anaphylaxis is a severe, life-threatening, generalized hypersensitivity reaction, most often starting with urticaria and/or angioedema, that may involve cardiovascular and respiratory systems. Cardiovascular symptoms, including hypotension, cardiac arrhythmia and chest pain, are presumably linked to cardiac mast cell mediator release.

Case Report: We describe the case of a woman who experienced a profound reversible cardiomyopathy with typical features of Takotsubo's syndrome during an anaphylactic reaction.
Conclusion: Exposure to catecholamines and beta-receptor agonists used routinely during procedures and diagnostic tests can precipitate all the features of stress cardiomyopathy, including cardiac isoenzyme elevation and rapidly reversible cardiac dysfunction. These observations strongly implicate excessive sympathetic stimulation as central to the pathogenesis of this unique syndrome.

*Keywords: Takotsubo syndrome, Ballooning apical, Anaphylaxis, C*atecholamines*, Case report*

1. INTRODUCTION

“Takotsubo cardiomyopathy (TTC), also known as broken heart syndrome, apical ballooning syndrome, or stress cardiomyopathy, occurs when a stressful emotional or physical event causes the left ventricle of the heart to dilate, leading to acute heart failure” (1). “TTC in the setting of anaphylaxis is rare, but has been reported previously. Most of these reports have been in patients treated with significant epinephrine therapy. Dose-dependent adverse effects of epinephrine on cardiac function have been described, and these are now backed up by recently elucidated elaborate molecular mechanisms” (2).
“Anaphylaxis and Takotsubo syndrome are linked in cases of severe allergic reactions where stress and catecholamine surges play critical roles. Takotsubo cardiomyopathy, can occur as the body releases high levels of catecholamines in response to anaphylaxis. This surge can provoke cardiac dysfunction, particularly in the setting of allergic reactions where inflammatory mediators exacerbate coronary spasms. This relationship is part of a complex known as the ATAK complex (Adrenaline, Takotsubo, Anaphylaxis, and Kounis syndrome), which highlights how anaphylactic reactions can instigate cardiac events, sometimes leading to simultaneous coronary and myocardial involvement in otherwise healthy individuals” (19).

We present the case of a patient who suffered from stress-induced cardiomyopathy with severe left ventricular dysfunction immediately after the initiation of anesthesia for a rotator cuff surgery.

2. **CASE PRESENTATION**

A 61-year-old female was scheduled for a right rotator cuff surgery. Preoperative evaluation revealed a nervous patient quoting a very unpleasant experience regarding prior uneventful operations (appendectomy, tonsillectomy, cure of herniated disc).

Her medical history included bipolar disorder under sodium valproate. Cardiovascular and respiratory clinical examination was normal on admission (blood pressure (BP): 119/67 mmHg, heart rate (HR): 69 beats per minute, and SpO2 98%). Preoperative 12-lead ECG, chest X-ray, and routine laboratory tests were normal. She was under intense stress the day before her surgery.

Upon arrival at the operating room, vital signs recordings were BP: 123/71 mmHg, HR: 78 bpm, and SpO2 96% (room air). The procedure involved making an interscalene right block with 10 ml of Ropivacaine, then injection 30 mg of Ketamine, 300 mg of Propofol, 10 mg of Sufentanil, and 40 mg of Atracurium. Then, endotracheal intubation was performed successfully.

Soon after the induction, she presented a prolonged sudden decrease in blood oxygen level to 70%, with global cyanosis, bilateral rhonchi perceptible at auscultation, and hypotension at 70/30 mmHg with no peripheral pulse. Later, she had a nearly complete rash on her body, red-brown and urticaria-like (Figure 1).

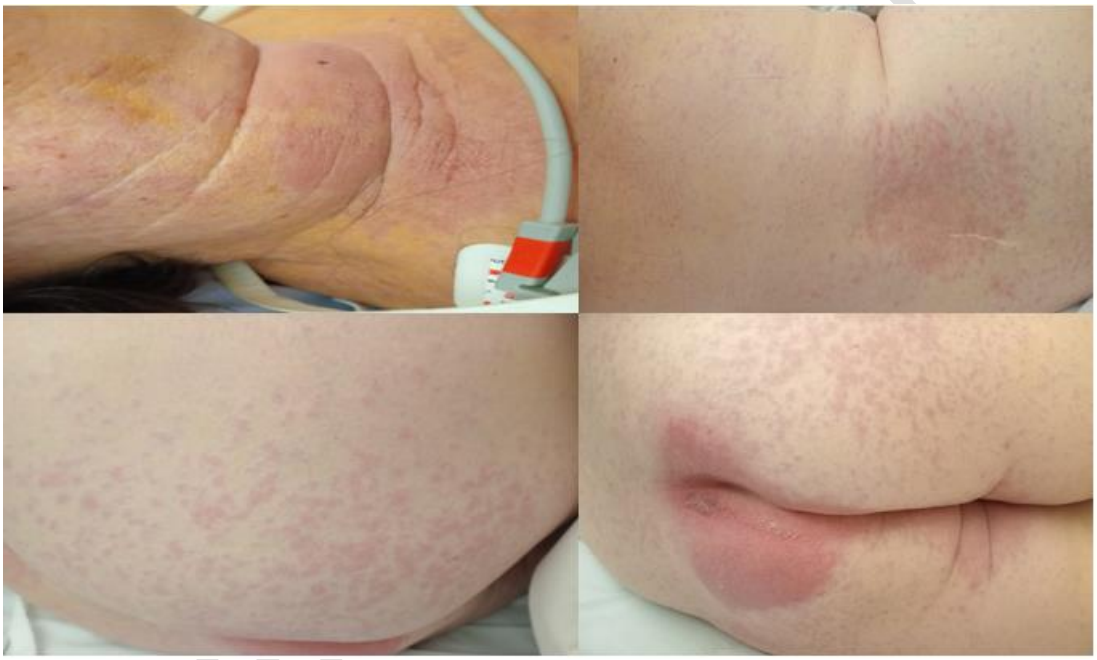

Figure 1 showing a skin rash urticaria and red-brown in color.

The initial management consisted of an increase in the fraction of inspired oxygen (FiO2) to 100% , alveolar recruitment, protective lung ventilation , Salbutamol by the endotracheal intubation tube, Vascular filling with crystalloids and introduction of vasopressors: epinephrine in titration (1 mg in total) and norepinephrine 16 gamma/ml (5 ml/h max).

The electrocardiogram showed a regular sinus rhythm with repolarization abnormalities.

The patient was then admitted to the intensive care unit. Within the next hour, she presented a new episode of vascular collapse refractory to vascular filling, associated with a
severe hypoxia and bilateral pulmonary overload on chest X-ray suggestive of acute pulmonary edema.

A transthoracic echocardiogram (TTE) was immediately performed and showed signs of global left ventricular failure (LV EF evaluated at 30%) associated with slight ballooning of the left ventricle.

The electrocardiogram performed on admission to intensive care showed ST segment elevation in leads V1-V4. Biologically: troponins at 1400 ng/l, BNP at 8740 ng/l, d-dimers at 2500 ng/ml and arterial blood gas showed mixed acidosis.

The evolution was favorable: left ventricular function partially recuperated, but akinesia persisted in the septum and free wall of the left ventricle (Figure 2). ST segment elevation disappeared, but T wave inversion was observed in the anterior and lateral territories.

Treatment with antiplatelet agents and low-molecular weight heparin was initiated, as part of the usual treatment for acute coronary syndrome.

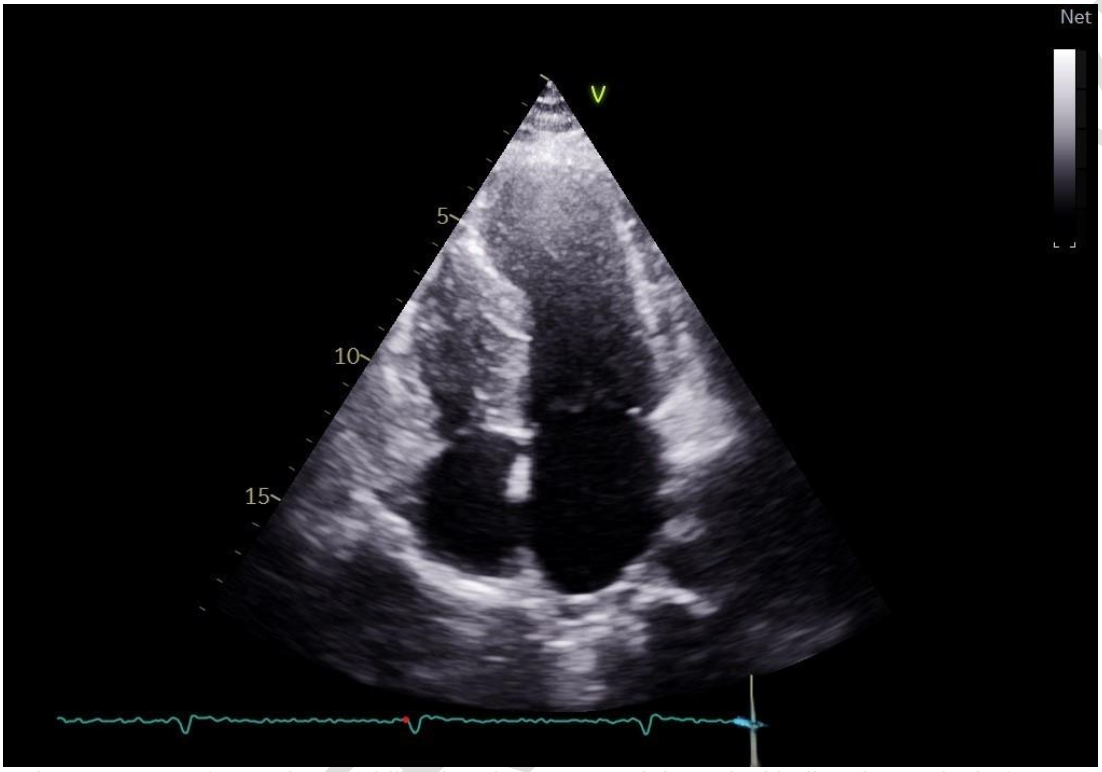

Figure 2: TTE after patient stabilization demonstrated the apical ballooning typical of stress cardiomyopathy.

There were no significant lesions observed in the coronary angiography. The ventriculography showed apical akinesia giving a ballooning aspect. The left ventricular ejection fraction was calculated at 48%.

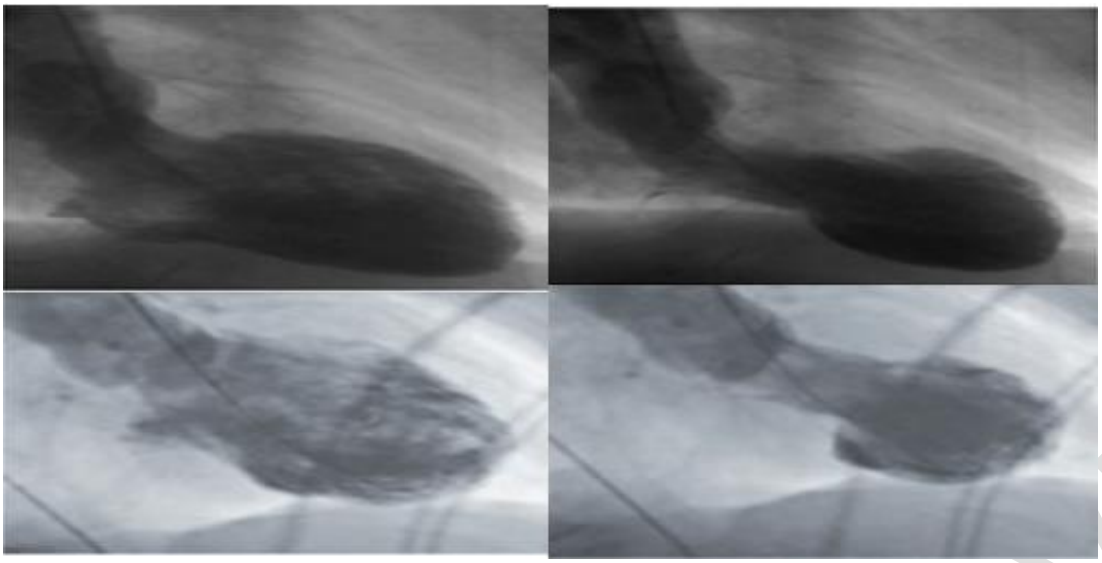

Figure 3: Ventriculography typical of Takotsubo syndrome performed after normal coronary angiography.

The patient, asymptomatic, returned home on the sixth day with beta-blocker and angiotensin-converting enzyme (ACE) inhibitor. She was reviewed after 1 month with an echocardiogram showing a remarkable improvement in left ventricular ejection fraction and regression of apical akinesia.

3. DISCUSSION

“Takotsubo cardiomyopathy (TTC), also known as stress-induced cardiomyopathy or broken heart syndrome, is a transient cardiac condition that mimics the symptoms of an acute coronary syndrome (ACS) but typically lacks obstructive coronary artery disease” (3).
“Originally described in Japan in the early 1990s, TTC is named for the Japanese "takotsubo" pot, which has a shape similar to the left ventricular ballooning observed in affected patients” (14). TTC predominantly affects postmenopausal women and is triggered by sudden physical or emotional stress.

“Patients with TTC commonly present with acute chest pain, elevated cardiac biomarkers, and characteristic left ventricular apical ballooning on imaging. Although it is often reversible, TTC can result in severe complications, including heart failure, arrhythmias, and thromboembolism” (3).

“Takotsubo syndrome is increasing in incidence, which may reflect the rising prevalence of modern life stressors and the greater awareness and detection of the condition by the clinical cardiology community” (3,5).
“The exact pathophysiological mechanism of takotsubo cardiomyopathy remains unclear. Its pathophysiology varies, including coronary vasospasm, microcirculatory dysfunction, catecholamine surge, and sympathetic overdrive” (4,5).

“It has been suggested that the response to catecholamines (such as epinephrine and norepinephrine, released in response to stress) leads to heart muscle dysfunction that contributes to takotsubo cardiomyopathy” (6). “The effects of this toxicity can be greater in those with a predisposition to anxiety or panic disorders” (7). “Delivery of catecholamines (epinephrine, norepinephrine) via circulating blood and through direct delivery from cardiac nerves is increased by the stimulation of stress control centers of the brain” (7).

“Plasma catecholamine levels in patients with TTC are approximately two to three times higher compared with patients presenting with myocardial infarction, suggesting that this is the primary mechanism underlying TTC” (11).

During an emotionally or physically stressful event (such as the allergic reaction), brain centers initiate the sympathetic nervous pathways and increase myocardial activity.

“In the perioperative setting, there are a number of potential factors, which may contribute to the hyper-catecholaminergic state. Agarwal *et al*, in a review, identified factors such as inadequate depth of anesthesia, exogenous administration of epinephrine, anaphylaxis secondary to release of inflammatory mediators (Kounis syndrome) and ergometrine use after cesarean as potentially contributing to a hyper-catecholaminergic state” (12). Hessel estimated that TTC occurs in approximately 1/6700 cases (10). In Hessel’s review, of 131 cases, 37% presented during anesthesia or surgery.

“Excessive catecholamine stimulation has a toxic effect on cardiac muscle cells which creates necrosis of the contractile units of cells similarly seen during acute myocardial infarction” (6,8). “The increased workload of cardiac muscle created by the stimulation of catecholamines, increases the need for more blood and oxygen to these muscles to sustain function. When these demands are unable to be met, the heart is starved of blood and oxygen and begins to die” (7). Included in the cytotoxic sequela of catecholamine toxicity is the molecular transformation of the cardiac myocyte to produce apical stunning.

“Factors favoring myocardial ischemia as part of an anaphylactic reaction in general anesthesia are the patient's cardiovascular background, possible ventilatory difficulties linked to bronchospasm that may lead to a lack of oxygenation of the patient, hyperexcitability and increased inotropism induced by histamine stimulation of myocardial H2 receptors, and the inotropic and chronotropic effect on beta 1 adrenaline receptors” (9).

“Worldwide, adrenaline is considered the first-choice therapy in the international guidelines for the management of anaphylaxis. However, the heart and cardiovascular apparatus are strongly involved in anaphylaxis; for that reason, there are some cardiac conditions and certain anaphylaxis patterns that make epinephrine use problematic without adequate heart monitoring” (13).

“The onset of Kounis syndrome, Takotsubo cardiomyopathy, or the paradoxical anaphylaxis require great attention in the management of anaphylaxis and adrenaline administration by clinicians, who should be aware of the undervalued evolution of anaphylaxis and the potential cardiologic complications of epinephrine administration. Numerous case reports and studies describe the unexpected onset of cardiac diseases following epinephrine treatment, despite the latter being the recommended therapy for anaphylaxis” (13).

“The literature reports that this syndrome is known as ATAK complex (Adrenaline, Takotsubo cardiomyopathy, Anaphylaxis, and Kounis syndrome) which is a complex clinical syndrome often associated with endogenous or exogenous adrenaline. Due to its rapid onset, severity and therapeutic challenges, it deserves significant attention from clinicians. This article reports a typical case of Kounis syndrome type 1 combined with stress cardiomyopathy (ATAK complex) triggered by anaesthesia-induced allergy” (15,16).

“Therefore, if a patient is diagnosed with Kounis syndrome, caution should be exercised in using epinephrine to prevent ATAK. This indirectly indicates that the concept of ATAK has not been widely discussed, but is of some importance in clinical practice. There is currently no systematic treatment plan for ATAK. Antihistamines, antiplatelet agents, relief of vasospasm and prompt opening of occluded vessels are important methods of treating Kounis syndrome. Treatment of Kounis syndrome is challenging because both cardiac and allergic symptoms need to be treated simultaneously. Drugs given to treat the cardiac manifestations may worsen the allergy, and drugs given to treat the allergic symptoms may worsen the cardiac dysfunction” (15,16).

“According to the literature, the use of intravenous corticosteroids such as hydrocortisone at a dose of 5 mg/kg and H1 and H2 antihistamines such as diphenhydramine at a dose of 1 to 2 mg/kg and ranitidine at a dose of 1 mg/kg is sufficient for type I. Vasodilators such as calcium channel blockers and nitrates may stop the hypersensitivity vasospasm. Intravenous or sublingual nitroglycerin seems reasonable and safe in patients with Kounis syndrome if blood pressure is satisfactory. Bolus administration of antihistamines should be done slowly as these drugs may induce hypotension and compromise coronary flow” (16,17).

“Care should be taken to ensure that all infusible drugs, including antihistamines, steroids and cardiac drugs, are alcohol-free. Since anaphylactic reactions can also induce takotsubo syndrome, measurement of anaphylactic inflammatory mediators such as histamine, tryptase, chymase, leukotrienes, thromboxane, and PAF, or the use of corticosteroids or mast cell stabilizers for prevention and treatment, may shed light on its etiology and pathophysiology” (18).

4. CONCLUSION

This case report discusses a 61-year-old woman undergoing surgery who experienced a unique medical condition termed the ATAK complex, involving adrenaline, takotsubo, anaphylaxis, and Kounis syndrome. Following an episode of anaphylaxis and the inadvertent administration of intravenous epinephrine, the patient exhibited symptoms of takotsubo

cardiomyopathy. The case underscores the importance of prompt recognition and management of this rare but potentially life-threatening condition. The discussion highlights the challenges in diagnosing and treating Kounis syndrome, emphasizing the need for increased awareness and caution in epinephrine administration. Further research is suggested to refine the diagnostic and treatment guidelines for this complex syndrome.