Stress-Related Cardiomyopathy in a 31-Year-Old Woman

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Stress-related cardiomyopathy (SRC), initially referred to as Tako-Tsubo cardiomyopathy and later as apical ballooning syndrome, has been largely observed in postmenopausal women. It is frequently precipitated by a stressful event.

Keywords: Apical ballooning syndrome, “broken heart syndrome,” stress-related cardiomyopathy, Tako-Tsubo cardiomyopathy.

This is a case report of a 31-year-old woman who experienced SRC immediately after a bilateral mastectomy.

The syndrome of Tako-Tsubo cardiomyopathy was first described in the Japanese literature in 1990 and is now typically referred to as stress-related cardiomyopathy (SRC). This syndrome is usually identified in postmenopausal women and is characterized by acute left ventricular (LV) failure in the absence of obstructive coronary disease. It is often observed in the setting of major stress. We present a case of SRC in a 31-year-old woman, in the setting of major breast surgery, to increase the awareness of SRC and to highlight the need to include SRC in the differential diagnosis for patients who present with an apparent acute coronary syndrome.

Case Report
A 31-year-old woman, gravida 2, para 2, was scheduled for bilateral radical mastectomy for the treatment of invasive ductal carcinoma. In addition, sentinel node biopsies and the insertion of bilateral tissue expanders were planned. Her medical history revealed she had chronic allergic rhinitis, which she was treating with flunisolide nasal inhalation spray (25 µg in each nostril twice daily) and loratadine (10 mg/d), as well as lower back pain due to a bulging disk at L5-S1, which she was treating as needed with naproxen (500 mg twice daily) and tramadol hydrochloride (up to two 50-mg tablets 4 times daily). The patient reported she had experienced shortness of breath as a result of a drug allergy to prochlorperazine. She denied any cardiac, pulmonary, gastrointestinal, renal, or endocrine problems and reported that she had never smoked or used illicit drugs. On physical examination, her blood pressure was 109/76 mm Hg, pulse rate was 75/min, body temperature was 37.1°C, and oxygen saturation was 97% on room air. Her weight and height were 66.6 kg and 167.6 cm, respectively, and body surface area was 1.7 m². She had no jugular vein distention, calf discomfort, or pedal edema. On heart auscultation, there was a regular rate and rhythm, with no murmurs or clicks. Her chest was clear to auscultation, with equal breath sounds in all fields. Her laboratory values were within normal limits at the time of surgery.

Her preoperative electrocardiogram (ECG) was normal (Figure 1), as was a chest x-ray film. A multigated acquisition (MUGA) scan done the day before surgery revealed a normal LV systolic function (ejection fraction or EF of 54%). The MUGA scan was ordered by the Hematology-Oncology Service as a prerequisite to chemotherapy. Doxorubicin (Adriamycin) and paclitaxel (Taxol) were to be given postoperatively. Doxorubicin in accumulative dosages can cause cardiotoxicity.

The patient requested that bilateral mastectomies, sentinel node biopsies, and insertion of tissue expanders all be done as 1 surgical procedure. This resulted in a surgical procedure lasting more than 6 hours. The surgery took place without incident. A total intravenous anesthesia technique was administered using propofol (Diprivan) and remifentanil (Ultiva). She was relatively stable throughout the procedure but did require a phenylephrine drip for the last 1.5 hours of the case for pressure support.

After surgery, the patient was extubated and was responding to verbal commands before transfer to the postanesthesia care unit (PACU). Upon arrival in the PACU, the patient was noted to be ashen and pale. She was connected to the monitor and found to be tachycardic, with a heart rate of 130/min, and blood pressure of 65/35 mm Hg. She was minimally responsive and complained of being thirsty and feeling cold. Approximately 1 minute later, she became unresponsive and cyanotic, with a loss of pulse and blood pressure. Cardiopulmonary resuscitation was initiated immediately, and the patient was reintubated. Multiple pressors were given during the code, including dopamine, norepinephrine, epinephrine, and dobutamine.

A chest x-ray revealed florid bilateral pulmonary
edema. A bedside transthoracic echocardiogram revealed global hypokinesis with a LV ejection fraction of approximately 20%, but no other abnormalities (Figure 2). Unsure of the mechanism for the patient’s cardiopulmonary arrest, the care team considered a differential diagnosis of transfusion-associated acute lung injury or anaphylaxis, and she was given methylprednisolone (Solu-Medrol) and diphenhydramine (Benadryl). Sepsis was also considered, and the patient was started on a regimen of broad-spectrum antibiotics. (Antibiotics were stopped after 2 days of therapy when cultures were found to be negative for bacteria). An ECG revealed tachycardia and T-wave inversion in leads II, III, aVF, and V3 through V6 (Figure 3). A flow-directional pulmonary catheter was inserted at the bedside. Initial readings revealed a pulmonary capillary wedge pressure of 34 mm Hg, central venous pressure of 12 mm Hg, systemic vascular resistance of 700 dynes · s/cm² and a reduced cardiac index of 2.29 L/min/m2 while she was receiving pressors.

She was taken to the cardiac catheterization laboratory for further evaluation. A right heart catheterization confirmed the elevated right- and left-sided filling pressures. The decision was made not to perform left heart catheterization because of an elevated serum creatinine level, the absence of ST segment elevation, and the suspicion for SRC. Given the findings on echocardiography and the right heart catheterization, the most likely cause of this patient’s acute episode was thought to be acute LV failure. She was continued on an intravenous drip infusion with dobutamine and dopamine and was slowly weaned off these medications over the next 48 hours. Troponin levels peaked at 5.09 ng/mL.

Once the treatment with pressors was discontinued, she was started on a regimen of a low-dose β-blocker—extended-release metoprolol (25 mg/d)—and an angiotensin-converting enzyme (ACE) inhibitor (first captopril, then lisinopril, 10 mg/d) for afterload reduction. A left heart catheterization performed 5 days after surgery revealed no obstructive coronary disease, further supporting the diagnosis of SRC. Before discharge, the patient’s LV function had returned to normal by echocardiography.

The patient was seen for follow-up in the Cardiology Clinic 1 month later and underwent a repeated echocardiogram and ECG. Her echocardiogram revealed normal LV function with an EF of 64%. Her ECG was normal.
with sinus rhythm, normal axis, and normal R-wave progression (Figure 4).

**Discussion**

Stress-related cardiomyopathy is characterized by a sudden, reversible reduction in LV systolic function. It was first described in Japan in 1990 and was labeled “Tako-Tsubo syndrome,” because the characteristic appearance of the left ventricle in end systole resembles a ceramic octopus trap (Figures 5 and 6). This cardiomyopathy has also been labeled as apical ballooning syndrome, but the term currently accepted for this syndrome is stress-related cardiomyopathy.

- **Etiology.** The etiology and pathophysiology of SRC...
are poorly understood. Several mechanisms have been reported as potential physiologic causes for SRC including catecholamine-mediated cardiotoxicity, impaired myocardial perfusion, LV outflow tract obstruction, and/or myocyte injury.\textsuperscript{1-5} More recently, hypercontractility of the basal portion of the heart causing outflow tract or mid-ventricular obstruction and subsequent apical ischemia has been suggested as the primary mechanism for SRC. This may be particularly relevant in elderly women with a sigmoid-shaped interventricular septum that predispose them to outflow tract obstruction.

Although the mechanism of SRC remains unclear, what does seem to be prevalent is the association of SRC with emotional or physical triggers. Myocardial stunning due to elevated levels of catecholamines at the time of a stressful event is thought to play a role.\textsuperscript{9,10} Observation of this finding has been noted in at least two-thirds of the patients in whom SRC was diagnosed. Dimsdale\textsuperscript{9} reviewed data from earthquake victims and noted that although stressors may trigger acute onset of LV failure, it is less clear that stress “causes” the event. Neurologists have also identified an association between subarachnoid

**Figure 5.** Left Ventriculogram Revealing Hyperdynamic Basal Contraction With Akinesis
Arrows at right indicate akinesis of mid and apical segments.
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**Figure 6.** Left Ventriculogram With Akinesis of Midsegment and Preserved Function at Base and Apex
Arrows at right indicate akinesis of midsegment.
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hemorrhage and SRC. Multiple studies have looked at potential causes for SRC, but findings have not been consistent. Prasad et al listed the stressors reported to trigger SRC, as seen in the Table.

Ninety percent of all reported cases of SRC have occurred in postmenopausal women between the ages of 58 and 75 years. Case reports show that the youngest reported case was in a 10-year-old and the oldest in an 88-year-old. Most patients experienced emotional problems at the time of onset of symptoms, which led to the syndrome also being identified as the “broken heart syndrome.” Wittstein et al pointed out that women do seem to be more vulnerable to sympathetically mediated myocardial stunning. The reason for the syndrome occurring in women is unclear, although reduction in estrogen levels may be a contributing factor.

- **Diagnosis.** In 50% to 60% of the patients with SRC, chest pain will be the presenting symptom. In some cases, dyspnea may be the initial presenting symptom. Physical examination will reveal rales, tachycardia, hypotension, and elevated jugular venous pressure. The ECG will demonstrate ischemic changes with ST-segment elevation in 46% to 100% of cases, which may mimic ST-segment elevation myocardial infarction (STEMI). In fact, 1% to 3% of patients who present with a clinical picture of STEMI actually have SRC. T-wave inversion, as observed in our case (see Figure 3), is found in 15% to 44% of patients. The finding of Q waves on ECG is rare. The ECG changes are usually transient, resolving in 3 to 4 months. Cardiac biomarkers are often elevated with a moderate rise in troponin levels, which peak at 24 hours. When taken to the cardiac catheterization laboratory, the patients are found to have normal coronary anatomy. The left ventriculogram often reveals the Tako-Tsubo appearance with ballooning of the cardiac apex (see Figures 5 and 6).

Given that the clinical presentation of SRC is often indistinguishable from a myocardial infarction, 4 criteria have been outlined by the Mayo Clinic for the diagnosis of SRC. These include:

1. Transient hypokinesis, akinesis, or dyskinesis of the LV midsegments 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, present.

2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.

3. New electrocardiographic abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin levels.

4. Absence of pheochromocytoma and myocarditis.

- **Treatment.** Initial treatment is typically the same as that for STEMI and includes continuous ECG monitoring and placement of an intra-aortic balloon pump during the acute phase in patients with cardiogenic shock. Once the diagnosis of SRC is determined, therapy is supportive. Medical therapy includes the use of inotropes for treatment of severe LV failure and cardiogenic shock. Intravenous heparin and aspirin are given in the acute phase. Longer term anticoagulation with warfarin (Coumadin) should be administered for thromboembolic protection in the presence of persistent LV dysfunction. The patient is typically discharged on a regimen of a β-blocker and an ACE inhibitor, to be continued for 3 to 6 months until there is full recovery of LV function. The value of treatment with an ACE inhibitor or a β-blocker beyond this period is unclear, as no studies have been done evaluating the efficacy of long-term use in this setting. Annual follow-up is recommended because the course of SRC is unknown.

- **Prognosis.** Systolic LV dysfunction associated with SRC is usually transient, returning to normal within days to weeks. In those patients who survive the initial hospitalization, prognosis is good and is similar to that in the general population. In-hospital mortality is 1% to 2%. In a small group of patients with physical triggers of major surgery or illness, the prognosis is somewhat worse. In up to 10% of patients, SRC may recur.

The recurrent theme found throughout our literature search is that this syndrome occurs primarily in postmenopausal women. Complete recovery of LV function is also observed.

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### Table. Stressors That May Trigger Stress-Related Cardiomyopathy

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<th>Stressor</th>
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<tr>
<td>Death or severe illness or injury of a family member, friend, or pet</td>
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<tr>
<td>Surprise party</td>
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<td>Move to a new residence</td>
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### Emotional stress

- Death or severe illness or injury of a family member, friend, or pet
- Receiving bad news—diagnosis of a major illness, daughter’s divorce, spouse leaving for war
- Severe argument
- Public speaking
- Involvement with legal proceedings
- Financial loss—business, gambling
- Car accident
- Surprise party
- Move to a new residence

### Physical stress

- Noncardiac surgery or procedure—cholecystectomy, hysterectomy
- Severe illness—asthma or chronic obstructive airway exacerbation, connective tissue disorders, acute cholecystitis, pseudomembranous colitis
- Severe pain—fracture, renal colic, pneumothorax, pulmonary embolism
- Recovering from general anesthesia
- Cocaine use
- Opiate withdrawal
- Stress test—dobutamine stress echocardiogram, exercise sestamibi
- Thyrotoxicosis
Our patient’s clinical syndrome is uncommon among young, otherwise healthy women. Although she did not exhibit the Tako-Tsubo feature often seen on left ventriculography, she did have other characteristics commonly found in SRC. Those symptoms consisted of pulmonary edema, diffuse T-wave abnormality, severe LV dysfunction, and elevated troponin levels. Surgery appeared to be the trigger. As also occurs in SRC, our patient had normal coronary anatomy and made a complete recovery of LV function in a brief time. The impact of the breast tumor on this patient’s hormones is unknown, but the patient denied variation in her menstrual cycle at any time before surgery. She did not have preoperative chemotherapy that could have altered natural hormone production. We do not have access to presurgical laboratory results of her hormones to indicate otherwise. As is typical in this syndrome, she recovered normal LV function quickly, demonstrating the reversibility of the syndrome. Prolonged catecholamine release during a lengthy surgery may have contributed to our patient’s response. Whether increased oxygen demand in the presence of tachycardia played a part is also unknown. As suggested by Grayburn and Hills, postoperative pain, withdrawal of anesthesia, or shifts of intravascular volume may contribute to cardiac events in patients undergoing noncardiac surgery. In this case, remifentanil anesthesia was discontinued, and she was maintained on a phenylephrine drip at the end of the case. These circumstances, however, usually surround acute myocardial infarction in the perioperative setting rather than SRC.

The importance of emotional stress should also be considered in this case. Our patient had no risk factors for early-onset breast cancer and no family history of breast cancer. She was found to have an invasive, aggressive form of the cancer. In addition, the patient’s perception of the loss of her breasts and her new self-image may have been contributing emotional factors. Her long-term treatment will include β-blockade through the completion of reconstructive surgery.

Conclusion

This case highlights an atypical presentation of SRC in a premenopausal woman, seemingly precipitated by a major surgical procedure. Stress-related cardiomyopathy should be considered in the differential diagnosis when a sudden onset of LV failure is observed in patients in the perioperative setting, especially in women. It is not known if the number of cases of SRC is increasing or if there is now an increased awareness of the syndrome that was not previously known. It is unusual in a 31-year-old woman. With increased awareness of this syndrome, earlier identification and institution of appropriate treatment may lead to improved clinical outcomes for this patient cohort. Recently published articles seem to bear out similar experiences and outcomes with complete recovery.15,16

REFERENCES


AUTHORS

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