Case series

Two case studies of cardiac arrest occurring in medically fit patients undergoing radical hysterectomy for cervical cancer

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ABSTRACT

We report case histories of two young women who had an intraoperative cardiac arrest, potentially caused by preoperative emotional stress, while undergoing open radical hysterectomy for cervical cancer. Neither had any history of heart disease or other comorbidities. Takotsubo cardiomyopathy, a form of stress cardiomyopathy characterized by acute reversible ventricular dysfunction that can occur in the perioperative period, was the cause in one patient. A vasovagal episode during the exploration of the abdomen was the cause in the other. Successful resuscitation and stabilisation of both patients made it possible to continue the surgery and successfully complete both procedures. Takotsubo cardiomyopathy should be considered in any patient showing significant preoperative stress who has a cardiac arrest, even if there is no preoperative morbidity. It is difficult to differentiate from a vasovagal episode intraoperatively. Surgical and anaesthetic teams should be aware of importance of countering severe preoperative stress.

1. Introduction

We describe two cases of cardiac arrest which occurred during radical hysterectomy for cervical cancer at the Royal Hospital for Women in Sydney. Both occurred in otherwise healthy young women, and both patients had their cardiac arrest on assessment of the peritoneal cavity, prior to undertaking any surgery. The cardiac arrest was caused in one patient by the 'broken heart syndrome', also known as Takotsubo cardiomyopathy, stress-induced cardiomyopathy, or apical ballooning syndrome. The other patient suffered severe sudden sinus bradycardia rapidly degenerating to asystole, likely caused be a vasovagal episode.

Takotsubo syndrome is a stress related cardiomyopathy which can occur in otherwise healthy patients. This heart condition is of interest to gynaecologists, because almost 90% of cases occur in women (Gianni et al., 2006; Pilgrim and Wyss, 2008; Sharkey et al., 2011). First described in 1990 by Sato and colleagues in Japan, "Takotsubo" stands for octopus (Tako) pot (Tsubo) (Shthu, 1990), after the resemblance of the left ventricle to a traditional Japanese octopus trap during systole.

Takotsubo cardiomyopathy presents with ECG changes mimicking a myocardial infarction with ST-segment elevation, it occurs in the absence of coronary artery obstruction (Kurowski et al., 2007), is associated with elevated troponin titers, and usually with ballooning of the left ventricle due to impairment of apical systolic contraction. The pathogenesis of this disorder is not well understood. Physical or emotional stress triggering a catecholamine increase, or administration of catecholamines, may be responsible for microvascular spasm and endothelial dysfunction causing the cardiomyopathy (Nef et al., 2007).

It has also been suggested that affective or anxiety disorders may be predisposing factors (Templin et al., 2015). The diagnosis of Takotsubo Cardiomyopathy is based on the Mayo Clinic diagnostic criteria (Scantlebury and Prasad, 2014) (Table 1).

2. Case presentations

2.1. Case 1

A 43-year-old woman, gravida1 para 0, presented with post-coital bleeding. She had a grossly apparent lesion on the cervix and was diagnosed with a FIGO Stage IbI squamous cell carcinoma of the cervix. She had no significant medical history, did not take any regular medication, and was adopted, so had no knowledge of her family history. She

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Table 1

Mayo Clinic Criteria for Takotsubo cardiomyopathy.

1. 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 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.
4. Absence of:
a. Pheochromocytoma
b. Myocarditis

did not plan to have any children. Preoperative chest radiography and routine laboratory studies were normal. A PET/CT scan showed no evidence of suspicious lymph nodes or distant metastases.

In the two weeks prior to her admission, the patient suffered severe anxiety, including several episodes of panic. Our clinical psychologist noted a Distress Thermometer reading of 10 out of 10 preoperatively. The distress thermometer is an assessment tool originally developed to identify cancer patients at significant risk of needing psychological support (Roth et al., 1998).

On May 25th, 2016, she underwent a midline laparotomy, radical hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy. She developed bradycardia following the opening of the abdominal wall, while exploration of the peritoneal cavity was being undertaken. The heart rate rapidly dropped from 75 beats per minute to asystole.

Chest compression was commenced, and she was given a total of 2400 µg of atropine. Spontaneous rhythm and cardiac output returned within 90 s. An arterial line was inserted. The patient remained stable and the decision to continue surgery was made jointly between the surgical and anaesthetic teams. The procedure was completed without any further issues. The operating time was 160 min, and the blood loss was 350 ml. The pathology showed a squamous cell carcinoma of the cervix which was 20 mm wide and invaded to a depth of 3 mm. There were 27 negative lymph nodes.

The cause of the cardiac arrest was attributed to a vasovagal episode due to vagal stimulation during peritoneal exploration. Postoperative ECG and echocardiogram were normal. She was discharged on the 5th post-operative day and referred to a cardiologist for outpatient follow-up, but she did not attend. She remained alive and well at 58 months.

2.2. Case 2

A 37-year-old female was diagnosed with an 8 cm FIGO Stage Ib3 adenocarcinoma of the cervix. Her last PAP smear 5 years earlier was normal. She had no co-morbidities and was on no regular medication. She was gravida one, para one and had regular periods. An MRI did not show any evidence of parametrial or bladder invasion.

Her family history included a paternal grandmother who had breast cancer at a young age. Based on her family history, and the increased likelihood of ovarian metastases with adenocarcinoma, the decision was made to proceed with a midline laparotomy, radical hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy (Shimada et al., 2006; Hacker et al., 2013).

The patient was assessed preoperatively by our clinical psychologist, and the distress thermometer recorded a score of 9 out of 10. This severe anxiety was also noted preoperatively by the anaesthetic team, and they administered the anxiolytic agent Midazolam prior to induction of anaesthesia.

A midline laparotomy was performed on May 8th, 2017, and during routine assessment of the peritoneal cavity, before any clamps were applied to the uterus, the patient developed sinus bradycardia; her heart rate dropped from 80 beats per minutes to asystole within 1 min. Prior to asystole, she was given 600 µg of atropine intravenously.

Cardiopulmonary resuscitation was initiated as per Australian Resuscitation Council guidelines, during which she received 2 min of chest compression and 1 mg of adrenaline intravenously. Return of sinus rhythm and cardiac output were achieved after 2 min, whereupon the cardiac monitor displayed sinus tachycardia of 150 bpm, new profound ST elevation of 8 mm on the ECG tracing and a systolic blood pressure of 70 mm Hg on non-invasive recording. Surgery was temporarily suspended, and she was treated supportively without further need for adrenaline while her condition stabilised. After 30 min, the ST segment elevation was less than 1 mm and her heart rate and blood pressure were within the normal range. The anaesthetic team was happy for the operation to proceed.

On exploring the pelvis, the uterine corpus was not enlarged, but the cervix was expanded to about 8 cm and there was a suspicious right external iliac lymph node. This was sent for frozen section and metastatic adenocarcinoma was reported. The patient then underwent radical hysterectomy, bilateral salpingo-oophorectomy, and resection of bulky pelvic lymph nodes (Derks et al., 2017). The surgery was completed uneventfully. The patient required low doses of metaraminol to maintain normotension during the later stages of the surgery, which continued into the recovery period. The operation lasted for 250 min including the time lost from the cardiac event; the blood loss was 450 ml. The pathology showed an 80 mm wide, 70 mm long poorly differentiated adenocarcinoma which was confined to the cervix but invaded to a depth of 16 mm. Vascular space invasion was present, and 2 of 8 left and right external iliac lymph nodes were positive. There were 5 negative common iliac nodes.

Post-operatively, she was reviewed by cardiology. Her troponin titre initially rose from 2 to 301 ng/L (ULN 14 ng/L), before falling back to normal within 24 h. Her transthoracic echocardiogram suggested segmental impairment of left ventricular systolic function with mid and apical akinesis typical of Takotsubo Cardiomyopathy (Fig. 1). She was admitted to the Coronary Care Unit for cardiac telemetry and was treated with an ACE inhibitor (Ramipril 2.5 mg) and a beta blocker (Bisoprolol 2.5 mg). Given her recent surgery, and suspected diagnosis, she was not given any antithrombotic treatment.

A subsequent coronary angiogram showed normal coronary arteries. A repeat transthoracic echocardiogram at 48 h showed improvement in the LV systolic function, and an echocardiogram at outpatient follow-up at 6 weeks showed normal left ventricular systolic function. The patient was counselled about the incident and subsequent management and was discharged on post-operative day 5.

She was treated with pelvic chemoradiation 6 weeks postoperatively. She was reviewed by her cardiologist 6 months following the event and she had returned to her usual function with no cardiac symptoms. She was alive with lung and cerebellar metastases at 37 months.

3. Discussion

Cardiac arrest requiring cardiopulmonary resuscitation (CPR) is a major public health problem; one event occurs every 90 s in the US (Cooper et al., 2006). Cardiac arrest in the operating theatre is a rare event with an incidence ranging from 1.1 to 34.6 cardiac arrests per 10,000 anaesthetics (Braz et al., 2006; An et al., 2011). There is a wide variation in the reported incidence, but the case fatality of intraoperative cardiac arrest has remained consistently high at approximately 60–80% since the 1950s (Goswami et al., 2012).

Takotsubo cardiomyopathy plays a special role in intraoperative cardiac arrest since it is a reversible left ventricular dysfunction and has a much lower mortality (Hessel, 2016; Struzkova et al., 2014; Kraft et al., 2017; Bhojraj et al., 2014). It is also an exception since patients can have no comorbidities, like the case we described, and it is therefore difficult to anticipate. The fact that we saw two cases of intraoperative cardiac arrest within a 12-month period prompted this report.

In some cases, an acute emotional or physical stressor can be
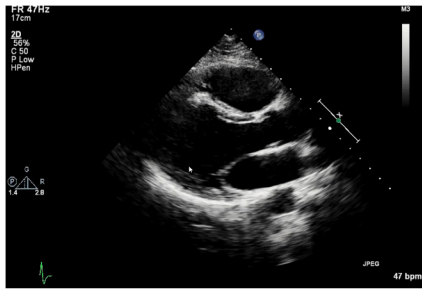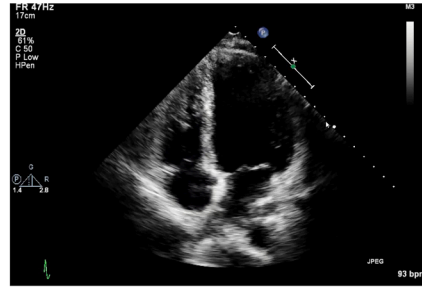
a) Parasternal long axis view
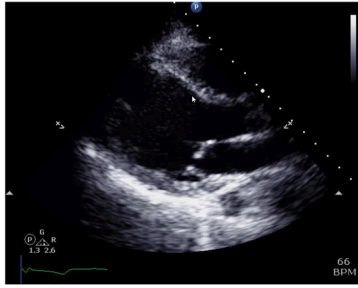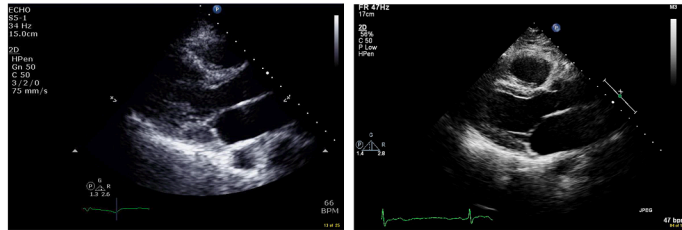
b) Apical 4 chamber
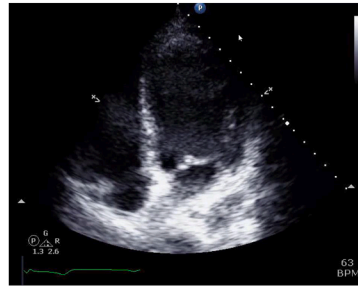
c) Parasternal long axis view, 1 month later

d) Apical 4 chamber, 1 month later

e) Parasternal long axis view in systole – TTE 1
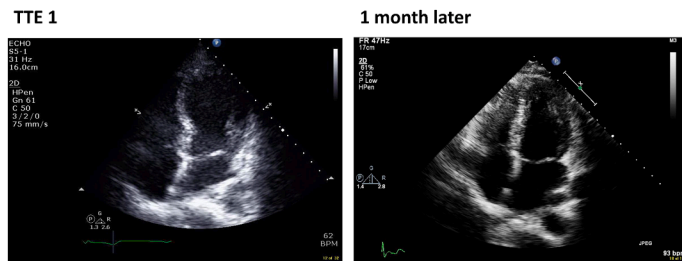(left) and TTE 1 month later (right)

f) systole, apical 4 chamber

Fig. 1. Two-dimensional transthoracic echocardiograms obtained from Patient 2 postoperatively and one month after the event. a) showing a short clip of a parasternal long axis view of patient 2 on the postoperative echocardiogram. The left ventricle is dilated and there is mild to moderate segmental impairment of systolic function. The mid and apical segments are involved, there is basal sparing, consistent Takotsubo cardiomyopathy. b) short video clip of the 4-chamber view on the postoperative echocardiogram. The left ventricle is dilated with mild to moderate segmental impairment of systolic function, basal segments are spared thereby giving the typical "apical ballooning" appearance in diastole. c) short video clip of the parasternal long axis view, 1 month after surgery; the left ventricle is normal size with normal systolic function. d) short video clip of the apical 4 chamber view 1 month after surgery; normal size and systolic function of the left ventricle. e) image - parasternal long axis view in systole postoperatively (left) and 1 month later (right). The first image demonstrates the lack of contraction in the mid and apical segments in systole; there is normal LV contraction on the right image. f) image - apical 4 chamber view showing the left ventricle in systole postoperatively (left) and 1 month later (right). The first image demonstrates the lack of contraction in the mid and apical segments in systole; there is normal LV contraction on the right image.

recognized as a triggering factor for Takotsubo cardiomyopathy (Wang et al., 2015; Szardien et al., 2013; Lyon et al., 2008). The diagnosis of a gynaecological malignancy combined with the anxiety related to the incipient surgery, on top of the increasing pressure of work and modern life, may trigger Takotsubo cardiomyopathy unexpectedly. Young people are often under physical and/or mental stress, particularly in larger cities. As such, the incidence of Takosubo Cardiomyopathy in this particular cohort of young, otherwise healthy women, warrants attention (Reimann and Lohmann, 2013).

In young patients, physical stress rather than mental stress may trigger Takotsubo cardiomyopathy. Such stressors may include drugs, trauma, anaesthesia, surgery, chronic pain, subarachnoid hemorrhage, smoking, allergic reactions, high blood pressure, and asthma (Wang et al., 2015). If physical stressors are combined with mental stress, such as that caused by a gynaecological cancer diagnosis, the combination may increase the likelihood of a cardiac arrest during a procedure. Whereas our cases had anaesthesia and surgery, they were otherwise in good health and neither smoked nor took recreational drugs.

Vigilant psychological assessment should be included in case notes of all new patients with a gynaecological cancer. The literature does not provide sufficient evidence for a risk stratification approach or pre-treatment with beta blockers for patients with a high stress score, but it does suggest the team (anaesthetists and surgeons) should be more aware of warning signs and manage triggers with caution (Hessel, 2016).

The clinical manifestations of Takotsubo cardiomyopathy and acute myocardial infarction are similar, so Takotsubo cardiomyopathy may be misdiagnosed as an acute myocardial infarction. Treatment and prognosis are quite different in the two entities. More than 95% of patients with Takotsubo cardiomyopathy have a good prognosis with full recovery of left ventricle function. Serious complications such as heart failure, malignant arrhythmia, and death are rare.

Medical treatment during the postoperative period should be in conjunction with a cardiologist. As catecholamine-mediated cardiotoxicity is one of the pathophysiological mechanisms of Takotsubo cardiomyopathy, beta receptor blockers and angiotensin-converting enzyme inhibitors are a favourable treatment option rather than thrombolytic agents, coronary artery stents, or long-term antiplatelet or lipid-lowering drugs (Fazio et al., 2008).

It is not possible to be certain whether a patient has Takotsubo cardiomyopathy in the acute intraoperative situation. Ventricular morphology with apical ballooning cannot immediately be assessed with a ventriculogram and echocardiogram (Kawai et al., 2007). Patients have elevated cardiac enzymes and changes in the ECG similar to acute myocardial infarction (e.g. ST segment elevation and T-wave inversion). Differential diagnosis in this situation includes segmental ventricular dysfunction secondary to adrenaline administered according to the advanced life support protocol.

Cardiac arrest in the first case was caused by a reflex mediated vasovagal episode. Similar to Takotsubo cardiomyopathy, a precipitating event or situation such as emotional stress, trauma, or pain is usually identifiable. In our case, exploration of the peritoneal cavity must have promoted the parasympathetic drive, although it was not different to any other exploration. Echocardiographic changes like those seen in Takotsubo cardiomyopathy are not present in vasovagal syncope.

In the situation of an intraoperative cardiac arrest, Resuscitation Council guidelines should be followed, although in the specific situation of Takotsubo cardiomyopathy, adrenaline may be disadvantageous, or may even aggravate the condition.

In these two cases, the immediate question was whether the procedure should be continued or cancelled. In both cases, radiation therapy would have been a reasonable option. However, each patient was young and in a stable condition after sinus rhythm was restored. It was the decision of the anaesthetic team to continue with the surgery, and both procedures were completed without further incident.

In summary, we present two cases of cardiac arrest occurring in otherwise healthy young women at the time of exploration of the peritoneal cavity prior to radical hysterectomy for cervical cancer. One case was considered to be a vasovagal episode, and the other a case of Takotsubo cardiomyopathy. In both cases, the common factor was severe preoperative anxiety.

4. Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Bernd C. Schmid: Conceptualization, Methodology, Investigation, Writing - original draft. **Rex Yuan:** Data curation, Investigation, Writing - review & editing. **Leonie Watterrson:** Investigation, Writing - review & editing. **Jennifer Yu:** Investigation, Writing - review & editing. **Neville Hacker:** Writing - review & editing, Supervision, Project administration, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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