CASE REPORT

Takotsubo cardiomyopathy and anaesthesia: Case report and review of the literature

H.D. de Boer a,*, L.H.D.J. Booij b

a Department of Anaesthesiology and Pain Medicine, Martini Hospital, Groningen, The Netherlands
b Department of Anaesthesiology, Pain Medicine and Palliative Care, Radboud University Medical Centre, Nijmegen, The Netherlands

Received 12 March 2013; accepted 17 April 2013
Available online 21 June 2013

KEYWORDS
Tako-tsubo; Pseudocholinesterase deficiency; Cardiomyopathy

Abstract Takotsubo cardiomyopathy is an acute syndrome characterized by cardiac failure from disturbances in the contractility of the left ventricle. It is presumably caused by sympathetic over stimulation. We describe a case of postoperatively developed Takotsubo cardiomyopathy in a 69-year-old female. The syndrome developed in connection with awareness during complete residual paralysis. The literature on this syndrome is reviewed and implications for anaesthesia described.

© 2013 Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor. Published by Elsevier España, S.L. All rights reserved.

PALABRAS CLAVE
Takotsubo; Déficit de pseudocolinesterasa; Miocardiopatía

La miocardiopatía de Takotsubo y la anestesia: caso clínico y evaluación de la bibliografía

Resumen La miocardiopatía de Takotsubo es un síndrome agudo que se caracteriza por una insuficiencia cardíaca debida a alteraciones de la contractilidad ventricular izquierda. Posiblemente derive de una sobreestimulación simpática. Presentamos el caso de una mujer de 69 años con miocardiopatía de Takotsubo que se produjo en el postoperatorio. Durante la parálisis residual completa, el síndrome apareció cuando la paciente recuperó la consciencia. Se analiza la bibliografía con respecto a este síndrome y se describen las implicaciones anestésicas.

© 2013 Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor. Publicado por Elsevier España, S.L. Todos los derechos reservados.

Takotsubo cardiomyopathy is an acute syndrome of cardiac failure due to disturbances in the contractility of the left ventricle wall. It is presumably evoked by sympathetic over activity from physical or psychological stress. Cases are described in relation to anaesthesia and surgery, but also on relation to other stressful situations. Therefore stress should be prevented to occur at induction, during and after anaesthesia.

* Corresponding author.
E-mail address: hd.de.boer@mzh.nl (H.D. de Boer).
Case report

A 69-year-old healthy female (80 kg, 176 cm, 25.8 kg/m², ASA class 2) was admitted for elective microscopic removal of a vocal cord polyp. Her medical history revealed three uncomplicated gynaecologic surgical procedures, two of which were performed under general and one under spinal anaesthesia.

Preoperative physical and laboratory examination revealed no abnormalities and a standard general intravenous (propofol TCI and remifentanil) anaesthetic procedure was chosen. Standard monitoring of respiratory and haemodynamic parameters was performed. Neuromuscular function was monitored with a TOF Watch SX (Organon, Oss, The Netherlands). Induction was uncomplicated and the endotracheal intubation was performed under neuromuscular blockade with mivacurium 0.25 mg/kg (total 20 mg). During the procedure signs of hypoxia or cardiovascular changes were not seen. At the end of surgery neuromuscular monitoring showed two posttetanic count (PTC) responses, which is a profound neuromuscular blockade. This was surprising because the duration of the surgical procedure, which was 53 min, exceeded the usual duration of action of mivacurium. Since the duration of action of mivacurium depends on plasma-cholinesterase activity the existence of a plasma-cholinesterase deficiency was suspected.

The patient was transferred to the Intensive Care Unit where anaesthesia was maintained with intravenous midazolam and fentanyl and the lungs artificially ventilated. Neuromuscular monitoring was continued and after 9 h and 55 min neuromuscular monitoring showed the recovery to a train-of-four >0.9. The patient was extubated without problems. Routine ECG and blood analysis (by ICU protocol) were performed. ECG showed changes in the ST-segment suspicious for myocardial infarction and blood analysis showed a mild increase in troponine (1.71 μg/l, normal values 0–0.014 μg/l). Clopidogrel and aspirin treatment was started according to the existing local protocol for treatment of acute myocardial ischaemia. Echocardiography, coronary angiography and MRI imaging were performed and showed ballooning of the left ventricle wall and diagnosed the existence of a Takotsubo cardiomyopathy without coronary abnormalities. Further evaluation showed a markedly low plasma cholinesterase activity (2860 U/l, normal 4000–10,000 U/l) explaining the prolonged effect of mivacurium. Retrospectively it was noticed that sedation during the Intensive Care episode had been insufficient and patient reported to have been awake and extremely anxious for some time. We hypothesized that this may have resulted in extreme emotional stress leading to the Takotsubo cardiomyopathy. After detailed explanation the patient was discharged from the hospital in good condition. Follow up eleven months later was without residual effects.

Discussion

Prolonged effect of succinylcholine and mivacurium as a result of low plasma cholinesterase activity has been frequently described in anaesthesia. The cause of such low activity can be inherited low production of the enzyme or presence of an aspecific cholinesterase with decreased activity. Experience of residual paralysis is stressful and can lead both to physical and psychological complications. The treatment of residual paralysis is artificial ventilation or in case of use of non-depolarizing muscle relaxants reversal with cholinesterase inhibitors. During residual paralysis, anaesthesia or deep sedation should be maintained until the neuromuscular blockade has disappeared. It is important to prevent occurrence of psychological stress.

On the other hand, in the postoperative period in apparently healthy persons cardiovascular complications may occur. Its incidence in the non-cardiac surgery population is estimated to be around 1%. Although in most patients there are cardiac risk factors, in some there are no such indicators. Sometimes a perioperative ECG alteration with slight increase in cardiac enzymes without coronary angiography abnormalities is observed. In our patient, the confluence of both, the insufficient depth of sedation leading to awareness and the stress this event produced, might develop the stress-related Takotsubo cardiomyopathy.

Literature review

Incidence

In Japan a Takotsubo syndrome is diagnosed in 1–2% of the hospital admissions for chest pain, and in the USA the syndrome is diagnosed in 2–2.2% of the patients with an ST-segment elevation, symptoms of acute myocardial infarction, or unstable angina. Presumably the incidence is underestimated. The syndrome especially develops in women of the post-menopausal age group of 50–70 years, presumably as a result of decreased oestrogen production. One of the possible reasons is that the cardiac vagal tone and the baroreflex sensitivity are decreased in postmenopausal female. However, the syndrome is also found in younger age groups and in male. In one study the syndrome was found in 28% of patients admitted to a non-surgical intensive care unit. In many of Takotsubo patients was later a malignancy detected.

Pathogenesis

The pathogenesis of the Takotsubo syndrome is not known. Catecholamine induced cardiac myotoxicity, coronary vasospasm, microvascular dysfunction, outflow obstruction of the left ventricle, and cardiac imbalance of the autonomic nervous system are considered possible causes. Because of the observed high catecholamine concentration is due to excessive sympathetic nervous system stimulation from emotional or physical stress this is considered the most likely causative factor. This thought is strengthened by the fact that in Japan there was an increase in its incidence during recent earth quakes. Furthermore, it was found that the catecholamine levels during the acute phase of a Takotsubo episode is two to three times higher than during an acute myocardial infarction, and 20 times higher than in healthy people. These increased levels remain for more than a week and the catecholamines involved have been demonstrated to be produced in the heart. It is known that high levels of catecholamines can produce damage to...
cardiac muscle cells. Especially the apex is more sensitive for catecholamines than other areas. Vasospasm and micro-vascular dysfunction are less likely causes because they used to result in longer lasting effects and cannot be induced by administration of acetylcholine. Genetic predisposition is not excluded. In female strong emotional stress frequently precedes the syndrome; in male patients it is more frequently the result of physical stress. Also administration of drugs with a strong sympathetic stimulating action like amphetamine, atropine, dobutamine, or adrenaline cannot result in Takotsubo syndrome. In some cases there are no clear factors.

### Symptoms

In 76% of the Takotsubo cases hypertension exists before its development. The syndrome simulates an acute coronary syndrome with pre-cordial pain, dyspnoea and changes in the ECG (elevation or depression of the ST-segment, reversed T-wave and prolonged QTc-interval) and slightly increased levels of cardiac enzymes. As a result of the left ventricle wall contractility alteration, heart failure can occur with pulmonary oedema and pulmonary hypertension.

### Types of Takotsubo cardiomyopathy

Based on the anatomic location of the disorder there are 4 types of the syndrome described. The most common is the classic apical ballooning. The second is the rarely occurring reversed type with a hyperdynamic apex and akinesia of the basal segments of the left ventricle. In the third type is the middle of the left ventricle involved with the base and apex saved. The fourth type is characterized by localized abnormal motility of part of the left ventricle wall, most frequently the front wall.

### Diagnosis

In the past the diagnosis was frequently missed because it was difficult to obtain heart catheterization, echocardiography and other imaging examinations of the heart. However, nowadays it is much more easily diagnosed by the typical image of the ballooning heart characterizing the transient dysfunction of the middle and apical segment and the hyperkinesia of the basal segments. These abnormalities result in the ballooning of the apex during systole. This image remains for 4–8 weeks. In most cases there is none (in 81% of cases) or only mild (19%) stenosis of the coronary arteries. The Mayo clinic criteria for the diagnosis of Takotsubo cardiomyopathy are the general accepted guidelines and are described in Table 1. In 70% of the patients with Takotsubo an increased catecholamine level is detected.

### Differential diagnosis

Because the symptoms resemble acute myocardial ischaemia is this the most frequent differential diagnosis.

### Complications and prognosis

As a result of the change in ventricle wall contractility cardiogenic shock developed in 6.5%, heart failure in 3.8–44%, dynamic intra-ventricular obstruction in 13–18%, severe mitral valve insufficiency, ventricular arrhythmia, formation of apical thrombosis, rupture of the left ventricle wall, or sudden death in 5.2% of the cases.

A mortality of 9–10% is observed during the first 30 days. Another study showed an overall mortality of 1% and a reoccurrence of the syndrome in 11% of patients.

### Treatment and prevention

During the acute phase aspirin, clopidogrel, nitrates, heparin and β-blockers are indicated. Coronary angiography and echocardiography must be performed to exclude coronary obstruction. When the diagnosis Takotsubo cardiomyopathy is confirmed β-blockers and angiotensin converting enzyme inhibitors (ACE-inhibitors) are used. The β-blockers decrease stress responses; combination of α and β blockers solve the ST-changes in the ECG. Further treatment is symptomatic with special attention to cardiogenic shock, arrhythmias and thrombi formation and emboli. Administration of diuretics and vasodilators are indicated when heart failure occurs. Sometimes cardiac support in order to increase cardiac output with intra-aortic balloon pumping is necessary. Sympathetic stimulating drugs like dobutamine and dopamine are contra-indicated. Cardiac and haemodynamic monitoring use to be needed during several days.

The occurrence of Takotsubo cardiomyopathy can be decreased by blockade of α and β-adrenergic receptors before and during anaesthesia.

### Takotsubo cardiomyopathy and anaesthesia

Many cases of Takotsubo cardiomyopathy described in the literature have occurred in the peri-operative period. Anxiety and fear for anaesthesia and surgery, stress from endotracheal intubation, pain from surgical stimulation and postoperative pain might play an important role because they release catecholamines. Takotsubo cardiomyopathy is not only observed in relation to general anaesthesia, but also to loco-regional anaesthesia, and especially after administration of vasoactive medication (adrenalin, phenylephrine, ephedrine, dopamine, etc.) and possibly anticholinergic drugs (atropine). However, loco-regional anaesthesia in combination with a heavy sedative premedication are advisable in patients known to have had a Takotsubo syndrome. During general anaesthesia higher levels of aldosterone, ACTH and cortisol can be observed.
of aldosterone can result in cardiac dysfunction.\textsuperscript{79} Also increase in the cardiac biomarker brain natriuretic peptide (BNP) is less under loco-regional anaesthesia.\textsuperscript{80} The administration of catecholamines for the treatment of hypotension of bradycardia might theoretically also evoke an attack of Takotsubo. Severe postoperative pain\textsuperscript{91,82} and the stress from postoperative residual paralysis\textsuperscript{83} have been described as evoking factors. The case should be cancelled if Takotsubo occurs before or immediately after the induction of anaesthesia. Only when the ventricle wall motility and ventricular function have completely recovered can the case be scheduled again. In this situation the case should in our opinion be probably performed under protection with β-blockers and close cardiovascular monitoring. A heavy sedative premedication should be administered and outpatient surgery prohibited. Patients who have suffered from the cardiomyopathy probably needed deep anaesthesia before new stressful manipulations like endotracheal intubation or surgery.\textsuperscript{84} Vasoactive and cardiotoxic medications must be avoided in such patients.\textsuperscript{58,85,86} Connection of Takotsubo cardiomyopathy and anaphylactoid reactions during anaesthesia has been described in a case report.\textsuperscript{58,87} For its treatment atropine and catecholamines were used.

Takotsubo cardiomyopathy may occur during and after anaesthesia as a result of stressful responses. These demands for avoidance of stress before, during and after the procedures.

Conflict of interest
The authors declare no conflicts of interest.

References
Takotsubo cardiomyopathy and anaesthesia


