Takotsubo cardiomyopathy associated with sepsis due to *Streptococcus pneumoniae* pneumonia

Shuren Geng, Dan Mullany and John F Fraser

ABSTRACT

A 65-year-old woman was transferred from another hospital with a diagnosis of acute myocardial infarction associated with shock. An initial electrocardiogram (ECG) showed ST-segment elevation in leads V_1–V_6. A transoesophageal echocardiogram showed akinesis of the distal anterior septum and apical regions and hyperkinesis of the basal segments, with an ejection fraction of 20%–25%. The coronary angiogram showed trivial coronary disease. By Day 6 of admission, the ECG showed normal left ventricle size and systolic function, with an ejection fraction of 65% and no regional abnormalities of wall motion. Sputum examination subsequently revealed typical *Streptococcus pneumoniae*. Our case demonstrates for the first time an association between sepsis and takotsubo cardiomyopathy. We analyse the possible role of sepsis and the systemic inflammatory response syndrome caused by severe infection as the initial causative mechanism of this syndrome.

Crit Care Resusc 2008; 10: 231–234

Clinical record

A 65-year-old woman was referred for emergency coronary angiography from another hospital where she had been diagnosed with acute myocardial infarction and acute pulmonary oedema. Her past medical history included type 2 diabetes and hypertension, but she had no clinical history of coronary artery disease. On the day before presentation, she had been normally active during the day but developed central chest pain during the evening, which was not relieved by repeated self-administration of her husband's nitrate spray. Her condition deteriorated, and she developed orthopnoea with blood-stained sputum. While being transferred via ambulance, she had several episodes of self-limiting ventricular tachycardia.

On arrival in the emergency department, the patient was noted to be in respiratory distress, with blood pressure of 214/124 mmHg, heart rate of 110 beats/minute, and Spo_2 of 90% while breathing 6.1 L/min supplemental oxygen. An initial electrocardiogram (ECG) showed ST-segment elevation in leads V_1–V_6 (Figure 1A). Respiratory function deteriorated rapidly, and she developed pulmonary oedema followed by respiratory arrest. She was intubated, mechanically ventilated and received tenecteplase for presumed ST-segment elevation myocardial infarction.

The patient underwent emergency transfer to our hospital. On arrival, her blood pressure was 110/60 mmHg, heart rate was 106 beats/min, and Pao_2 was 56 mmHg while ventilated with 100% oxygen. A second ECG, recorded within 6 hours of the first, showed non-specific T wave changes (Figure 1B). A transthoracic echocardiogram showed severe left ventricular dysfunction with an ejection fraction of 20%–25% with apical akinesis. Results of laboratory investigations are shown in Table 1. The patient underwent emergency coronary angiography, which showed trivial coronary disease. An intra-aortic balloon pump (IABP) was inserted via the right femoral artery for hypotension and severe ventricular dysfunction which persisted despite high-dose inotropes. Transoesophageal echocardiography after angiography showed akinesis of the distal anterior septum and apical regions and hyperkinesis of the basal segments (Figure 2). Takotsubo cardiomyopathy was diagnosed.

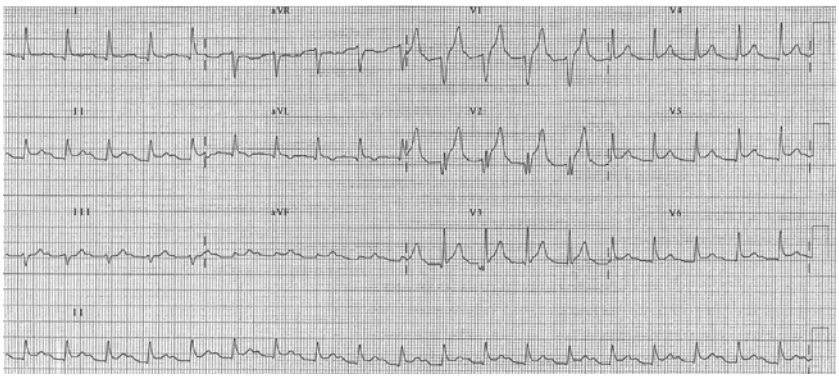
The IABP was removed the following day. By Day 6, a transthoracic echocardiogram showed normal left ventricle size and normal systolic function, with an ejection fraction of 65% and no regional abnormalities of wall motion. Peak serum concentration of troponin I was 3 μg/L (reference range [RR], ⩽ 0.2 μg/L), and of creatine kinase was 153 U/L (RR, < 200 U/L).

Streptococcus pneumoniae with high-level resistance to penicillin was grown from the endotracheal tube aspirate. Chest x-ray revealed bilateral areas of opacification, predominantly in the lower and middle lobes. Blood cultures showed no growth. The patient was treated empirically with vancomycin and ticarcillin–clavulanate.

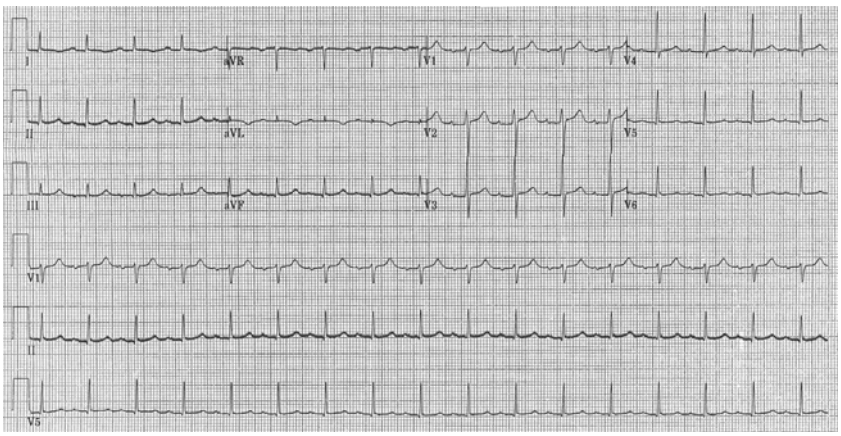
The patient's ICU course was complicated by the need to repair a femoral artery false aneurysm and by a parapneumonic effusion, which was sterile and was managed by drainage via an intercostal catheter. The patient was mechanically ventilated for 16 days; on Day 18, she was discharged from the ICU, and on Day 26 from the hospital.

After ICU discharge, results of iron studies, catecholamine, angiotensin-converting enzyme and autoantibody concentrations, and thyroid function were within the reference ranges.

Figure 1. Serial electrocardiograms (ECGs) in a patient with takotsubo cardiomyopathy



A. *At presentation in the emergency department, an ECG showed ST-segment elevation in leads V_1–V_6.*



B. *An ECG on arrival at our hospital, within 6 hours of the first ECG, showed non-specific T wave changes.*

Discussion

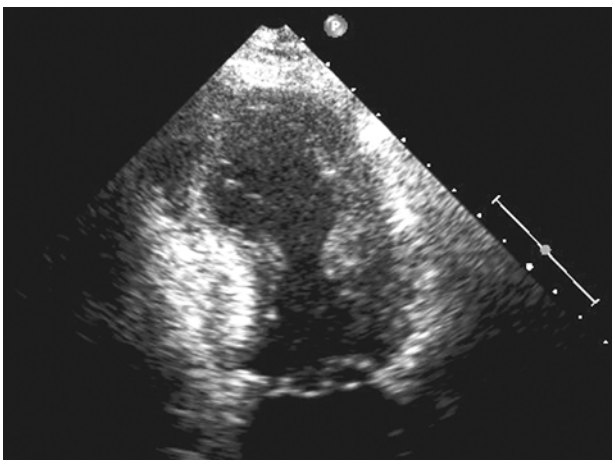
Takotsubo cardiomyopathy, also known as transient left ventricular apical ballooning syndrome, is characterised by transient regional systolic dysfunction involving the left ventricular apex and mid-ventricle, with hyperkinesis of the basal left ventricular segments. The syndrome was initially recognised and reported in the Japanese population.[1-6] Dote and colleagues named it after a narrow-necked, round-bottomed Japanese fishing pot used for trapping octopus, which is morphologically similar to the echocardiographic appearance of the heart.[1] Subsequent reports have documented the syndrome in other racial groups.[7,8] Clinical presentation is similar to that of acute myocardial infarction, despite the absence of obstructive epicardial coronary artery disease. Arrhythmias, dynamic intraventricular outflow tract obstruction and mechanical complications, such as mitral regurgitation, left ventricular mural thrombus formation, and even left ventricular free-wall rupture, may occur.[9]

An episode of acute emotional or physiological stress, such as overexertion or surgery,[10,11] may precipitate the syndrome. Patients seem to have a favourable in-hospital prognosis despite the development of acute left-sided heart failure and haemodynamic instability. The cause of the syndrome, reported most frequently in postmenopausal women, is not yet known.

Several mechanisms have been proposed, including multivessel epicardial spasm, myocardial dysfunction mediated through catecholamine-induced damage, microvascular coronary spasm or dysfunction, and neurogenically mediated myocardial stunning.[9,12-17] Transient multivessel epicardial spasm may be responsible for some cases,[3,5,15-17] but was probably not the cause in our patient, who had no identifiable epicardial spasm or stenosis on angiography.

Diffuse abnormalities of coronary microvascular function have been seen in takotsubo cardiomyopathy when patients were assessed immediately after presentation by invasive measurements of coronary flow reserve and TIMI (Thrombolysis In Myocardial Infarction) frame count techniques.[5,7,14,18-22] In addition, injection of nicorandil into the coronary arteries during the acute phase of the syndrome reduces

Figure 2. Echocardiogram in a patient with takotsubo cardiomyopathy



A transoesophageal echocardiogram showed apical ballooning typical of takotsubo cardiomyopathy.

Table 1. Results of laboratory investigations on admission

	Patient result	Reference range
Peripheral blood		
White blood cell count ($\times 10^9$/L)	25.0	4.0–11.0
Red blood cell count ($\times 10^{12}$/L)	4.9	4.5–6.0
Haemoglobin (g/L)	143	135–180
Platelet count ($\times 10^9$/L)	252	140–400
Coagulation		
Prothrombin time ($\times 10^9$/L)	16	12–16
Activated partial thromboplastin time (s)	40.0	25–38
Fibrinogen (g/L)	2.8	1.5–4.0
D-dimer (mg/L)	7.09	< 0.28
International normalised ratio	1.2	0.9–1.3
Biochemistry		
Cortisol (nmol/L)	1270	200–700
Glucose (mmol/L)	8.0	3.0–7.8
Total protein (g/L)	71	62–83
Albumin (g/L)	31	33–47
Creatinine (μmol/L)	171	70–120
Urea nitrogen (mmol/L)	17.1	3.0–8.0
Aspartate aminotransferase (U/L)	185	< 40
Alanine aminotransferase (U/L)	114	< 45
Lactate dehydrogenase (U/L)	361	110–250
Creatine kinase (U/L)	128	< 200
Troponin I (μg/mL)	3.0	< 0.2
Amylase (U/L)	208	25–130
Normetadrenaline (μmol/24 h)	2.9	< 2.3
Dopamine (nmol/24 h)	26300	200–3500
Serology and microbiology		
C-reactive protein (mg/L)	54	< 5.0
Sputum culture	*Streptococcus pneumoniae*	

the extent of ST-segment elevation, further suggesting that microvascular spasm may be the causative mechanism.[23] Our patient had a long history of diabetes, which may be a potential cause. It remains unclear whether coronary microvascular dysfunction is the primary mechanism in pathogenesis of the syndrome, or whether it is simply an associated secondary phenomenon.

Catecholamines probably play an important role in the syndrome.[10,18,24] Elevated catecholamine levels decrease the viability of myocytes through cyclic AMP-mediated calcium overload, and are also a potential source of oxygen-derived free radicals that may cause myocyte injury. Free radicals can interfere with sodium and calcium transporters, possibly resulting in myocyte dysfunction through increased transsarcolemmal calcium influx and cellular calcium overload. Kawai et al recently reported histological findings in patients with apical ballooning that are similar to those described in catecholamine-induced cardiomyopathy.[25] Some researchers have suggested that the syndrome could be a result of catecholamine-associated stunning of the myocardium, which is provoked by emotional or physiological stress.[11] Patients presenting with the syndrome appear to have abnormalities of cardiac sympathetic innervation, with evidence of sympathetic hyperactivity at the cardiac apex.[26,27]

Sepsis can induce myocyte injury, either directly or by raising levels of catecholamines,[28,29] thereby decreasing the viability of myocytes. Sepsis is associated with increased levels of nitric oxide, tumour necrosis factor alfa (TNF-α), interleukin-6 and other mediators.[30,31] Several studies support a role of infection in altering vascular integrity, which could mediate myocardial abnormalities.[28,29,32,33]

Our patient demonstrates, to our knowledge for the first time, the combination of sepsis and takotsubo cardiomyopathy. The cause of the syndrome in this case is unknown, but the close relationship to infection, physical stress and diabetes may indicate a multifactorial aetiology. Takotsubo syndrome should be considered in patients presenting with sepsis or systemic inflammatory response syndrome and cardiac dysfunction.

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