Basal Takotsubo syndrome induced by pheochromocytoma rupture

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Abstract

Takotsubo syndrome (TTS), characterised by transient left ventricular systolic dysfunction, is divided into five types: (1) apical ballooning, (2) mid-ventricular, (3) basal or inverted, (4) and focal wall-motion patterns, and (5) other types, including biventricular type, isolated right ventricular and global type. The common clinical features of TTS are similar to acute coronary syndrome, which makes them indistinguishable in the early stages. TTS has a wide spectrum of emotional or physical triggers. Pheochromocytoma has been widely recognised as a distinct physical trigger of TTS. Although reports of pheochromocytoma causing TTS are not uncommon, spontaneous rupture of pheochromocytoma causing TTS is extremely rare because of the low incidence of tumour rupture. Here we report on a case of a 31-year-old man with adrenal pheochromocytoma rupture developing basal TTS.

Keywords: Takotsubo syndrome, pheochromocytoma, spontaneous rupture, cardiogenic shock, heart failure

Case report

A 31-year-old man was admitted to hospital due to sudden severe abdominal pain. Prior to this event, he had experienced intermittent abdominal pain, headache and palpitations for two years without any treatment. On arrival at a local hospital, his blood pressure (BP) was 206/115 mmHg and heart rate was 120 bpm. Plain computed tomography (CT) showed a 3.7-cm mass of uneven density in the left adrenal gland (Fig. 1A). An ECG showed ST-segment elevation on the precordial leads V3–V6 and limb leads I and aVL, and ST-segment depression on limb leads II, III and aVF. Troponin I (TnI) and creatine kinase isoenzyme MB (CK-MB) levels were normal at that time.
In less than 12 hours, his abdominal pain progressively intensified, and BP dropped to 90/60 mmHg. He was transferred to our hospital. The repeat CT scan revealed the mass had expanded to 6.5 cm in diameter, with accumulation of fluid surrounding the left pararenal and parapancreatic space (Fig. 1B).

Haemoglobin and red blood cell counts were in the normal range. Levels of serum and urine epinephrine (E), serum and urine norepinephrine (NE), serum metanephrine (MN) and normetanephrine (NMN), and urine vanillylmandelic acid (VMN) were found to be markedly elevated (serum E: 767.66 pg/ml, reference range 0–100 pg/ml; serum NE: 2148.52 pg/ml, reference range 0–600 pg/ml; urine E: 66.74 μg/day, reference range 0–20 μg/day; urine NE: 240.15 μg/day, reference range 0–90 μg/day; serum MN: > 20.56 nmol/l, reference range ≤ 0.5 nmol/l; serum NMN: > 20.56 nmol/l, reference range ≤ 0.9 nmol/l; urine VMN 46.7 mg/day, reference range ≤ 12 mg/day).

Repeat ECG showed elevated/depressed ST-segments somewhat recovered, but retest of cardiac biomarkers showed a TnI level of 12.4 ng/ml (reference range 0–1 ng/ml) and CK-MB of 29.5 ng/ml (reference range 0–4.3 ng/ml). A transthoracic echocardiogram (TTE) showed severely impaired LV systolic function [ejection fraction (EF) 27%] with akinesis/hypokinesis of the basal and middle LV segments and hyperkinesis of the apical segments (Fig. 2A, B).

The patient soon developed heart failure and shock. He was transferred to the intensive care unit (ICU) for life support, utilising vasoactive drugs (noradrenaline), intra-aortic balloon pump (IABP) and ventilator assistance. During treatment, the TnI level, which peaked within 24 hours, began to drop from the fourth day, and returned to normal in one week. CK-MB, which peaked within 24 hours, began to drop from the third day, and returned to normal on the 10th day.

During his hospitalisation, we paid close attention to the
change in cardiac function and checked his heart regularly with TTE. TTE showed a distinct improvement in wall motion of the LV basal and middle segments on the 12th day with an EF of 36%, so the IABP and ventilator were withdrawn on the 13th and 14th days, respectively. On TTE, the wall motion of the LV returned to almost normal after 17 days.

After discharge from hospital, the patient received adrenergic alpha-receptor blockers. Three months later he had a repeat TTE and the results were normal.

He thereafter underwent a left adrenalectomy. The pathology examination revealed adrenal pheochromocytoma with haemorrhage and rupture (Fig. 3A, B). After the patient was discharged, he took no beta-blockers or angiotensin converting enzyme inhibitors (ACEIs). His BP was in the normal range and activity tolerance returned to normal levels. TTS did not recur after the tumour was removed during follow up of a year.

Discussion

Pheochromocytomas are uncommon catecholamine-secreting tumours. Intractable hypertension is one of the most common symptoms, accompanied by headache, palpitations and perspiration. Pheochromocytoma crisis, with an occurrence rate of about 10%, induced by sudden release of large amounts of catecholamines, is a dreaded and potentially lethal complication of pheochromocytoma. Clinical manifestation consists of severe hyper- and/or hypotension, high fever, encephalopathy and multiple organ system failure.

Haemodynamic abnormality of pheochromocytoma crisis has a variety of causes such as cardiomyopathy, myocardial infarction, arrhythmia, pulmonary oedema, cerebrovascular accident, encephalopathy, liver and kidney failure, adrenal haemorrhage and others. Spontaneous rupture of adrenal pheochromocytoma, one cause of pheochromocytoma crisis, is rare, and most of such rare cases present as haemorrhagic shock. Here we discuss a case of a young man with adrenal pheochromocytoma rupture developing pheochromocytoma crisis, which presented with basal TTS and cardiogenic shock.

Pheochromocytoma serves as a distinct physical trigger of TTS, and TTS may be found in up to 3% of patients with pheochromocytoma and paraganglioma. The types of pheochromocytoma-induced TTS (pheo-TTS) suffer significantly in all patients with TTS (all-TTS), with the basal type in almost 30% of pheo-TTS and the global type in 20% of pheo-TTS. Both types are rare in all-TTS, with the basal type only accounting for 2.2% of all-TTS and the global type even less. Patients with pheo-TTS are significantly younger than all-TTS, with a relatively high proportion of men. In addition, pheo-TTS is characterised by a dramatic clinical presentation with high complication rates, especially in patients under 50 years, and a relatively high recurrence rate.

Common complications are heart failure (occurrence rate 51%), pulmonary oedema (45%) and cardiogenic shock (34.6%), which occurs more frequently in the global and basal patterns of pheo-TTS than the apical type. As reported in most previous cases, levels of cardiac biomarkers are slightly or moderately elevated, but were significantly increased in our patient. In this case, the patient presented as acute myocardial infarction initially, with ECG changes presenting as ST-segment elevation and depression, cardiac biomarkers significantly elevated, and wall-motion abnormality of the LV on TTE. However, this young man had no chest pain, no history of hypertension, diabetes mellitus, smoking, or family history of early-onset coronary heart disease. TTE showed akinesis/hypokinesis of the entire basal and middle LV segments, which extended beyond a single epicardial vascular distribution. These features and the presence of physical stress of pheochromocytoma rupture pointed to the basal type of TTS. Regular TTE showed LV wall motion distinctly improved on the 12th day and almost recovered after 17 days, which indicated LV dysfunction was transient and confirmed the diagnosis of TTS.

A coronary CT angiogram should be performed to exclude coronary artery diseases, but at that critical time, with life support of IABP and ventilator, the patient had no chance of getting a CT angiogram. In this patient, severely impaired LV systolic function with an EF of 27% caused by TTS was one of the main causes of shock. His haemoglobin and red blood cell count were in the normal range, so haemorrhagic shock was excluded.

The precise pathophysiological mechanisms of TTS are incompletely understood, but there is considerable evidence that...
catecholamine excess and sympathetic stimulation is central to its pathogenesis.8,9 Catecholamine levels of this patient were significantly elevated. We supposed that the sudden release of large amounts of catecholamines from the ruptured pheochromocytoma played an important role in the pathogenesis of TTS in this patient. However, the reason why the basal type of TTS has a high incidence in pheo-TTS remains unclear.

Although reports of pheochromocytoma causing TTS are not uncommon, spontaneous rupture of pheochromocytoma causing TTS is extremely rare because of the low incidence of tumour rupture. So far, only one case diagnosed with apical TTS caused by pheochromocytoma rupture has been reported around the world.10 This case of pheochromocytoma rupture-induced basal TTS is the first explicit report in the literature.

Conclusion
This case provides us with three insights: (1) young patients with abdominal pain and clinical evidence of ACS should be checked for pheochromocytoma; (2) the impaired LV systolic function recovered in two to three weeks with timely mechanically assisted therapy; (3) TTS did not re-occur even without taking any beta-blockers or ACEIs after the tumour was removed.

References