

# Takotsubo-Like Cardiomyopathy in Pheochromocytoma



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## INTRODUCTION

Takotsubo cardiomyopathy (TTC) is commonly triggered by acute illness or by physical or emotional stress and has been associated with excess catecholamine. The presentation of TTC can be various, and the condition is associated with a risk for serious complications. In patients with unstable vital signs, mechanical circulatory support can be lifesaving.

We report a case of pheochromocytoma-induced cardiogenic shock managed using extracorporeal membrane oxygenation (ECMO). The final diagnosis was confirmed during online consultations.

## CASE PRESENTATION

A 31-year-old woman was admitted to the emergency department with recurrent choking sensation for 2 days, exacerbated with nausea and vomiting for 24 hours. She had a history of hypertension but was not receiving any treatment. On admission, she was sweaty and her limbs were cold and wet, with a body temperature of 38.1°C. During the subsequent hours, the patient's blood pressure ranged widely from 90/50 to 159/122 mm Hg, and her pulse rate fluctuated between 70 and 140 beats/min. Laboratory tests revealed that troponin I (>50 pg/mL), creatine kinase MB (81.03 nmol/L), and brain natriuretic peptide (10,683 pg/mL) were elevated (Figure 1). Blood catecholamines were 5 times the normal upper limit: epinephrine 586.98 pg/mL, norepinephrine 921.04 pg/mL, and dopamine 150.9 pg/mL. White blood cell count was  $25.29 \times 10^9/L$ , and the granulocyte ratio was 84.2%. Electrocardiography showed sinus tachycardia and 1- to 2-mm ST-segment elevation in leads II, III, and aVF, with no changes in other leads. Emergency transthoracic echocardiography revealed mildly hypercontractility of the basal segments, with systolic ballooning of the apical and middle portions of the left ventricle. Velocity of the left ventricular (LV) outflow tract was normal. There was no systolic anterior motion of the mitral leaflet. LV diastolic diameter was 47 mm. Ejection fraction, calculated using the biplane Simpson formula, was 35% (Figure 2, Videos 1-3). Coronary artery obstruction was excluded by subsequent coronary angiography (Video 4). TTC was our first

diagnosis. Myocarditis also could not be excluded. The patient had acute LV failure, and she had aggravation of dyspnea. ECMO was deployed immediately, and anti-infective therapies including cefuroxime, piperacillin, ganciclovir, and oseltamivir were administered. Besides an angiotensin-converting enzyme inhibitor, a  $\beta$ -blocker, an aldosterone antagonist, and diuretics were also started, with trimetazidine and a vitamin C tablet. Subsequent electrocardiographic showed that ST segments dropped gradually, and T waves in all leads except aVR inverted (Figure 3). Serial transthoracic echocardiography during the following days showed gradually improved LV systolic function (Video 5, Figure 4). The patient tolerated the treatment well. After stabilization, she was discharged on the 13th day.

We reported the case as myocarditis on an online network for medical consultation. Experts in echocardiography considered the high possibility of pheochromocytoma-induced TTC. Abdominal computed tomography was completed and showed a right adrenal tumor (Figure 5). The patient was put on phenoxybenzamine and a  $\beta$ -blocker. After 4 weeks, the patient underwent uncomplicated laparoscopic removal of the adrenal mass. Pheochromocytoma was confirmed on histopathology (Figure 6). Repeated urine catecholamine measurements and ambulatory blood pressure monitoring values were within the normal range. On 3-month follow-up after surgery, the patient was asymptomatic, and LV systolic function had recovered fully (Figure 7).

## DISCUSSION

Although myocardial enzymology and electrocardiographic changes support the diagnosis of acute coronary syndrome and coronary artery dissection as a possible cause of acute coronary syndrome in young women, we could not explain a regional wall motion abnormality as due to acute coronary syndrome. Subsequent coronary angiography also excluded coronary artery obstruction and dissection. Combined with an elevated white blood cell count, myocarditis could not be excluded. Given that the patient had worsening heart failure symptoms and that the early mortality rate of fulminating viral myocarditis is as high as 80%,<sup>1</sup> we made a rapid decision to deploy ECMO. Subsequent transthoracic echocardiography showed gradually recovered wall motion. With the guidance of echocardiography experts on an online network, the final diagnosis of pheochromocytoma-induced TTC was confirmed.

In a review including 254 cases of TTC and 38 cases of pheochromocytoma-induced TTC, although 65.7% of patients in the TTC review had identifiable antecedent stressors, most of which were acute medical illnesses or intense physical or emotional stress, only 28.9% of patients with pheochromocytoma-induced TTC patients had antecedent stressors.<sup>1</sup> In our case, what triggered TTC is still disputable. Pheochromocytoma-induced excess catecholamine releasing can be a trigger, as excess catecholamine release can disrupt cardiac contraction and cause myocardial injury,<sup>2-4</sup> which can be detected by echocardiography and electrocardiographic changes. The

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**VIDEO HIGHLIGHTS**

**Video 1:** Echocardiography on the day of admission. Wall motion abnormalities involved the apical and midventricular segments of the opposite wall. Video demonstrates hypercontractility of the interventricular septum and lateral wall in the four-chamber view.

**Video 2:** Echocardiography on the day of admission. Wall motion abnormalities involved the apical and midventricular segments of the opposite wall. Video demonstrates hypercontractility of the anterior and inferior wall in the two-chamber view.

**Video 3:** Echocardiography on the day of admission. Wall motion abnormalities involved the apical and midventricular segments of the opposite wall. Video demonstrates hypercontractility of the anteroseptal and inferolateral wall in the three-chamber view.

**Video 4:** Coronary angiography on the day of admission showed absence of obstructive coronary disease and evidence of dissection.

**Video 5:** Echocardiography on the following day revealed restoration of LV motion and improved LV systolic function.

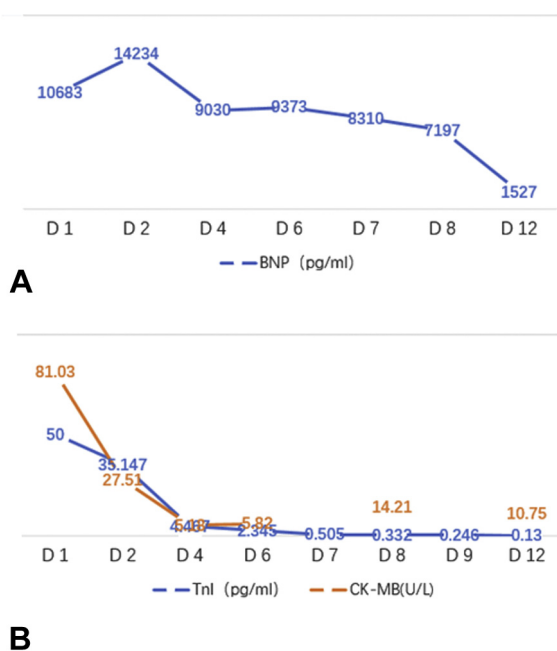
View the video content online at [www.cvcasejournal.com](http://www.cvcasejournal.com).

trigger can also be myocarditis. However, because we did not perform an endomyocardial biopsy, the causes of myocarditis could not be confirmed. Both regional wall motion abnormalities and myocardial injury can lead to hemodynamic instability. In our case, once the initial critical context had been controlled, the patient's heart failure was fully reversible, suggesting that a regional wall motion abnormality rather than myocardial injury was the primary factor resulting in circulatory failure. By comparing delayed electrocardiographic recovery with earlier recovery of myocardial synchrony in our patient, we hypothesize that myocardial injury will not delay the cardiac mechanical recovery.

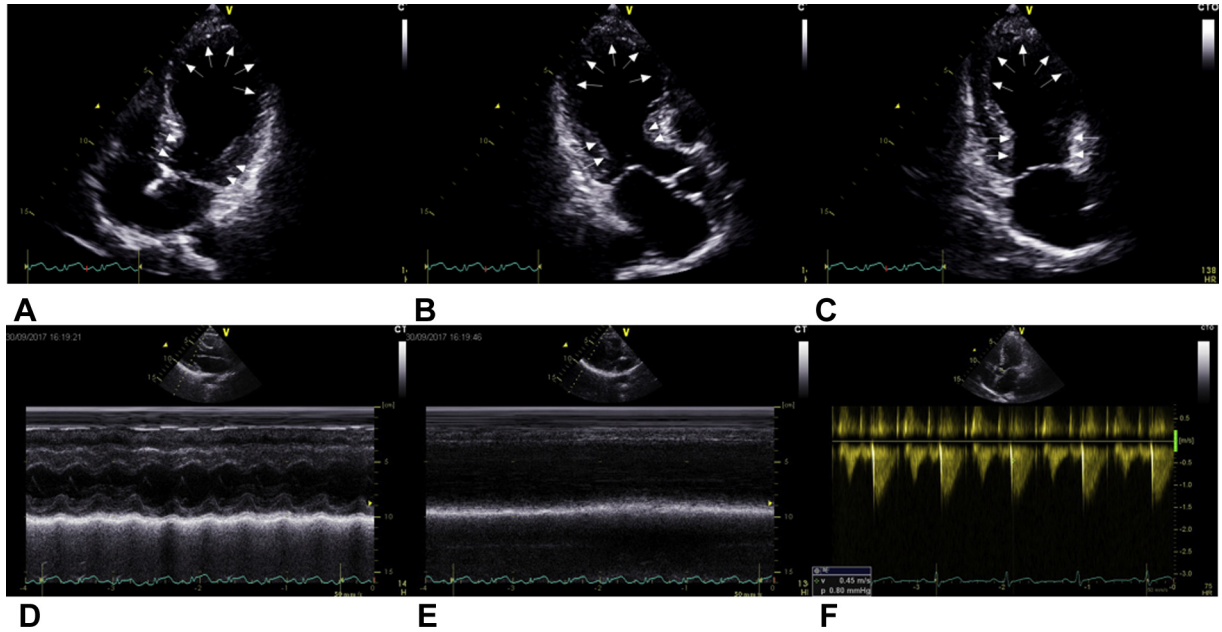
Most cases of TTC feature complete resolution of LV function, in which only conservative treatment is sufficient.<sup>5</sup> However, a small subset of patients have potentially life-threatening complications during the initial presentation.<sup>2</sup> In patients who develop fatal complications and are misdiagnosed with acute coronary syndrome, commonly used vasoactive drugs may cause iatrogenic worsening hemodynamics.<sup>6</sup> In our case, the patient experienced pump failure. ECMO extended the diagnostic window while improving tissue perfusion.

**CONCLUSION**

Diagnosis of pheochromocytoma-induced TTC has important implications for clinical management at presentation and afterward. In patients diagnosed with symptoms of acute coronary syndrome without coronary artery stenosis or spasm, a more comprehensive examination should be taken to decode wall motion abnormalities.



**Figure 1** (A) Brain natriuretic peptide (BNP) changes from the first day (D1) of admission to the 12th day (D12). (B) Troponin I (TnI) and creatine kinase MB (CK-MB) changes from the first day of admission to the 12th day. BNP release was increased compared with cardiac enzymes, which were also increased on admission, but BNP was disproportionately higher than cardiac enzymes.



**Figure 2** Transthoracic echocardiography revealed mildly hypercontractility of the basal segments (*inward arrows*), with ballooning of the apical and middle portions of the left ventricle (*outward arrows*) at the end of systole. Four-chamber view (**A**), three-chamber view (**B**), and two-chamber view (**C**) are demonstrated. M-mode imaging showed hypercontractility at basal segments (**D**) and hypokinesis at apex (**E**). Continuous-wave Doppler (**F**) showed that the velocity of the LV outflow tract was normal, and there was no obvious mitral valve regurgitation.

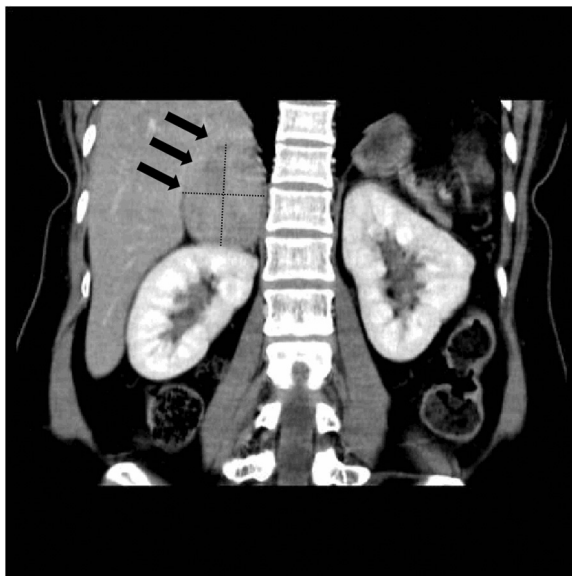


**Figure 3** Electrocardiography showed ST-segment elevation in leads I, II, V<sub>4</sub>, V<sub>5</sub>, and V<sub>6</sub> on the second day of hospitalization; during the third to sixth days, the ST segments returned to baseline; on the seventh day, T waves in leads I, II, aVL, V<sub>2</sub>, V<sub>3</sub>, V<sub>4</sub>, V<sub>5</sub>, and V<sub>6</sub> became inverted.

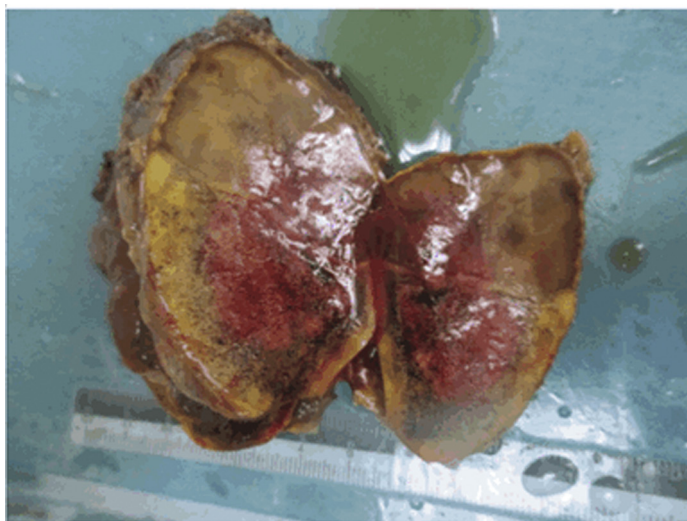


	LA (mm)	LV (mm)	EF (%)	Decreased left ventricular wall motion
Day2	32	52	33	General LV ventricle
Day3	33	52	16	General LV ventricle
Day4	35	50	49	Mid to apical portion of LV
Day5	30	47	48	Apical segment of ventricular septum
Day7	28	45	57	Apical wall of LV ventricle
Day10	27	42	73	Apical wall of LV ventricle
Day13	27	41	80	None

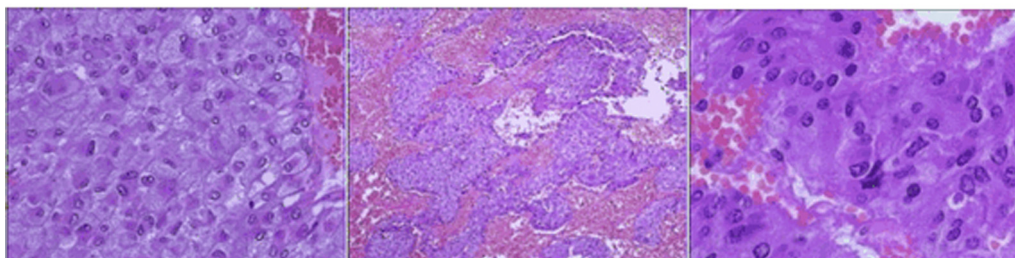
**Figure 4** Serial transthoracic echocardiography during the following days showed gradually improved LV contraction. *EF*, Ejection fraction; *LA*, left atrium.



**Figure 5** Longitudinal computed tomographic scan demonstrating a right adrenal mass.

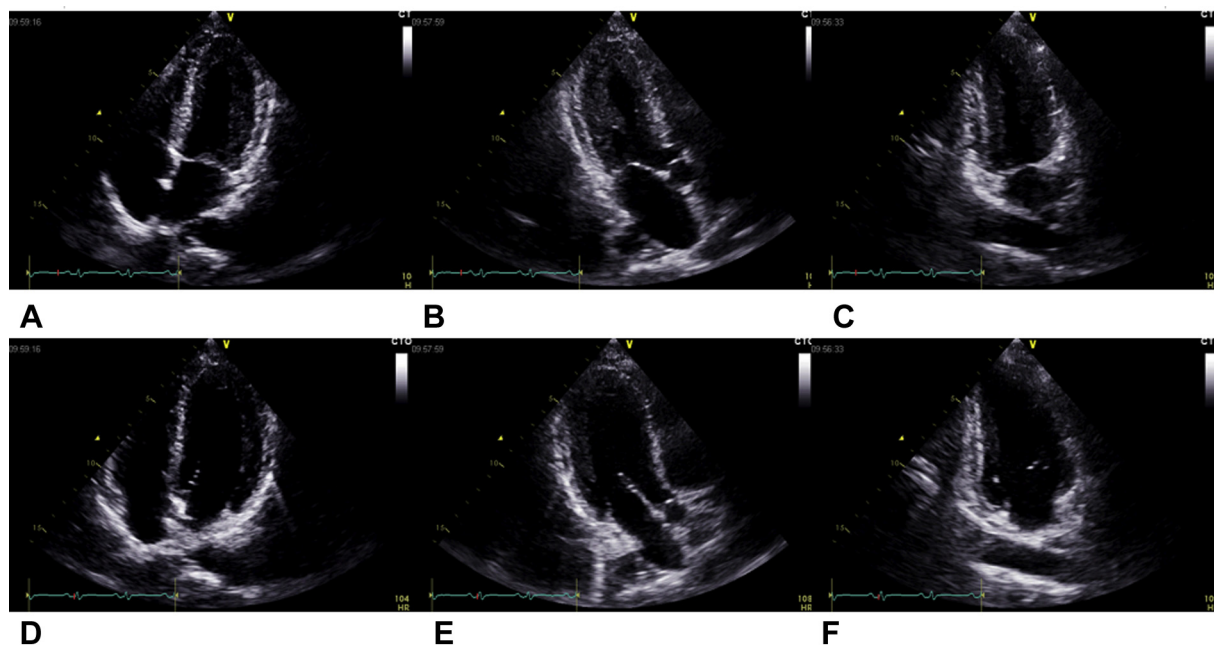


**A**



**B**

**Figure 6 (A)** Surgically removed right adrenal mass. **(B)** Under the microscope, trabecular patterns of polygonal and spindle-shaped cells in a rich vascular network could be seen. Cells had finely granular basophilic cytoplasm and intracytoplasmic hyaline globules and round or oval nuclei with prominent nucleolus and variable inclusion-like structures.



**Figure 7** Transthoracic echocardiography revealed normal motion of the left ventricle at end-systole (**A–C**) and end-diastole (**D–F**).

#### **SUPPLEMENTARY DATA**

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2019.04.006>.

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