Pheochromocytoma-Induced Takotsubo Cardiomyopathy

Pheochromocytoma is a rare, catecholamine-secreting neuroendocrine tumor that arises from the chromaffin cells of the adrenal medulla. The typical clinical manifestations are paroxysmal hypertension, tachycardia, diaphoresis, and headache. Less often, the tumor will cause severe cardiovascular complications such as myocardial infarction, arrhythmias, and heart failure. We report the case of a patient whose pheochromocytoma presented as cardiogenic shock and severe heart failure, and we discuss our diagnostic and management insights.

Case Report

In August 2016, a 66-year-old woman with no relevant medical history presented with a 2-day history of nausea and of epigastric pain radiating to her back. Her heart rate was 135 beats/min; her blood pressure, 153/87 mmHg; and her respiratory rate, 24 breaths/min. Laboratory findings included a white blood cell count of 15,400/µL (normal range, 4,000–9,000/µL), a cardiac troponin I level of 19 ng/mL (normal, <0.05 ng/mL), a brain natriuretic peptide level of 1,403 pg/mL (normal, <50 pg/mL), acute kidney injury with a creatinine level of 3.2 mg/dL (normal, <1 mg/dL), and a lactate level of 8.9 mmol/L (normal, <1.8 mmol/L). All were markers of end-organ damage in the presence of what appeared to be the early stages of shock, intravascular volume depletion, or both. An electrocardiogram showed 0.5-mm ST-segment elevation in leads III and aVF; PR depression in leads II, III, and aVF; and PR elevation in lead aVR (Fig. 1). The patient’s troponin I level peaked at 49.5 ng/mL. Despite aggressive fluid resuscitation, she remained tachycardic and became severely hypertensive. A transthoracic echocardiogram (TTE) showed a left ventricular ejection fraction (LVEF) of 0.15 with severe hypokinesis of the mid-distal anterior, lateral, inferior, and inferolateral walls. The electrocardiographic changes and troponin I elevation prompted same-day coronary angiography to investigate possible acute myocardial infarction; however, the patient’s coronary arteries were normal. Right-sided heart catheterization revealed a right atrial pressure of 11 mmHg, a mean pulmonary artery pressure of 25 mmHg, a pulmonary capillary wedge pressure of 22 mmHg, and a substantially reduced Fick cardiac output and index of 2.43 L/min and 1.55 L/min/m², respectively. The systemic vascular resistance was 3,028 dynes·s/cm⁵.

The patient was admitted to the cardiac intensive care unit. She was given intravenous milrinone (0.25 µg/kg/min) as inotropic therapy for cardiogenic shock, along with intravenous nitroprusside and concomitant up-titration of oral hydralazine and isosorbide dinitrate for afterload reduction.
We began evaluating the patient’s leukocytosis and abdominal pain on her 3rd day of intensive care. An ultrasonogram showed an apparently solid mass in the right upper quadrant, characterized on computed tomograms (CT) as a 111.5-mm right adrenal mass (Fig. 2). Cardiac magnetic resonance (CMR) images obtained 6 days after admission revealed dramatic improvement in left ventricular (LV) function (LVEF, 0.50), a small thrombus in the LV apex, and delayed gadolinium enhancement in the basal and mid inferoseptum (Fig. 3). Despite some CMR evidence of LV trabeculation, the patient’s rapid hemodynamic recovery ruled out LV noncompaction as a cause of cardiomyopathy.

On day 6, we suspected endocrinologic dysfunction, so we requested analyses of the patient’s 24-hour urinary metanephrine, catecholamine, and vanillylmandelic acid levels (these results took 7 d to receive). Given the patient’s hemodynamic recovery and improved renal and end-organ function, we started her on oral metoprolol succinate and continued the isosorbide dinitrate and hydralazine. After a 9-day hospitalization, she was discharged with a prescription for enoxaparin and plans for outpatient treatment.

A week later, the patient visited our cardiology clinic. Her urinary levels of catecholamines and metanephrine were substantially elevated (Table I). Her speed of recovery, normal angiographic findings, and TTE findings of depressed LVEF with severe hypokinesis of the mid-distal LV and sparing of the basal segments supported the diagnosis of takotsubo cardiomyopathy (TC). The substantially elevated urinary findings, the large adrenal mass, and the rapid onset of and recovery from hemodynamic instability indicated that the TC was due to pheochromocytoma.

Consequent to this diagnosis, we changed the metoprolol to labetalol for combined α- and β-blockade. Ten days after the patient’s discharge from the hospital, we consulted with our endocrinologists and additionally

![Image](image1.jpg)

**Fig. 1** Electrocardiogram on presentation shows 0.5-mm ST-segment elevation in leads III and aVF; PR depression in leads II, III, and aVF; and PR elevation in lead aVR, suggesting acute myocardial injury.

![Image](image2.jpg)

**Fig. 2** Abdominal computed tomogram (coronal view) shows a 111.5-mm mass in the right upper quadrant.

![Image](image3.jpg)

**Fig. 3** Cardiac magnetic resonance image (short-axis view) of the left ventricle shows delayed gadolinium enhancement of the A) basal and B) mid inferoseptum.
prescribed doxazosin for further α-blockade, a regimen to be maintained for approximately 3 weeks before elective surgical resection of the adrenal mass. A TTE 19 days after initial presentation showed preserved LVEF (0.70) and resolution of the LV thrombus. We discontinued labetalol on day 27 because of the patient’s intermittent orthostatic hypotension and relied on doxazosin alone, titrated up to a maximal 3-mg dose. Two days preoperatively, we prescribed propranolol (10 mg twice/d) to prevent reflex tachycardia. On the 46th day after initial presentation, we performed right adrenalectomy; the mass was confirmed to be pheochromocytoma. Postoperatively, the patient no longer needed anti-hypertensive or heart failure medications, and she was discharged from the hospital after 7 days. At her 2-week and 2-month follow-up cardiology appointments, she was asymptomatic and doing well. Subsequent periodic endocrinologic screenings revealed no disease recurrence, and test results for genetic causes of pheochromocytoma were negative.

Discussion

Our patient had an unusual presentation of pheochromocytoma–TC with cardiogenic shock, which we diagnosed while evaluating abdominal pain in an otherwise seemingly healthy patient.

In the presence of new-onset cardiomyopathy and normal coronary arteries, the differential diagnosis includes TC, acute myocarditis, and pheochromocytoma. Takotsubo cardiomyopathy, also called apical ballooning syndrome or broken-heart syndrome, is a transient, reversible cardiomyopathy that most often occurs in postmenopausal women after intense emotional or physical stress, which our patient did not report. Increased circulating catecholamines are associated with TC. The proposed mechanisms of cardiac dysfunction include direct toxic effects of catecholamine byproducts on the myocardium, direct catecholamine receptor-mediated effects, coronary vasospasm, and microvascular dysfunction.1-3 Hemodynamic collapse or cardiogenic shock can occur in TC or be caused by a pheochromocytoma alone from combined catecholamine-induced myocardial injury, LV mid cavity obstruction, and intravascular volume depletion.4-6 Our patient’s acute systolic heart failure with cardiogenic shock, normal coronary arteries, TTE findings of LV apical hypokinesis with preserved basal segments, elevated catecholamine levels with a documented adrenal mass, and rapid recovery all supported the diagnosis of pheochromocytoma-induced TC.

Pheochromocytoma has been associated with TC.6-10 In addition to typical presentations, descriptions have included cardiogenic shock necessitating intra-aortic balloon pump support or extracorporeal membrane oxygenation. In an analysis of 38 patients who had pheochromocytoma-associated TC and 254 who had primary TC, the investigators found higher complication rates in the former group but similar outcomes between the groups, suggesting similar underlying cardiac pathophysiologic processes. Our patient had TC with mid-distal LV hypokinesis, an apical LV thrombus, and preserved contraction of the LV base. Pheochromocytoma has also been associated with inverted TC syndrome in which LV apical contraction is preserved while basilar LV segments are hypokinetic or dyskinetic.6-9

When our patient was treated with intravenous fluids, brief inotropic support, and pulmonary artery catheterization, her cardiogenic shock, renal failure, LV systolic dysfunction, and heart failure improved. Vasopressors and inotropic agents can magnify the clinical presentation of TC because of further increase in adrenergic insult and altered vascular function; however, we observed a positive impact of these agents on our patient’s hemodynamic status. Accordingly, patients with TC might not all react the same to vasoactive medications. We prescribed enoxaparin for LV thrombus anticoagulation along with metoprolol, hydralazine, and oral nitrates before the pheochromocytoma diagnosis was confirmed by contrast CT and post-discharge analyses of catecholamine levels. The results of CMR (day 6) showed considerable improvement in LV function, and a repeat TEE (day 19) showed an LVEF of 0.70 with resolved LV thrombus. Doxazosin was prescribed and titrated over 3 weeks to provide adequate α-blockade, and propranolol was added to control reflex tachycardia before right adrenalectomy (day 46). Despite some CMR evidence of LV trabeculation, the rapidly recovered LV systolic function excluded noncompaction cardiomyopathy as a diagnosis.

Our patient’s abdominal pain prompted abdominal imaging and catecholamine testing. We suggest that cardiology providers who encounter TC patients remember the link between pheochromocytoma and TC or inverted TC, and consider catecholamine and metanephrine testing plus abdominal imaging if abdominal pain or other pheochromocytoma symptoms are present.

| TABLE I. The Patient’s Urinary Analysis Results One Week after Hospital Discharge |
|---|---|---|
| Urine Component (24-hr) | Reference Range | Value |
| Metanephrine (µg) | 52–341 | 8,045 |
| Normetanephrine (µg) | 88–444 | 16,034 |
| Total metanephrines (µg) | 140–785 | 24,079 |
| Epinephrine (µg) | 0–20 | 65 |
| Norepinephrine (µg) | 15–80 | 147 |
| Total catecholamines (µg) | 15–100 | 212 |
| Metanephrine (µg) | 52–341 | 8,045 |
| Normetanephrine (µg) | 88–444 | 16,034 |
| Total metanephrines (µg) | 140–785 | 24,079 |
| Epinephrine (µg) | 0–20 | 65 |
| Norepinephrine (µg) | 15–80 | 147 |
| Total catecholamines (µg) | 15–100 | 212 |
| Vanillylmandelic acid (mg) | 1.8–6.7 | 52.7 |
References

1. Rathi MS. Pheochromocytoma mimicking an acute coronary syndrome: a case report and review of its cardiovascular manifestations. Endocrinologist 2010;20(5):214-6. Abstract available from: https://journals.lww.com/theendocrinologist/Abstract/2010/09000/Pheochromocytoma_Mimicking_an_Acute_Coronary.4.aspx.

2. Kassim TA, Clarke DD, Mai VQ, Clyde PW, Mohamed Shakeri KM. Catecholamine-induced cardiomyopathy. Endocr Pract 2008;14(9):1137-49.

3. Leissner KB, Mahmood F, Aragam JR, Amouzgar A, Ortega R. Catecholamine-induced cardiomyopathy and pheochromocytoma. Anesth Analg 2008;107(2):410-2.

4. Baratella MC, Menti L, Angelini A, Daliento L. An unusual case of myocarditis. Int J Cardiol 1998;65(3):305-10.

5. Schifferdecker B, Kodali D, Hausner E, Aragam J. Adrenergic shock—an overlooked clinical entity? Cardiol Rev 2005;13(2):69-72.

6. Wu GY, Doshi AA, Haas GJ. Pheochromocytoma induced cardiogenic shock with rapid recovery of ventricular function. Eur J Heart Fail 2007;9(2):212-4.

7. Wu XM, Chen JJ, Wu CK, Lin LY, Tseng CD. Pheochromocytoma presenting as acute myocarditis with cardiogenic shock in two cases. Intern Med 2008;47(24):2151-5.

8. Flam B, Broome M, Francnker B, Branstrom R, Bell M. Pheochromocytoma-induced inverted takotsubo-like cardiomyopathy leading to cardiogenic shock successfully treated with extracorporeal membrane oxygenation. J Intensive Care Med 2015;30(6):365-72.

9. Marcovitz PA, Czako P, Rosenblatt S, Billecke SS. Pheochromocytoma presenting with takotsubo syndrome. J Interv Cardiol 2010;23(5):437-42.

10. Agarwal V, Kant G, Hans N, Messerli FH. Takotsubo-like cardiomyopathy in pheochromocytoma. Int J Cardiol 2011;153(3):241-8.