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Atypical Takotsubo cardiomyopathy presenting as acute coronary syndrome: A case report and literature review

Wang ZH *et al.* Atypical Takotsubo caused by pheochromocytoma, presenting as acute coronary syndrome

Zi-Han Wang, Jia-Rong Fan, Gao-Yu Zhang, Xian-Lun Li, Lin Li

Abstract

BACKGROUND

Takotsubo cardiomyopathy (TS) is a rare acute cardiac disease with clinical features, symptoms, and electrocardiographic manifestations similar to those of acute myocardial infarction. We present the case of a patient with TS caused by a pheochromocytoma, which was confirmed by the postoperative pathology. Furthermore, we present the patient's subsequent management, treatment, and outcome.

CASE SUMMARY

A 64-year-old woman was admitted to the hospital with episodic chest pain and palpitations, electrocardiogram (ECG) findings suggestive of high lateral wall myocardial infarction, echocardiogram showing left ventricular wall segmental motion abnormalities, and elevated levels of the myocardial marker troponin. The patient underwent coronary angiography, which revealed unobstructed blood flow without obvious stenosis. During their hospitalization, the patient had paroxysmal elevation of blood pressure accompanied by palpitations and profuse sweating, with elevated blood catecholamine levels during seizures. Subsequent computerized tomography of the adrenal glands revealed the presence of a nodule in the right adrenal, which was resected and determined to be an adrenal pheochromocytoma. Therefore, the diagnosis of pheochromocytoma-induced atypical TS was made. The patient had an uneventful postoperative recovery.

CONCLUSION

Cardiologists should consider pheochromocytoma in patients with TS. Early detection allows timely intervention, benefiting patients.

Key Words: Takotsubo cardiomyopathy; Acute coronary syndromes; Pheochromocytoma; Diagnose; Prognosis; Case report

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Core Tip: Pheochromocytomas are a common class of endocrine tumors that can cause cardiovascular pathology, often resulting in stress cardiomyopathy due to the intermittent or sustained release of catecholamines. We report a patient with a postoperatively confirmed diagnosis of Takotsubo cardiomyopathy caused by pheochromocytoma.

INTRODUCTION

Takotsubo cardiomyopathy (TS) is a rare acute cardiac disease that was first reported by a Japanese physician in 1991^[1] but has not been widely recognized. TS mainly occurs in women, with a higher incidence in postmenopausal women^[2], which may be related to the loss of estrogen protection^[3]. Because TS is closely related to emotions and external stimuli, it is also called “broken heart syndrome”. At present, more attention has been paid to the increase of blood-derived catecholamines in the pathogenesis of TS. Pheochromocytoma is a common type of endocrine system tumor^[4] that can cause cardiovascular pathology due to the intermittent or persistent release of catecholamines, which can lead to the development of TS. There are few previous reports in the literature on this secondary stress cardiomyopathy, especially caused by

pheochromocytoma. Here we report a case in which atypical TS occurred due to the presence of a pheochromocytoma with massive release of catecholamines.

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CASE PRESENTATION

Chief complaints

A 64-year-old Chinese woman was admitted to the Department of Integrative Cardiology of the China-Japan Friendship Hospital with severe chest pain.

History of present illness

The patient presented with left-sided chest pain confined to the precordial region, accompanied by panic, shoulder and back pain, dizziness, and profuse sweating for several hours after receiving acupuncture treatment on the scapula 12 d prior.

History of past illness

The patient had hyperlipidemia and homocysteinemia but was not taking medications. She denied a history of hypertension and diabetes mellitus.

Personal and family history

The patient did not smoke or drink alcohol. She became menopausal at age 50 without the use of chemotherapy drugs. She also confirmed no family history of genetic disorders.

Physical examination

General examination revealed no cardiopulmonary or abdominal abnormalities. The patient had a heart rate of 60 beats/min and a BMI of 31.6. At the time of admission, her blood pressure was elevated to 20.0/14.7 kPa; however, when she was at rest, a stable blood pressure of 16.0/10.7 kPa was measured. During the patient's hospitalization, we found that her blood pressure was unstable, occasionally up to 26.7/14.7 kPa.

Laboratory examinations

Blood test results were as follows: Creatine kinase-MB 15.67 ng/mL (reference range: < 5.00); cardiac troponin I 5.31 ng/mL (reference range: < 1.00); myoglobin 78.6 ng/mL (reference range: < 70.0); and N-terminal pro-brain natriuretic peptide 3578 pg/mL (reference range: < 300). Further examinations revealed a fasting blood-glucose of 8.73 mmol/L (reference range: 3.90-6.10), normal C-reactive protein, normal renal function, and negative tumor markers. Importantly, catecholamine levels were significantly elevated during episodes of elevated blood pressure, with epinephrine of 11.60 pmol/L (reference range: 0.164-0.519) and norepinephrine of 56.19 pmol/L (reference range: 1.182-2.364).

Imaging examinations

The electrocardiogram (ECG) showed ST-segment elevation in lead I and AVL and ST-segment depression in leads II, III, and AVF (Figure 1). Echocardiogram findings showed reverse motion of the posterior wall of the left ventricle and septum, normal motion of the posterior septum and posterior ventricular wall, and loss of motion of the rest of the ventricular wall, with an ejection fraction of 50%. Re-examination of the ECG showed T-wave inversion in leads I and AVL, while the echocardiogram showed normal wall motion in each compartment. Imaging results showed no meaningful stenosis in the coronary arteries and unobstructed blood flow (Figure 2). Computed tomography scan of the adrenal glands showed the presence of nodules in the right adrenal gland, on the basis of which we suspected the presence of a pheochromocytoma (Figure 3A).

FINAL DIAGNOSIS

Considering the patient's history, laboratory examinations, and imaging results, we determined that she had developed atypical TS with involvement of the lateral wall caused by a pheochromocytoma.

TREATMENT

At the time of admission, we gave the patient aspirin (100 mg, qd, po), clopidogrel (75 mg, qd, po), metoprolol (47.5 mg, qd, po), and atorvastatin (20 mg, qn, po) to prevent recurrence of cardiovascular events, isosorbide mononitrate (60 mg, qd, po) to improve cardiac circulation, and acarbose (50 mg, tid, po) to lower blood glucose. The patient underwent laparoscopic surgical resection of the pheochromocytoma, and doxazosin mesylate (4 mg, qd, po) was applied. The postsurgical pathologic diagnosis was right adrenal pheochromocytoma (size: 3.5 cm + ACo-3.5 cm + ACo-3 cm) (Figure 3B-D).

OUTCOME AND FOLLOW-UP

After tumor resection, the patient had a smooth postoperative recovery without adverse events and was treated only with atorvastatin 10 mg qd for lipid-lowering. Repeat ECG examination showed no ST-segment abnormality, and the echocardiogram showed normal motion of all ventricular walls. We followed the patient for one year, and she did not have any further cardiac-related diseases, while the ECG and echocardiogram were normal.

DISCUSSION

The electrocardiographic changes and clinical presentation of TS are similar to acute coronary syndromes (ACS) without the presence of coronary occlusion. The typical patient with TS has a distinctive abnormal contour of ventricular annular contraction with a peculiar circumferential pattern and apical ballooning of the left ventricle extending beyond the coronary blood supply region^[5]. In our present report, the heart showed abnormal activity of the lateral wall and was judged to be an atypical case of TS. This abnormal motion is reversible, and ventricular dysfunction returns to normal within hours to weeks. Coronary angiogram is the key test to distinguish ACS from TS^[6].

The pathogenesis of TS is unclear, and pathophysiological mechanisms such as myocardial ischemia, left ventricular outlet tract obstruction, blood-borne

catecholamine myocardial toxicity, adrenergic-induced signal transduction abnormalities, and autonomic nervous system dysfunction have been proposed^[7]. More attention is currently focused on elevated blood-borne catecholamine levels and excessive activation of cardiac sympathetic nerves. The rapid elevation of plasma catecholamine levels leads to vasospasm and activation of cardiac sympathetic nerves, inducing TS and acute reversible myocardial dysfunction^[8]. Pheochromocytomas produce large amounts of catecholamines when stimulated, which have been reported to induce TS^[9] and were the final etiologic diagnosis in this case. Previously, many guidelines for the diagnosis of TS required the exclusion of pheochromocytoma, such as the Mayo diagnostic criteria^[10] that had been used for many years; however, the European Journal of Heart Failure introduced new diagnostic principles^[7] in recent years, and pheochromocytoma is no longer an exclusion criterion for TS. Typical apical balloon-like changes account for approximately 80% of all TS, and the current literature is dominated by these cases, while the remaining atypical subtypes are rarely reported. Epidemiologic studies show^[11] that the incidence of secondary forms of TS is about 3.4 hospitalizations per 100000 person-years, and TS caused by pheochromocytoma is rarely reported.

TS is broadly classified into four subtypes according to the site of involvement, apical, midventricular, basal, or focal^[6]. In mammalian studies, it has been reported^[12] that sympathetic nerve endings and β -adrenergic receptors are unevenly distributed across the myocardium, thus providing some evidence that different sympathetic nerve branches in the affected heart can lead to different lesion sites. One report^[13] shows a significant difference in heart rate variability between apical and midventricular TS, which also suggests that differences in sympathetic activation may be a potential mechanism for the different sites of TS pathology. Atypical TS has different clinical features from typical TS in that its patients have a younger age of onset, more frequent ST-segment alterations, and a higher prevalence of neurological disease, whereas a decrease in left ventricular ejection fraction and an increase in brain natriuretic peptide values are not evident^[14]. Atypical TS is more difficult to detect in the clinical setting.

In this case, the patient had the classical symptoms of myocardial infarction, such as episodes of chest tightness and breathlessness, ST-T segment abnormalities on ECG, wall dyskinesia on echocardiogram, and elevated troponin levels, as well as newly discovered unexplained paroxysmal palpitations, sweating, and elevated blood pressure and blood glucose levels. Although cardiac imaging did not reveal typical apical spherical changes, the diagnosis of TS could be made based on the absence of significant abnormalities on coronary angiogram, echocardiographic findings suggesting a basic loss of proximal apical lateral wall motion and abnormal segmental ventricular wall motion, and a repeat echocardiogram showing normal motion, which could further be classified as an atypical focal type of TS. The postoperative pathology clearly showed the presence of pheochromocytoma, which was the underlying cause of TS.

Pheochromocytomas are a significant pathogenic factor in TS. The sudden production of large doses of catecholamines is directly toxic to the myocardium, producing catecholamine-induced myocarditis, diffuse myocardial fibrosis, and induced heart failure^[15]; most patients can recover normal cardiac function after removal of the primary tumor^[16].

CONCLUSION

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In conclusion, we report a case of TS caused by pheochromocytoma. The leading causes of death in patients with TS are the sudden onset of illness and failure to receive prompt emergency treatment; therefore, the patient's prognosis depends on timely detection of the cause of the illness. Pheochromocytoma as the causative factor should not be overlooked in the management of TS, since early intervention can effectively improve myocardial remodeling, and clinicians should pay attention to this.

ACKNOWLEDGEMENTS

³
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⁵ Figure Legends

Figure 1 Electrocardiogram images. ST-segment elevation in leads I and AVL and ST-segment depression in leads II, III, and AVE; we initially predicted a high lateral wall myocardial infarction.

Figure 2 Coronary angiogram images. A-D: Coronary angiogram results showed no meaningful stenosis in the coronary arteries and unobstructed blood flow.

Figure 3 Adrenal computed tomography scan and pathology. A: Mass-like soft tissue shadow with heterogeneous density was present in the medial branch of the right adrenal gland; B: Immunohistochemical staining showed Chromogranin A (+), which was confined to the adrenal gland and did not invade the peri-adrenal tissue; C: HE stained tissue ⁸observed under 200 × light microscope; D: HE stained tissue observed under 400 × light microscope. HE: Hematoxylin-eosin.

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