Recurrent Left Ventricular Apical Ballooning Syndrome in a Patient with Pheochromocytoma

Huseyin Celebi, M.D.¹ Refik Erdim, M.D., F.E.S.C.¹ Kanber Ocal Karabay, M.D.¹
Ozlem Yildirimturk, M.D., F.E.S.C.¹ Vedat Aytekin, M.D., F.E.S.C.¹

¹ Department of Cardiology, Florence Nightingale Hospital, Istanbul, Turkey

Address for correspondence and reprint requests Refik Erdim, M.D., F.E.S.C., Abide-i Hurriyet Caddesi No: 290, Istanbul 80220, Turkey (e-mail: errefik@hotmail.com).

Int J Angiol 2012;21:63–68.

Abstract

Transient left ventricular apical ballooning syndrome is characterized by reversible left ventricular wall motion abnormalities, chest pain or dyspnea, ST-segment elevation, and mild elevation of cardiac enzyme levels in the absence of obstructive coronary artery disease. The pathophysiology of the syndrome is still unknown. The probable mechanism is supposed to be a catecholamine discharge. We report the case of a 66-year-old woman with recently diagnosed pheochromocytoma who presented with chest pain and ST-segment elevation. Coronary angiography revealed normal coronaries and apical dyskinesia at ventriculography. A similar episode of chest pain occurred 4 years ago with same angiographic findings and reversible inferobasal akinesia. In-hospital course was uneventful and the patient was discharged from the hospital 4 days later with treatment of aspirin 1 × 100 mg, metoprolol 1 × 50 mg, lisinopril 1 × 10 mg, and atorvastatin 1 × 20 mg. At 2 years follow-up after the event, the patient remained asymptomatic.

Keywords

- ▶ apical ballooning syndrome
- ▶ pheochromocytoma
- ▶ catecholamine

Transient left ventricular apical ballooning syndrome or “takotsubo” cardiomyopathy is characterized by acute onset of reversible left ventricular wall motion abnormalities including apical and mid-ventricular dyskinesia described as ballooning, with basal hyperkinesia.^{1,2} This syndrome usually mimics acute coronary syndrome consisting of chest pain or dyspnea, electrocardiographic changes, and mild elevation of cardiac enzyme levels in the absence of obstructive coronary artery disease.³ The incidence of apical ballooning syndrome is estimated at 1 to 2% among acute coronary syndrome patients.⁴ The pathophysiology of the syndrome is still unknown. The probable mechanism is supposed to be a catecholamine discharge triggered by various factors.^{5–7} We present a unique case of a 66-year-old woman who had recurrent chest pain and was recently diagnosed with pheochromocytoma.

Case Report

A 66-year-old woman was admitted to the emergency department because of sudden onset chest pain during the past 3

hours. Physical examination was normal and electrocardiogram (ECG) showed ST-segment elevations in leads I, II, aVL, aVF, and V2 through V6 by 0.1 to 0.4 mV on admission (▶ Fig. 1). Risk factors included diabetes mellitus, hyperlipidemia, and hypertension. At admission her blood glucose level was 165 mg/dL and total cholesterol level was 270 mg/dL. She had been investigated for labile hypertension 1 month ago and a right surrenal mass was found in abdominal ultrasonography and surrenal computed tomography. She was diagnosed with pheochromocytoma after the measurement of catecholamine levels and its metabolites on a 24-hour urine sample. She was waiting for surgical treatment. In her history, similar episode of chest pain occurred 4 years ago and the patient had been diagnosed with acute coronary syndrome. At that time, coronary angiography revealed normal coronary arteries and inferobasal dyskinesia (▶ Fig. 2). She had been followed-up with medical treatment including β-blocker, angiotensin-converting enzyme inhibitor, aspirin, and statin. At the current admission, the patient's medication consisted of β-blocker, angiotensin-converting enzyme inhibitor, and statin. Aspirin therapy was withdrawn for the past 5 days because of planned surgery. After

Figure 1 Electrocardiogram shows ST-segment elevations in leads I, II, aVL, aVF, V2 through V6 by 0.1 to 0.4 mV on admission.

the first evaluation, the patient underwent emergency cardiac catheterization due to a diagnosis of acute coronary syndrome. The coronary arteries were patent without any obstruction (►Fig. 3) and ventriculography demonstrated mid-ventricular and apical dyskinesia, basal hyperkinesia, and apical ballooning during ventricular systole (►Fig. 4). The echocardiography (ECHO) showed sigmoid septum and regional systolic dysfunction of the left ventricle walls with dyskinesia of the mid-apical segments and hyperkinesia of the basal segments with ejection fraction of 39% (►Fig. 5A). Laboratory analysis showed a peak serum troponin-T level of 1.2 ng/mL (normal range, 0.03 to 0.1) during admission. ECG showed T-wave inversion in leads I, II, aVL, aVF, and V2 through V6 on 2nd day (►Fig. 6). With supportive therapy, she recovered over the next few days and was discharged with aspirin 1 × 100 mg, metoprolol 1 × 50 mg, lisinopril 1 × 10 mg, and atorvastatin 1 × 20 mg. At discharge,

her blood glucose level was 130 mg/dL and total cholesterol level was 230 mg/dL. At follow-up two-dimensional ECHO demonstrated recovery of the ejection fraction to 58% and complete regression of left ventricular dysfunction 1 month after discharge (►Fig. 5B). Laparoscopic surgery was performed for the right surrenal mass. Histopathological examination confirmed the diagnosis of pheochromocytoma. The postoperative course was uneventful. At 2-year follow-up after the event, the patient remained asymptomatic.

Discussion

The cause of the transient left ventricular apical ballooning syndrome is still unknown. Several mechanisms have been proposed, including diffuse epicardial coronary spasm, microvascular dysfunction, and direct catecholamine-induced

Figure 2 Left ventriculography in year 2003. (A) End-systolic and (B) end-diastolic morphology of the left ventricle with inferobasal dyskinesia in end systole.

Figure 3 Coronary angiography. (A) Left coronary arteries and (B) right coronary artery were normal.

myocyte injury.^{8–11} High plasma catecholamine levels may play a role in this syndrome. Unfortunately, we could not measure plasma catecholamine levels in our case. A previous study suggested that the apical ballooning syndrome might be a result of catecholamine-associated stunning of the myocardium, which is provoked by emotional or physical stress.¹² There was no history of emotional or physical stress in this case. Increased sympathetic stimulation is also characteristic for pheochromocytoma. Takizawa et al¹³ reported a case of transient left ventricular ballooning with pheochromocytoma, supporting the pathogenetic role of catecholamines. Spes et al¹⁴ published a case of recurrent takotsubo phenomenon that proved to have a pheochromocytoma as most likely underlying diagnosis. In that case apical involvement was predominant in both episodes, but in our case the first episode was with inferobasal dyskinesia and the second

episode was with apical dyskinesia. Similarly, in our case, the patient had labile hypertension and was diagnosed with pheochromocytoma 1 month ago, probably recurrent hypotension and hypertension attacks were related to pheochromocytoma. Undulation of the plasma catecholamine levels could cause hemodynamic instability, which lead to apical ballooning syndrome.

It is interesting to study why the apex and mid-ventricular segments of the heart are affected and the basal segments are spared. However, this may be related to increased adrenergic receptor density in cardiac apical segments or increased apical myocardial responsiveness to adrenergic stimulation.¹⁵ In contrary to this, there was only inferobasal dyskinesia on the left ventriculography in the first presentation of our patient in 2003. However, there was typical appearance of the apical ballooning syndrome on the left ventriculography

Figure 4 Left ventriculography at the current admission. (A) End-systolic and (B) end-diastolic morphology of the left ventricle with the typical appearance of apical ballooning in end systole.

Figure 5 Transthoracic echocardiography on (A) admission and (B) 1 month later. LA, left atrium; LV, left ventricle.

Figure 6 Electrocardiogram shows T-wave inversion in leads I, II, aVL, aVF, V2 through V6 on 2nd day.

at the current admission in the same patient. The apical ballooning syndrome mostly occurs in postmenopausal women.¹⁶ Our patient was also a 66-year-old woman. The explanation of this entity is also unclear. However, it may be related to postmenopausal alterations of endothelial function in response to reduced estrogen levels and microvascular vasomotor reactivity in response to adrenergic stimuli.¹⁷ In conclusion, differential diagnosis between atherosclerotic coronary artery disease and apical ballooning syndrome seems to be only verified by coronary angiography. It is believed that medical management of apical ballooning syndrome is safe and compatible with good long-term outcome. Clinical symptoms and left ventricular dysfunction usually recover completely within several weeks. In particular, clinicians should suspect this syndrome, especially in postmenopausal women who present with acute coronary syndrome and normal coronary arteries. Further research is needed to identify risk factors and the underlying mechanisms for this syndrome.

References

- 1 Tsuchihashi K, Ueshima K, Uchida T, et al; Angina Pectoris-Myocardial Infarction Investigations in Japan. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol* 2001;38(1):11-18
- 2 Kurisu S, Sato H, Kawagoe T, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* 2002;143(3):448-455
- 3 Bybee KA, Kara T, Prasad A, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med* 2004;141(11):858-865
- 4 Cangella F, Medolla A, De Fazio G, et al. Stress induced cardiomyopathy presenting as acute coronary syndrome: Tako-Tsubo in Mercogliano, Southern Italy. *Cardiovasc Ultrasound* 2007; 5:36-
- 5 Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005;111(4):472-479

- 6 Lentschener C, Vignaux O, Spaulding C, Bonnichon P, Legmann P, Ozier Y. Early postoperative tako-tsubo-like left ventricular dysfunction: transient left ventricular apical ballooning syndrome. *Anesth Analg* 2006;103(3):580–582
- 7 Shaw TR, Rafferty P, Tait GW. Transient shock and myocardial impairment caused by phaeochromocytoma crisis. *Br Heart J* 1987;57(2):194–198
- 8 Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352(6):539–548
- 9 Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Sasaka K. Reversible left ventricular dysfunction “takotsubo” cardiomyopathy related to catecholamine cardiotoxicity. *J Electrocardiol* 2002;35(4):351–356
- 10 Mann DL, Kent RL, Parsons B, Cooper G IV. Adrenergic effects on the biology of the adult mammalian cardiocyte. *Circulation* 1992;85(2):790–804
- 11 Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. *J Am Coll Cardiol* 1994;24(3):636–640
- 12 Mori H, Ishikawa S, Kojima S, et al. Increased responsiveness of left ventricular apical myocardium to adrenergic stimuli. *Cardiovasc Res* 1993;27(2):192–198
- 13 Takizawa M, Kobayakawa N, Uozumi H, et al. A case of transient left ventricular ballooning with pheochromocytoma, supporting pathogenetic role of catecholamines in stress-induced cardiomyopathy or takotsubo cardiomyopathy. *Int J Cardiol* 2007;114(1):e15–e17
- 14 Spes C, Knape A, Mudra H. Recurrent tako-tsubo-like left ventricular dysfunction (apical ballooning) in a patient with pheochromocytoma - a case report. *Clin Res Cardiol* 2006;95(5):307–311
- 15 Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005;111(4):472–479
- 16 Celermajer DS, Sorensen KE, Spiegelhalter DJ, Georgakopoulos D, Robinson J, Deanfield JE. Aging is associated with endothelial dysfunction in healthy men years before the age-related decline in women. *J Am Coll Cardiol* 1994;24(2):471–476
- 17 Ueyama T, Hano T, Kasamatsu K, Yamamoto K, Tsuruo Y, Nishio I. Estrogen attenuates the emotional stress-induced cardiac responses in the animal model of Tako-tsubo (Ampulla) cardiomyopathy. *J Cardiovasc Pharmacol* 2003;42(Suppl 1):S117–S119