INNOVATIVE COLLECTIONS

COMPLEX CASE STUDY

Pheochromocytoma Presenting as Recurrent Stress Cardiomyopathy with Multiple Monomorphic Ventricular Tachycardias

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ABSTRACT. Adrenergic crisis due to pheochromocytomas is a recognized cause of transient left ventricular dysfunction mimicking stress cardiomyopathy, and isolated cases of pheochromocytomas presenting like stress cardiomyopathy have been reported. Pheochromocytomas have been associated with both typical (apical ballooning) and reverse (basal and mid-ventricular ballooning) types of stress cardiomyopathy and, rarely, pheochromocytomas have also presented with ventricular arrhythmias. In this report we describe a patient presenting with recurrent stress cardiomyopathy episodes, alternating patterns of wall motion abnormalities, and distinct monomorphic ventricular arrhythmias who was subsequently diagnosed with pheochromocytoma.

KEYWORDS. pheochromocytoma, reverse stress cardiomyopathy, stress cardiomyopathy, takotsubo cardiomyopathy, ventricular tachycardia.

Introduction

Pheochromocytomas are uncommon neuroendocrine tumors that typically present with paroxysmal headache, nausea, palpitations, and hypertension. Rarely, catecholamine secretion from pheochromocytomas induces a clinical syndrome mimicking takotsubo or stress cardiomyopathy manifest by acute left ventricular systolic dysfunction without coronary artery obstruction.1–4 Even more unusual, pheochromocytomas present with life-threatening ventricular arrhythmias and cardiogenic shock.5–8 Additionally, pheochromocytomas have been associated with recurrent episodes of stress cardiomyopathy1,4 as well as the reverse type of stress cardiomyopathy.3,9–11 This report highlights an atypical presentation of pheochromocytoma characterized by recurrent episodes of stress cardiomyopathy of both typical and reverse patterns as well as coincident multifocal monomorphic ventricular tachycardias.

Case

A 65-year-old female with a history of hypertension presented to her local emergency room with chest pain, nausea, and vomiting for several hours. She also had an episode of syncope with no prodrome, resulting in a fall. Her symptoms came on suddenly and were not related to exertion. She had an ailing grandchild but otherwise had no acute psychological stressor. Prior to this episode she was in her state of usual health. She had never experienced similar symptoms and never had any formal cardiovascular testing. Her past medical history was notable for hypertension. Her surgical history consisted of carpal tunnel surgery. She took olmesartan for hypertension and had no drug allergies. She had a 35 pack-year tobacco history and consumed one to two glasses of wine a week. There was no family history of early coronary artery disease, arrhythmias, or sudden cardiac death. Her father had colon and liver cancers.

Her general appearance was a well-nourished female in mild distress. She was afibrile and her heart rate and blood pressure were normal. She was found to have 1–2 mm ST elevation in leads V2–V5 prompting emergent left heart catheterization (Figure 1a). Her coronary angiograms revealed non-obstructive coronary artery disease with normal flow. Left ventriculogram revealed...
depressed systolic function, apical hypokinesis with mid-ventricular hyperkinesis (Figure 1b), consistent with an apical ballooning pattern. Her course was complicated by cardiogenic shock requiring intraortic balloon counterpulsation and inotropic support. She was weaned off chemical and mechanical support within 48 h; a subsequent transthoracic echocardiogram demonstrated recovery of systolic function. She was diagnosed with stress cardiomyopathy and discharged on carvedilol, aspirin, plavix, furosemide, and digoxin with plans for outpatient follow-up.

One month later, she developed headache, palpitations, and nausea that began during sleep. Her palpitations were accompanied by syncopal episodes. On arrival to the emergency room, her symptoms had resolved and she was in sinus rhythm (Figure 2a) with T-wave inversion in V3–V5 without evidence of ST segment elevation. Her blood pressure was 89/59, and she had no evidence of congestive heart failure or low-perfusion state on initial examination. Her initial laboratory tests was relatively unremarkable (Na 134, K 3.6, Cl 96, HCO₃ 25, BUN 17, Creat 1.0, Glc 172; WBC 7.5, HCT 42%, Plt 417; INR 1.3; CK 237, CK-MB 2.1, Trop 0.09). She developed recurrence of nausea and palpitations and was found to be in a wide complex tachycardia with a right bundle branch block morphology and right axis deviation (Figure 2b). She became hypotensive and was initiated on a phenylephrine infusion as well as intravenous lidocaine. Subsequently, her rhythm converted to a different monomorphic ventricular tachycardia with left bundle branch morphology and left axis deviation (Figure 2c). Ultimately she converted to sinus rhythm and was transferred to our institution for further care.

Repeat electrocardiogram (ECG) demonstrated prolongation of the QTc interval and progression of anterior T-wave inversion (Figure 3a). Laboratory studies revealed interval rise in troponin-I to 3.8. She was successfully weaned off the phenylephrine and lidocaine infusions. Although she had undergone left heart catheterization demonstrating normal coronary arteries 1 month previously, the combination of ventricular arrhythmias with cardiac biomarker elevation and shock prompted re-evaluation for an ischemic etiology. Again, the left heart catheterization demonstrated normal coronary arteries. Left ventriculogram demonstrated basal akinesis with mid-ventricular variant or ‘reverse’ stress cardiomyopathy (Figure 3b). Cardiac magnetic resonance imaging (MRI) revealed no infiltrative or valvular heart disease, and there was no evidence of prior infarct. She had an ejection fraction of 45%, and there was basal and mid-ventricular hypokinesis with preserved apical contractility. There were no intracardiac masses, and the visualized portions of the liver, spleen, kidneys, and adrenal glands were normal. Based on her history of syncope and ventricular tachycardias, the electrophysiology service was consulted for consideration of implantable cardioverter-defibrillator (ICD) placement. Although there were no reproducible ventricular tachycardias on electrophysiology study, an ICD was placed given her history of multiple distinct ventricular tachycardias, syncope, and recurrent stress cardiomyopathy. She was discharged on carvedilol 6.25, lisinopril, 2.5, aspirin 81 mg, furosemide 20 mg qd, and plavix 75 mg.

Several months later, she presented with nausea, palpitations, and multiple ICD shocks. Device interrogation revealed sustained ventricular tachycardia between 160 and 180 bpm. She received appropriate antitachycardia pacing and defibrillation sequences twice, for a total of 12 attempts of anti-tachycardia pacing and 14 defibrillations (Figure 4a). The rhythm was refractory to both antitachycardia pacing algorithms and sequential defibrillations. She remained in sustained ventricular tachycardia with a rate of approximately 160 bpm for approximately 2 h until she spontaneously converted to sinus rhythm. She was placed on an amiodarone infusion and underwent emergent left heart catheterization that again revealed normal coronary arteries. Echocardiogram demonstrated severe global hypokinesis with

Figure 1: (a) A 12-lead electrocardiogram (ECG) with 1–2 mm ST elevation in leads V2–V5. (b) A left ventriculogram with typical stress cardiomyopathy wall motion abnormalities characterized by basal hyperkinesis and apical ballooning.
ejection fraction of approximately 20%. The rest of her hospitalization was unremarkable and she was discharged with amiodarone and high-dose β-blockers. Three weeks later a repeat echocardiogram showed marked improvement in ejection fraction to 50% with normal wall motion (Figure 4b).

Approximately 2 months later, she presented with severe headache, palpitations, abdominal pain, and nausea. She was in sinus rhythm with left bundle branch block, and her blood pressures were markedly labile ranging from 90 to 180 mmHg systolic. A computed tomography (CT) scan of the abdomen revealed a 4.1 × 4.6 cm cystic L adrenal mass. Urinary metanephrines were markedly elevated, strongly suggesting the presence of a neuroendocrine tumor. After consultation with endocrinology and endocrine surgery, she underwent successful left adrenalectomy. The tissue stained positive for S100, synaptophysin, and neurofibromatosis-1,

Figure 2: Serial electrocardiograms demonstrate (a) sinus rhythm with anterolateral ischemic ST/T wave changes, (b) wide complex tachycardia with right bundle branch block morphology, and (c) wide complex tachycardia with left bundle branch block morphology.
consistent with a diagnosis of pheochromocytoma. In the 3 months following her tumor removal, she has not had any recurrent symptomatic episodes or arrhythmias noted on device interrogation.

Discussion

Stress or takotsubo cardiomyopathy is a recently defined clinical entity that has become increasingly understood over the past two decades. The classic presentation is usually triggered by severe emotional or physical stress, causes severe transient left ventricular apical hypokinesis with basal hyperkinesis, and mimics acute coronary syndrome. The distinguishing features of stress cardiomyopathy according to proposed Mayo Clinic criteria include: 1) transient left ventricular dyskinesis not represented by a single epicardial artery vascular territory; 2) absence of obstructive coronary artery disease; 3) ECG changes such as ST elevation and/or T-wave inversion; and 4) the absence of head trauma, intracranial hemorrhage, obstructive coronary artery disease, pheochromocytoma, myocarditis, and hypertrophic cardiomyopathy. Although there is a 2% mortality in the initial phases of the syndrome, most patients experience full recovery with rare reports of recurrence. Of the alternative causes of stress cardiomyopathy phenotypes, neuroendocrine tumors have a seemingly disparate representation in the literature for causing the reverse stress cardiomyopathy pattern; however, this may be the result of publication bias. Furthermore, there are scattered reports of recurrent episodes of stress cardiomyopathy associated with an underlying pheochromocytoma or paraganglioma. This care report highlights several interesting features of the stress cardiomyopathy phenotype and pheochromocytomas. This is an atypical presentation of a pheochromocytoma with the initial episode characterized by cardiogenic shock, anterior ST segment elevation and typical stress cardiomyopathy wall motion. The “typical” features of the pheochromocytoma paraneoplastic syndrome were not evident. Additionally, an MRI scan showed no evidence of adrenal tumor during her initial presentations. During the subsequent event 1 month later, the patient exhibited normotension, sustained ventricular tachycardia of multiple morphologies, and deep T-wave inversion without ST segment elevation and the reverse stress cardiomyopathy pattern. These findings are consistent with observations that typical stress cardiomyopathy is more likely to cause shock and to be associated with anterior ST elevation, whereas reverse stress cardiomyopathy usually exhibits diffuse, deep T-wave inversions. Typical and reverse forms of stress cardiomyopathy occurring in the same patient have been reported only a few times in

Figure 3: (a) Sinus rhythm with anterolateral T-wave inversion with QT prolongation. (b) A left ventriculogram with atypical stress cardiomyopathy wall motion abnormalities characterized by basal hypokinesis and apical hyperkinesis.
the literature, and to our knowledge has never been reported in a patient with pheochromocytoma. Furthermore, multiple distinct ventricular tachycardias associated with pheochromocytomas have only been reported once. In this case, the underlying mechanism of the ventricular tachycardias was consistent with abnormal automaticity and/or triggered activity, as evidenced by a lack of efficacy with ATP or ICD shocks. These mechanisms would be more likely in the case of a high catecholamine state associated with paraneoplastic syndrome associated with pheochromocytoma, rather than a re-entrant mechanism which would be associated with a scar-mediated tachycardia (i.e. ischemic or dilated cardiomyopathy). Additionally, this report is consistent with other case reports of patients with recurrent ventricular tachycardia in the setting of pheochromocytoma whose arrhythmias resolve with removal of the tumor. Therefore, ICD implantation could be avoided with prompt identification of underlying pheochromocytomas that present as recurrent ventricular tachycardia.

**Conclusions**

In this case report we show a patient presenting with recurrent stress cardiomyopathy with varying morphologies.
and multiple sustained ventricular tachycardias who had an underlying diagnosis of pheochromocytoma. Although there are case reports of patients with pheochromocytomas presenting with recurrent stress cardiomyopathy, both typical and variant type of wall motion abnormalities, and multifocal ventricular tachycardias, this is to our knowledge the first patient who has displayed all of these clinical features. This case will hopefully add to the growing body of literature linking pheochromocytomas and catecholamines to stress cardiomyopathy and ventricular arrhythmias to help understand the pathogenesis and future treatment of these processes.

References