Case Report and Review of Literature

Catecholamine induced cardiomyopathy in pheochromocytoma

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ABSTRACT

Catecholamine induced cardiomyopathy in the setting of pheochromocytoma is an unusual clinical entity. Earlier studies have reported left ventricular dysfunction in around 10% of subjects with pheochromocytoma.[1] Catecholamine induced vasoconstriction, direct toxic effect of byproducts of catecholamine degradation and direct receptor-mediated mechanisms are thought to contribute to cardiomyopathy in subjects with pheochromocytoma. The presentation remains a diagnostic challenge as patients may already have hypertensive heart disease and acute coronary syndrome on account of uncontrolled secondary hypertension. We report a case of a 42-year-old male, who presented with features of pheochromocytoma induced cardiomyopathy.

Key words: Pheochromocytoma, catecholamines, cardiomyopathy, milrinone, India

Introduction

Pheochromocytomas are catecholamine producing tumors. They may be adrenal or extra adrenal in location or may occur as part of endocrine syndromes. The classical clinical manifestation of this tumor is the triad of diaphoresis, palpitations, and headache. Cardiomyopathy on account of excess catecholamines is a relatively rare and clinically challenging complication of pheochromocytoma.

Case Report

A 42-year-old male working as a clerk, presented elsewhere with episodic palpitations, headache, and sweating of 2 years duration. The frequency of these paroxysms gradually increased over the past 6 months. On evaluation elsewhere, he was found to have hypertension, which was difficult to control with three antihypertensive drugs. He was hence evaluated for secondary hypertension.

An ultra sonogram of the abdomen was performed initially, as he had undergone left side nephrectomy for voluntary kidney donation 9 years ago. The ultra sonogram revealed a right adrenal mass and he had a positive metaiodobenzylguanidine scan suggesting a right adrenal pheochromocytoma. He was started on three antihypertensive agents, elsewhere.

He was referred to our institute for further management. A computerized tomography of the abdomen revealed a heterogeneously enhancing mass of size 4.9 × 5.3 × 5.0 cm [Figure 1] in the right adrenal gland. Left adrenal appeared normal [Figure 2]. He was evaluated further and was found to have elevated 24-h urinary metanephrin and normetanephrin levels {2050 μg (normal <350 μg/24 h) and 6240 μg (normal <600 μg/24 h) respectively}. He was admitted to the ward at 8.30 PM. At admission his heart rate was 120/min and blood pressure was 160/100 mmHg in the right upper limb in the supine position with no significant postural drop. Cardiovascular examination was unremarkable; few basal crackles were heard on auscultation of chest. Central nervous system examination including optic fundii did not show any significant abnormality.

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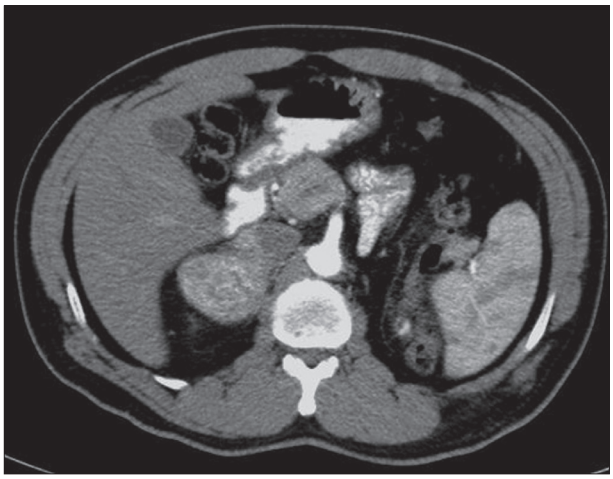

Figure 1: CT abdomen showing mass in right adrenal

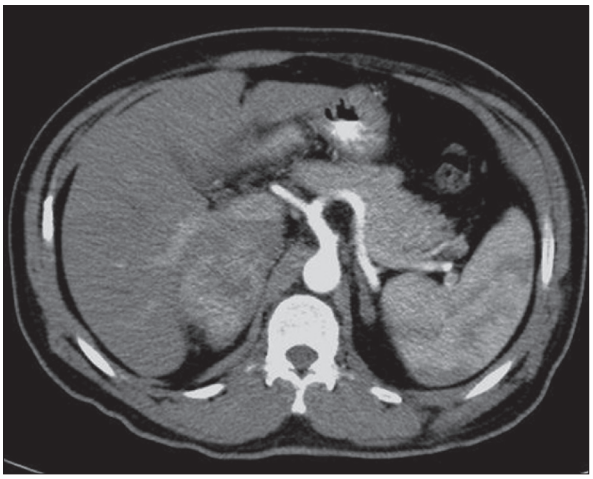

Figure 2: CT abdomen showing normal left adrenal

Examination of the abdomen was unremarkable except for a 12 cm nephrectomy scar on the left side.

He did not have any features suggestive of syndromic association including multiple endocrine neoplasiae, Von Hippel Lindau syndrome, or neurofibromatosis.

An electrocardiogram done at admission was within normal limits.

In view of pheochromocytoma, he was started on an alpha blocker. Forty five minutes after administering 2.5 mg of Prazosin, he developed giddiness and had a fall. His systolic blood pressure at that point of time was 60 mm of Hg. First dose effect of alpha blocker was thought of at that point of time. However, the bibasal crepitations, which he already had, worsened progressively. An electrocardiogram done revealed a new onset left anterior fascicular block. Cardiac enzymes were grossly elevated creatinine kinase-muscle brain faction {CKMB: 35 ng/ml (normal <6.7 ng/ml); Troponin T: 1234 pg/ml (normal <14 pg/ml)}. The possibility of a myocardial injury was considered and cardiology opinion was sought.

An emergency echocardiogram was performed. This revealed global hypokinesia with no regional wall motion abnormality. Left ventricular ejection fraction was 31%. This was not consistent with an acute coronary syndrome. The patient was shifted to coronary care unit for further management. Cardiac enzymes were repeated after 4 h. This did not show an elevation.

Given the absence of regional wall motion abnormality on echocardiogram and lack of serial rise of cardiac enzymes, the possibility of catecholamine induced cardiomyopathy was considered to be more likely than an acute coronary event.

Patient was started on Milrinone (a phosphodiesterase 3 inhibitor) infusion along with a loop diuretic. He improved gradually, blood pressure stabilized over the next 48 h. He was restarted on beta blockers and continued on alpha blocker prazosin and was shifted out of cardiac intensive care unit (CCU). Phenoxybenzamine was also started within the next 24 h, which he tolerated well.

He was prepared for surgery and underwent the same uneventfully after 2 weeks. During laparoscopic adrenalectomy, a 6 × 5 cm vascular tumor arising in right adrenal gland was found and excised. Immediate postoperative period was managed in surgical intensive care unit as he had a hypertensive surge. After control of blood pressure, he was shifted to ward on the second postoperative day. His blood pressure stabilized and remained within normal limits there after without any antihypertensives.

His cardiac function improved and he did not have any features of failure thereafter.

Discussion

The presentation of catecholamine induced cardiomyopathy is similar to stress-induced cardiomyopathy (Takotsubo cardiomyopathy). In both these conditions the overwhelming effect of catecholamines results in vasoconstriction of small arterioles. Metabolites of catecholamines also cause direct toxic effect on myocardium. Though these two conditions have similar clinical presentation and histology,[2] Takotsubo is classically described in postmenopausal women[3] and is usually self limiting.

The key to management of catecholamine induced cardiomyopathy associated with pheochromocytoma is early intervention in the form of surgery. There are reports

of complete reversibility of the myocardial dysfunction with surgical treatment.[4] The myocardial function improved as early as 8 days after intervention.[5]

In this patient, the management of hypotension was a challenge. He had LV dysfunction and could not be overloaded with fluids. He could not be given the conventional vasopressors as he already had catecholamines in abundance due to pheochromocytoma. Further administration of ionotropes would not help in the management of hypotension in LV failure.

As he had only one kidney, severe vasoconstriction and hypotension would have proved detrimental. Hence he was started on milrinone, an ionodilator. This drug, a phosphodiesterase 3 inhibitor induces peripheral vasodilatation and improves cardiac contractility. Cardiac contractility is enhanced by increased contraction of the left ventricle by increasing Cyclic Adenosine Monophosphatase (cAMP) activity and there by increasing calcium influx into the cardiac sarcoplasmic reticulum.[6] Milrinone (Phosphodiesterase 3 inhibitor) inhibit the degeneration of intracellular cAMP. In the vascular smooth muscle, cAMP inhibits myosin light chain kinase, an enzyme responsible for phosphorylating smooth muscle myosin and causing contraction. Milrinone thus serves to decrease vascular smooth muscle tone, without a negative ionotropic action on the heart.[7]

We report this case because of the diagnostic challenges involved as he had a single kidney and cardiomyopathy, and to stress on the management issues of hypotension in the presence of catecholamine excess. In view of the complete reversibility of this condition, it is imperative to diagnose and intervene early.

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