Severe Dilated Cardiomyopathy After Propranolol Treatment in an Undiagnosed Adrenal Pheochromocytoma

Rachel Krasnow McEntee, BA; David Coyle, MD; Markus Meyer, MD

A 43-year-old woman presented to an outside hospital with 3 hours of newly onset substernal chest pressure, associated nausea, vomiting, shortness of breath, palpitations, and diaphoresis. Her medical history was significant for 18 months of episodic headaches that were diagnosed as atypical migraines and being treated with daily propranolol 60 mg initiated 1 week before the current presentation. Blood pressure on presentation was 144/112 mm Hg, initial ECG showed T-wave inversions in leads I and aVL (Figure 1A), and troponin I level was 0.497 ng/mL (normal, <0.034 ng/mL). The chest pain was relieved by nitroglycerin infusion, which was discontinued after 40 minutes secondary to a decrease in blood pressure to 95/72 mm Hg. The patient was treated with aspirin, clopidogrel, and heparin and transferred to our hospital for urgent left heart catheterization.

On presentation to our hospital, blood pressure was 97/50 mm Hg, troponin I was 4.54 ng/mL (positive, >0.8 ng/mL), and the ECG showed partial resolution of T-wave inversion and sinus tachycardia (Figure 1B). Coronary angiography showed no clinically significant coronary artery disease. Transthoracic echocardiogram revealed moderate dilation of the left ventricle (LV), diffuse LV hypokinesis, and moderate to severely decreased LV function with an LV ejection fraction of 25% to 30%. The patient developed symptomatic hypotension to 75/55 mm Hg with tachycardia and was transferred to the intensive care unit. A central venous catheter was placed, and she was monitored closely for further hemodynamic instability. She stabilized without further intervention. Plasma fractionated metanephrines were drawn on hospital day 3 to evaluate for pheochromocytoma given the patient’s history of episodic tachycardia, headache, and diaphoresis. Carvedilol 3.125 mg and lisinopril 5 mg were started. She remained hemodynamically stable and asymptomatic and was discharged home on hospital day 4 with carvedilol 3.125 mg BID and lisinopril 10 mg daily with plans to follow up with outpatient cardiology.

On the day of discharge, the patient was asymptomatic at home with palpitations, diaphoresis, presyncope, and a self-measured blood pressure of 160/110 mm Hg. A 24-hour Holter monitor was placed, which was negative, although she was asymptomatic during the monitoring period. On postdischarge day 3, laboratory results returned abnormal plasma fractionated metanephrines; these results were followed up with a 24-hour urine test, which also was markedly elevated (Table). Abdominal CT showed a 3.5×2.9×2.7-cm right-side adrenal mass (Figure 2A). Medical treatment was changed to metoprolol succinate 25 mg daily, phenoxybenzamine 10 mg daily, and lisinopril 15 mg daily. Repeat transthoracic echocardiogram 1 month after presentation and 2 weeks after initiating phenoxybenzamine therapy showed normal LV systolic function with an LV ejection fraction of 65% to 70% without wall motion abnormalities. Two months after initial presentation, the patient underwent laparoscopic adrenalectomy after preoperative tyrosine hydroxylase blockade. Surgery revealed a 3.6×3.0×2.8-cm adrenal mass consistent with pheochromocytoma, and immunohistochemical staining was positive for the neuroendocrine markers synaptophysin and chromogranin (Figure 2B through 2D).

Discussion

Cardiovascular complications and cardiotoxicity as a result of pheochromocytoma have been documented. They include LV hypertrophy, myocardial infarction, arrhythmias, heart failure, and cardiogenic shock.1 In this case, a patient with an undiagnosed pheochromocytoma developed a symptomatic dilated cardiomyopathy and severe left-sided heart failure after initiation of β blockade with propranolol. The subsequent rapid structural and functional recovery of the myocardium after appropriate α blockade was administered highlights the importance of α blockade and its dramatic effect toward improving LV function in this setting. Although this patient’s symptoms were transiently improved with treatment with carvedilol, which provides α and β blockade in a ratio of 1:10, her symptoms and echocardiographic findings were most improved after the addition of phenoxybenzamine. In contrast, although she had chronic systemic symptoms, her acute presentation was likely facilitated by the initiation of propranolol and the resultant unopposed α-adrenergic stimulation.

This case contributes to the literature that seeks to understand the pathophysiology of catecholamine-induced damage to the myocardium. Mobine et al2 posited that the cardiomyopathy seen in pheochromocytoma is mediated by cell-
secreted factors in a synergistic fashion with norepinephrine (NE) exposure, based on their findings of increased LV dilation in rodents implanted with pheochromocytoma cells versus NE pumps and their observation that cardiomyopathy was induced in rodents with cell implants at serum NE levels significantly lower than those with NE infusion pumps. The present case and others,3,4 show that the reversal of pheochromocytoma-induced cardiomyopathy is achievable with aggressive α-adrenergic blockade before surgical removal of the tumor, suggesting that although it may not be the sole factor inciting damage to the myocardium, targeting the α-adrenergic NE effects is a useful pharmacological approach. Additional study into this area is warranted because although rare, pheochromocytoma provides an interesting model to elucidate the vulnerability of the myocardium to adrenergic stimulation.

Consideration of pheochromocytoma as a possible diagnosis is best pursued on an outpatient basis. This case serves as a poignant illustration of the importance of broad differentials and describes the pathophysiological cardiac effects of unopposed α stimulation in a primarily NE-secreting pheochromocytoma. Careful attention to the patient’s history should be paid to evaluate for pheochromocytoma in any patient with an unexplained, nonischemic cardiomyopathy before initiation of β blockade.

Disclosures
Dr Meyer has received research grant from the National Institutes of Health (R21 NIH Cardiorenal Protection of N-Acetylcysteine) and honoraria from Gilead Sciences.

**Table.** Results of Fractionated Metanephrines Showing Elevated Plasma Normetanephrine and Elevated Urine Normetanephrine and Total Metanephrines

<table>
<thead>
<tr>
<th></th>
<th>Result</th>
<th>Normal</th>
</tr>
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<tbody>
<tr>
<td><strong>Plasma (drawn hospital day 3)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normetanephrine</td>
<td>7.60 nmol/L</td>
<td>&lt;0.90</td>
</tr>
<tr>
<td>Metanephrines</td>
<td>0.22 nmol/L</td>
<td>&lt;0.50</td>
</tr>
<tr>
<td><strong>24-h urine (collected postdischarge day 9)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metanephrines</td>
<td>148 μg</td>
<td>30–180 (normotensive)</td>
</tr>
<tr>
<td>Normetanephrine</td>
<td>2998 μg</td>
<td>156–561 (normotensive)</td>
</tr>
<tr>
<td>Total metanephrines</td>
<td>3146 μg</td>
<td>156–561 (normotensive)</td>
</tr>
</tbody>
</table>

**Figure 2.** A, Abdominal CT showing a 3.5×2.9×2.7-cm right-side adrenal mass. B, Intraoperative laparoscopic image of mass. C, Gross pathology specimen. D, Histological image showing positive chromogranin staining (magnification ×20).
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