Undiagnosed Pheochromocytoma Presenting with Takotsubo-Pattern Cardiomyopathy  
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INTRODUCTION

- Pheochromocytomas (PCC) are rare neuroendocrine tumors most commonly arising from adrenal chromaffin cells. Patients classically present with symptoms of catecholamine excess, such as headaches, palpitations, diaphoresis, hypertension and tachycardia.
- Cardiovascular manifestations of pheochromocytomas include Takotsubo-pattern cardiomyopathy (TCCM), dilated cardiomyopathy (DCM), and hypertrophic cardiomyopathy (HCM), and may present as left ventricular dysfunction or overt heart failure.
- We present a case of Takotsubo-pattern cardiomyopathy associated with undiagnosed pheochromocytoma, which was likely induced by exogenous corticosteroid injection.

CASE PRESENTATION

- A 73-year-old female with past medical history of hypertension, hyperlipidemia, stage I breast cancer, presented to emergency department with a 6-day history of epigastric pain, nausea, vomiting, diaphoresis and headaches.
- Patient reported symptoms started right after receiving a trigger finger methylprednisolone injection with subsequent oral methylprednisolone taper starting from 24mm.
- On admission she was tachycardic (125/min), normotensive (112/70 mmHg), saturating 93-96% on room air, and found to have significantly elevated troponin (8th gen. Troponin: 1649-2191), leukocytosis (25.6 x10³/µL) and creatinine (1.32 mg/dL) and NT-pro-BNP >7000 pg/mL.
- CT scan of chest to pelvis (Figure 1) revealed bilateral ground-glass opacities concerning for multi-local pneumonia vs pulmonary edema, 4.2x3.6 cm right adrenal mass, no other significant findings in GI tract.
- There were no ECG findings to suggest acute coronary syndrome, and echocardiogram (Figure 2) showed reduced ejection fraction (35-40%), hyperdynamic LV base with akinesis in other segments.
- Given lack of chest pain, no further ECG changes and flat trend of troponins consistently between 1852-2330, diagnosis of Takotsubo (stress-initiation of CICMPP): dilated CMP, Takotsubo-like cardiomyopathy (TCCM), and hypertrophic CMP (HCM).

FURTHER INVESTIGATION

- Repeat echocardiogram done 6 weeks post-discharge showed a normalized ejection fraction (60-65%), and resolution of previously-noted regional wall motion abnormalities and left ventricular thrombus.
- For right adrenal mass, there was initial concern of breast cancer metastasis, which was previously treated with lumpectomy, radiation therapy and hormonal therapy. PET-CT was done, revealing very low grade activity in right breast, modest activity in right adrenal mass.
- Workup was initiated for adrenal mass revealed extremely high epinephrine, metanephrine and normetanephrine levels in 24-hr urine collection, suggestive of pheochromocytoma (Table 1).
- Patient underwent alpha blockade and successful resection of right adrenal mass 2 months after discharge. Surgical pathology confirmed diagnosis of pheochromocytoma.

Figure 1. CT scan of chest to pelvis revealed (A) bilateral ground-glass opacities concerning for multi-local pneumonia vs pulmonary edema (lung window), and (B) 4.2 x 3.6 cm right adrenal mass with possible central necrosis (liver window).

Figure 2. End-systole echocardiogram demonstrating Takotsubo pattern, along with reduced EF, hyperdynamic LV base with akinesis of mid-apical inferior, mid anterospetal, mid inferoseptal, mid-apical inferior, mid interlateral, apical septal, apical lateral walls and apex.

Table 1. 24-hr urine study for catecholamines and metanephrines, with total urine creatinine and volume. Units are mcg/24hr if not specified.

<table>
<thead>
<tr>
<th>Catecholamines</th>
<th>Metanephrines</th>
<th>Reference range</th>
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<tbody>
<tr>
<td>Epinephrine</td>
<td>Metanephrines</td>
<td>N/A</td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
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<tr>
<td>Noradrenaline</td>
<td></td>
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<tr>
<td>Metanephrines</td>
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<tr>
<td>Creatinine</td>
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<td>Urine volume</td>
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DISCUSSION

- The clinical presentation of PCC is caused by excess catecholamine release, can be quite variable and is often paroxysmal in patients. In literature only 10-20% of patients present with PCC-induced cardiomyopathy.
- Pheochromocytoma crisis (PC), as defined by severe hypertension or hypotension resulting in end-organ damage, can be potentially triggered by certain medications, and there have been several case reports of PC precipitated by exogenous corticosteroids as in our patient (9).
- Takotsubo (stress-induced) cardiomyopathy, on the other hand, is often a reversible condition triggered by intense emotional or physical stress. Although of similar pathogenesis related to excessive catecholamines, pheochromocytoma should be excluded before making a diagnosis per the Mayo Clinic Criteria (10).
- Literature suggest that there are 3 main categories of presentation in catecholamine-induced cardiomyopathy in PCC (CICMPP): dilated CMP, Takotsubo-like cardiomyopathy (TCCM), and hypertrophic CMP (HCM). There is no consensus on treatment, and management would need to be tailored according to the variable clinical presentations.
- In patients with PCC, initiation of β-blockers before a-blockade may be detrimental, since it may cause unopposed α-agonistic stimulation and hypertensive crisis. Although hypertension is more common in PCC, hypotension is also seen, more in epinephrine-secreting tumors. This is probably due to chronic excessive circulating epinephrine causing downregulation of β-receptors and cardiac contractility (11).
- Our patient was never hypertensive during this admission, initiation of metoprolol likely caused further cardiac dysfunction and drastic hypotension. Upon discharge, she received carvedilol. 6 weeks later EF normalized. Carvedilol’s partial α-blocking effect was likely beneficial.

CONCLUSIONS

- Our case illustrates that pheochromocytoma should be part of the differential diagnoses of stress-induced cardiomyopathy. High clinical suspicion is still necessary for the diagnosis of pheochromocytoma.
- Patients with pheochromocytoma should be started on α-blockers prior to β-blockade. Cardiac dysfunction after initiation of β-blockers should also caution clinicians of the possibility of pheochromocytoma.

REFERENCES