

## Acute cardiomyopathy and multiorgan failure in a patient with pheochromocytoma and neurofibromatosis type 1

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### Abstract

Pheochromocytomas are catecholamine secreting tumours of the adrenal gland, discovered in 0.1% of patients with hypertension. Our case highlights an atypical presentation of pheochromocytoma in a patient with Neurofibromatosis type 1 who developed cardiogenic shock with multi-organ failure. The patient demonstrated reversible dilated cardiomyopathy during her hospital stay, and her blood pressure fluctuated widely. Discovery of right adrenal mass followed by biochemical testing facilitated the diagnosis. Judicious medical management led to an uneventful surgical removal of the tumour followed by marked stabilization of her blood pressure. We discuss the characteristics of pheochromocytoma associated with Neurofibromatosis type 1 via reversible cardiac dysfunction.

**Keywords:** Pheochromocytoma, Cardiomyopathy, Neurofibromatosis, Hypertension.

### Introduction

Pheochromocytomas are rare catecholamine secreting tumours of adrenal gland and extra-adrenal chromaffin tissue.<sup>1</sup> Mostly sporadic and associated with paroxysmal or sustained hypertension, they can be associated with hereditary syndromes and atypical presentations posing diagnostic challenges.<sup>2</sup> We describe a case of Neurofibromatosis type 1 associated pheochromocytoma presenting with reversible cardiomyopathy and cardiogenic shock.

### Case Report

A 49-year-old female with neurofibromatosis type 1 (NF1) and hypertension presented to the hospital with acute onset of severe left sided chest pain and dyspnoea.

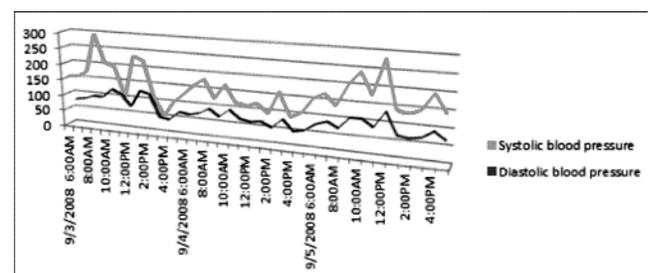
On examination, the patient appeared agitated. Her initial set of vital signs on triage were: blood pressure of 220/120 mmHg; temperature of 102.9°F, heart rate of 133;

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respiratory rate of 36 and oxygen saturation of 98% on room air. Lungs auscultation revealed bilateral crackles. No jugular venous distention was noted and there was no lower extremity oedema or peripheral cyanosis. Initial laboratory studies demonstrated elevated serum creatinine (1.4mg/dl), lactic acidosis (13.1mmol/L), hyperglycaemia (484mg/dl), leukocytosis (WBC: 24,000) elevated pancreatic enzymes (lipase 628 U/L; amylase 943U/L), and elevated liver enzymes (ALT 372U/L; AST 868U/L). Furthermore, there was a subsequent elevation in cardiac enzymes (troponin 16.8 ng/mL; CKMB 14.3mg/mL). Urine drug screen was negative. A chest x-ray confirmed bilateral pulmonary oedema and CAT scan of the chest ruled out pulmonary embolism. CAT scan of abdomen showed presence of right adrenal mass measuring 4.7x3.8cm with a central area of necrosis. EKG showed no acute ischaemic changes but evidence of left ventricular hypertrophy and tachycardia. An emergent bedside echocardiogram revealed diminished severe global hypokinesia and diminished left ventricular function with ejection fraction of 10%.

The patient was admitted to the intensive care unit and given empirical antimicrobial therapy for suspected sepsis. She was put on ventilator support secondary to her respiratory distress. Intravenous Nitroglycerin infusion and Furosemide were administered for treatment of hypertensive emergency, following which the patient became hypotensive. She was started on IV Dopamine, Dobutamine and Neo-syneprine infusion in addition to IV fluids. She remained on IV vasopressors and inotropic support for another 72 hours. Her hyperglycaemia was



**Figure:** Labile Systolic and Diastolic blood pressure readings in mmHg plotted over time in hours during the first 3 days after admission.

**Table:** Functional evaluation of the adrenal mass.

Laboratory Test	Result	Normal Range
Plasma Metanephrine	7243 pg/ml	0-62 pg/ml
Plasma Normetanephrine	10601 pg/ml	0-145 pg/ml
24-hr urine Metanephrines	11318 mcg	35-460 mcg
24-hr urine Normetanephrines	8674 mcg	110-1050 mcg
24-hr urine Cortisol	218 mcg	0-50 mcg
Serum DHEA	1876 ng/dl	110-554 ng/dl
Serum Aldosterone	55.4 ng/dl	1-16 ng/dl
Plasma Renin Activity	15.3 ng/ml/hr	1.9-3.7 ng/ml/hr

initially managed by IV insulin infusion and resolved as patient's condition improved. Her empiric antibiotics were discontinued when no evidence of infection was found.

Her BP fluctuated widely over the next few days (Figure). The presence of labile hypertension and significant fluctuations in heart rate along with presence of adrenal mass lead to the suspected diagnosis of pheochromocytoma, which was confirmed by elevated metanephrine levels both in serum and urine (Table-1).

The patient responded favourably to phenoxybenzamine for alpha-blockade and was weaned off ventilatory support. Within a few days, her pancreatic, renal and liver parameters returned to normal ranges. Echocardiography repeated after 6 days of admission showed normal left ventricular systolic function and absence of regional wall motion abnormalities that were observed previously.

Surgical removal of right adrenal mass was planned and therapy with beta-blockade was initiated after 7 days of adequate alpha blockade. Captopril was added to the medical regimen for enhanced blood pressure control, and IV Phentolamine and Nicardipine were used for acute elevations. The patient had a myocardial perfusion imaging study as part of an ischaemic workup that showed no evidence of ischaemia and an ejection fraction of 64%.

The patient remained stable haemodynamically and underwent an uneventful right adrenalectomy to remove a 5.5x5.5x4.1cm right adrenal mass weighing 54 grams with a central area of cavitation which was confirmed to be pheochromocytoma with no suspicious malignant features. Her pheochromocytoma of adrenal gland scaled score (PASS) score was 2 [profound nuclear pleomorphism-1, hyperchromasia-1] consistent with benign nature of the tumour.

## Discussion

Pheochromocytomas are tumours of adrenal gland or extra-adrenal chromaffin tissues discovered in 0.1% of

patients with hypertension.<sup>1</sup> About 4% patients with incidentally discovered adrenal nodules are found to have pheochromocytoma.<sup>3</sup> An overwhelming majority of these tumours are benign with malignancy reported in approximately 10% of cases at diagnosis. While most of these tumours are sporadic, about 10-15% of cases are thought to have hereditary basis. The hereditary cases tend to run in families as a component of disease syndromes of the genetic origin, such as von Hippel Lindau disease, Multiple Endocrine Neoplasia type II, Neurofibromatosis type I (NF1), familial carotid body tumours and paraganglioma syndromes.<sup>4</sup>

Neurofibromatosis type-1 affects about 1 in 3500 individuals and demonstrates autosomal dominant inheritance with complete penetrance. The susceptibility gene, NF1, a tumour suppressor gene is located on the long arm of chromosome 17 (17q11.2). NF-1 is characterized by multiple neurofibromata and café-au-lait spots on the skin, axillary or inguinal freckling, optic glioma and iris hamartomas. Although the prevalence of pheochromocytoma is relatively rare in NF-1 patients overall (0.1-5.7%), if these patients have co-existing hypertension, pheochromocytoma occurs at a much higher frequency of 20-50%. The mean age of pheochromocytoma onset in NF-1 patients is 42 years.<sup>5</sup>

Pheochromocytoma is associated with arterial hypertension in 90-100% of cases which can be intermittent rather than persistent in almost 50% of patients. The classic triad of palpitation, headache and sweating occur in only 15-24% patients.<sup>6</sup> Intermittent nature of symptoms can be explained due to intermittent catecholamine excess. Unusual presentations such as a reversible tako-tsubo like cardiomyopathy with transient left ventricular dysfunction has been linked to sporadic pheochromocytoma.<sup>7</sup> Significantly high plasma catecholamine levels have been reported in a series of patients with tako-tsubo like cardiomyopathy and it is postulated that exaggerated sympathetic stimulation found in pheochromocytoma could induce a state of transient cardiac stunning and myocardial impairment resulting in cardiogenic shock and pulmonary oedema as witnessed in our patient.

Our case demonstrates an unusual presentation of pheochromocytoma with hypertensive emergency followed by rapid decompensation resulting in pulmonary oedema, acute cardiogenic shock and multiple organ failure. Crisis due to untreated catecholamine excess can lead to cardiac insufficiency, pulmonary oedema, respiratory distress, cardiac arrhythmias, intracerebral bleeding and death.<sup>6</sup>

Aggressive multidisciplinary management along with supportive care as carried out in our patient is critical to reverse excess mortality and morbidity associated with such patients

In patients and family members with NF1 mutation, it is recommended that blood pressure should be monitored at least twice a year and plasma or urinary metanephrines be checked on yearly basis to screen for pheochromocytoma.<sup>8</sup> In our patient with a pre-existing history of concomitant NF-1 and hypertension, appropriate timely screening for pheochromocytoma carried out on an outpatient basis could have potentially prevented the acute morbid hospital course described above.

It is well known that the only curative treatment for a pheochromocytoma is surgical removal. Unfortunately, surgery does not always lead to long-term cure of hypertension or pheochromocytoma, even in patients with benign tumour. In a study of 176 patients, pheochromocytoma recurred in 16%, out of which half of recurrences were due to malignant tumours. In the same study, recurrence occurred more frequently in patients with familial pheochromocytoma. Thus long term monitoring with radiological imaging and biochemical tests is indicated in all patients, even those apparently cured, and most patients should have annual biochemical screening.<sup>9</sup>

Our case demonstrates that pheochromocytoma should be considered in differential diagnosis of patients presenting with wide fluctuations of arterial blood

pressure and cardiogenic shock. Although rare, pheochromocytoma can present as cardiovascular collapse and multiple organ injury rather than the more typical presentation of arterial hypertension. Therefore, a high index of suspicion is essential to reduce morbidity and mortality in these patients.

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