

Pheochromocytoma: A Curable Cause of Hypertension

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Table 1

Patient investigation

Physical examination:

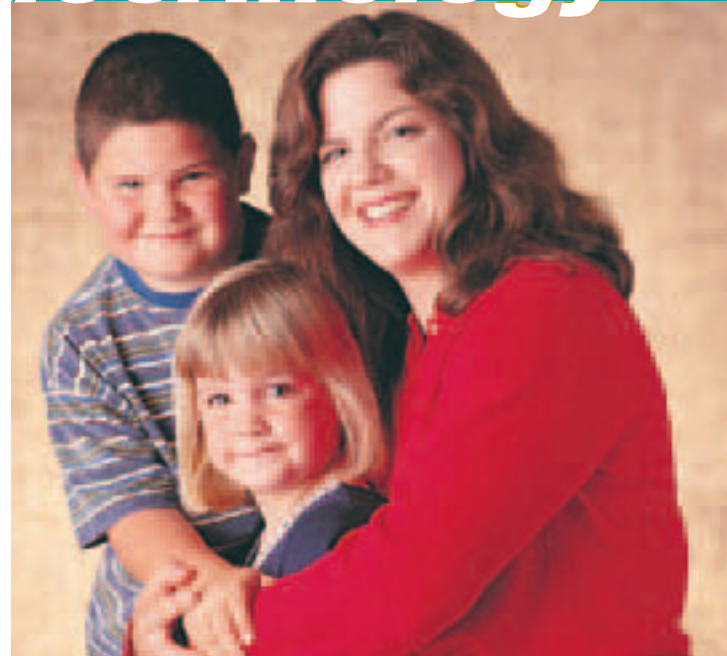
- supine blood pressure (BP) 205/110 mmHg
- erect BP 160/105 mmHg
- weight 150 lbs
- 5'4" height
- sinus pulse rate of 98 beats a minute
- soft ejection systolic murmur

It was otherwise unremarkable for:

- thyromegaly
- thyroid or neck nodules
- rales
- organomegaly/tenderness on abdominal palpation
- leg edema
- café au lait skin spots
- visual or neurological deficits

Lab panel:

- hyperglycemia (9.9 mmol/L)
- normal creatinine
- potassium 4.1 mmol/L (normal range 3.5-5.0)
- aspartate aminotransferase
- normal alanine aminotransferase
- thyroid stimulating hormone of the hip
- free thyroxine
- hemoglobin A1C (HbA1C)
- thyroid ultrasound
- electrocardiogram (no LVH)
- echocardiogram (ejection fraction 60%)



Sheila's hypertension

Sheila, a 40-year-old mother of two, was referred for evaluation regarding her hypertension of five years. It was uncontrolled, despite triple antihypertensive therapy with maximum doses of verapamil, cilazapril, and labetalol. Historically, Sheila had episodic headaches, diaphoresis, and tachycardia accompanied with shakes, pallor, and nausea. These symptoms worsened over the last few months, and were precipitated, particularly after bending (due to her work as a motel maid). Apart from hypertension, she had hypothyroidism (on synthroid), and impaired glucose tolerance. A hysterectomy, from a few years back, was not accompanied with any hypertensive crisis. Sheila is not a smoker, she doesn't abuse alcohol, and she sustained no episode of renal lithiasis in the past (Table 1).

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After a computed tomography (CT) scan of the abdomen, endocrine evaluation was sought for a left-sided 4 cm adrenal mass (Figure 1).

Subsequently, 24-hour urine studies confirmed the diagnosis of pheochromocytoma:

- Norepinephrine was 7549 nmol/24 hours (normal < 600),
- epinephrine was 356 nmol/24 hours (normal < 60), and
- vanillylmandelic acid was 85 umol/24 hours (normal < 35).

Pheochromocytomas and paragangliomas

Catecholamine producing tumours that arise from chromaffin cells of the adrenal medulla or sympathetic ganglia are termed pheochromocytomas, and paragangliomas respectively. Although rare (annual incidence of two to eight people per million), it is important to suspect, confirm, localize, and resect because the associated hypertension is curable with surgical removal of the tumour.¹ The “rule of 10” is sometimes used for pheochromocytomas:

- 10% are extra-adrenal (of those, 10% are extra-abdominal),
- 10% are malignant,
- 10% are found in patients who do not have hypertension, and
- 10% are hereditary.

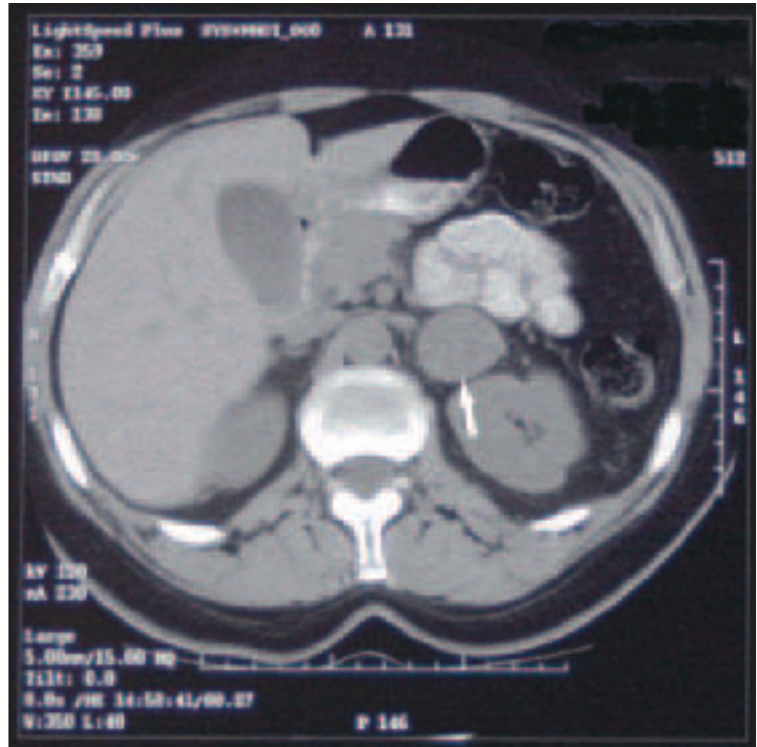


Figure 1. A CT scan of the abdomen showing left-sided 4 cm adrenal

Table 2

Other signs and symptoms of pheochromocytoma

- Pallor
- Orthostatic hypotension
- Visual blurring
- Weight loss
- Hyperglycemia
- Dilated cardiomyopathy
- Constipation
- Megacolon

Some studies show higher incidence of familial pheochromocytomas. Familial pheochromocytoma is inherited as an autosomal dominant

trait alone, or as a component of the multiple endocrine neoplasia Type 2 syndromes (MEN-2A and MEN-2B), von Hippel–Lindau disease, or in rare cases, neurofibromatosis Type 1. The remaining 90% of pheochromocytomas are classified as sporadic or nonsyndromic.^{2,3} The classic triad of pheochromocytoma consists of episodic headache, diaphoresis and tachycardia (Tables 2 and 3).⁴⁻⁷

Commonly used tests

Biochemical testing can establish the diagnosis in more than 95% of patients. The 24-hour urinary excretion of catecholamines, and their metabolites (vanillylmandelic acid, metanephrine and normetanephrine) are the test of choice to screen for catecholamine-secreting tumours. Since catecholamines are normally produced by sympathetic nerves, and by the adrenal medulla, high plasma catecholamine levels are not specific to pheochromocytoma, and may accompany other conditions or disease states. In addition, sometimes pheochromocytomas do not secrete enough catecholamines to produce positive test results, or typical signs and symptoms. In few instances, pheochromocytomas secrete catecholamines episodically.

Between episodes, levels of catecholamines may be normal. Commonly used tests of plasma or urinary catecholamines and other

biochemical tests, such as measurements of plasma chromogranin A levels, do not always reliably exclude or confirm a tumour. A recently developed biochemical test, involving measurements of plasma levels of free metanephrines (o-methylated metabolites of catecholamines), circumvents many of the above problems, and offers a more effective means to diagnose pheochromocytoma than other tests.⁸ In some patients clonidine suppression, and glucagon stimulation tests have been used when urinary levels had not been diagnos-



Table 3

Differential diagnosis of pheochromocytoma

- Thyrotoxicosis
- Insulinoma
- Hypoglycemia
- Carcinoids, arrhythmias
- Pulmonary edema
- Syncope
- Migraine
- Panic attacks perimenopause

tic, or diagnosis is strongly suspected on clinical grounds. Medications may alter measured levels of catecholamines and metabolites. Although it is best to evaluate patients who are not taking any medications, it is not always feasible. Treatment with most medications may be continued with some exceptions. Labetalol is the most frequently used antihypertensive agent that interferes with metanephrine and catecholamine assays, and should be discontinued for four to seven days before diagnostic evaluation of a catecholamine-secreting tumour. Tricyclic antidepressants, methyl, and levo-dopa also commonly interfere with interpretation of 24-hour studies.⁹ Serum chromogranin is costored and cosecreted with catecholamines, and its plasma levels are high in 80% to 90% of patients with catecholamine secreting tumours.¹⁰

Localization studies should not be initiated until biochemical evaluation has confirmed the diagnosis. CT and magnetic reso-

nance imaging can locate adrenal pheochromocytomas with greater than 95% sensitivity. Occasionally, however, these imaging studies are negative despite the presence of pheochromocytoma. A metaiodobenzylguanidine (MIBG) scan can be helpful, not only in these cases, but also in localization for extrarenal or metastatic disease.¹¹

After securing the diagnosis, surgical excision with at least two weeks of appropriate medical preparation prior to procedure, is advisable. Alpha blockers (phenoxybenzamine or prazosin) followed by nonslective beta blockade are used commonly for hypertension, and to overcome tachycardia.¹²

Metyrosine can be used for less fluctuant perioperative blood pressure, and minimum intraoperative blood loss.¹³ In recent years, laparoscopic adrenalectomy has evolved as a promising new technique with faster post-operative recovery, decreased blood loss, and less incidence of complications associated with laparotomy.¹⁴ A 24-hour urine sample should be obtained two weeks post-operatively, to measure catecholamines and metanephrines, and to confirm cure.

Surgical removal is the primary therapy for malignant pheochromocytomas. Five-year survival may be less than 50%. Metastatic lesions should be resected if feasible. Apart from lifelong alpha blockade, MIBG and chemotherapy are other options.¹⁵

Sheila's case revisited

Sheila was started on prazosin, and later propranolol, with good response in orthostatic

hypotension and heart rate. Metyrosine was added later while labetalol and verapamil were held. Repeat 24-hour urine studies revealed:

- high catecholamines and metabolites,
- norepinephrine 11256 nmol/24hr (normal < 600),
- epinephrine 607 nmol/24 hours (normal < 60),
- metanephrine 35 umol/ 24 hours (normal < 5.5), and
- vanillylmandelic acid 121 umol/24 hours (normal < 35).

Sheila's serum calcium, calcitonin, total testosterone, progesterone, androstenedione, and pregnenolone were normal. A chest X-ray was also normal.

Sheila underwent successful laparoscopic adrenalectomy after three weeks of medical treatment. She has been off all antihypertensives, and remains only on synthroid. To date, three sets of repeat postoperative 24-hour urine evaluations have been negative on her followups. [CME](#)

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