

# 41-Year-Old Man with Severe Headaches and Heart Palpitations: A Case of a Recurring, Extra-Adrenal Pheochromocytoma

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## Clinical Points:

- Extra adrenal pheochromocytoma should be considered in the differential diagnosis for patients presenting with severe headaches and heart palpitations.
- Investigations that are used to diagnose a pheochromocytoma include a 24 hour urine catecholamine collection, magnetic resonance imaging, computerised tomography and I<sup>131</sup> metaiodobenzylguanidine scans.
- Surgery is the mainstay treatment, though some pheochromocytomas may respond to radiotherapy or chemotherapy.
- An annual follow up is important in patients who are susceptible to recurring pheochromocytomas.
- Pheochromocytomas are tumours of the rule of 10 – 10% of tumours are malignant, 10% are extra adrenal 10% occur in children, 10% are bilateral and 10% are familial.

## PRESENTATION OF CASE

Patient K, a 41 year old man, presented to a surgical outpatient clinic as a general practitioner (GP) referral because he was suffering from severe headaches and heart palpitations. The patient described the headache as a sharp pain that rated 9 on a scale of 0 -10 (with 10 representing the most severe pain) that encapsulated the whole of the cranium which was sometimes so severe that he would have to stop working and lie down to find relief. He reported that analgesia was not helpful and that physical exercise exacerbated the symptoms. At time of presentation the headaches occurred 2-3 times every day and varied in duration between 10 minutes to an hour. In addition, there were no associated visual disturbances, photophobia, phonophobia or aura. The patient also reported random heart palpitations, which would last 20-30 minutes occurring throughout the day even when lying down. They were not brought on by any single action and were not associated with any pain or shortness or breath, but they sometimes preceded a headache.

K had a background history of pheochromocytoma for which a right adrenal mass was excised in his home country of Pakistan nine years previous to presentation. The headaches and heart palpitations had initially developed six years previous to the current presentation and since then K had presented to his GP eight times with the same complaint but with worsening severity. During this time, his blood pressure remained within normal limits and 24 hour blood pressure monitoring was also found to be normal. A computed tomography (CT) scan, carried out three years previous to the current presentation,

was unremarkable. Over the previous six months, K had started to experience numbness in the extremities, uneasiness and general mood changes as he found himself becoming more anxious. The patient stated that the mood changes occurred around the same time as the onset of the headache, and that he was not usually an anxious person. K denied any loss of weight, heat intolerance, change in bowel habit and any history of anxiety disorder or panic attacks. K had no significant family history of hypertension, malignancies, thyroid or heart disorders. K worked as a GP and lived with his wife and two children and reported good family support. He claimed he did not drink alcohol but was a smoker of five pack-years. K denied any illicit drug use. K had no known drug allergies and was not on any regular medication. Review of systems was non-contributory.

On presentation, K was given an urgent appointment for a CT scan which detected a mass in the paraaortic area, caudal to the superior mesenteric artery. He was admitted into the surgical unit for further investigations. At the time of admission, K was afebrile and had a weight of 71.1kgs, standing blood pressure of 138/82 mmHg and lying blood pressure of 128/82 mmHg. K had a sinus heart rate of 99 beats per minute. He was sweating and looked a little flushed but had a good nutritional state. K did not have any positive findings on clinical examination.

## INVESTIGATIONS AND DIAGNOSIS

Although K's history of pheochromocytoma and his symptoms of headache and palpitations pointed strongly to a recurrence of a pheochromocytoma, several differential diagnoses were considered, including: (i) anxiety disorder, (ii) carcinoid tumour, (iii) essential hypertension, (iv) hyperthyroidism, (v) migraine, (vi) paroxysmal supraventricular tachycardia, (vii) renovascular hypertension and (viii) insulinoma. Blood was drawn for laboratory investigations which revealed normal full blood counts, renal profile, liver function tests, urea and electrolytes, thyroid function test and blood

sugar. He also had a normal electrocardiogram and urine dipstick showed no abnormalities. The following radiological investigations were carried out, spiral CT of abdomen and chest,  $^{131}\text{I}$  metaiodobenzylguanidine (MIBG) scan, magnetic resonance imaging (MRI), positron emission tomography (PET) and in order to rule out local adrenal infiltration by the tumour a fine slice helical CT of both adrenals. A 24 hour urine catecholamine collection was also performed.

The results from the spiral CT, MRI, PET and MIBG scan were able to pinpoint the location of a tumour in the area caudal to the superior mesenteric artery called the organ of Zuckerkandl. Fine slice helical CT of both adrenals excluded any involvement of the adrenals. The results also ruled out the existence of metastases. These findings were supported by a positive uptake on the MIBG scan in the paraaortic area and also increased levels of norepinephrine and metanephrines in the urine detected by a 24 hour catecholamine test (see Table 1). The nature of this tumour is to secrete catecholamines periodically, which gives rise

Catecholamine	Conc. in Urine	Normal Range
Norepinephrine	572 nmol	50 – 500 nmol
Epinephrine	2 nmol	5 -120 nmol
Dopamine	12.2 nmol	300–3900 nmol
Metanephrines	1.19 mg	0 – 0.9 mg

**Table 1. Results of a 24hr urine catecholamine and metabolite collection for Patient K.**

to the biochemical picture depicted in Table 1, in which norepinephrine is raised while epinephrine and dopamine are decreased (probably due to decreased innate production). Metanephrines are always raised in this disease and thus do not depend on periodic secretion. In some cases 24 hour urine vanillylmandelic acid (VMA) is measured, however it is not measured in this case as urine VMA has been found to be the least specific of the tests available and false positives may arise from coffee, tea, raw fruits and drugs such as (alpha methyl dopa). Other tests, such as clonidine and glucagon suppression tests have been used in the past but are no longer common place.

## MANAGEMENT

Phaeochromocytomas are amenable to surgical resection and based on the results of our investigations, it was decided that patient K required admission for surgical resection of the phaeochromocytoma. Contraindications to surgery, such as metastatic disease, did not exist.

### Pre-operative Management

Before a resection of a phaeochromocytoma, strict surgical criteria must be adhered to ensure the best possible outcome. The main pre-operative preparation before the surgery is adequate adrenergic blockade and adequate hydration of the patient. Patient K was prescribed a non-selective alpha antagonist, oral phenoxybenzamine (which was started at 10mg BD and eventually titrated up to 130mg BD) to facilitate complete alpha-blockade in order to

prevent a hypertensive crisis during the procedure as manipulation of the tumour may release catecholamines into the blood stream. K was also prescribed a low molecular weight heparin, subcutaneous enoxaparin (40mg OD) for surgical prophylaxis of embolism. The patient was also started on aggressive fluid hydration of normal saline (1L, 4 hourly) to prevent a hypotensive crisis after the removal of the phaeochromocytoma which would cause a sudden drop in the catecholamine levels in the body. K was weighed daily before breakfast and his haematocrit was monitored regularly as a good indicator of sufficient fluid hydration is a 10% increase in body weight and a 10% decrease in haematocrit. K's blood pressure was also taken regularly while lying and standing as a 10% decrease in the blood pressure together with symptoms of postural hypotension was taken as an indication of complete alpha blockage. When the patient was sufficiently hydrated and alpha blocked he was sent for surgery.

### Surgical Procedure

Patient K underwent open laparotomy under general anaesthetic. The tumour in the area caudal to the superior mesenteric artery was identified and excised without encountering haemostatic difficulties. The margins were checked and found to be clear and the tumour was sent to the pathology department for further histological staining and microscopy where it was found to be a benign tumour.

### Post-operative Management

Post-operatively, K received a detailed management plan. He was admitted into the coronary care unit (CCU) as he required constant 24 hour blood pressure monitoring. This was necessary due the fluctuations in the blood pressure that can occur post resection of a phaeochromocytoma as the body needs to equilibrate to the lesser levels of catecholamine. Urine catecholamines tests were also carried out whilst in CCU to set up a baseline for the catecholamine levels post resection. K also received serial glucose concentration monitoring as there is a risk of rebound hyperinsulinaemia from catecholamine - induced suppression of insulin secretion.

### FOLLOW UP AND OUTCOME

Patient K had an normal, uneventful recovery and is doing well. He is seen annually for analysis of 24-hour urinary catecholamines and metanephrines at the outpatient clinic.

## DISCUSSION OF PHAEOCHROMOCYTOMA

### Introduction

Phaeochromocytomas, first described by Pick in 1912 (1) are rare tumours which secrete catecholamines such as epinephrine and norepinephrine that affect more women than men and have no specific geographical patterns. Phaeochromocytomas are found to be the cause of increased blood pressure in 0.1% of all hypertensive patients (2) and are well known as the "10% tumour". This term was coined due to the nature of the tumour, of which 10% are bilateral, 10% are extra-adrenal, 10% are familial, 10% are in children and 10% are malignant. In this case, patient K is one of the 10% of patients that has the phaeochromocytoma located extra-adrenally. Bilateral

adrenal phaeochromocytomas occur in familial syndromes including multiple endocrine neoplasia (3). Other genetic links with phaeochromocytoma include von Hippel – Lindau gene and the Neurofibromatosis type I gene which is associated with von Recklinghausen's disease. Phaeochromocytomas produce catecholamines and in some cases, adrenocorticotrophic hormone, therefore patients may have Cushing's syndrome alongside the clinical symptoms of anxiety attacks, episodic or sustained hypertension (4). Extra adrenal phaeochromocytomas can occur at any site where the chromaffin tissue is located such as the organ of Zuckerkandl as occurs in Patient K's case.

### Recurrence

The presented case is an example of a recurrence of a phaeochromocytoma. The incidence of recurrence ranges, from 10% (5) to 60% (6), most of which recur in the five year period following resection. With a vast difference in the recurrence rate, it suggests that malignant tumours might have a higher rate of incidence than previously thought (7). The rate of recurrence depends on several factors: the time of patient follow up and the volume of residual adrenomedullary tissue left post surgery. Therefore, post-operative patients require periodic blood pressure measurements, yearly urinary catecholamine estimations and, where there is a high suspicion of recurrence, an MIBG scan should be carried out.

### Complications

The major complications of phaeochromocytomas are associated with hypertension as they cause an increased risk of cerebral haemorrhage, renal dysfunction and myocardial infarction. Other complications include cardiac arrhythmias, hypertensive encephalopathy and heart failure. Interestingly, patients may present with hypotension and shock, which is due to a myriad of reasons such as intravascular volume depletion, abrupt cessation of catecholamine secretion due to tumour necrosis and desensitisation of adrenergic receptors (8).

### Prognosis

Prognosis in well prepared patients undergoing resection is good, with low mortality and low morbidity (9). Advances in localisation techniques, medical management and anaesthetic management have resulted in improved surgical outcomes (10). Survival data of patients with malignant phaeochromocytoma is difficult to obtain due to the rarity and indolence of the tumour (11). The Mayo clinic has reported a five year survival rate of 36%, in one study (12) whereas another report showed a five year survival rate of 60% (13). Surgical excision of a benign phaeochromocytoma has a good prognosis as the elective surgery in well prepared patients has low morbidity and mortality rates. Recent papers suggest mortalities between 2 - 4% (14, 15). A review of patients with recurrent phaeochromocytoma showed a five year survival rate of between 32% and 60% (16).

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