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Case Report

Phaeochromocytoma – an unusually large tumour: a case report

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Introduction

Catecholamine-producing tumours may arise in the adrenal medulla or in extra-adrenal chromaffin cells [1]. Those which arise from the adrenal medulla are referred to as 'phaeochromocytomas' while the latter are called 'catecholamine-secreting paragangliomas' or 'extra-adrenal phaeochromocytomas' [2]. The prevalence of catecholamine-producing tumours in patients with hypertension is around 0.2% to 0.6% [3] Incidence of phaeochromocytoma is estimated to be 0.8 per 100,000 person-years but this is often considered to be an underestimate. Phaeochromocytomas may occur at any age but are most common in the fourth to fifth decade and occur equally in both sexes. In over half of the patients, the tumour is discovered incidentally during computed tomography (CT) or magnetic resonance imaging (MRI) [2].

Case presentation

A 75-year-old man with type 2 diabetes mellitus (DM), hypertension (HTN) and a very recent history of troponin positive acute coronary syndrome (ACS) four days prior to admission, was transferred from District General Hospital (DGH) Mullaitivu to Teaching Hospital, Jaffna (THJ) for further evaluation of fluctuating blood pressure. He complained of giddiness, episodic headache and excessive sweating of three weeks duration. He also had intermittent chest pain, exertional shortness of breath and paroxysmal dyspnoea. He denied swelling of feet, cough and fever. His urine output was normal but he complained of constipation. His appetite was reduced and he had noticed loss of weight during the last couple of months. He was an ex-smoker and ex-alcohol user and denied any other substance abuse.

On examination, he was lean built and afebrile. He did not show signs of congestive heart failure. His blood pressure on admission was 173/103 mmHg with a pulse rate of 108 beats per minute. Abdominal examination revealed a palpable, non-tender mass in the

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right hypochondrium, measuring about 9cm that appeared to originate from the right kidney. All other systems examinations were normal. After admission, he was ~~also~~ found to have fluctuating blood pressure.

Random blood sugar was normal. 12 lead electrocardiogram (ECG) showed sinus tachycardia. Troponin I was negative. Other basic investigations showed mild elevation of transaminases, normal inflammatory markers, elevated serum creatinine and normal thyroid function (Table 1). He underwent urgent ultrasonography (USS) of the abdomen which showed a mass originating from the right suprarenal gland suggestive of a phaeochromocytoma. There were no liver lesions or intra-abdominal lymph node enlargement. He was started on oral prazosin 0.5 mg t.i.d with continuous blood pressure monitoring. Contrast enhanced computed tomography (CECT) of the abdomen and pelvis confirmed the USS findings (Figure 1). Both the 24-hour urinary vanillyl mandeleic acid (VMA) and 24-hour urinary metanephrine tests were elevated confirming the clinical diagnosis of phaeochromocytoma. (Table 1)

He was referred to the surgical team for adrenalectomy which was successfully done under careful pre-, peri- and post-operative anaesthetic preparation and care. (Figure 2) Resected tissue was sent for histology that confirmed the presence of a phaeochromocytoma. (Figure 3 & 4). Patient improved clinically and was discharged from hospital. He is being followed up at the Mullaitivu District General Hospital and his blood pressure is well under control.

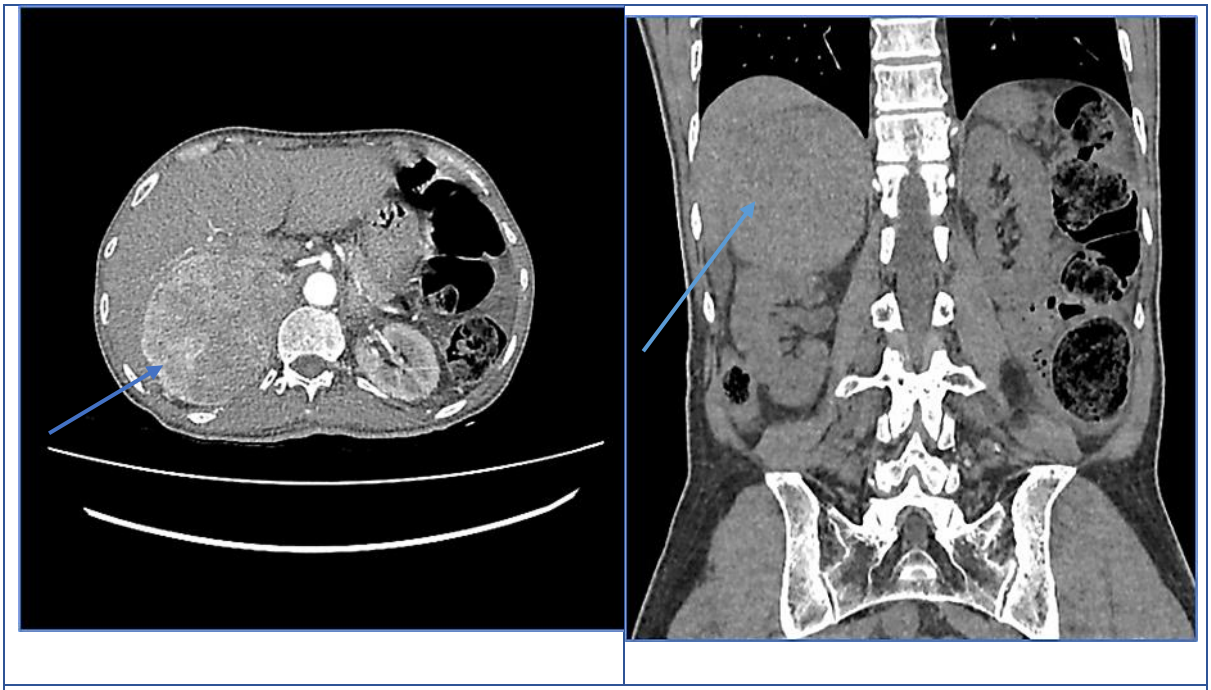

Figure 1: CECT of abdomen and pelvis – axial view (left) and coronal reconstruction (right) shows a large mass arising from right suprarenal gland impinging on the liver

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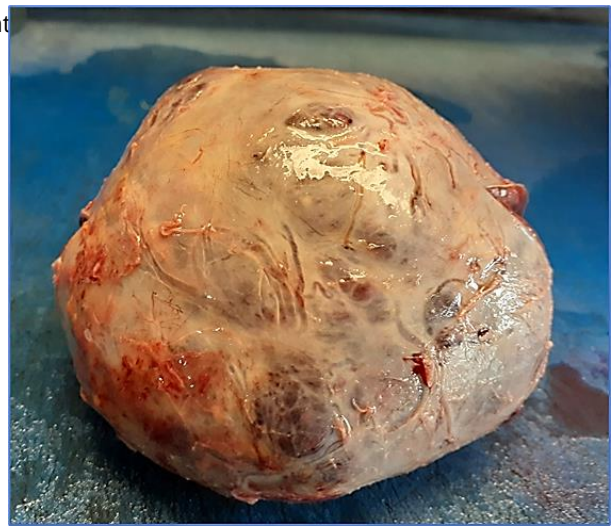

Figure 2: Resected right sided suprarenal mass

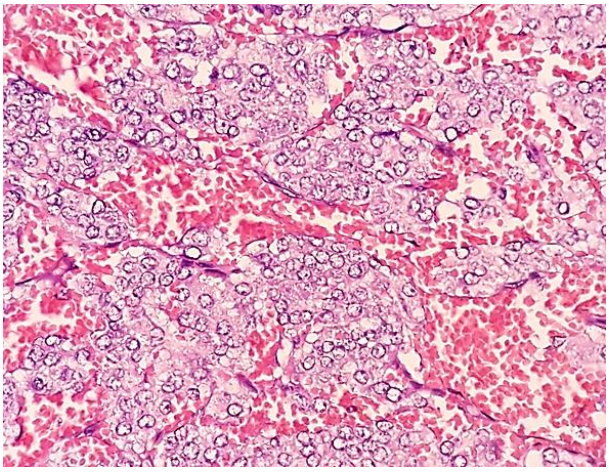

Figure 3: Phaeochromocytoma cells with characteristic abundant basophilic granular cytoplasm

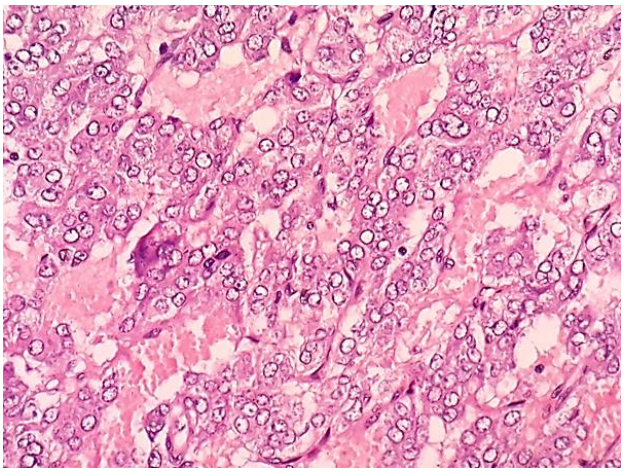

Figure 4: Fibrous bands produce nested architecture of phaeochromocytoma

Table 1: Summary of investigations

Investigations	Results
Full blood count (FBC)	White blood cells (WBC): 7.59/µL (4-11) Neutrophils: 60.5% Lymphocytes: 23.6% Monocytes: 7.4% Eosinophils: 8.0% Red Blood Cells (RBC): 4.52 × 10^3/µL (3.5-5.5) Haemoglobin (Hb): 11.6 g/dL (11.0-16.0) Platelets (Plt): 219/µL (150-450)

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Liver function test (LFT)	Alanine transaminase (ALT): 72 U/L (16-63) Aspartate transaminase (AST): 48 U/L (15-37) Alkaline phosphatase (ALP): 159 U/L (46-116) Total protein (TP): 78 g/L (64-82) Albumin: 39 g/L (34-50) Globulin: 39g/L (22-48) Total bilirubin: 10.8 µmol/L (0-17)
Blood urea	8.9 mmol/L (2.5-6.4)
Serum creatinine	135 µmol/L (62-115)
Serum electrolytes	Sodium (Na): 131 mmol/L (136-145) Potassium (K): 3.7 mmol/L (3.5-5.1) Calcium (Ca): 2.49 mmol/L (2.10-2.54) Phosphorus (PO4): 1.08 mmol/L (0.81-1.45)
Erythrocyte sedimentation rate (ESR)	30 mm/1st hour
C-Reactive Protein (CRP)	10.8 mg/L (0-3)
Thyroid function test (TFT)	Thyroid stimulating hormone (TSH): 0.66 mIU/L (0.465-4.680) Free thyroxine hormone (fT_4): 1.41 ng/dL (0.78-2.19)
Serum cortisol (09:00)	614 nmol/L (123-626)
Serum testosterone	95.2 ng/dL (71.8-623)
24-hour urinary vanillyl mandeleic acid (VMA)	19.8 mg/24 hours (1-11 mg/24 hrs)
24-hour urinary metanephrines	4.27 mg/ 24 hours (Up to 1 mg/24 hrs)

Discussion

The majority of phaeochromocytomas are sporadic while a significant number of patients have the disease as part of a familial disorder. Many autosomal dominant familial diseases are associated with phaeochromocytomas, such as von Hippel-Lindau (VHL) syndrome, multiple endocrine neoplasia type 2 (MEN2) and neurofibromatosis type 1 (NF1) [2]. This patient did not have any clinical or biochemical abnormalities suggestive of these disorders. Review of this patient's family history also did not reveal any hint of familial disease.

Around 50% of patients with phaeochromocytoma are symptomatic which is often paroxysmal in nature [2]. The most common symptoms are headache, sweating and palpitation which constitute the "classic triad". Other common findings are persistent or paroxysmal hypertension, fatigue, tremor and shortness of breath. Orthostatic hypotension, blurring of vision, loss of weight, polyuria, increased appetite and thirst, constipation and hyperglycaemia are also observed but in low frequency. Rarely, patients may develop phaeochromocytoma crisis characterized by hypertension or hypotension, hyperthermia, altered mental status and evidence of organ dysfunction. Takotsubo cardiomyopathy is a rare complication in this setting and secondary polycythaemia may also occur [2]. This patient had the symptoms of the classic triad as well as most of the other commonly observed symptoms. Interestingly, he also had fluctuating blood pressure (hyper and hypotensive episodes) without any other signs of

phaeochromocytoma crisis. Although he had had a recent episode of ACS, coronary angiogram revealed dual coronary vessel disease rendering the diagnosis of phaeochromocytoma crisis in doubt.

Indicated initial biochemical testing is 24-hour urinary fractionated metanephrines or plasma fractionated metanephrines [4] Although, measurement of plasma fractionated metanephrines is useful to exclude phaeochromocytoma, a positive test is not adequate to confirm the diagnosis [2]. Once biochemical confirmation is achieved, radiological evaluation should follow to locate the tumour. Computed tomography (CT) is considered the first-choice imaging modality because of its excellent spatial resolution for thorax, abdomen, and pelvis when compared to MRI [4]. If CT or MRI is negative in the background of strong clinical and biochemical evidence of phaeochromocytoma, scintigraphy could be performed. Other imaging modalities include fludeoxyglucose-positron emission tomography (FDG-PET) and Gallium-68 DOTA-0-Phe1-Tyr-3 octreotate-positron emission tomography (Ga-68 DOTATATE PET) [2].

Surgical resection of the phaeochromocytoma is the recommended treatment. Laparoscopic adrenalectomy is advocated (6) but in this patient the large size of the tumour and anomalous blood supply of the tumour required open laparotomy. Preoperative preparation is very important in all patients. Alpha-adrenergic blockade with phenoxybenzamine is the pre-operative treatment to control blood pressure. Beta-adrenergic blockade is used only after adequate alpha-adrenergic blockade [4].

The average tumour size of a phaeochromocytoma is 4.9 cm. (2) The largest phaeochromocytoma reported in Sri Lanka, by Wickramarachchi *et al*, was ~~of~~ 26 x 25 x 11 cm in size and 3800g in weight [5]. The phaeochromocytoma resected in this patient measured 11 x 8.5 x 7.2 cm.

Approximately 10 percent of all phaeochromocytoma are malignant and they are histologically and biochemically similar to benign tumours. Local invasion into surrounding tissues and organs or distant metastases are the only features that could help in distinguishing malignant tumours from benign tumours. Metastasis had been observed to occur as long as 53 years after resection [2]. So, long term post-operative follow-up is essential in these patients.

Conclusion

Phaeochromocytomas, though rare, are of significant clinical importance as they produce a wide range of symptoms. These tumours are one of the causes of refractory hypertension. Early diagnosis is very important as the pharmacological and surgical treatment of these tumours is highly specific. These tumours have malignant potential necessitating long term follow up.

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