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Teaching Case Report

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Macular star: An unusual sign of pheochromocytoma

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Abstract

Introduction: Pheochromocytoma is a rare neuroendocrine tumour that produces catecholamines and other neuropeptides, originating in the adrenal gland medulla. The majority of cases are sporadic, but could be associated with genetic syndromes.

Case Presentation: Here we report a 37-year-old female with a history of recent onset diabetes mellitus and hypertension who presented to an ophthalmologist with blurred vision and headache. On slit lamp examination she was found to have bilateral optic disc oedema and macular star. On further evaluation by medical team she was diagnosed to have phaeochromocytoma based on hormonal and radiological assessment. She underwent surgical resection of the tumor after the medical intervention.

Discussion: Pheochromocytoma usually presents as a classical triad of symptoms which includes headache, sweating and tachycardia. However, there are other presentations of pheochromocytoma namely hypertension, hyperthermia and cardiomyopathy.

Keywords: Arterial hypertension, Pheochromocytoma, catecholamines, Optic disc oedema, macular star.

INTRODUCTION

Arterial hypertension (AHT) is a common disease worldwide and overall prevalence of hypertension in adults is 24% in men and 20% in women respectively. But 5–10% of cases have a potentially curable secondary cause[1].

Among the causes of secondary AHT are endocrine (primary hyperaldosteronism, pheochromocytoma, Cushing syndrome and hyperparathyroidism), renal (parenchymal and renovascular) or others such as obstructive sleep apnoea, coarctation of aorta and intracranial tumours are worth to note[2].

Pheochromocytoma is a rare neuroendocrine tumour that produces catecholamines and other neuropeptides, originating in the adrenal gland medulla. The majority of cases are sporadic, but 10–25% can be associated with genetic syndromes such as Von Hippel-Landau (VHL) disease, type 1 neurofibromatosis (NF1) and multiple endocrine neoplasia type 2 (MEN 2), implying genetic testing in selected cases[3].

Sustained or paroxysmal ATH is the most frequent sign, possibly associated with the classic triad:

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episodic headaches, sudoresis and tachycardia[4]. Cardiovascular complications due to adrenergic stimulation can potentially be fatal, emphasising the importance of timely diagnosis and an effective therapeutic strategy.

Here we discuss a patient presented to ophthalmologist with blurring of vision leading to the diagnosis of pheochromocytoma.

Patient information

A 37-year-old female with a past medical history of recent onset diabetes mellitus and hypertension were referred by the ophthalmologist for the evaluation of bilateral optic disc edema and macular star. She had early morning headache associated with vomiting for the past two years and also had some constitutional symptoms. She also had on and off palpitation but did not have any other features to suggest hyperthyroidism. Although she had poor sleep, her appetite was good and had normal bowel habits. Her blood sugar was well controlled with oral hypoglycemic agents however her blood pressure readings were fluctuating and was not optimized

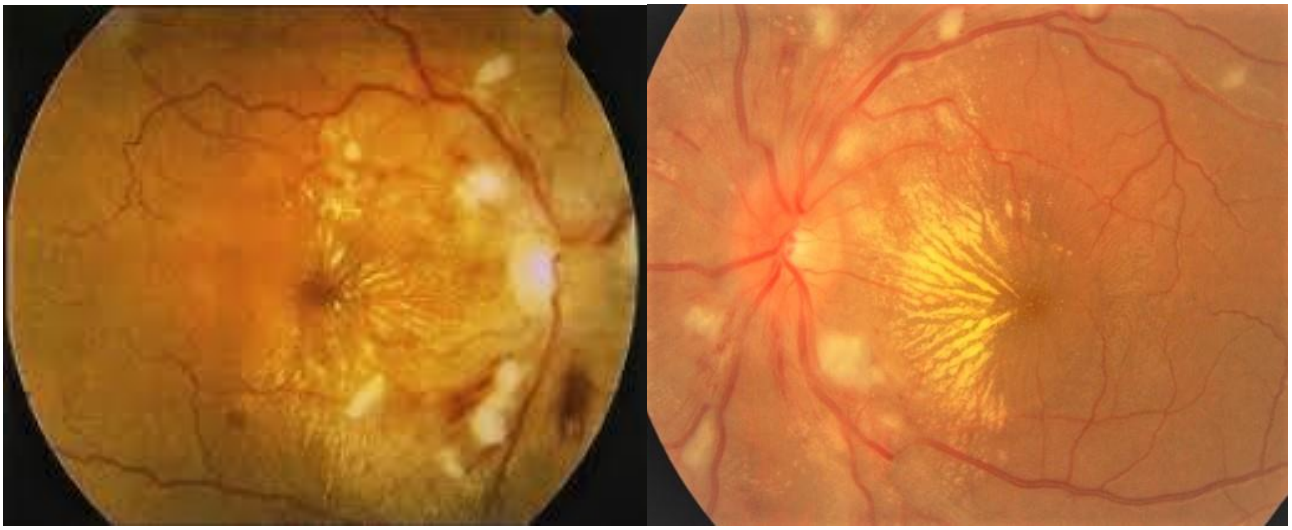


Figure 1: Fundus shows Disc oedema and macular star

On admission she was afebrile and not pale. Her blood pressure was 190/120mmhg in both arms and a pulse rate was 90beats/minute. The respiratory rate was 18 breaths/minute and oxygen saturation on ambient air was 97%. She also had grade 4 hypertensive retinopathy with macular star bilaterally (figure 1). Her other systemic examination findings were within normal limits. The ambulatory blood pressure monitoring (ABPM) showed high variability in spite of administration different classes of anti-hypertensive agents (figure 2).

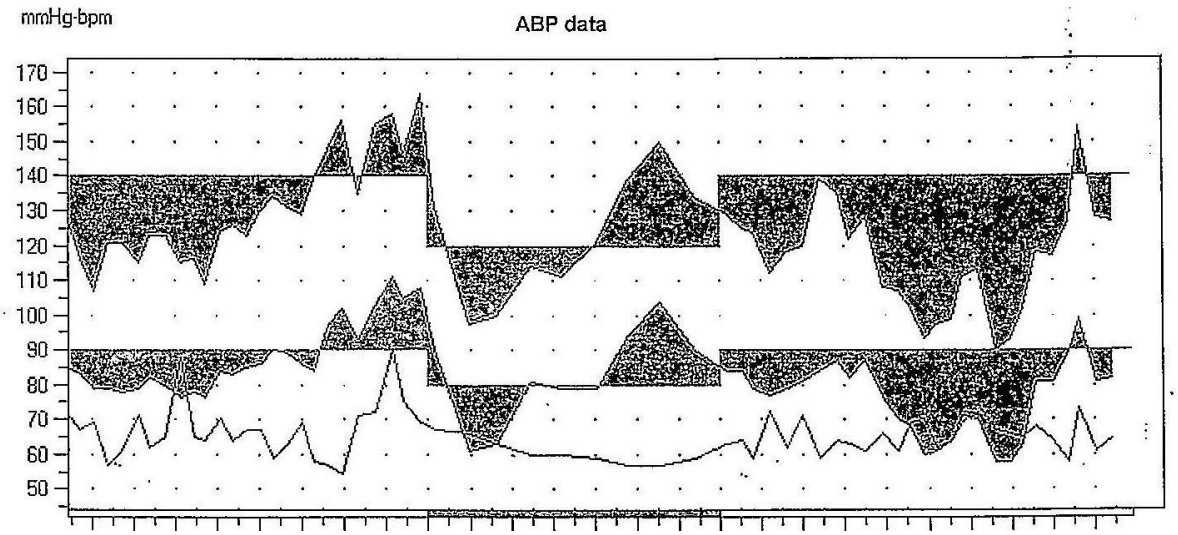


Figure 2: 24 hours' ambulatory blood pressure monitoring shows fluctuation if blood pressure

Her basic investigations were normal including serum electrolytes. The ultrasound scan of the abdomen showed a small hypo echoic lesion between liver and upper pole of the right kidney measuring 4cm x 2.5cm suspicious of a right supra renal mass.

The contrast enhanced CT scan of the abdomen showed enhancing mass lesion in the right suprarenal gland measuring 4.5cm x 2.9cm (figure 3). Urine for Vanillyl Mandelic Acid (VMA) was 30.8mg/day (normal range 2-7mg/day) and the 24hour urinary fractionated metanephrine was 7362µg/24hrs (normal<1300µg/24hrs). Clinical, radiological and biochemical findings favored the diagnosis of Pheochromocytoma.

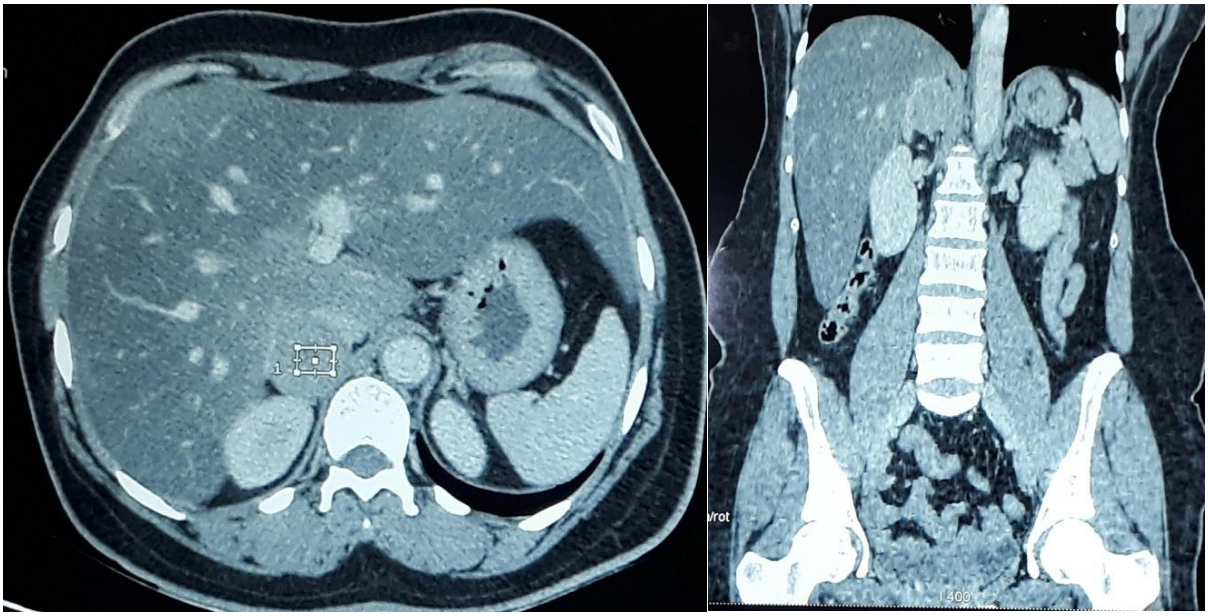
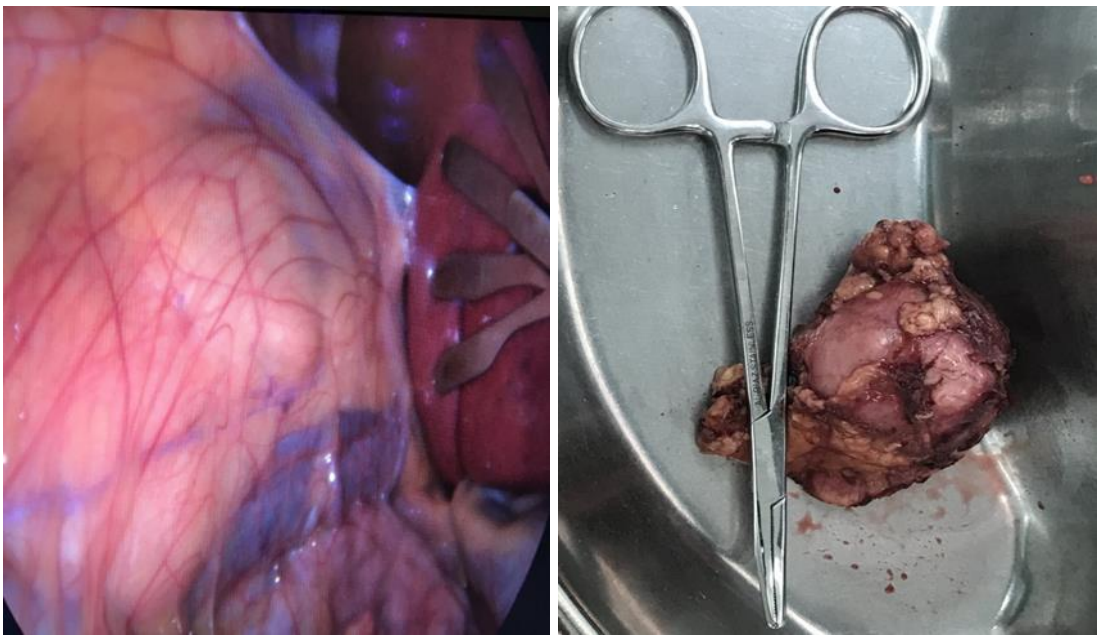


Figure 3: CECT abdomen showed enhancing mass lesion in the right suprarenal gland favours Pheochromocytoma

Therapeutic intervention

She was started on an alpha blocker phenoxybenzamine. A beta blocker (Propranolol) was then added to control the blood pressure. She was referred to the endocrinology and surgical team and underwent laparoscopic right sided adrenalectomy after careful preoperative preparation. The post-operative haemodynamic fluctuations were managed in the intensive care unit with arterial blood pressure monitoring, intravenous fluids and inotropes. She made an uneventful recovery and her regular antihypertensives were discontinued.



(a) **(b)**

Figure 4: (a) Laparoscopic view of the adrenal tumour and (b) Adrenal gland with the tumour

Follow up

A medical clinic followed up was arranged and she was advised on Home Blood Pressure Monitoring (HBPM) to decide upon routine antihypertensive therapy. However, she remained normotensive on follow up clinic visits. Follow-up ophthalmological examination shows disappearance of retinopathy changes including macular star and optic disc oedema.

DISCUSSION

Tumours that arise from chromaffin cells of adrenal medulla which secret catecholamines are called pheochromocytomas and the tumours arise from sympathetic ganglia are called paragangliomas. The diagnosis made by measurement of plasma levels of free metanephrins. This has a high sensitivity (99%) and specificity (89%) [(5)]. Catecholamine levels might be normal in between the episodes of catecholamine release that necessitate the measurement of metabolites rather than catecholamine itself. The sensitivity and specificity of urinary catecholamine are high but it's still less comparing to plasma free metanephrins[5].

There are some distinct features seen in retinal blood vessels, which differentiate them from other blood vessels[6], they don't have sympathetic nerve supply, auto regulation of blood flow and presence of blood-retinal barrier. So increase blood pressures directly transfer to the vessels and constrict them. But further increase in pressure

overcomes this compensatory to mechanism and damage to the muscle layer and endothelium.

There are three phases in hypertensive retinopathy[7]. The first is vasoconstrictive phase. Here the local auto regulatory mechanisms play a major role. This leads to vasospasm and retinal arteriole narrowing. The second is sclerotic phase. Here, intima layer thickening, media layer hyperplasia and arteriolar wall hyaline degeneration occurs due to persistent increase in blood pressure. The third is Exudative Phase. This occurs in patients with very high blood pressure leads to disruption of autoregulatory mechanisms and breach of blood-brain barrier and leakage of blood and plasma into the vessel wall. Retinal signs occur in this stage, such as hard exudate formation, retinal hemorrhage (flame-shaped and dot blot), necrosis of smooth muscle cells and retinal ischemia (cotton-wool spots). At this stage patient can also develop macular changes which include macular star formation and optic nerve changes such as optic disc swelling which is also known as hypertensive optic neuropathy. Macular star formation is caused by the deposition of lipid exudates along the outer plexiform layer of the macula. Neuroretinitis, papillodema are associated with lipid deposits with this peculiar pattern.

The presented case had hypertensive retinopathy with macular star formation which is secondary to phaeochromocytoma. This case illustrates important information regarding the need of detailed clinical assessment of any patient with ocular manifestations. It also emphasizes the importance of vigilant search for a secondary cause of hypertension which is potentially curable.

In this report the arterial hypertension with end organ damage is secondary to phaeochromocytoma. A supra renal mass confirmed by CT imaging with elevated urinary metanephrines and an elevated VMA level characteristically leads to the diagnosis of phaeochromocytoma with the clinical context. This patient did not have any clinical features in favor of genetic syndromes and hence they were not evaluated.

Once the phaeochromocytoma is confirmed the definitive treatment is surgical removal of the tumor after adequately controlling the hypertension with pharmacological treatment. The surgical removal of tumor which reduces the cardiovascular morbidity of this patient population[8]. In patients with pheochromocytoma, when hormones are released epinephrine acts on α and β adrenergic receptors while norepinephrine acts on same receptor except β_2 adrenergic receptor. The cumulative effect is potent peripheral vasoconstriction by α receptor agonism and increase heart rate by β_1 receptor agonism[9]. Thus management of hypertension is very specific which includes initial alpha antagonism followed by beta antagonism after 2 days[10].

It is achieved with initial adequate α blockade followed by β blockade and other antihypertensives as needed. Once normotension is achieved, laparoscopic resection of the tumor is performed with optimal pre-operative management. Stringent preparation to combat phaeochromocytoma crisis due to catecholamine surge during tumor manipulation and sudden decrease in peripheral vascular resistance following tumor excision needs to be monitored.

Patients need careful monitoring during intraoperative and post-operative period for expected intra vascular volume depletion and hypotension. This patient did not require any antihypertensive medications in the immediate post-operative period and at three months of follow up.

CONCLUSION

A patient with pheochromocytoma may not always present with the classical triad of symptoms described in medical literature but could present with an array of symptoms and signs particularly related to hypertensive end organ damage or dysfunction. Clinical suspicion and proper diagnostic assessment would be of paramount importance to diagnose the disease early and plan for a prompt curative intervention. This scenario further emphasizes the importance of in-depth medical history and thorough physical examination in the clinical evaluation of a physical sign.

Author declaration
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Author contribution
All authors contributed to the diagnosis and management of this patient.

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Availability of data and materials
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Ethics approval and consent to participate
Informed written consent was obtained from the patient.

Competing interests
The authors declare no competing interests.

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