Pheochromocytoma and Secondary Amenorrhoea: A Rare Combination

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Case Report

Abstract: Pheochromocytoma is a rare tumour originating from the adrenal medulla and is chromaffin cell catecholamine secretor. We report a case of a previously healthy young lady presenting with symptoms of palpitations, sweating, and giddiness along with secondary amenorrhoea which is a rare presentation due to pheochromocytoma. Resolution of symptoms occurred 3 months after resection of tumour.

Keywords: Secondary ammenorohea, pheochromcytoma, ammenorrhoea, rare manifestation of pheochromocytoma.

Introduction

Pheochromocytoma is a relatively rare (<0.1% of hypertensives), catecholamine secreting tumour[1] that typically presents with catecholamine stimulated symptoms. Ranging from incidental detection to classical triad of episodic headache, palpitation and sweating due to hypersecretion of catecholamines resulting in labile hypertension.[1] But secondary amenerrhoea, potentially through activation of alpha receptors along with classical symptoms is very rare.

Case Report

A 20 yrs old unmarried nulliparous female patient presented with repeated episodes of giddiness, palpitations and sweating. The giddiness used to get aggravated by upright posture. She did not have preceding headache, aura, nausea, photophobias or loss of consciousness. There was no history of chest pain, seizures, eating disorder or recent weight loss. There was no family history of relevance including autoimmune disease. On further enquiry she gave 6 months history of secondary amenorrhoea. She had regular menstrual cycle since the age of 13, she had not consumed contraceptive pill and was a non smoker and non alcoholic. Physical examination revealed a lady with normal body mass index, secondary sexual characters were normal. She seemed anxious during examination. She had a pulse rate of 120/ min and Blood pressure of 190/ 130mmHg in right arm supine position and 150/90 mmHg on standing.. Blood pressure fluctuated during her stay in ward. All peripheral pulses were normal. She had mild pallor; there was no renal or carotid bruit and no cutaneous pigmentation. Fundoscopic examination was normal, gynaecological examination was normal. Systemic examination did not detect any abnormality. Her investigations revealed iron deficiency anaemia. The electrocardiogram ECG, chest radiograph and blood glucose were normal except for sinus tachycardia present on ECG. Blood urea level, serum creatinine, serum electrolytes, urine examination, liver function tests, coagulation parameter were normal. Her thyroid function tests were normal. Echocardiogram revealed concentric left ventricular hypertrophy and normal ejection fraction. Ultrasound of abdomen revealed well defined echogenic solid lesion measuring 3.9 by 3.2 cm in right suprarenal region with cystic areas in the centre. She underwent CT scan of the abdomen which revealed a well defined homogeneously enhancing lesion anteromedial to the upper pole of right kidney which was 3.8x2.8cm in size, was of adrenal origin. (Figure 1). Further investigations like 24hrs urinary fractionated catecholamine showed excess secretions of Norepinephrines 1161 mmol/L. (normal 70-550) with normal epinephrine and dopamine secretion.

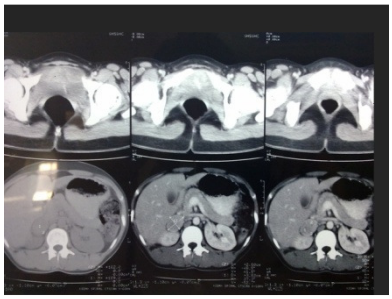

Figure 1: Showing well defined homogenously enhancing lesion anteromedial to upper pole of right kidney measuring 3.8x2.8cm in size.

Her investigations for secondary ammenorrohea revealed iron deficiency anaemia, Hb. 8.9 g/dl, microcytosis. She had luteal phase FSH, LH, oestradiol and progesterone of 5.5 iu/L (0–5), 5.0 i.u/L (2–9), <65pmol/L (150–1000)

and 1 nmol/L, respectively. Her prolactin was 300 mU/L (0–550) and testosterone was 1.6 nmol/L (0–4.1). Her ultrasound of the pelvis revealed normal ovaries and normal endometrial thickness and hysterosalpingography showed patent fallopian tubes. She was diagnosed as hypertensive urgency, right adrenal pheochromocytoma and was started with oral phenoxybenzamine 10mg initially twice daily and increased to 10mg 4 times a day. Propranalol was added a week later up to 20mg 3 times a daily. After controlling blood pressure, right open adrenalectomy confirmed the presence of an encapsulated pheochromocytoma that was completely excised. Her blood pressure returned to normal immediate post-operatively. She regained her menses, 3 months after resection of tumour.

Discussion

Pheochromocytomas are catecholamine secreting highly vascular tumour that arises from the cells derived from the sympathetic system .The term pheochromocytoma (in Greek pheo – means dusky, chroma – means colour and cytoma means tumour) refers to colour, the tumour cells acquire when stained with chromium salt.[2] The etiology of most tumours is sporadic or may be inherited. The etiology of most sporadic pheochromocytoma is unknown. However 25% are inherited as a feature of Multiple Endocrine Neoplasia 2A or B, or several other pheochromocytomas associated syndrome eg. Neurofibromatosis and Von Hippel Lindau disease.[2] It is estimated to occur in 2-8out of 1 million persons / yr. The mean age at diagnosis is about 40 yrs .The "rule of ten" for pheochromocytoma states that about 10% are bilateral, 10% are extrarenal, 10% are malignant, 10% familial, 10% recur and 10% are discovered incidentally.[2] Pheochromocytomas secrete nor epinephrine predominantly as in our case also, whereas secretion from normal adrenal medulla are composed of roughly 85% epinephrine and so in familial variety.[2] The clinical presentation is variable ranging from an adrenal incidentalomas to a patient in hypertensive crises with associated cerebrovascular accidents or cardiac complication. The dominant sign is hypertension. Classically patients have episodic hypertension. Catecholamine crises can lead to heart failure, pulmonary oedema, arrhythmia and intracranial haemorrhage.[2] Amenorrhoea is unusual presentation of pheochromocytoma . Only a single case report on extensive survey of literature was found.[3] One possibility is that ovarian granulose luteal cells in human and animals have alpha and beta adrenergic receptors. It was shown recently that activation of alpha receptors causes inhibition of LH and HCG mediated progesterone release through intracellular Ca and Phosphoinositide pathways.[4]Ovarian progesterone production atleast in rats has been shown to be regulated by nor adrenaline through a mechanism in which Renin Angiotensin System is involved with a main role of Angiotensin.[4] A less likely possibility is interaction of Norepinephrine at the level of the hypothalamus. The median pre optic area of the hypothalamus is innervated by ascending noradrenergic fibres from the locus coeruleus and these fibres stimulate GnRH and LH release.[5] Animal studies have shown that alpha adrenergic receptors in the hypothalamus play a role in modulating GnRH and LH release. In a study on rats, stimulating the ascending noradrenergic bundle has resulted in partial or complete inhibition of the LH pulse pattern.[6] However, this was not found in human studies.[7] Other likely explanation to this rare combination of presentation which are confirmed experimentally could be presence of functioning adrenergic receptors on human granulosa lutin cells.Catecholamines most likely acting via the alpha adrenergic receptors inhibits the LH/HCG induced release of progesterone.[4]

Abbreviations

Hb: haemoglobin; FSH: follicular stimulating hormone; LH: leutinizing hormone; HCG: human chorionic gonadotropin; GnRH: gonadotropin releasing hormone; Ca: calcium.

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