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CASE REPORT

Normotensive Pheochromocytoma As An Adrenal Incidentaloma: A Case Report

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ABSTRACT

Pheochromocytomas and paragangliomas are catecholamine producing tumours that arise from the sympathetic or the parasympathetic nervous system. If the tumour is confined to the inner part of the adrenal gland, it is called as pheochromocytoma and if it has extra adrenal location, it is called as paraganglioma. Pheochromocytoma is a rare cause of hypertension with about 0.1 % incidence in hypertensive patients. Adrenal masses are found in about 2% of the abdominal CT scans which are performed for other reasons (e.g. incidentalomas) and of these, 5.1% to 23% are considered to be pheochromocytomas. Nonfunctional pheochromocytoma is usually an asymptomatic adrenal tumour, even if it is associated with hypercatecholaminaemia. In this paper, we report a rare case of normotensive pheochromocytoma which was discovered incidentally while assessing abdominal discomfort. Despite the presence of excess catecholamines in the circulation, the patient was normotensive without any other sign of pheochromocytoma. Surgical excision of the adrenal tumour revealed pheochromocytoma.

Key Words: Incidentaloma, pheochromocytoma, adrenal tumour

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Introduction

The diagnosis of adrenal incidentaloma is based on imaging studies like CT scanning and MR imaging. If a tumour bigger than 1 cm is incidentally discovered in the adrenal gland in radiological assays, it is called an incidentaloma. The prevalence of adrenal incidentaloma is about 2% of all the abdominal CT scans, of which 5.1% to 23% are considered to be pheochromocytomas [1], [2].

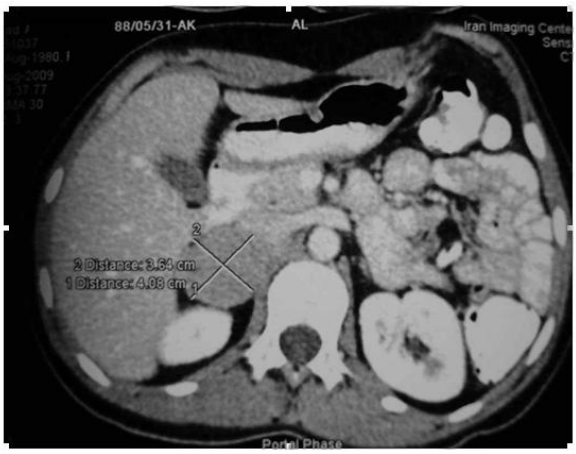
In general, pheochromocytomas are rare and silent pheochromocytomas are even much rare; consisting approximately 5% to 15% of all pheochromocytomas [3]. It is important to know whether incidentaloma is hormonally active and malignancy has to be ruled out, failure to detect and treat it can result in fatalities. Here, we report a case of silent pheochromocytoma.

Case Report

A 31-year-old married woman was presented with generalized abdominal discomfort. There was no positive family history.

The review of her systems and physical examination were unremarkable. The blood pressure and heart rate were 104/75 and 84/min, respectively. By using ultrasonography for the evaluation of her abdominal pain a hypoechoic solid mass between the liver and the right adrenal gland was detected. For further evaluation, abdominal CT scan was performed with IV contrast; the result was indicative of a soft tissue mass without calcification or fatty component measuring

43×32×51 mm in the right adrenal gland [Table/Fig 1] .



(Table/Fig 1) Axial enhanced CT scan at the right adrenal level shows a well-defined solid homogenous soft tissue mass lesion with mild enhancement anterior to the upper pole of the right kidney in the right adrenal. No fatty component or calcification is evident.

Endocrine evaluation of this patient included a plasma cortisol assay following an overnight dexamethasone suppression test, serum sodium and potassium levels and a 24-hour urinary metanephrine estimation [Table/Fig 2].

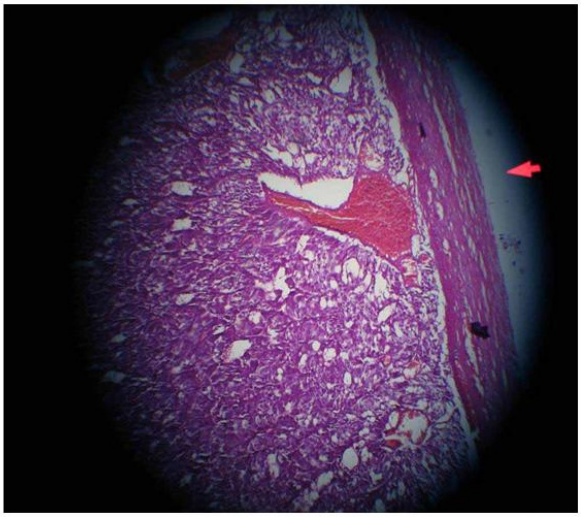
(Table/Fig 2) Preoperative laboratory findings

Parameters	Result	Reference range
K (mEq/l)	3.5	3.5-5.5
Serum Cortisol (µg/dl)	0.83	4.5-24
Normetanephrine (µg/day)	2511	<350
Metanephrine (µg/day)	1500	<600
VMA (mg/day)	7	<13.6

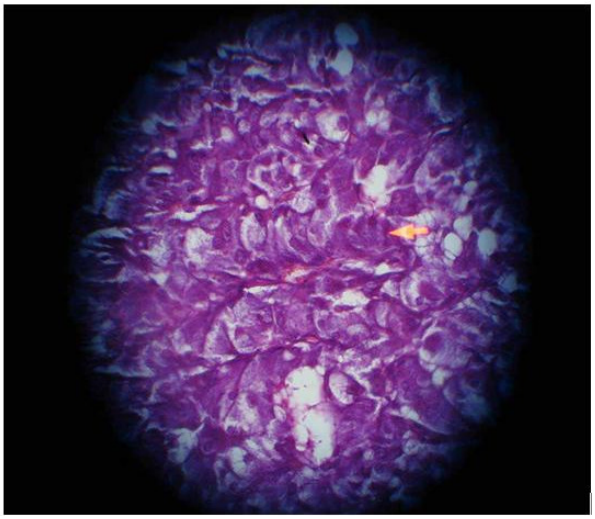
With the suspicion of pheochromocytoma, the patient received 10mg/day phenoxybenzamine 2 weeks before the surgery and the laparatomic adrenalectomy was performed with no complication during the operation.

Gross pathology revealed a grey ovoid fragment of the adrenal specimen, with a dimension of 4cm, which weighed 37 grams together with the absorbed formalin. Cross section revealed an encapsulated solid mass with haemorrhagic foci and with cystic areas.

In the microscopic examination, the proliferation of the cells in the nests with hypervascular stroma was observed. The neoplastic cells had abundant fine granular eosinophilic cytoplasm with vesicular round oval nuclei, some of which had prominent nucleoli and minimal atypia [Table/Fig 3] , [Table/Fig 4] .



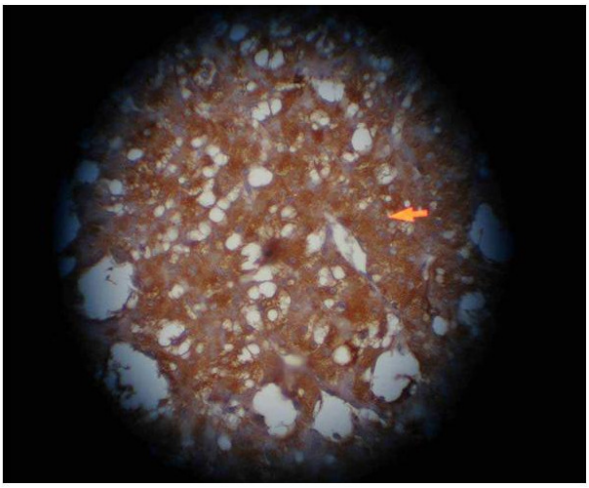
(Table/Fig 3) The medium power view (×100 obj) shows the nesting pattern of the neoplastic cells.



(Table/Fig 4) The high power view (×400 obj) shows fine granular cytoplasm of the cells.

Immunohistochemical staining revealed that neuron specific enolase (NSE) was strongly positive in the cytoplasm of most of the tumoural cells and S100 staining was positive in the peripheral spindle cells of the tumoural nests [Table/Fig 5]. These findings

confirmed the diagnosis of paraganglioma of the adrenal medulla.



(Table/Fig 5) IHC study: Neuron specific enolase (NSE) is strongly positive in the cytoplasm of the tumoural cells.

Discussion

The detection of an adrenal lesion should prompt biochemical evaluation unless it is an obvious myelolipoma.

Any hormonally hyperfunctioning adenoma needs to be surgically resected. Patients are screened for SCS with a 1-mg overnight dexamethasone suppression test. Patients with hypertension who have a ratio of plasma aldosterone concentration (PAC) (ng/dL) to plasma rennin activity (PRA) (ng/mL per hour) of >20, while not taking spironolactone and mineralocorticoid receptor blockers, should undergo further assessment for the presence of primary aldosteronism. Finally, elevated plasma free metanephrine and normetanephrine levels, 24-hour total urinary metanephrines and fractionated catecholamines suggest the presence of a pheochromocytoma. In general, testing the patient for the production of excess sex hormones is not indicated unless the patient has obvious clinical stigmas [4].

The term pheochromocytoma, as a catecholamine-releasing tumour, may arise sporadically or may be an inherited form as the feature of multiple endocrine neoplasias [3]. The incidence of this tumour is estimated to be about 2-8 out of 1 million persons per year and accounts for 0.1% of hypertension causes. The prevalence of this tumour in autopsy series was seen to be approximately 0.2% [3]. Although these tumours can occur at any age, the mean age at diagnosis is about 40 [3]. There is no gender difference in the occurrence [5],[6]. The prevalence of non-functional pheochromocytoma is also rare, which accounts for about 5-15% of all pheochromocytomas. The manifestation of these tumours varies greatly; hence, it has been termed “the great masquerader” [3]. Hypertension is the most common presentation of pheochromocytoma, as 90%-100% of patients with functional pheochromocytoma represent hypertension [7]. Sustained hypertension is seen in half, episodic hypertension in a third and the normotensive form is seen in less than a fifth of the patients [7]. The less common manifestations of this tumour include tremor, Raynaud’s phenomenon, mass effect of the tumour and livedo reticularis [6],[7],[8]. Amit Agarwal et al reported nine cases of normotensive Pheochromocytoma [9]. This is the first report from India from such a series [Table/Fig 6] .

(Table/Fig 6) Summery of previously reported cases outcomes

Patient No	Intraop. events	Size (cm) and slide	Weight (g)	Pathology
1	Hypotension	9 × 6 × 3 Right	160	P
2	Hypertension, hypotension	7 × 6 × 5Left	160	P
3	Hypertension, hypotension	8.5 × 8 × 9.5Left E	110	Para
4	Hypertension, hypotension	5 × 5.5 × 3.6 Right	50	P
5	Hypertension, hypotension	4.5× 4.5 × 2 Left	45	P
6	Hypotension	10.3 × 7.2×7.8 Left	200	P
7	Hypertension, hypotension	7.5 × 6.5Left E	70	Para
8	Hypertension	6.5 × 5.9 × 6.4 Right	NA	P
9	Hypotension, tachycardia	7.5 × 7.5Left	100	P

E: extraadrenal mass; P: pheochromocytoma; Para: paraganglioma;NA: not available

It is interesting to know that in this study, all the patients with normotensive pheochromocytoma had

abdominal or flank pain as their primary complaints [9]. This was similar to our patient's presentation.
No association existed between catecholamine concentration and blood pressure.

The lack of correlation can be explained as follows:
[1] Long-term exposure to high levels of catecholamine which can lead to desensitization of the cardiovascular system to catecholamine.
[2] Low circulatory volume in these patients.
[3] The presence of vasodilator components derived from pheochromocytomas such as dopamine, vasoactive intestinal peptide, calcitonin gene-related peptide, adrenomedullin, metenkephalin, atrial natriuretic peptide and neuropeptide Y.
[4] And finally, varying responsiveness to circulatory catecholamine attributed to some factors such as the rate of catecholamine inactivation and the rate of reaching to the target cells [10],[11],[12],[13].
At diagnosis, it is important to evaluate hormone excess, even in normotensive patients by using various biochemical tests. In addition, pre operation α-adrenergic blockading should be carried out even for the non-functional form of pheochromocytomas, at least 2 weeks before the surgery, since there is a possibility for the occurrence of hypertensive crisis with manipulation during the operation [14],[15] .Non-functional pheochromocytomas can be large in size [15]. Most of the studies show that the mean diameter of incidental tumours is significantly greater than the symptomatic ones, while in tumours smaller than 50 gm, it is observed that they release free catecholamines into the circulation and exhibit persistent signs and symptoms [16].

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