Article published online: 2022-07-07

CASE REPORT

Atypical Pheochromcytoma: Haemorrhagic Cyst and Abdominal Pain in a Normotensive Patient

Fathima P. Kunjumohammed

Department of Endocrinology, The Royal Hospital, Muscat, Oman.

Corresponding author: Dr. F P Kunjumohammed Email: fathya01@gmail.com
Published: 11 July 2013
Ibnosina J Med BS 2013,5(4):218-222
Received: 07 December 2102
Accepted: 06 January 2013
This article is available from: http://www.ijmbs.org

Abstract
Pheochromocytomas are catecholamine-secreting tumors. They show a considerable variation in clinical presentation ranging from adrenal incidentaloma in a normotensive individual to a patient in hypertensive crisis or with cerebrovascular or cardiac decompensation. We report here a case of fifty years old Omani female patient was referred to the endocrine clinic from a regional hospital, for further investigation of a an incidental left adrenal cyst that was detected on US abdomen being performed for evaluation of abdominal pain. Pheochromocytoma was eventually confirmed and an abdominal CT showed a large haemorrhagic cyst. The course and management is described and a focused review of the pitfalls of diagnosis and management is provided.

Key words: Catecholamine secreting tumors, Adrenal incidentalomas, Hypertension, Cystic Pheochromocytoma.

Introduction

Pheochromocytomas are rare tumors found in less than 1% of patient with hypertension. The diagnosis of pheochromocytoma is that "of exclusion" based on high index of suspicion. The classical triad of symptoms include paroxysmal headache, palpitation and profuse sweating. The presence of all these symptoms in association with hypertension makes a pheochromocytoma a very likely diagnosis (1). However, it can present with non-classic symptoms such as abdominal pain, vomiting, dyspnoea, heart failure, hypotension and sudden death (2). In one autopsy study at Mayo clinic, a large number of patients with pheochromocytoma had these non-classic symptoms previously documented (2). Among patients with adrenal incidentaloma approximately 6.5% are proved eventually to have pheochromocytoma (3). It is therefore crucial that the functional status and malignant potential of these incidentally detected adrenal tumors should be identified. We report here an illustrative case of pheochromocytoma, detected on abdominal CT as a haemorrhagic cyst in a normotensive patient who presented with abdominal pain. A focused review of the pitfalls of diagnosis and management is provided.

Table 1. Summary of the Laboratory Evaluations	
CBC, LFT, RFT, Electrolytes, Calcium	Normal
24 hour Urine Metanephrine	7.93umol/L(NR 0-1.8)
24 hour Urine Normetanephrine	7.26umol/L (0-3.3)
24 hour Urine adrenaline	697nmol/24hr(3-197)
24 hour urine noadrenaline	508 nmol /24hr(89-473)
Plasma Metanephrine	2.60nmol(0-.5)
Plasma Normetanephrine	1.90nmol(<1)
Chromogranin A	22 (Normal <22)

Table 2. Comparison of the values of plasma catecholamines before and after adrenalectomy. Reference range is also given to inform the comparison**.**

Measurement	Pre-operative	Postoperative	Reference Range
Plasma Metanephrine	2.60 nmol/L	0.22 nmol/L	0.0-0.5 nmol/L
Plasma Normeta nephrine	1.90 nmol/L	0.41 nmol/L	0.0-1.0 nmol/L

Case report

50 year old Omani female, was referred to our endocrine clinic from a regional hospital, for an incidental left adrenal cyst detected on US abdomen. She presented with a 6 month history of abdominal pain. The pain was constant and dull in nature with no radiation or relation with meal. She denied any history of headache, palpitation, flushing, dizziness or sweating. She was diagnosed to have hyperlipidemia in the past and was on simvastatin 20 mg. There was no other significant past relevant medical history such hypertension, stroke or any heart disease. On examination, she was in mild abdominal pain. She was normotensive (107/70mmHg) with a pulse rate of 84 per minute. There was mild generalized abdominal tenderness with no guarding, and no palpable masses. Biochemical evaluation revealed normal levels of complete blood count, renal and liver function tests and serum calcium (Table 1). Her 24 hour urinary and plasma metanephrine and normetanephrine levels, 24 hour urinary cathecholamines were high. Urinary metanphrine was sent (twice) after 3 days metanephrine-free diet. Plasma Chromogranin A level was in the upper reference range. Computed tomography (CT) of the abdomen showed a large cystic lesion measuring 7.3x7cm in close proximity to left upper renal pole demonstrated high signal intensity on T1 and T2 WI with fluid level (Figure 1). No evidence of calcification or enhancing solid component. These features are in keeping with a large hemorrhagic cyst likely related to left adrenal gland. MIBG scan could not be performed due to isotope shortage. A 12-lead ECG showed no changes suggestive of left ventricular hypertrophy (LVH). Echocardiogram showed ejection fraction (EF) of 60 %, with normal left ventricular size and thickness. As the risk for hypertensive crisis in clinically silent case is same as that for symptomatic patient, she was started on anti hypertensive but she could neither tolerate alfa-blocker (Prazosin 0.5 mg qd) nor calcium channel blocker (Amlodipine 5mg qd). She was referred for surgical management and transferred to the surgical department. She received 2 units of blood transfusion preoperatively. She underwent left adrenalectomy uneventfully (neither hypertensive crisis nor hypotension). Fluid status and BP were monitored by central venous pressure and intra-arterial line respectively. Intra operative findings report stated “a large cystic mass originating from the left adrenal gland, with no adhesion to adjacent structures. Histopathology reported as sections from the cystic mass shows a well defined neoplasm. Immuno histochemical studies showed that neoplastic cells are strongly positive for chromogranin and synaptophysin (Figure 2). The appearance was consistent with cystic pheochromocytoma”. Her abdominal symptoms improved and her plasma metanephrine level dropped dramatically and got normalized within 4 weeks (Table 2).

Table 3. Genetic Mutation associated with Pheochromocytoma & paraganglioma

Syndrome	Mutated Gene	Type of Tumour	Main secretion	malignancy
MEN-2A	RET-oncogene	40-50 % pheo PGL- rare	metanephrine	< 3 %
MEN-2B	RET-oncogene	Up to 50 %-pheo PGlL-rare	metanephrine	< 5%
VHL	VHL-gene	10 to 20 %pheo PGL -5%	Normetanephrine	< 5%
NF-type 1	NF-1 gene	<5 % pheo PGL rare	Metanephrine/ normetanehrine	10 %
Pheo/PGL	SDHD SDHB SDBC SDHAF2	Head &neck PGL Abdominal PGL Head & Neck PGL Head &neck PGL	Parasympathetic <5%catachoLamine Normetanehrine Parasympathetic Parasympathetic	Rare 40 % Rare Rare

MEN = Multiple Endocrine neoplasia, VHL = von Hippel Lindau, NF = neurofibromatosis, PGL = paraganglioma, SDH = Succinate Dehydrogenase

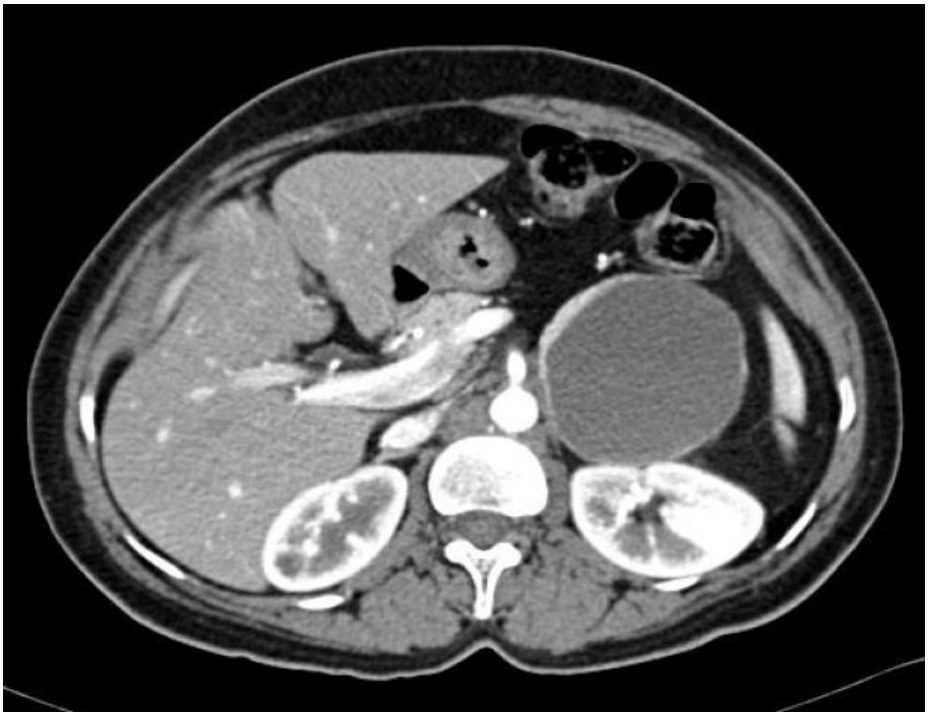

Figure 1. CT Abdomen showing the left adrenal cystic mass

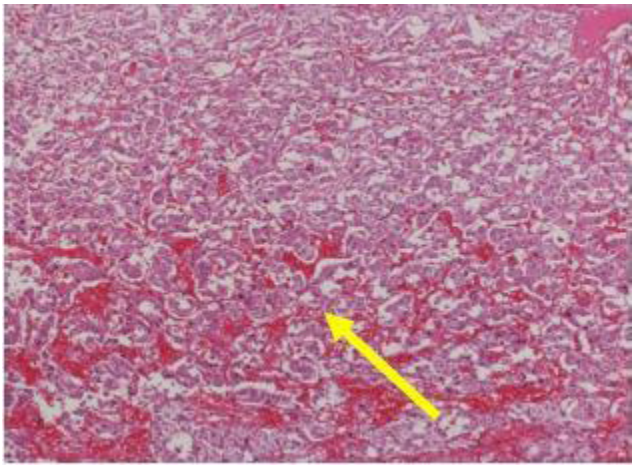

Figure 2. The histopathological appearance of the tumor: Sections from the cystic mass shows a well-defined neoplasm compsed of nests or strands of polygonal cells with round vesicular nuclei and granular eosinophilic cytoplasm (arrow). No abnormal mitosis is seen. The tumor is highly vascular with extensive areas of fresh and old hemorrhages seen. Compressed, but otherwise unremarkable adrenal tissue is seen at the edges.

Discussion

Pheochromocytomas are neuroendocrine tumors derived from chromaffin cells of adrenal medulla. Tumors originate from extra adrenal Chromaffin cells are called paraganglioma (4). Most pheochromocytomas occur sporadically, but around 20-30% of patients with pheochromocytoma carry germ line mutations as are summarized in Table 3 (5,6). Although most patients present with episodic headache, palpitation or diaphoresis, gastro intestinal symptoms may predominate in some patients (7). Around 90 % of patients with this tumor are hypertensive. This can be sustained or paroxysmal. Interestingly, some patients with pheochromocytomas and paragangliomas have no hypertension despite having chronically elevated serum norepinephrine. The hypotheses behind it include down regulation of adrenergic receptors or polymorphism of B2-adrenergic receptors that allow continued B2 mediated vasodilatation, counteracting the pressor effect of alfa-1 receptor stimulation or secreted catecholamines being metabolized within the tumor itself especially when the tumor has cystic component (1). The key to diagnosis of pheochromocytoma is the high index of clinical suspicion on presentation, documentation of catecholamine excess by biochemical testing and localization of tumor by imaging. No single biochemical test is absolutely sensitive and specific for pheochromocytoma. Measurement of fractionated plasma metanephrine is a highly sensitive and specific test (98% and 92% respectively). Similarly measurements 24 hour urinary fractionated metanephrine and catecholamines provide sensitivity and specificity in the order of 98% (4). Additionally, raised chromogranin A level is a relatively sensitive test (86%) in diagnosing pheochromocytoma (8, 9). Anatomical localization can be achieved by CT or MRI and functional localization is performed using radio tracers including ^{123}I-MIBG and ^{111}In-somatostatin analogues, or PET scanning (10). MIBG scanning is also useful in locating an occult paraganglioma or in confirming whether an extra adrenal mass is paraganglioma or screening patients for metastases. On CT scan, adrenal adenoma usually appears as small well-defined homogenous mass with intra cytoplasmic fat contents that results in low attenuation (<10 HU) and shows rapid wash out of intra venous contrast (40-50%). On the other hand malignant lesions are large (>5cm) and heterogeneous with high signal intensity. Pheochromocytomas show soft tissue intensity in the region of 40-50 HU on non-contrast CT. Administration of non-ionic intravenous contrast is safe in pheochromocytoma without any prior alpha-blockade (11). MRI is excellent in delineating the tissue character. On T2 weighted MRI imaging, they are typically very hyperintense to fat. They frequently manifest with partial or focal cystic degeneration. Totally cystic forms are not common (12,13). Surgery is the definitive treatment for pheochromocytoma. Preoperative preparation include, control of blood pressure with alpha blockade initially followed by beta blockade to avoid hypertensive crisis consecutively (14). Patients with pheochromocytoma, even with normal BP, are at risk for hypertensive crisis and should be prepared same as that for hypertensive patients. An incidentally detected pheochromocytoma on US abdomen in a normotensive

lady was reported in the literature (4). Her BP increased up to 220/120 during surgery and was managed with nitroprusside infusion. In emergency surgery, intravenous Nitroprusside, Phentolamine or Nitroglycerine can be used to control intraoperative hypertension. Initiating adequate hydration including blood transfusion 24 hours prior to surgery, to avoid post-operative hypotension is the next important step-as there would be volume contraction or down regulation of alpha receptors, may result in persistent hypotension after tumor resection (15). Postoperative surveillance of these patients includes annual quantification of 24 hour urine or plasma metanephrine level for at least 5 years.

In conclusion, a small percentage of patients with pheochromocytoma can be asymptomatic or presented with unusual symptoms. In our case her main symptom was abdominal pain and she was normotensive. She was screened for pheochromocytoma only because of adrenal lesion detected on imaging studies. Clearly, physicians must become more vigilant for pheochromocytoma and employ appropriate screening tests for all patients in whom pheochromocytoma enters into the differential diagnosis. To avoid, possible lethal outcome in patients with asymptomatic pheochromocytomas, they should be carefully evaluated and managed in accordance to the hemodynamic parameters and cardiac status.

Acknowledgments

The author would like to acknowledge the support of Dr. Hilal Musalhi, Dr. Mohamed Lamki, Dr. Noor Busaidi of the Department of Endocrinology, Dr. Waad-Allah Sharef Mula-Abed, Dr. Manal Khalifa Al Kindi of the Department of Biochemistry and Dr. Susan and other colleagues from Histopathology at Royal Hospital, Muscat, Oman.

References

1. FitzGerald PA. Chapter 12. Adrenal Medulla & Paraganglia. In: Gardner DG, Shoback D (eds.) Greenspan's Basic & Clinical Endocrinology. Ed 8th. McGraw-Hill 2007.
2. Sutton MG, Sheps SG, Lie JT. Prevalence of clinically unsuspected pheochromocytoma. Review of a 50-year autopsy series. Mayo Clin Proc 1981; 56: 354-60.
3. Shen SJ, Cheng HM, Chiu AW, Chou CW, Yang CY, Chen SY. Clinically silent pheochromocytoma in adrenal incidentaloma: a case report and review of the literature. J Intern Med Taiwan 2003;14: 248-54.
4. Bravo EL, Tagle R. Pheochromocytoma: state of the art and future prospects. Endocr Rev 2003; 24;539
5. Karagiannis A, Mikhailidis DP, Athyros VG, Harsoulis F.Pheochromocytoma: an update on genetics and management. Endocr Relat Cancer 2007;14:935-56.
6. Waguespack SG, Rich T, Grubbs A, Ying AK, Perrier ND, M Ayala *et al*. A current review of etiology, diagnosis and treatment of paediatric pheochromocytoma and paraganglioma, The Journal of clinical Endocrinology and metabolism 2010;95:2023-37
7. Sibal L, Jovanovic A, Agarwal SC, Peaston RT, James RA, Lennard TW, Bliss R *et al* pheochromocytoma presenting as acute crises after beta-blockade therapy. Clinical Endocrinology 2006;65:186-90
8. Eisenhofer G, Siegert G, Kotzerke J, Bornstein SR, Pacak K. Current progress and future challenges in the biochemical diagnosis and treatment of pheochromocytomas and paragangliomas. Horm Metab Res 2008;40:329-37.
9. d'Herbomez M, Gouze V, Huglo D, Nocaudie M, Pattou F, Proye C *et al*. Chromogranin A assay and (131)I-MIBG scintigraphy for diagnosis and follow-up of pheochromocytoma. J Nucl Med. 2001;42:993-7.
10. Brink I, Hoegerle S, Klisch J, Bley TA. Imaging of pheochromocytoma and paraganglioma. Familial Cancer 2005;4:61-8
11. Bessel-Browne R, O'Malley ME. CT of Pheochromocytoma and paraganglioma: risk of adverse events with IV administration of non-ionic contrast material. Am J Roentgenol 2007;188:970-4.
12. Goldberg A, Pautler SE, Harle C, Dennis A, Rachinsky, Dhir A *et al*. Giant Cystic pheochromocytoma containing high concentrations of catecholamines and metanephrines. The Journal of Clinical Endocrinology & Metabolism 2011;96:2308-9.
13. Inan M, Besim H, Tuloy S, Kobatt I. Giant symptomatic cyst in a patient with ectopic kidney. Can J Surg 2009; 52: E25-6.
14. Kantorovich V, Pacak K. A new concept of unopposed beta-adrenergic overstimulation in a patient with pheochromocytoma. Ann Intern Med 2005;142:1026-8.
15. Bhajwa SJS, Bhajwa SK. Implications and considerations during pheochromocytoma resection; A challenge to anesthesiologist. Indian J Endocrinol Metab 2011;15(suppl 4):S337-44.