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Case Report

ROLE OF CT IN INVESTIGATION OF AN INCIDENTAL ADRENAL LESION LATER CONFIRMED TO BE A PHAEOCHROMOCYTOMA

Debashis Dakshit and Averee Gangopadhayay*

Department of Radio-Diagnosis, Medical College, Kolkata, 88, College Street, Kolkata-700073

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ABSTRACT

Adrenal "incidentalomas" are defined as adrenal masses detected during USG, CT or MRI examination in patients for whom imaging studies are being performed for an unrelated indication. Approximately 3 to 4 percent of CT and MRI studies of the abdomen reveal an adrenal incidentaloma. The overwhelming majority of these lesions comprise benign nonfunctioning adenomas in the asymptomatic patient with no history of malignancy. However, this does not hold true for oncologic patients, as the adrenal glands are a common site for metastatic disease. Adrenal metastasis may be found in 25% of patients with known primary. Adrenal incidentalomas (5cm or larger) are detected in 1-10% of abdominal CT and MRI scans, 2-9% of autopsies, 4% of chest CT scans. Adrenal incidentaloma is higher in whites than blacks and in obese, diabetic, hypertensive patients. 3-7% of adrenal incidentalomas are pheochromocytomas. Of additional concern are lesions that are hormonally active and the rare primary adrenocortical carcinomas. 35% of adrenal tumours are non-functioning and may not need treatment. For this reason, differentiating the lesions that warrant treatment from those benign, inconsequential masses that should be left alone is essential.

INTRODUCTION

Adrenal "incidentalomas" are defined as adrenal masses detected during USG, CT or MRI examination in patients for whom imaging studies are being performed for an unrelated indication. Approximately 3 to 4 percent of CT and MRI studies of the abdomen reveal an adrenal incidentaloma. The commonest tumours of the adrenal medulla, adrenal phaeochromocytomas constitute 90% of all paragangliomas. The most important hormonally silent Adrenal Incidentaloma is Phaeochromocytoma. It is present in 1 in 1000 autopsies. Pheochromocytomas are a type of paragangliomas; catecholamine secreting tumours arising from neural crest cells (chromaffin cells). They typically demonstrate a nesting (Zellballen) pattern on microscopy. This pattern is composed of well-defined clusters of polygonal to spindle-shaped chromaffin cells surrounded by supporting sustentacular cells that are supplied by a rich vascular network.

Prevalence increases with age (mean age 44 years). The rate is < 1% for patients younger than 30 years and 7% for patients 70 years or older. In genetically predisposed individuals the mean age is 25 years. Paediatric phaeochromocytoma has a higher incidence of malignancy (47% vs 10% in adults).

*Corresponding author: **Averee Gangopadhayay**
Department of Radio-Diagnosis, Medical College, Kolkata, 88, College Street, Kolkata-700073

Incidence in teenage girls is slightly higher than boys, but no such sex predilection exists in adults.

The majority are sporadic. In 5-10% of cases Phaeochromocytoma is a manifestation of underlying condition including

- MEN II (both A and B); 3% of all phaeochromocytoma. Never extra-adrenal, almost always bilateral.
- Von Hippel-Lindau disease
- Von Recklinghausen disease(NF1)
- Sturge Weber disease
- Carney Triad for extra-adrenal phaeochromocytoma
- Tuberous Sclerosis

Adrenal Phaeochromocytomas are usually hyper-functioning tumours that secrete norepinephrine and epinephrine into the blood.

We report a case of a 48 year old man presenting at ENT OPD with complaints of recurrent episodes of epistaxis associated with hypertension. A complete biochemical and radiological evaluation revealed elevated plasma and urinary levels of catecholamines along with a solid-cystic space occupying lesion at the upper pole of right kidney on USG. Further CT evaluation suggested the mass to be an Adrenal Phaeochromocytoma. The diagnosis of a phaeochromocytoma is made clinically and biochemically by detection of elevated plasma and urinary levels of catecholamines and their metabolites, vanillylmandelic acid(VMA) and metanephrine.

Once a clinical and biochemical diagnosis has been made, imaging studies are performed to localize the tumour and to aid in surgical planning for resection.

CASE REPORT

A 48 year old male patient with complains of recurrent episodes of dizziness, headache and epistaxis for the past two years. Previously he had hypertension and was treated with anti-hypertensive medications. With recurrence of epistaxis, he was advised USG whole abdomen along with other tests by ENT surgeon of our institution, which revealed an adrenal incidentaloma. Further radiological and biochemical tests were undertaken to confirm the nature of the incidentaloma.

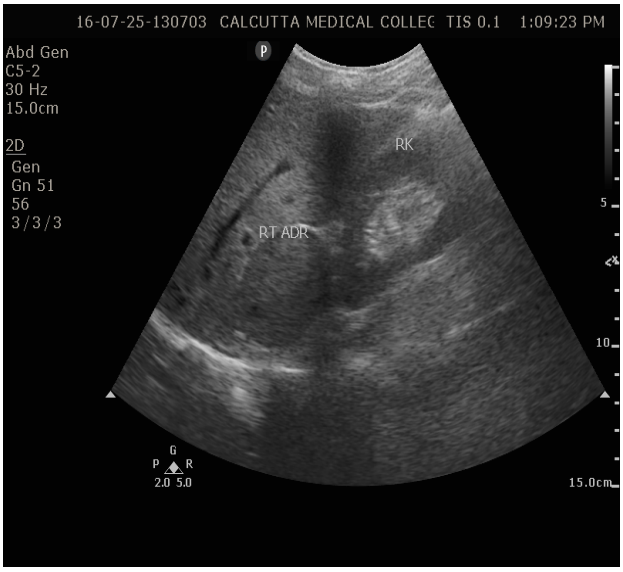

Fig 1 USG - 5 X 4 cm well-defined heterogeneously hypoechoic space occupying lesion above the upper pole of right kidney

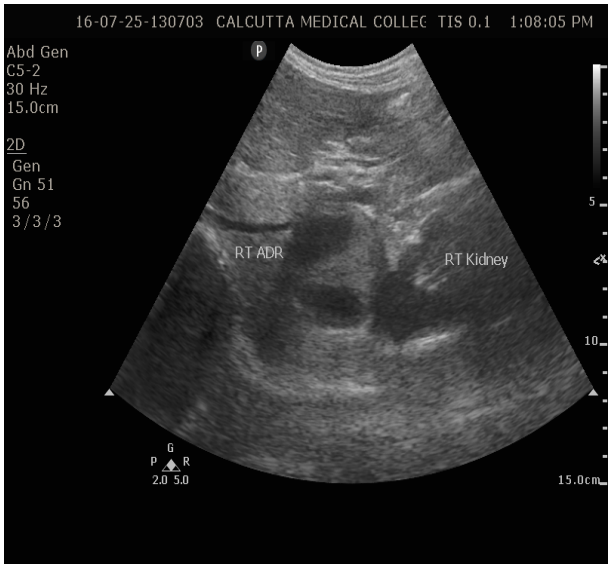

Fig 2 USG - Few cystic areas within the mass

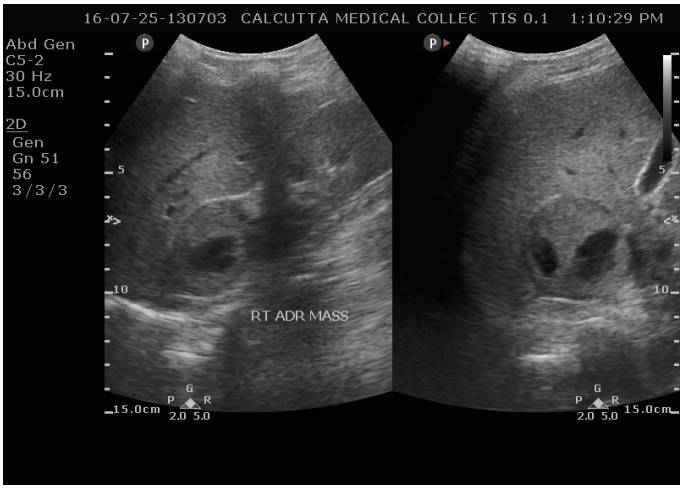

Fig 3 USG – Relationship of mass with IVC On further CT evaluation of whole abdomen, the following images were acquired:

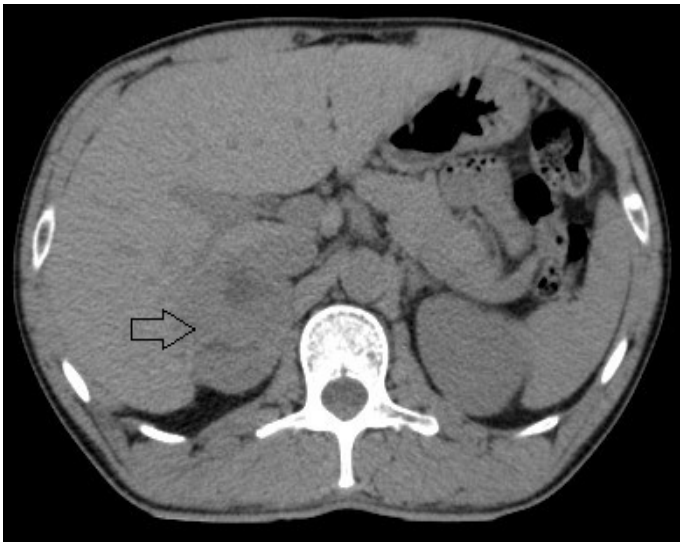

Fig 4 Plain CT image of mass

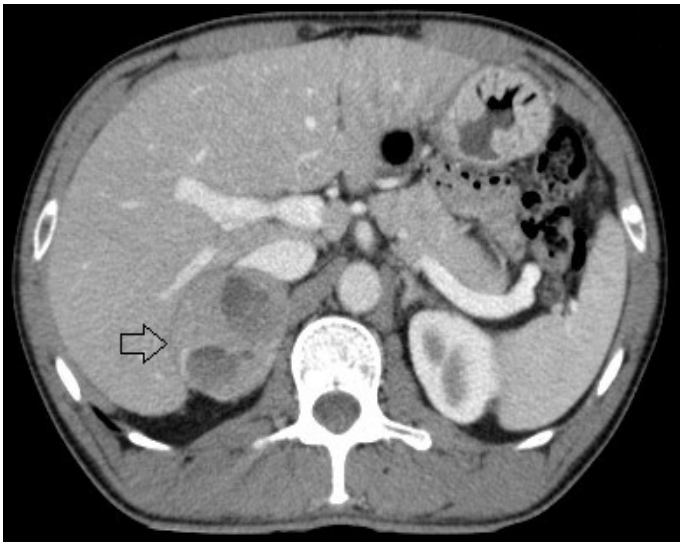

Fig 5 CECT showing the mass: Early Phase-homogenous post contrast enhancement

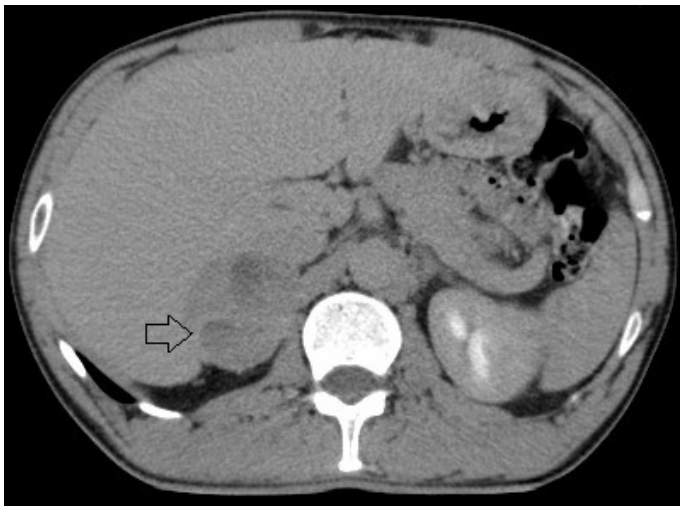

Fig 6 CECT: Delayed Phase-the mass is showing absolute washout of contrast

A 4.9 × 4.08 cm iso-attenuating lesion (Average 43 HU) with few internal hypodensities was noted in the Right adrenal region in NECT. 1 minute and 15 minute post contrast films were taken in which there is homogenous contrast enhancement with delayed absolute washout - less than 65% in 15 minutes post contrast CT. Lt adrenal appeared normal. Kidneys: RK and LK measuring 9.8 cm and 8.0 cm respectively. Both the kidneys have irregular lobulated cortical outline with multiple tiny simple renal cortical cysts bilaterally but largest one exophytic in the lower pole of Left Kidney. Normal excretory function was on both sides. Perirenal fat plane is maintained on either side.

Urine Metanephrine level was 2340.9 µg/24hrs (normal levels <350) while the Metanephrine: Creatinine ratio was 2622.86 µg/g creatinine (normal levels 33-109). In view of the above clinical, biochemical and radiological findings, the patient was diagnosed to be a case of Right Adrenal Phaeochromocytoma and was advised right adrenalectomy.

DISCUSSION

It is not possible to distinguish benign and malignant pheochromocytoma by appearance. Distinction is made by direct tumour invasion into adjacent organs/structures and presence of metastasis. High pre-operative 24 hours dopamine, extra-adrenal tumour location, high tumour weight (>80 gm), tumour dopamine concentration and persistent post-operative hypertension increases possibility of malignant phaeochromocytoma.

Ten percent of adrenal phaeochromocytomas are multiple, 10% are malignant with the incidence increasing in tumours larger than 6cm, 10% occur in children, 10% are familial, 10% are associated with hypertension and calcification, 10% are associated with neuroectodermal syndromes and 10% are non-functioning tumours. They are usually solitary although 10% are bilateral. Extra-adrenal phaeochromocytomas occur in 10% of patients and have been described in the Organ Of Zuckerkandl, sympathetic nerve chains, aortic and carotid chemoreceptors, bladder, prostate and chest. The tumours may also secrete dopamine, parathyroid hormones, calcitonin, gastrin, serotonin and ACTH with or without the catecholamines. Symptomatic patients present with paroxysmal hypertension, headaches, visual blurring, sweating and vasomotor changes caused by the transient elevation in catecholamines.

Their variable clinical presentation and biologic behavior often make accurate diagnosis challenging. A wide spectrum of imaging appearances—some of which may also mimic other diseases—has been recognized..

Sporadic adrenal phaeochromocytomas are usually large at time of diagnosis (90% larger than 2cm) and readily detected on imaging. They are generally well-defined oval or round masses and occasionally have foci of calcification, central necrosis or cystic change. Phaeochromocytomas occurring in association with neuroectodermal syndromes (MEN, VHL, Neurofibromatosis) are smaller at the time of detection, as these patients are generally actively screened by MRI.

The differential diagnoses of an Adrenal mass include:

- Cortical mass-Adenoma, Nodular Hyperplasia, Carcinoma
- Medullary mass- Phaeochromocytoma, Ganglioneuroma, Ganglioneuroblastoma
- Metastasis-Breast, Lung, Lymphoma, Leukemia
- Others - Myelolipoma, Neurofibroma, Hamartoma, Teratoma, Xanthomatosis, Amyloidosis, Cyst, Haematoma, Granulomatosis
- Pseudoadrenal mass – Renal, Pancreas, Spleen etc.

Adrenal cortical adenoma is a common benign tumour arising from the cortex of adrenal gland. Commonly occurs in adults but can be found in persons of any age. It has no potential for malignant transformation. Surgical excision is not indicated. Treatment for hormonally active (functional) adrenal tumour is surgery.

Approximately 85% of adrenal incidentalomas are non-functional (hormonally silent) and benign. The other 15% are either functional or malignant and require further evaluation and treatment. About 3.7% of adrenal incidentalomas prove to be phaeochromocytomas. Phaeochromocytomas may result in substantial complications including death if not recognized. They should be considered in all adrenal incidentalomas because they are more common than previously thought; diagnosis is often overlooked and a failure to recognize it may lead to patient death.

The adrenal gland is the 4th most common site of metastasis. Phaeochromocytoma should be excluded prior to FNAC/biopsy of adrenal incidentaloma to avoid hypertensive crisis.

The first step in the diagnosis of a pheochromocytoma is the biochemical confirmation of catecholamine excess. Diagnosis of phaeochromocytoma to be confirmed by measurement of plasma fractionated metanephrines and non-metanephrines or 24-hours total urinary metanephrines and fractionated catecholamines, or both plasma and urine studies. The biochemical diagnosis is followed by the localization of the pheochromocytoma and/ or metastases. On ultrasound, phaeochromocytomas are well-defined, ovoid or round suprarenal masses. They frequently have an inhomogeneous internal architecturedue to haemorrhage and necrosis. Ultrasound has a lower sensitivity for the detection of phaeochromocytomas than CT or MR imaging as smaller lesions particularly on the left may be obscured by bowel gas. CT is preferred as it is cost-effective than MRI to delineate size, shape and appearance. On unenhanced CT, the tumours have a soft-tissue density and speckled calcification is present

in up to 12% of tumours. A smooth homogenous lesion less than 4cm with low Hounsfield Unit is usually benign. A larger inhomogenous lesion with irregular margins and higher Hounsfield Units should be considered for malignancy.

To perform contrast-enhanced CT, nonionic contrast has been shown to be safe for patients with phaeochromocytomas without the use of adrenergic blockade. Contrast-enhanced CT is highly accurate in the detection of adrenal phaeochromocytomas, with the reported sensitivities between 93 and 100% and a positive predictive value exceeding 90%.

Contrast washout

Absolute washout: {Enhanced CT(HU)-Delayed CT(HU)}/{Enhanced CT(HU)-Unenhanced CT(HU)} X 100%
Relative washout: {Enhanced CT(HU)-Delayed CT(HU)}/Enhanced CT(HU) X 100%

Adenoma: Absolute washout > 60%, Relative washout > 40%. Phaeochromocytomas characteristically demonstrate intense contrast enhancement due to vascularity.The internal architecture of the tumours is variable, depending on the degree of central necrosis. In tumours with a large amount of central necrosis, the tumour may appear cystic. Even in these tumours a peripheral rim of intensely enhancing soft tissue can still be demonstrated.

Most phaeochromocytomas are iso- or hypointense to the liver on spin-echo (SE) T1-weighted MRI. High T1-weighted signal intensity corresponding to areas of haemorrhage has been reported in up to 20% of phaeochromocytomas. On spin-echo T2-weighted images the typical phaeochromocytoma has very high signal intensity with light bulb appearance. Larger tumours tend to be inhomogeneous, containing cystic central necrosis, calcification or haemorrhage.

Two main concerns in Adrenal incidentaloma are

1. Whether it is hormonally active
2. Whether it is malignant

Presence of intra-cytoplasmic lipid is fairly specific for adrenal cortical adenoma. Approximately 70% have high percentage of intra-cytoplasmic lipid. This unique characteristic distinguishes adenoma from others. Major exception is clear cell carcinoma of kidney with metastasis to the adrenal gland with an identical appearance with adenoma. On CT scan, benign adenoma typically reveals low HU and rapid washout of contrast 50% or more at 10 minutes. Malignancy is suggested on CT by large diameter >6cm, irregular border, inhomogeneity, a washout of contrast after 15 minutes of <40% and calcifications.

4-7% of incidentalomas are phaeochromocytomas. 10% have typical triad of symptoms (sweating, headache and palpitations) and 12.5% of incidentally found cases are normotensive.

Phaeochromocytomas are hormonally active in 90% cases. Morphological features - large, variation in size, homogeneity, margination and signal enhancement is seen in most cases. Low signal on T1WI and high signal on T2WI (Light Bulb Appearance) is characteristic of Phaeochromocytoma. Phaeochromocytoma enhances strongly on CECT scan in arterial as well s portal venous phase (portal venous more than arterial). 110 HU of enhancement in arterial phase is compatible with Phaeochromocytoma.

Urine free metanephrines and catecholamines are less sensitive than plasma but more specific. Meta-iodobenzylguanidine (MIBG) is a noradrenaline analogue taken up by the chromaffin cells in paragangliomas including phaeochromocytomas. MIBG is most commonly labelled with iodine-123 (for diagnosis) or I-131 (for treatment) for whole-body scintigraphy in the detection and localisation of primary and metastatic paragangliomas. The sensitivity of MIBG is reported between 87 and 90%, lower than that for both CT and MRI, as the detection of lesions depends on ability of the tumour to take up the tracer. However, the strength of MIBG is its high specificity, which exceeds 90%. 18F Dopa PET is thought to be highly sensitive according to initial results.

Treatment of hormonally active adrenal tumour is surgery. Treatment of malignancy depends on cell type, spread and location of primary tumour. Laparotomy is preferred for bilateral diseases, large masses >10 cm, possible malignant disease and phaeochromocytoma. Metastatic disease is managed according to the type of primary cancer. Adrenal mass has to be removed if the diameter is >6cm. Otherwise follow-up is advised with routine CT at periodic intervals. Resection for phaeochromocytoma should be on a long follow-up because of high recurrence rate (10-15%).

Surgical resection of the tumour is the treatment of choice and usually results in cure of hypertension. Careful preoperative preparation with Alpha adrenergic blocker (phenoxybenzamine) 7-10 days before surgery is required to control blood pressure and to prevent intra-operative hypertensive crisis. Beta blocker may be added to control tachycardia and arrhythmia. Approximately 27% patients die unexpectedly during surgery, 27% from cardiovascular causes and 17% from CVA.

CONCLUSION

Classical Triad of symptoms e.g. sweating, headache and palpitations are non-specific. This patient presented with hypertension with recurrent episodes of epistaxis. With these symptoms, attention is to be given to a possibility of Phaeochromocytoma. If not recognized, it may lead to complications and eventually death. Imaging with USG followed by CT and MRI helps in the detection of adrenal incidentalomas.

Biochemical assessment of plasma and urinary level of catecholamines has to be done first to establish or exclude the diagnosis of phaeochromocytoma in a case of Adrenal Incidentaloma prior to FNAC or biopsy to prevent hypertensive crisis. Imaging has a role in localization and metastasis.

Two main concerns of adrenal incidentalomas are whether it is hormonally active and whether it is malignant. 90% of phaeochromocytomas are hormonally active. Definitive treatment of phaeochromocytoma is surgical excision. Rarely, in phaeochromocytoma not cured by surgery chemo and radiotherapy may be required. Careful pre-operative preparation with alpha adrenergic blockers (phenoxybenzamine) required for 7-10 days to control blood pressure and prevent intra-operative hypertensive crisis.

After resection, patients of phaeochromocytoma should be on a long follow-up because of high recurrence rate (10-15%).

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