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CT in the Workup of Patients with Adrenal Incidentaloma

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Abstract: ***An adrenal "incidentaloma" (Al) is an adrenal mass, which is discovered serendipitously during a radiologic examination performed for indications other than for evaluation of an adrenal disease which is increasing frequency due to the widespread application of non-invasive, high-resolution techniques. Incidentalomas could be associated with some of the most common clinical syndromes of adrenal hormonal overproduction (hyperaldosteronism, hypercortisolism, or phaeochromocytoma); the majority of them, however are clinically silent. The need for discovering these incidentalomas and characterizing them on imaging is crucial, so that they can be managed accordingly. These Al masses need to be discovered on CT, which will lead to further evaluation and better management of these conditions, which would otherwise be diagnosed wrongly as essential diabetes or essential hypertension and inevitably treated for life. Conclusion: Clinically silent adrenal masses ('Incidentalomas') are discovered incidentally during diagnostic testing or treatment for clinical conditions that are not related to suspicion of adrenal disease. The widespread use of high-resolution anatomic imaging techniques such as computed tomography (CT) and magnetic resonance (MR) imaging has led to the increased detection of these masses. When an adrenal incidentaloma is discovered, two main concerns need to be addressed. First, these lesions must be defined as benign or malignant. Second, it is important to define whether this adrenal mass is hormonally active or hormonally inactive.***

Keywords: Adrenal incidentaloma, benign, malignant, computed tomography, adenoma, non-adenoma

1. Introduction

Adrenal incidentalomas (AIs) are adrenal neoplasms discovered during a procedure not performed for suspected adrenal disease [1,2]. Their prevalence is age dependent (up to 10–15% in adults >60–70 years old), and their detection is increased in recent years, because of the large availability of imaging medical equipment such as computed tomography (CT) and magnetic resonance (MR), resulting in more than 200 CT and 100 MR scans for 1000 people [3].

Overt endocrine secretion (glucocorticoids, mineralocorticoids, and catecholamines, characterising, respectively, Cushing's syndrome, primary aldosteronism, and pheochromocytoma) should be ruled out in all patients with AI by the measurement of serum cortisol after 1 mg dexamethasone (the overnight suppression test), aldosterone-to-renin ratio, and plasma or urinary metanephrines [2,4,5]. Nevertheless, the majority of them are non-secreting cortical adenomas [1,2].

At the first evaluation, it is also recommended to rule out malignancy [2]. Malignant AIs could be a primary adrenal disease (adrenocortical cancer, ACC, or malignant pheochromocytoma), or metastases, whose prevalence in AIs is 7.5%. A medical history positive for extra-adrenal cancer or imaging prescription for active cancer are common: Metastatic AI was 22 times more likely during cancer staging [6], and 27% of malignant tumours (especially lung, breast, gastric, liver, and pancreatic cancer) cause adrenal metastasis on autopsy studies [7]. On the contrary, adrenal metastases could be excluded in 96% of Ais by multidisciplinary evaluation in patients affected by colorectal cancer and AIs (10.5% in 500 patients) [8].

2. Justification of the Study

1) The modality of choice for characterization of adrenal masses is Computed tomography (CT)[9].
2) Most adrenal incidentalomas are detected at CT, and can be differentiated into benign and malignant on the basis of non-enhanced, contrast enhanced and delayed enhanced CT scans[9].
3) Most adrenal lesions can be characterized at CT, by using both non-enhanced and contrast-enhanced CT scan attenuation measurements, and calculation of relative percentage washout on dynamic and delayed enhanced CT scans, thereby obviating the need for additional imaging, follow-up, or biopsy.
4) Depending on the various characteristic imaging features, CT can also help to characterize the adrenal incidentaloma into various categories (adenoma, cyst, hematoma, myelolipoma, pheochromocytoma, ACC, etc).
5) Al may manifest as clinically silent Cushing's syndrome [SCS], silent pheochromocytoma, hyperandrogenism or hyperaldosteronism. These may present as diabetes, hypertension, obesity or Addison's disease. The

discovery of these AI masses on CT will lead to further evaluation and better management of these conditions which would otherwise be diagnosed as essential hypertension or essential diabetes and treated for life and what would be inevitable is wrong diagnosis and treatment. absence of fistula, its course and relations, exact location of the internal opening, associated inflammatory conditions like abscesses or collections, and any other relevant information that can help in patient management.

3. Material and Methods

This retrospective prospective study was conducted from August 2023 to October 2024 in the Department of Radiodiagnosis and Imaging, Department of Radiology,

Pandit Deendayal Upadhyay Government Medical College & Civil hospital, Rajkot, Gujarat, India. This study was approved by the institutional ethics committee. A total of 82 patients were assessed in the study.

Inclusion Criteria

- Any patient undergoing CT abdomen and/or thorax without symptoms and signs denoting an adrenal pathology.
- Patients able to cooperate for the examination.

Exclusion criteria

- Any patient with signs and symptoms denoting an adrenal gland pathology or a patient with a known adrenal mass.
- Adrenal haemorrhage cases in patients with traumatic injury to the abdomen.
- Patients with unilateral adrenalectomy.
- Patients who are unwilling to cooperate for the procedure.

All the patients fulfilling selection criteria were explained about the purpose of study and a written informed consent was obtained to participate in the study before enrolment (Annexure I).

Data Collection

Thorough clinical history and clinical examination were done before CT scan. Details of the participants like age, sex, detailed history, were obtained and recorded on predesigned and pretested proforma (Annexure-II).

Preparation of Patients

After detailed explanation regarding the imaging procedure, a written informed consent was obtained from the patients prior to the scan, and from the parents in cases of paediatric patients, following which a detailed clinical history was taken and relevant clinical examination was done.

Scan Protocol for multi-detector row CT

CT imaging was performed using 128-slice single source CT scanner (CT Wipro GE 128 slice H-211) in all patients.

Axial plain sections of the thorax or abdomen (depending on what was asked for from the referring consultant) were taken using 5.0 mm sections and multiplanar reconstruction was done in 1.5 mm slice thickness.

The examination area extended from the lung apex to upper abdomen in CT chest and from the lower chest to the inferior margin of pubic rami in CT abdomen; i.e., the CT thorax studies were done in such a way as to include sections of the upper abdomen including the bilateral adrenal glands.

Depending on the need for further evaluation, plain study was followed by i.v. contrast study using non-ionic water-soluble contrast medium i.e. lomeron 350 mg % in a dose of 1 ml/kg body weight.

Images were taken in arterial and venous phases. Delayed scans were taken with special emphasis made on delayed scans at 15 min of the start of contrast bolus.

When an adrenal incidentaloma was detected with an attenuation of <10 HU on plain scan, no further study was required. If the plain attenuation of the Adrenal incidentaloma is >10 HU, contrast study with delayed study at 15 min were performed.

For all adrenal massed detected at CT (regardless of phase whether plain, enhanced or delayed), the attenuation was measured by using circular- region of interest (ROI) placed over the area of disease. The ROI circle was made as large as possible and lesion edges were avoided to preclude partial volume effects. Cystic, haemorrhagic, and necrotic components of the adrenal masses, were excluded if they were present.

Necrosis was defined as a region (within the mass) with an attenuation value similar to that of water (20 HU) at 70 seconds contrast enhanced CT.

Calcification was defined as a region with an attenuation value > 100 HU at non enhanced CT. Scans were reviewed in appropriate window settings.

4. Results

Our study comprised of 100 patients with ages ranging from 22 to 86 years with a mean age of 55.72 years. There were 58 males and 24 females. The reasons for imaging procedure were abdominal pain, including either ill-defined discomfort or biliary & renal colic, acute abdomen, post-surgery follow-up, fever under evaluation, vomiting under evaluation, nonspecific abdominal symptoms, chest complaints and others. No significant difference in the indications by gender was apparent.

Table 1: Comparison of Benign and Malignant adrenal incidentalomas with respect to Plain HU, Venous HU and Delayed HU values on right side by t test

Parameters		Benign	Malignant	Total	t – value	p – value
Plain HU	Mean	27.61	31.71	28.83	-0.2129	0.8324
	SD	71.43	10.62	59.87		
Venous HU	Mean	31.67	68.46	45.74	-2.0866	0.0450
	SD	61.60	18.26	52.45		
Delayed HU	Mean	14.76	53.08	29.41	-2.5838	0.0145
	SD	52.16	13.19	45.49		

The mean plain HU of the benign adrenal incidentalomas on right side was 27.6.

The mean plain HU of the malignant adrenal incidentalomas on right side was 31.7.

The mean venous HU of the benign adrenal incidentalomas on right side was 31.6.

The mean venous HU of the malignant adrenal incidentalomas on right side was 68.4.

The mean delayed HU of the benign adrenal incidentalomas on right side was 14.7.

The mean delayed HU of the malignant adrenal incidentalomas on right side was 53.0

Table 2: Comparison of Benign and Malignant with respect to Absolute washout and Relative washout percentage values on right side by t test

Parameters		Benign	Malignant	Total	t – value	p - value
Absolute washout	Mean	71.36	38.51	54.93	4.9495	0.0001
	SD	17.34	16.50	23.57		
Relative washout	Mean	41.88	21.18	31.53	3.8828	0.0007
	SD	16.83	9.29	16.99		

The mean Absolute percentage washout time of benign adrenal incidentalomas on right side was 71.3±17.3 with a p value of 0.0001.

The mean Absolute percentage washout time of malignant adrenal incidentalomas on right side was 38.5±16.5 with a p value of 0.0001.

The mean relative percentage washout time of benign adrenal incidentalomas on right side was 41.8 ±16.8 with a p value of 0.0007.

The mean relative percentage washout time of malignant adrenal incidentalomas on right side was 21.2±9.3 with a p value of 0.0007.

Table 3: Comparison of Benign and Malignant with respect to Plain HU, Venous HU and Delayed HU values on left side by t test

Parameters			Benign	Malignant	Total	t – value	p - value
Plain HU	Left	Mean	17.63	35.28	24.25	-1.6990	0.0961
		SD	42.96	11.63	35.52		
Venous HU	Left	Mean	39.06	71.44	55.71	-2.8864	0.0068
		SD	45.39	14.04	36.58		
Delayed HU	Left	Mean	18.47	56.83	38.20	-4.5237	0.0001
		SD	34.25	10.78	31.44		

The mean plain HU of the benign adrenal incidentalomas on left side was 17.6.

The mean plain HU of the malignant adrenal incidentalomas on left side was 35.3.

The mean venous HU of the benign adrenal incidentalomas on left side was 39.06.

The mean venous HU of the malignant adrenal incidentalomas on left side was 71.4.

The mean delayed HU of the benign adrenal incidentalomas on left side was 18.4.

The mean delayed HU of the malignant adrenal incidentalomas on left side was 56.8.

Table 4: Comparison of Benign and Malignant adrenal incidentalomas with respect to Absolute washout and Relative washout percentage values on left side by t test

Parameters		Benign	Malignant	Total	t – value	p - value
Absolute washout	Mean	75.27	39.06	54.04	4.0093	0.0004
	SD	12.54	29.32	29.70		
Relative washout	Mean	50.92	17.64	31.41	6.9671	0.0001
	SD	13.33	12.19	20.81		

The mean Absolute percentage washout time of benign adrenal incidentalomas on left side was 75.2±12.5 with a p value of 0.0004.

The mean Absolute percentage washout time of malignant adrenal incidentalomas on left side was 39.0+ 29.3. with a p value of 0.0004.

The mean Relative percentage washout time of benign adrenal incidentalomas on left side was 50.9 ±13.3 with a p value of 0.0001.

The mean Relative percentage washout time of malignant adrenal incidentalomas on left side was 17.6±12.2 with a p value of 0.0001.

5. Discussion

Despite its small size, the adrenal gland can harbour numerous abnormalities ranging from hormonal dysfunction, to primary and secondary neoplasia, to infiltrative disease.

Clinically silent adrenal masses (incidentalomas') are discovered incidentally during diagnostic testing or treatment for clinical conditions that are not related to suspicion of adrenal diseases. The widespread use of high-resolution anatomic imaging techniques such as computed tomography (CT) and magnetic resonance (MR) imaging has led to the increased detection of these masses. These masses form part of a long differential diagnostic list; most often, they are benign adrenal adenomas, but their discovery requires a clinical evaluation that is sufficiently broad to exclude clinically silent endocrine disease, metastases to the adrenal gland in patients with suspected or known malignancies, and rare adrenocortical carcinomas.

More recent research has been focused on different approaches to characterizing adrenal masses on cross-sectional images, including assessing lesion size, describing morphologic criteria, measuring attenuation or signal

intensity, calculating the percentage loss of enhancement, and determining the lipid content.

Prevalence

A total of 7148 (4143 males and 3275 females, age range 5-86 years) CT scans of abdomen and chest were reviewed over a period of 1 year and a total of 98 adrenal incidentalomas were found in 82 patients (Prevalence- 1.37%).

The prevalence of incidentalomas in CT examinations has varied from 0.35 to 5 %, [12,-18] and in the autopsy series adrenal adenomas are found in 1.4 to 8.7%, but these series include also small adenomas that cannot be found in radiologic examinations [10,11]

Davenport et al[18] reported a prevalence of approximately 1%. They performed a retrospective study of 3,705 CT scans (January 2006 to December 2007) of chest and abdomen and found 37 incidentalomas.

Benign And Malignant

Of the 98 adrenal incidentalomas in 82 patients, 65 lesions were diagnosed as benign and 33 as malignant.

A total of 65 benign adrenal incidentalomas; 34 (40.2%) on right side and 31 (37.8%) on left side were diagnosed.

A total of 33 malignant adrenal incidentalomas; 14 (17.1%) on right side and 19 (23.1%) on left side were diagnosed.

The criteria used were attenuation on unenhanced CT and washout characteristics on delayed CT scans. The other corroborative findings that were also used in interpretation were presence or absence of necrosis, hemorrhage, calcification and macroscopic fat.

Of the 82 patients with adrenal incidentalomas, benign lesions diagnosed were lipid poor adenomas, adrenal calcifications, adrenal cysts, ganglioneuromas, hematomas, lipoma, pheochromocytomas & myelolipomas and were seen in 29, 6, 4, 1, 1, 5, 6, 4, 4 & 1 patients respectively, malignant lesions diagnosed were adrenal carcinoma « metastasis in 1 & 26 patients respectively.

Adenomas (lipid poor & lipid rich adenomas) and metastasis were the most mamon entities constituting approx 43% and 32% respectively of all adrenal incidentalomas

Of the 35 patients with adrenal adenomas, most of them had adrenal incidentalomas with plain HU value‹ 10. The remaining adenomas were diagnosed on delayed studies with the help of the absolute and relative percentage washout

Hamrahsin et al[19] performed a study of 299 Al. They reported a sensitivity of 40.5% and specificity of 100% for a cut-off value of 10 HU for the diagnosis of adrenal adenoma.

ADENOMA AND NONADENOMA

Of the 82 patients with Al. 35 (43%) were adenomas and 47 (57%) were non almonas. Non adenomas included benign lesions like myelolipoma, cyst, hematoma, no chromocytoma and malignant lesions like adrenocortical carcinoma and metastases.

Pheochromocytomas can be benign or malignant depending on the histological characteristics, and it cannot be differentiated on imaging (unless they metastasize).

All of the various types of Al were more common in males. Though size was a major criterion, that helped to distinguish between benign and malignant Al or adenomas and non-adenomas, it was not of much help in differentiating between various types of benign Al.

Caoili et a[21] evaluated 166 adrenal masses using the adrenal protocol. They found 127 adenomas and 39 nonadenomas. They reported a mean diameter of 2.3 cm for adenomas and 4 cm for non adenomas.

The results of the present study indicate that at non-enhanced CT, both adrenocortical carcinomas and pheochromocytomas have mean attenuation values similar to those of metastases but significantly higher than those of adenomas.

On the 70 seconds contrast-enhanced CT scans, however, there was considerable overlap in attenuation between the adenomas and all three types of nonadenomas, and, hence, it was not possible to identify a threshold attenuation value at could he used to reliably differentiate the different masses. On the 15-minute delayed contrast-enhanced scans, both the mean attenuation and the mean percentage loss of enhancement for adenomas differed significantly from those observed for pheochromocytomas, adrenocortical carcinomas, and metastases. The enhancement loss in adrenocortical carcinomas, pheochromocytomas, and adrenal metastases was significantly less than that in adrenal adenomas.

At optimal threshold values of 60% for absolute percentage of enhancement loss and 40% for relative percentage of enhancement loss at 15 minutes, both the sensitivity and the specificity for the diagnosis of adenoma were 100% when adenomas were compared with carcinomas, pheochromocytomas, and metastases.

Korobkin et al[20] reported that adrenal adenomas have a much earlier and more rapid contrast material washout than do nonadenomas. In their study, the mean percentage loss of enhancement for adrenal adenomas was 51% at 5 minutes and 70% at 15 minutes after the start of the contrast material administration, as it compared with 8% and 20%, respectively, for nonadenomas.

By using both non-enhanced and contrast-enhanced CT scan attenuation measurements, and calculation of relative percentage washout on dynamic and delayed enhanced CT scans most adrenal lesions can be characterized at CT, thereby obviating the need for additional imaging, follow-up, or biopsy.

The limitation of the study is that, the study did not include the correlation of adrenal incidentalomas detected on CT with

the hormonal levels, histopathological findings and clinical features.

6. Conclusion

In spite of its small size, the adrenal gland can harbor numerous abnormalities raging tom hormonal dysfunction, to primary and secondary neoplasms, to
infiltrative diseases.

Clinically silent adrenal masses (incidentalomas) are discovered incidentally during diagnostic testing or treatment for clinical conditions that are not related to suspicion of adrenal disease. The widespread use of high-resolution anatomic imaging techniques such as computed tomography (CT) and magnetic resonance (MR) imaging has led to the increased detection of these masses.

When an adrenal incidentaloma is discovered, two main concerns need to be addressed. First, it is important to define whether this adrenal mass is hormonally active or hormonally inactive. Second, these lesions must be defined as benign or malignant.

The role of the radiologist is to-

1) To identify an adrenal incidentaloma.
2) To identify, whether an adrenal incidentaloma is benign or malignant.
3) To differentiate between adenomas and non-adenomas. If possible, to identify the type of non-adenoma, depending on various characteristic imaging features.
4) Finally, to refer the patient to endocrinology department for further evaluation, identify whether an adrenal incidentaloma is normally functioning, hyper or hypo-functioning.

The following radiological criteria can be used:

1) Size- greater is the size of Al, more is the chance of it being malignant.
2) Imaging features on non-enhanced ct- if the attenuation is <10 HU, the Al is almost always an adenoma and is benign. Other features that should be looked for in non-enhanced CT are presence or absence of calcification, haemorrhage and macroscopic fat.
3) Washout characteristics on delayed CT-lf the APW >60% or RPW >40%, the Al is it most likely to be benign, otherwise malignant. In our study, 7,148 CT scans of the chest and abdomen were reviewed over a period, of 1 year and 98 Al were found in 82 patients. The prevalence of Al was found to be 1.37%.

Of the total 98 AI, 65 Al were diagnosed as benign and 33 as malignant, on the basis of imaging features.

By using both nonenhanced and contrast-enhanced CT scan attenuation measurements, and calculation of relative percentage washout on dynamic and delayed enhanced ct scans most adrenal lesions can be characterized at CT, thereby obviating the need for additional imaging, follow-up, or biopsy.

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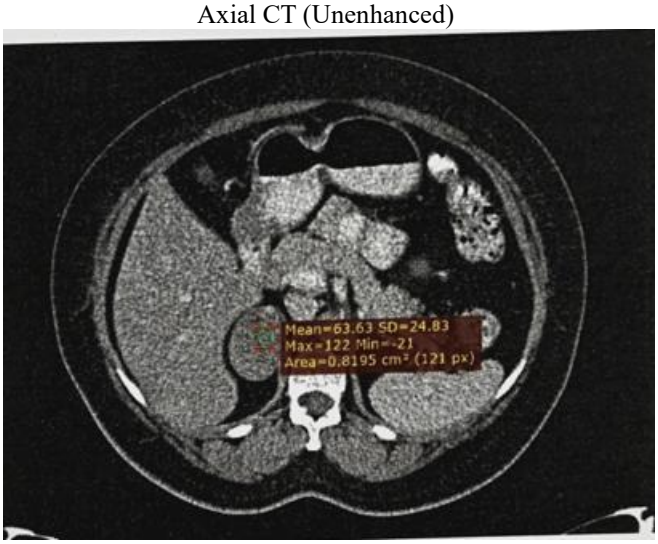
Figure 1: Adrenal adenoma (lipid rich)

A left adrenal mass with attenuation of 8.8 HU is seen on non-enhanced CT suggestive of lipid rich adrenal adenoma.

Axial CT (Unenhanced)

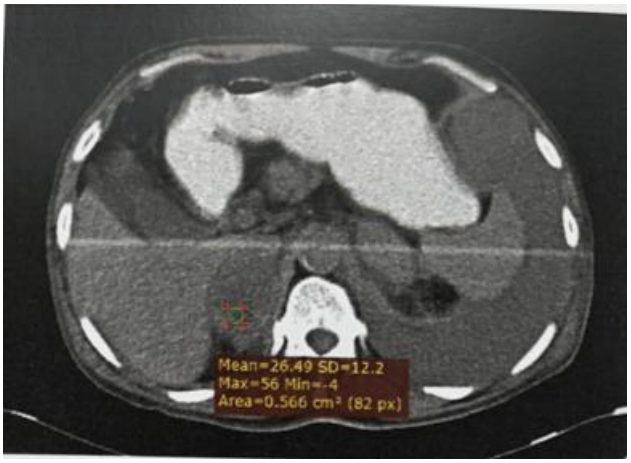


Axial CT (70s contrast enhanced)

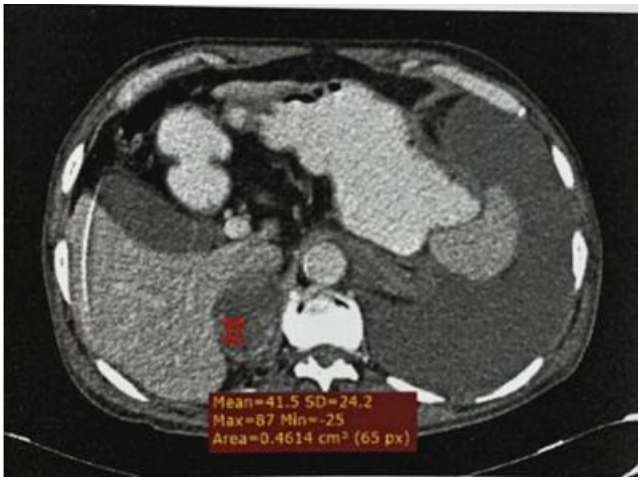
Axial CT delayed 15 minutes.

Figure 2: Adrenal adenoma (lipid poor)

An enhancing mass lesion is seen on the right adrenal gland showing attenuation value of 25.3 HU, 63.6 HU, 35.4HU on unenhanced, 70s (contrast enhanced) and delayed scans respectively. The APW and RPW were 73.6% and 44.3 % respectively suggestive of lipid poor adrenal adenoma.



Axial CT (Unenhanced)



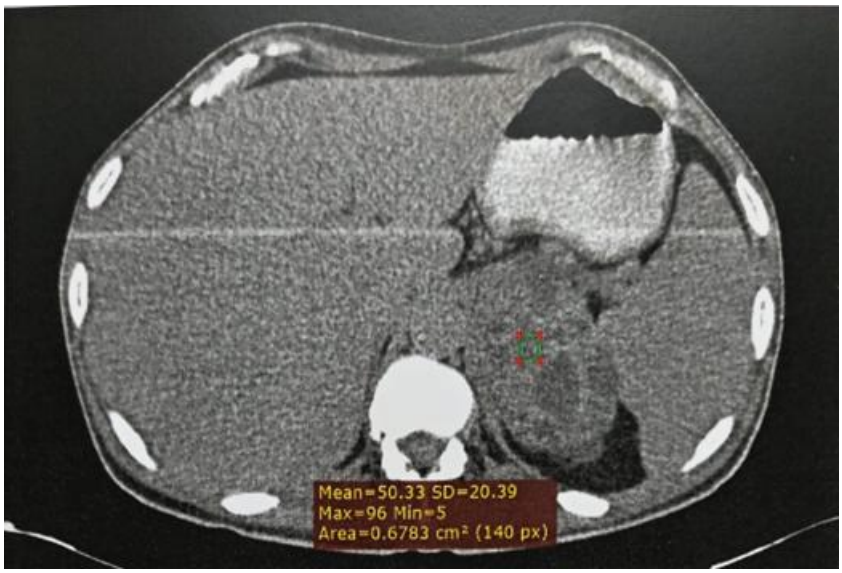
Axial CT (70s contrast enhanced)

Axial CT delayed

Figure 3: Adrenal metastasis

A heterogeneously enhancing mass seen on the right adrenal gland showing attenuation value of 26.5, 41.5 & 34.7 on unenhanced, contrast enhanced and delayed scans consistent with metastasis.

The APW and RPW were 45.3% and 16.4% respectively. It was a case of bronchogenic carcinoma on right side with adrenal metastasis.

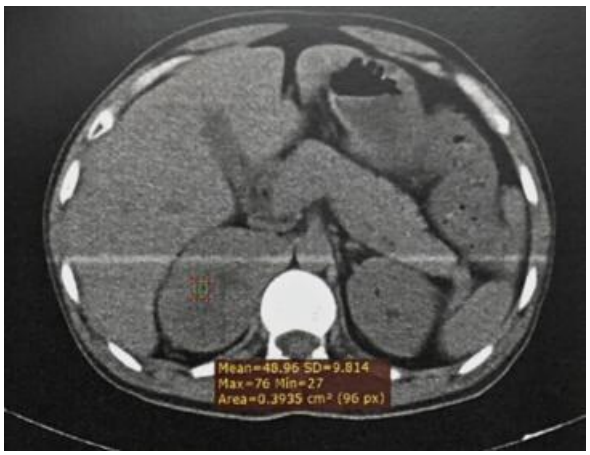


Axial CT (Unenhanced)

Axial CT contrast enhanced

Figure 4: Adrenocortical carcinoma

There is a large heterogeneously enhancing mass involving the left adrenal gland which shows enhancing solid and non-enhancing necrotic areas.



Axial CT (Unenhanced)

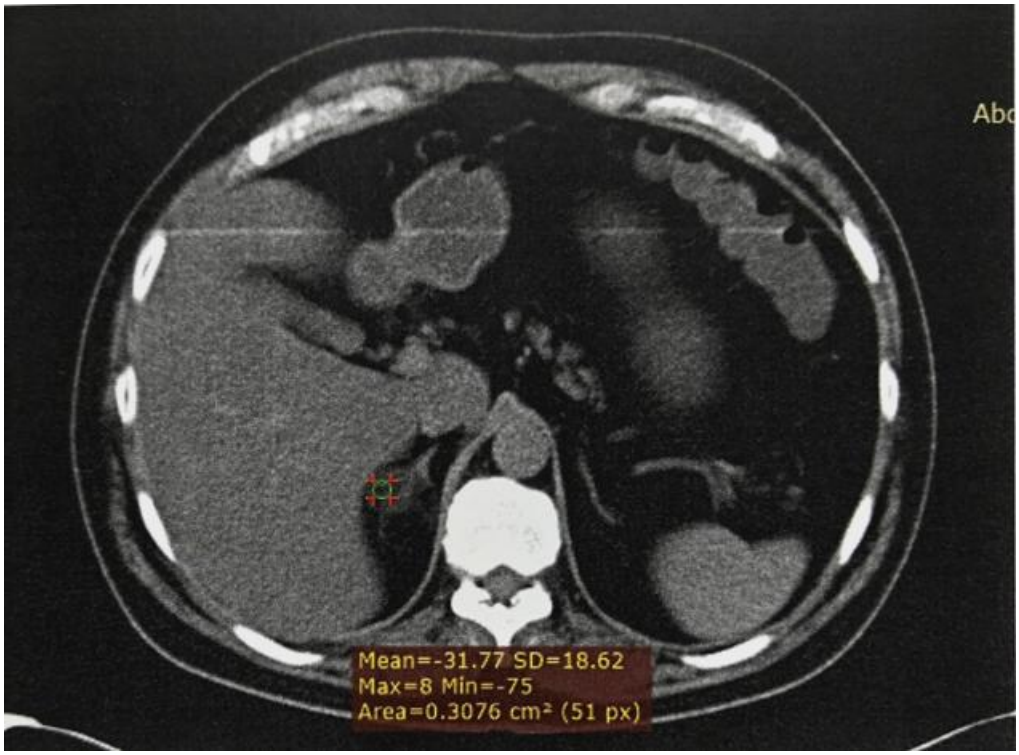
Axial CT contrast enhanced

Axial CT delayed

Figure 5: Pheochromocytoma

An intensely enhancing mass is seen involving the right adrenal gland with plain, enhanced & delayed attenuation values of 48.9 HU, 81.6 HU & 59.7 HU respectively.

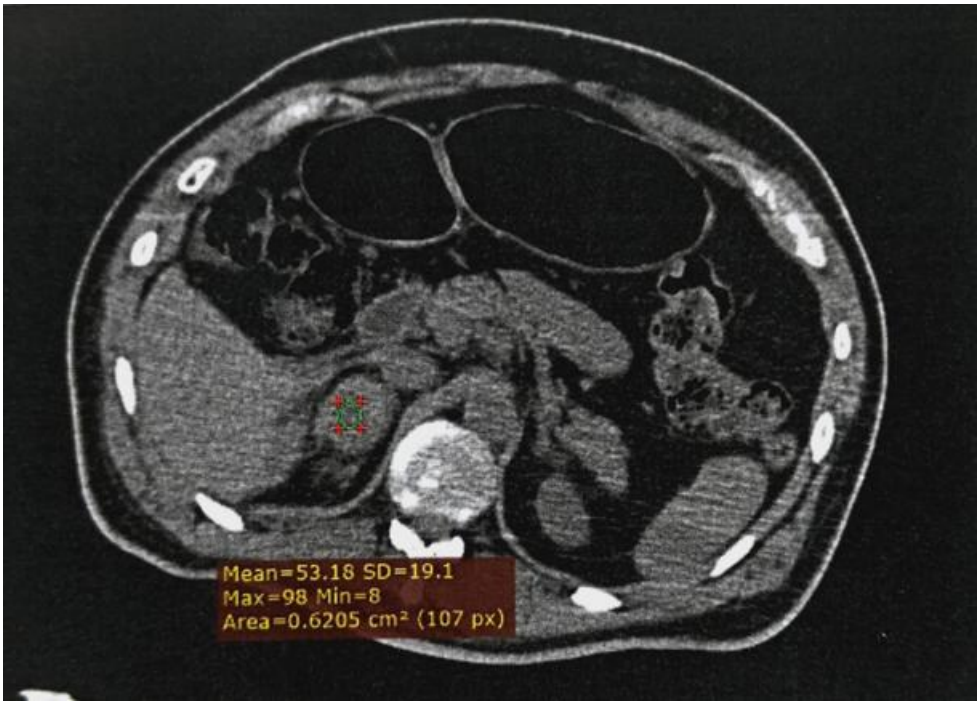
The APW and RPW were 66.9% and 26.8% respectively. The findings were consistent with pheochromocytoma.



Axial CT (Unenhanced)

Figure 6: Myelolipoma

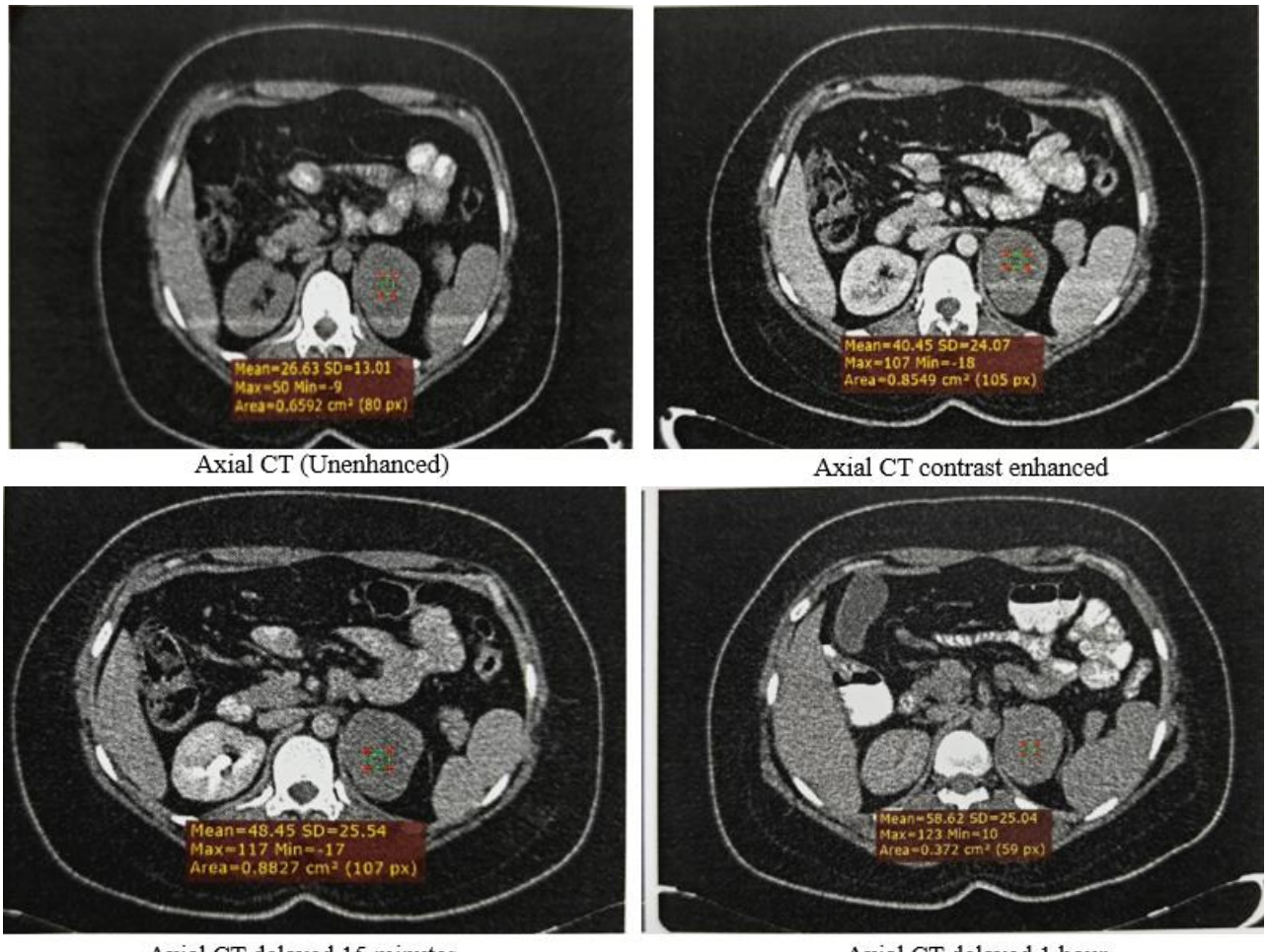
An Al is seen involving the right adrenal gland which shows macroscopic fat characteristic of a myelolipoma.



Axial CT (Unenhanced)

Figure 7: Adrenal hematoma

The right adrenal gland is diffusely bulky with increased attenuation suggestive of adrenal hematoma

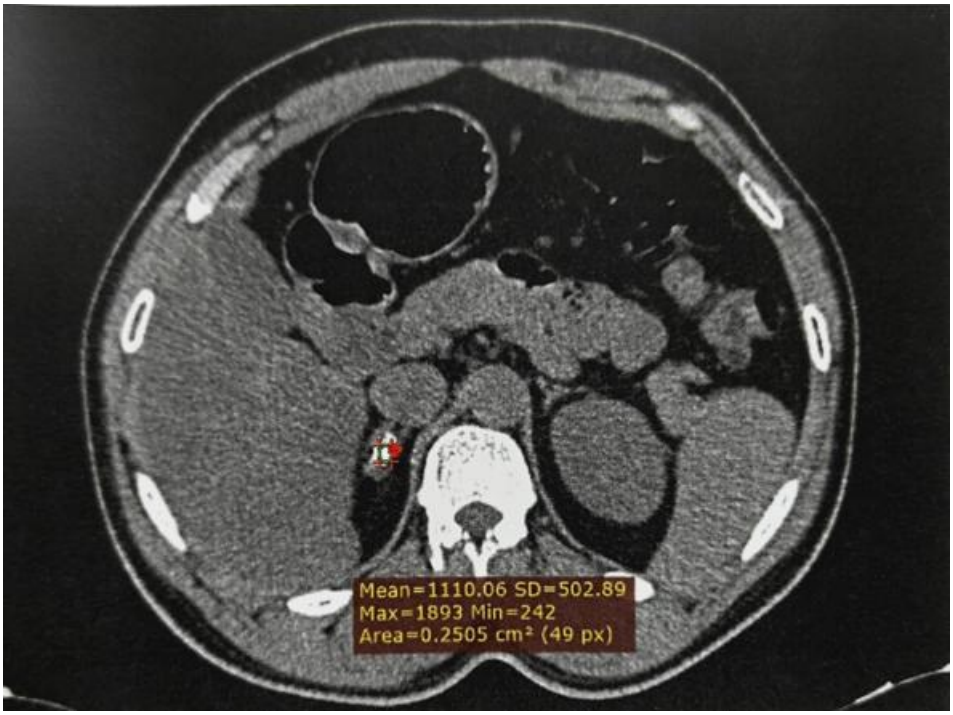


Axial CT (Unenhanced) Axial CT contrast enhanced

Axial CT delayed 15 minutes. Axial CT delayed 1 hour.

Figure 8: Adrenal ganglioneuroma

There is a large mass involving the left adrenal gland which showed persistent enhancement on the delayed scans suggestive of Ganglioneuroma.



Axial CT (Unenhanced)

Figure 9: Adrenal calcification

The right adrenal gland appears bulky and shows a hyperdense area with attenuation of 1100 HU suggestive of adrenal calcification.

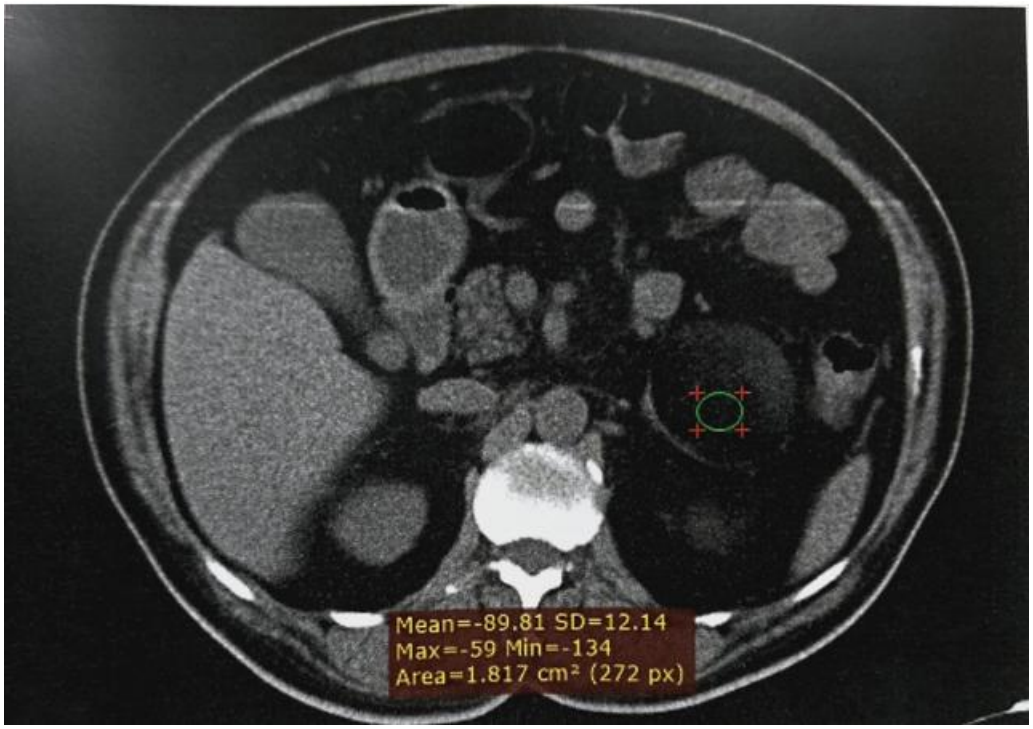


Figure 10: Adrenal lipoma

A well-defined large fat attenuating lesion along the lateral limb of the left adrenal gland suggestive of adrenal lipoma.