Imaging of Adrenal Tumors Using CT: Comparison of Benign and Malignant Lesions

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Abstract
Objective: The aim of the study was to see the CT features that most significantly useful to differentiate benign and malignant lesions of adrenal gland
Materials and Method: A retrospective analysis of CT of 35 patients with adrenal masses was done. Features such as size, margins, heterogeneous or homogeneous appearance, calcification, fatty attenuation, contrast enhancement patterns were assessed. Pathological and clinical diagnosis including biochemical parameters were obtained from the medical records library to make a final diagnosis.
Results: Size, irregular margins and heterogeneous enhancement pattern were found to be important discriminators for malignant from benign lesions.
Conclusion: Though the majority of tumors has similar appearances and cannot be characterized beyond size and location, CT criteria can often discriminate accurately between benign and malignant adrenal masses and, in particular, minimize the number of false-negative diagnoses of malignancy.
Keywords - Adrenal mass, CT, Computed Tomography, benign, malignant, pathology.

INTRODUCTION
The incidence of adrenal masses range from 0.6% to 5% on abdominal CT scans [¹,²] and on autopsies it varies from 1.4 to 2.9 % [³]. As a result of advances in imaging, the work up and clinical management of adrenal diseases has undergone improvement rapidly.
Adrenal masses are often incidentally detected when the patient is evaluated for some other suspected pathologies. The occurrence of incidental adrenal masses has been reported to be 0.5 to 5% of abdominal CT examinations. Whenever hyper or hypo functioning of adrenal glands are suspected CT becomes the primary mode for evaluation for localizing the pathology.

MATERIALS AND METHOD
Adrenal imaging was done on Siemens Somatom Definition AS 64 slice multi detector row CT or Toshiba X series (helical system-2B 250-064 EC). The adrenal scanning was done by using the following parameters: Scanning at 120 or 140 kVp and 200 to 300 mAs with a gantry revolution of 0.5 sec and beam width of 4 cm with a pitch of 1.2 to 1.5 mm. Reconstruction is done using standard algorithm in Syngo workstation. The patient is
scanned in supine position after at least 6 hours fasting. Scanning is done to include both the adrenal glands. Initially an unenhanced scan is done and the largest possible region of interest (ROI) is taken avoiding any calcifications or necrosis including more than half of cross sectional area\cite{4,5}. The mean attenuation value is calculated. 100 ml of nonionic contrast medium containing 300 mg of Iodine /ml of Iohexolis administered intravenously at the rate 3ml/sec using Medrad injector (Bayer HealthCare). Scanning is done in the immediate post contrast, 70 sec and after 15 minutes delay. All images were stored and analysed on a secondary workstation.

A total number of 35 patients with clinically suspected adrenal lesions between between 1998 and 2003 were included in the study. The main clinical symptoms of these patients included non-specific abdominal discomfort, palpable abdominal mass. A few patients had adrenal hormonal imbalance. The youngest patient was 2 months old and the oldest patient was 76 years old.

Majority of the patients were referred from the surgery department where the diagnosis was made on clinical evaluation, supplemented by biochemical laboratory parameters and ultrasound examination. All patients were clinically reassessed. Confirmation of diagnosis was accomplished with the help of histopathological evaluation whenever feasible and also by follow up scan of lesions. The size of adrenal lesion is taken as its largest diameter. Irregularity of margins was taken as presence of angulations or stranding in the borders with loss of a smooth contour. In addition, presence of calcification, homogenous or heterogeneous appearance on precontrast and post contrast scans and absence of contrast enhancement, and adjacent organ invasion were recorded. A difference of at least 20 CT numbers before and after contrast administration was taken to represent enhancement. Wherever CT attenuation values were not available, presence of contrast enhancement was judged subjectively by two radiologists.

RESULTS

Eleven cases of adrenocortical carcinoma were encountered (5 female and 6 male patients, aged 29 - 55 years). Unilateral adenomas were found in 6 patients (4 female and 2 male patients), 4 neuroblastomas in males (aged 2 months to 7 years aged 29-55 years). 6 had metastatic lesions (3 female and 3 male patients, aged 34 to 76 years). Two men (29 and 37 years) showed pheochromocytomas.

The mean age of patients with malignant tumors and benign tumors did not vary much (38 and 39 years respectively). (Table 2) Both malignant and benign masses were found to be more common in males. (Table 2) The occurrence of hypertension in patients with benign masses was more compared to malignant masses by a ratio of 3:1. While 75% of malignant masses were irregular only 20% of benign lesions showed irregularity of shape. Size comparison shows that 95% of malignant lesion was more than 5 cm in size, while majority of (67%) of benign lesions were smaller than 5 cm. This correlates with the data published by Wajchenberg et al \cite{6} In the authors study lesions less than 3 cm are considered probably benign, where as lesions more than 5 cm are probably malignant..However Berland et al in their study series reported that when size is less than 2 cm all the lesions to be benign \cite{7}.

While none of the malignant lesion showed macroscopic fat, only a single mass- a case of myelolipoma showed evidence of macroscopic fat.

### Table 1 Frequency of 35 adrenal masses

|   | Adrenocortical carcinoma | 11 |
|---|----------------------------|----|
| 2 | Adrenal metastasis         | 5  |
| 3 | Neuroblastoma              | 4  |
| 4 | Pheochromacytoma           | 3  |
| 5 | adrenal adenoma            | 6  |
| 6 | Benign cyst                | 3  |
| 7 | Adrenal myeloma            | 1  |
| 8 | Adrenal calcification      | 2  |
|   | **Total**                  | 35 |
Table 2 Mean Age and sex distribution of study population

| Factor                        | Malignant | benign |
|-------------------------------|-----------|--------|
| Mean age ( Standard deviation)| 38 (20)   | 39 (11)|
| Gender                        |           |        |
| Male                          | 12        | 10     |
| female                        | 8         | 5      |

Table 3 Comparison of adrenal mass pathology and CT study

| Size *                  | Malignant | Benign | Total |
|-------------------------|-----------|--------|-------|
| <5 cm                   | 1(5%)     | 10(67%)| 11%   |
| >5 cm                   | 19(95%)   | 35(33%)| 54%   |
| Margin #                |           |        |       |
| Regular                 | 5(25%)    | 12(80%)| 17%   |
| Irregular               | 15(75%)   | 3(20%) | 18%   |
| Contrast enhancement @  |           |        |       |
| Heterogeneous           | 20(100%)  | 4(27%) | 24%   |
| Homogeneous             | 0         | 6(40%) | 6%    |
| Absent                  | 0         | 5(33%) | 5%    |

"x²=15.1 p<.001, " p x²=10.38=<.001 "x² =21.3p<.00

Fig 1. Benign pheochromocytoma A. Large heterogeneous mass with smooth margins B. Markedly enhancing areas and poorly enhancing necrotic areas.

Fig 2. Benign adenoma of left adrenal gland in Conn’s syndrome. Poorly enhancing low density mass.

Fig 3. Carcinoma of right adrenal gland infiltrating the right lobe of liver shows heterogeneous enhancement.

The occurrence of calcification did not vary much between benign and malignant lesions. (70% and 75% respectively.

On analyzing the lesion attenuation, a heterogeneous appearance was seen in almost all cases of malignant lesion, while only 27% of benign lesion showed a heterogeneous appearance. Similarly almost all malignant lesion showed a heterogeneous enhancement pattern while 27 % of benign lesions showed heterogeneous pattern of enhancement. Majority of (40%) of benign lesions showed a homogeneous pattern and 33 % showed absent enhancement. All the lesions with absent enhancement were benign. Presence of metastasis was one criterion for excluding benign lesions.

Of the 11 cases reported as adrenal cortical carcinoma, 11 had large irregular masses ranging in size from 5 cm to 17 cm. Two cases showed evidence of tumor thrombus in the inferior vena cava. A study conducted in 105 cases of adrenalcortical carcinoma, 14% had major IVC invasion. [8] One of the cases had infiltration of right lobe of liver.
5 cases of metastasis to adrenal gland were diagnosed using CT. Of these 3 cases were metastatic from lung and two cases were from breast carcinoma. These patients were scanned for staging purposes. All these lesion were fairly large heterogeneous lesions except for one case were the lesion was less than 5 cm in size but heterogeneous. In this case a fine needle aspiration was done to reach the diagnosis. Strong clinical support with evidence of metastasis in other organs substantiated the CT impression in the remaining patients. The remaining two cases were incidentally detected on ultrasound.

Among the pediatric age group the commonest lesion detected was neuroblastoma 4 cases were reported as neuroblastoma. Of these 3 were pathologically proved to be neuroblastomas. All children were in the age group of two months to seven years. All were males. One had evidence of distant metastasis and one had intra spinal extension at the time of diagnosis. All these cases showed large heterogeneous lesions with calcification necrosis and hemorrhage. 3 cases affected the left adrenal while one affected the right. Out of the 35 lesions only three were surgically proven to be pheochromocytomas. Of these, two cases were prospectively identified on CT as these cases had clinical and laboratory parameters to support the diagnosis prior to scanning. In the remaining one patient the biochemical markers were found to be elevated following scan. All lesions were round or oval but variable densities were also seen. Pathologic specimen demonstrated necrotic tissue accounting for low-density areas. One mass had flecks of calcification.

6 cases of adrenal adenoma were diagnosed. Of these 3 patients presented with biochemical evidence of primary hyperaldosteronism. 2 cases showed less than two centimeter diameter size well defined predominantly hypodense lesions, mildly but homogeneously enhancing following contrast administration. However, in their study, Ctvrtilk et al[9] and Mayo-Smith WW et al [10] maintains that homogeneous attenuation is seen in 87% of adenomas on precontrast scans and 58 % on post contrast scans. No areas of calcification or hemorrhage were demonstrated. Both these cases were correlated with the laboratory finding of hyperaldosteronism and reported as Conn’s adenoma and histopathologically confirmed.

Three benign cysts of the adrenal gland were diagnosed on the basis of CT findings. Cysts showed sharply margined smooth round configuration and homogenous water density. One lesion that had a density calcified rim was excised and its benign nature proved.

We saw a presumptive case of adrenal myelolipoma, which is a rare tumor, composed of varying proportions of fat and myeloid elements. These lesions were well circumscribed and of a homogenous attenuation value, slightly higher than that of neutral fat. In enhanced scans, contrast the lesion in the right adrenal gland showed a mildly enhancing solid component. This lesion remained stable over a period of two years.

2 patients showed irregular dense calcification in the region of left adrenal gland with no associated soft tissue. Both these cases were asymptomatic and suspicious calcific density was detected on plain, x-rays taken for other purposes.

**DISCUSSION**

In this study, 35 patients with adrenal mass on CT were subjected to detailed evaluation. The age spectrum ranged between 2 months to 76 years. Findings at biopsy or FNAC whenever done were kept as the gold standard. In cases where pathological study was not done biochemical correlation or follow up scan was done to assess the progress.

The study results were compared to similar studies in current literature.

Of the adrenal masses the majority of lesions were adrenal cortical carcinomas (31 %). However according to the world literature the most common lesion is an adrenal adenoma[11] while the adrenal cortical carcinoma is a rare neoplasm [12]. This disparity could be because the study conducted was among patient population referred to a tertiary care center. In the case of adrenal cortical carcinoma, out
of the 11 cases, diagnosed by computed tomography histopathological correlation was obtained for 11 cases.

Distinguishing malignant from benign adrenal lesions is difficult because no single criterion is specific. Though the size of lesion, heterogeneous enhancement on contrast administration and irregular margins were more suggestive of a malignant lesion, the only definitive criteria for malignancy are the presence of metastasis or infiltration of adjacent structures. Size, contrast enhancement, and consistency are significant discriminators, on the CT image, between primary adrenal carcinomas and benign masses according to a study conducted by Adams et al. [13]

Fat containing adrenal tumors and simple adrenal cysts have characteristic CT appearance, but the majority of tumors has similar appearances and cannot be characterized beyond size and location. [14, 15]. The main limitation of adrenal CT is its lack of specificity.

But this is not an important draw back because correlation with the biochemical status is often distinctive.

The commonest mass that could be identified in the pediatric age group in this study was neuroblastomas, which accounted for 4 out of 5 cases. The single case in which the diagnosis was missed turned out to be adrenal cortical carcinoma.

The study has its own limitations. Firstly number of study population is small. However this could be due to the overall incidence of adrenal masses being less. [12,3] all the spectrum of adrenal lesions were not included in the study.

The ability of CT to demonstrate clearly normal as well as abnormal gland disease can provide valuable diagnostic information. Though the size of the case material does not warrant definitive conclusions, it is apparent that, CT can obviate the need for more invasive adrenal tests.

To conclude, size, irregular margins and heterogeneous enhancement pattern were found to be important discriminators for malignant from benign lesions.

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