

# CT Features of Adrenal Pheochromocytoma: Evaluation with Clinical and Pathological Correlation

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## ABSTRACT

**Objective:** To evaluate CT features of adrenal pheochromocytoma with clinical and histopathological correlation.

**Methods:** A retrospective study was approved by the ethics committee. Forty-four patients with proven adrenal pheochromocytoma from January 2002- December 2007 at our institution were included. Only 10 out of the 44 had available pre-operative computed tomography (CT). All 10 CT were interpreted independently by two abdominal radiologists, with correlation with clinical and histopathological analysis.

**Results:** All 10 patients had unilateral adrenal pheochromocytoma. Three were men and 7 were women. The mean age of patients was 45.1 years old. Eight out of 10 patients presented with hypertension. Four patients presented with neuroendocrine symptoms such as palpitation and diaphoresis. Other symptoms were palpable abdominal mass, headache and gastrointestinal symptoms (nausea, vomiting or abdominal pain). Pre-operative biochemistry tests for pheochromocytoma were performed in 8 patients. The tumor size varied from 2-15 cm in diameter. CT features of pheochromocytoma of this study showed 1 tumor of pure solid mass (2 cm tumor size) and 9 tumors of complex cystic masses. The range of density values at the solid part of tumors was 25-53 HU on non-contrast phase CT and the mean was about 41.4 HU. All 10 tumors showed enhancement of the solid part. Intratumoral hemorrhage and calcifications were detected. No intratumoral fatty component was detected.

**Conclusion:** CT findings of adrenal pheochromocytoma were typical heterogeneous soft tissue density mass and moderate enhancement. Tumors with cystic component and hemorrhage were common in our study. CT was useful for tumor characterization in patient with nonclassic clinical manifestation of pheochromocytoma and also for pre-operative management.

**Keywords:** Adrenal mass, pheochromocytoma

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**P**heochromocytoma is a catecholamine producing tumor that arises from the chromaffin cells of the adrenal gland. Although it is a rare tumor, it may precipitate life-threatening hypertension or cardiac arrhythmias because of excessive catecholamine secretion particularly in untreated cases.<sup>1</sup> However patients may be completely asymptomatic, with up to 10% of cases being clinically silent.<sup>1</sup> More than 90% are located within the adrenal glands. Extra-adrenal pheochromocytomas or paragangliomas develop in the paraganglionic chromaffin tissue of the sympathetic system at the neck, mediastinum, abdomen, and pelvis<sup>2</sup> which

are more likely to be malignant. In general they occur unilaterally with benign behavior, but can be bilateral and malignant in 10% of patients.<sup>1</sup> Occasionally, pheochromocytoma has been named the 10% tumor (10% risk of malignancy, 10% of the tumors are bilateral, and 10% of the tumors are extra-adrenal). Early detection may reduce the risk of metastasis.

The diagnosis of pheochromocytoma is depended on the imaging identification of an appropriately located mass with accompanying clinical and biochemical confirmation. Pheochromocytoma can have any imaging appearance.<sup>1-5</sup> It can undergo a variety of forms of pathological degeneration which affects its imaging features. This study will focus on CT features of pheochromocytoma and correlate with clinical and pathological findings.

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## MATERIALS AND METHODS

A retrospective study with approval by the Siriraj Institutional Review Board (SI 098/2008) and waiver informed consent were performed on 44 patients with pathological proven adrenal pheochromocytomas at Siriraj Hospital, from January 2002 - December 2007. Only 10 patients with available preoperative CT scan were included in this study, 3 were men and 7 were women. Their ages ranged from 15 to 72 years old (mean age = 45.1 years). Clinical symptoms and signs and biochemistry tests were recorded.

CT techniques: 5 patients were performed by Spiral CT Philip and another 5 patients CT were performed by multi-detector (16-slice or 64 slice MDCT; GE light speed VCT). All patients received an injection of non-ionic iodinated contrast medium. Our protocols included non-enhanced CT and dynamic contrast-enhanced CT (arterial phase: delayed 35 seconds after intravenous contrast agent injection, porto-venous phase (delayed 80 sec) and delayed full bladder (delayed 5 min). The images covered from the hepatic dome to the pubic symphysis to detect intra- and extra-adrenal lesion (for non-contrast CT, arterial and porto-venous phases).

The CT scan was retrospectively reviewed by two radiologists, with 8 and 4 years experience in abdominal radiology. The tumors were identified and described in these regards, tumor size, location (right, left or bilateral adrenal gland involvement), border (well- or ill-defined border), density on non-enhanced CT (homogeneous or heterogeneous density), presence of additional features (hemorrhage, necrosis, calcification or fat component), degree of enhancement on porto-venous phase (because some patients have no arterial phase). The region of interest for measurement of the degree of enhancement was performed at the solid part of the tumor on non-enhanced CT and contrast-enhanced CT on porto-venous phase (marked enhancement: if increase in density > 40 Hounsfield unit (HU), moderate enhancement: if increase in density 20-40 HU, mild enhancement: if increase in density 10-20 HU, non enhancement: if increase in density < 10 HU), and metastasis (lung, bone, liver, lymph node) and abnormal lymph node if the diameter was greater than 1 cm in the short axis. Imaging findings were correlated with operative findings, gross specimens, and pathological correlation.

## RESULTS

There were 10 patients diagnosed with adrenal pheochromocytoma with available CT scan in this study. Three were 3 men and 7 were women. The age range was from 15-72 years old. The mean age was 45.1 years old.

Eight patients presented with hypertension, 4 patients presented with neuroendocrine symptoms such as palpitation and sweating. Two of these 4 patients had a classical triad of headache, palpitation and diaphoresis. One patient presented with recurrent hypertension (known case of MEN IIa and past history of left adrenalectomy due to pheochromocytoma 8 years ago), so recurrent tumor was suspected. Five patients had non-specific symptoms such as nausea, vomiting, abdominal discomfort, palpable mass, etc. One of these 5 patients presented only abdominal pain.

Specific plasma catecholamine level and 24-hr

urinary catecholamine level or urine vanillylmandelic acid (VMA) were recorded. The biochemistry tests were performed before operation in 8 patients. An abnormal laboratory test was present in 7 of 8 patients.

Two radiologists individually reviewed the CTs of all patients. All patients had unilateral adrenal pheochromocytoma. One patient also had another extra-adrenal lesion at the pancreatic tail, but it was not pathologically proven. In 10 adrenal pheochromocytomas, 4 tumors were located at the right adrenal gland and 6 tumors were located at the left adrenal gland. The tumor size varied from 2-15 cm in diameter. The mean maximum diameter was approximately 7.6 cm. Six tumors showed marked enhancement and 4 tumors showed moderate enhancement. No tumor with a mild degree of enhancement or no enhancement was detected. The range of tumor density value of the solid part was 25-53 HU on the non-enhanced phase and the mean density was about 41.4 HU. One tumor was totally solid component and the other 9 tumors showed low density portions (density range from 15-40 HU), interpreted as cystic component. Three tumors showed a cystic component of less than 50% of lesion and 6 tumors showed more than 90%.

There were 2 contradicted points from 2 radiologists' reports, intratumoral hemorrhage and calcification. The first radiologist revealed no tumor with hemorrhage, while the second radiologist revealed 4 tumors with hemorrhage. After discussion, both agreed to report 4 cases of intratumoral hemorrhage. The first and second radiologists revealed calcification in 4 and 5 tumors, respectively. After discussion, both agreed to report 5 cases of intratumoral calcification. Most of the containing calcifications were tiny and punctate morphology. No evidence of metastasis was detected based on imaging and clinical information. The pathological findings of 10 tumors were shown on Table 1.

## DISCUSSION

CT has a sensitivity of greater than 93% and specificity of 95% in the diagnosis of this tumor. Magnetic resonance imaging (MRI) is as sensitive as CT with sensitivities ranging from 86-100%.<sup>1,2,6-9</sup> Ultrasonography has largely been replaced by CT and MRI due to being operator dependent. Nuclear medicine investigation, such as <sup>131</sup>I-MIBG specificity is as high as 99%.

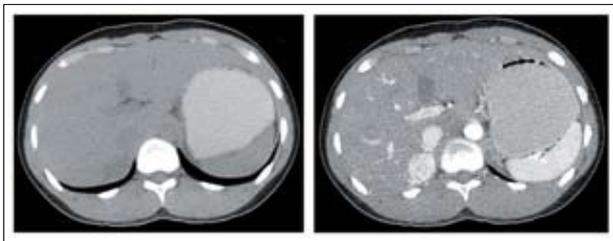
In this study, we will focus on the CT features of adrenal pheochromocytoma. Typically, tumor size is less

**TABLE 1.** Pathological findings of 10 adrenal pheochromocytoma.

Findings of pathology	Number of tumor
Location of adrenal mass	Unilateral (Right = 4 tumors, Left = 6 tumors)
Solid tumor	2
Mixed solid and cystic tumor	8
Hemorrhage	10
Hemorrhage in cystic part	7
Hemorrhage in solid part	3
Loose myxoid tissue	1
Calcification	none
Fat	none

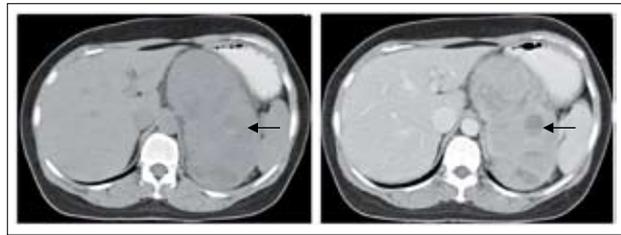
than 3 cm, with well-defined border and enhancement, and especially avid enhancement on the arterial phase CT.<sup>10</sup> All 10 adrenal pheochromocytomas in our study showed a well-defined border. One tumor was less than 3 cm in size with total solid component (Fig 1), and 9 tumors were greater than 3 cm in tumor size (2 tumors: about 3-5 cm and 7 tumors: more than 5 cm). Tumors that were greater than 3 cm in size showed a complex mass with a low density portion or cystic component at CT images (Fig 2) which is concordant to a previous study done by Blake M, et al., who reported that pheochromocytoma had CT features of homogeneous or heterogeneous density mass, solid or cystic complex masses, average attenuation higher than 10 HU, rarely contain intracellular fat to have an attenuation of less than 10 HU, some hemorrhage, some calcification and avid enhancement in the solid portion.<sup>1</sup>

Three in 10 tumors (30%) showed a marked degree of enhancement and 7 in 10 tumors (70%) showed a moderate degree of enhancement on the porto-venous phase. Two tumors showed avid enhancement on the arterial phase (available arterial phase in 8 CT studies) (Fig 1 and 3). Avid enhancement on the arterial phase CT is a typical finding for pheochromocytoma. The arterial phase CT study is helpful for tumor characterization and is useful for differential diagnosis or to exclude other tumors. Moreover, it is prudent to detect extra-adrenal lesions or multiple endocrine tumors if the tumor appears to have avid enhancement. One patient with clinical hypertension and non-specific GI symptoms underwent CT of the upper abdomen. CT showed a right adrenal mass with central low density and avid enhancement that is typical for pheochromocytoma. The radiologist also detected another avid enhancing mass at the pancreatic tail and suspected multiple endocrine neoplasms. The patient underwent further investigations and was finally diagnosed Von-Hippel-Lindau disease (surgically proven adrenal pheochromocytoma, pancreatic cystadenomas and cerebellum hemangioblastoma) (Fig 3). <sup>131</sup>I-MIBG scintigraphy was performed in this patient and revealed focal uptake lesion at the left upper abdomen, which corresponded with a hypervascular tumor at the pancreatic tail detected on CT. Six in 10 (60%) of CT examinations were performed without pheochromocytoma protocol due to unsuspected clinical signs of pheochromocytoma and 2 CT studies were CT whole abdomen protocol with no arterial phase. However, we noted that non-enhanced CT and porto-venous phase CT are still beneficial for tumor characterization



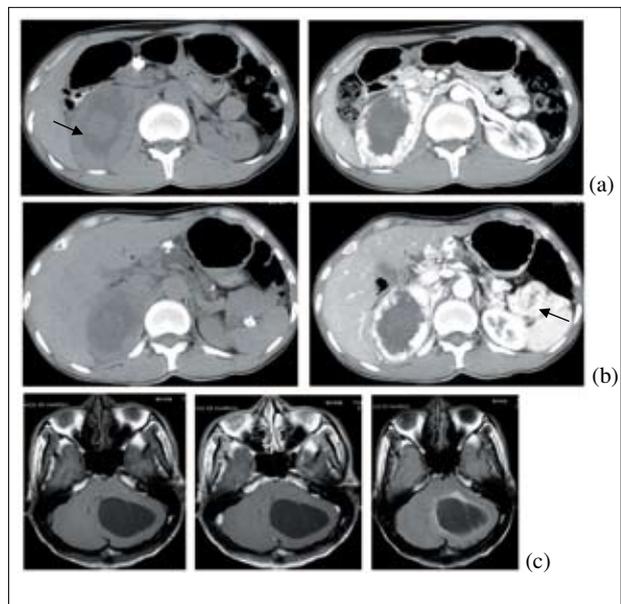
**Fig 1.** A 15-year-old boy had abdominal pain and hypertension.

Pre and post contrast enhanced CT images show heterogeneous markedly enhancing soft tissue mass at right adrenal gland (44 and 104 HU on pre and arterial phase contrast enhanced CT, respectively), 2.3 x 2.1 cm without cystic or necrotic component.



**Fig 2.** A 51-year-old female had palpable mass, abdominal pain and hypertension.

Pre and post contrast enhanced CT images show heterogeneous enhancing mass at left adrenal gland with cystic hemorrhage. CT demonstrates fluid-fluid level (arrow). Note - cystic portion is less than 50% of the mass.



**Fig 3.** A 55-year-old male had abdominal discomfort.

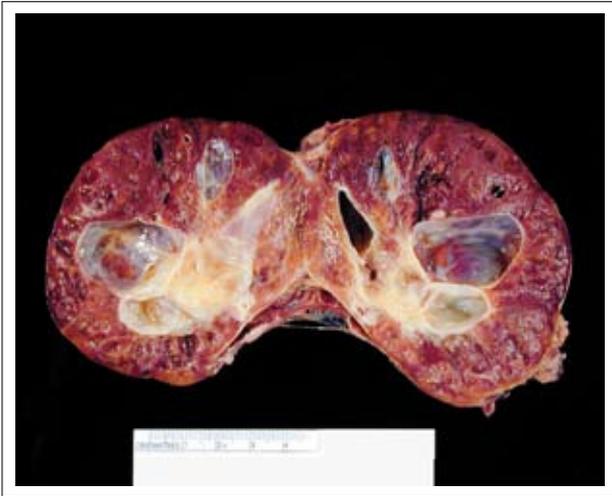
(a) CT images show avid enhancing mass at right adrenal gland. Tumor shows central low density with hyperdensity content (arrow). CT interpretation as cystic part with intratumor hemorrhage. Pathological feature reveals solid mass with loose connective tissue.

(b) CT images shows another hypervascular tumor at pancreatic tail (arrow). <sup>131</sup>I MIBG scintigraphy demonstrates neuroendocrine tumor.

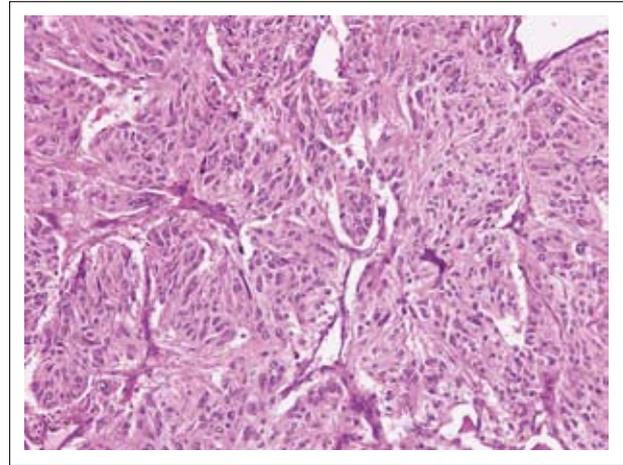
(c) MRI on T1W, T2 FLAIR and T1W post gadolinium images show a large well-defined hypointense mass with slightly rim enhancement at cerebellum is observed. Hemangioblastoma is diagnosis by pathological proven. Von-Hippel Lindau disease is definite diagnosis.

and for differential diagnosis. CT interpretation may guide patient management and also for patients who were not clinically suspected for pheochromocytoma before they underwent CT examination.

For the correlation between CT findings and clinical manifestation of adrenal pheochromocytoma, 2 patients had classical clinical manifestation, 1 patient had typical CT findings of pheochromocytoma: soft tissue mass with marked enhancement. Another patient with classical clinical manifestation had atypical CT findings of pheochromocytoma (cystic component greater than 90%) and moderate enhancement. Six patients who were clinically unsuspected for pheochromocytoma,



**Fig 4.** Gross pathology shows sharply circumscribed encapsulated mass with dark brown cut surface. Cystic change is noted.



**Fig 5.** Microscopic pathology shows polygonal tumor cells with moderate amount of granular, eosinophilic to amphophilic cytoplasm. Some tumor cells have lavender tint cytoplasm. The tumor cells are arranged in alveolar or nesting pattern (Zellballen pattern) and trabecular pattern.

had CT scans of their abdomens obtained with other indication. CT showed incidental adrenal pheochromocytoma with typical finding of hypervascular tumor in 1 patient and atypical CT findings of more than 90% cystic portion in 5 patients.

Some pheochromocytomas may demonstrate very high attenuation due to hemorrhage.<sup>1</sup> Non-enhanced CT examination is useful to demonstrate fluid-fluid level and hyperdensity material in the cystic component that probably indicates intratumoral hemorrhagic content. Awareness of intratumoral hemorrhage is recommended because it is difficult to identify in some cases. In this study, there was a different interpretation of intratumoral hemorrhage between 2 radiologists. The first radiologist revealed no tumor with hemorrhage, while the second radiologist revealed 4 tumors with hemorrhage. After consensus, CT showed fluid-fluid level in cystic part in 1 tumor and hyperdensity content in cystic part in 3 tumors (density about 35-40 HU), so the two radiologists made agreement of 4 intratumoral hemorrhage (Fig 2). Pathological correlation showed 10 tumors with hemorrhage. CT interpretation of intratumoral hemorrhage was correct in 4 tumors.

One solid tumor in our study, CT showed no evidence of hemorrhage (average density 33 HU on non-enhanced CT), but pathological finding revealed areas of hemorrhage. CT may have limitation to detect liquefied hemorrhage or small hemorrhage. CT interpretation with careful tumor characterization and adjusted window level on both non-enhanced CT and enhanced CT is helpful to correct this mistake.

In our series, there were 9 (90%) adrenal pheochromocytomas that appear complex masses with cystic component. Lee TH, et al., reported that total or subtotal cystic degeneration of pheochromocytoma is not common.<sup>10</sup> In this study, there were 6 tumors (60%) that showed more than 90% of cystic component on CT study. Of these 6 tumors, 1 tumor was 3.5 cm and 5 tumors are larger than 5 cm. This pattern is probably related with large tumor size that outgrows blood supply causing cystic degeneration or hemorrhage. We also noted that the low density portion on non-enhanced CT

which was interpreted as cystic portion in 9 tumors. Pathological features were old hemorrhage or cystic degeneration or necrosis in 8 tumors and loose connective tissue in 1 tumor. (Fig 4 and 5)

In our experience, differential diagnoses of the large complex mass with cystic portion of the adrenal gland are pheochromocytoma and adrenocortical carcinoma. If the tumor has these features including ill-defined border, local invasion and no avid enhancement on arterial phase, adrenocortical carcinoma is preferred. In this condition, a biochemistry test is helpful to guide diagnosis and for pre-operative planning. In this study, 1 patient with abdominal pain and CT showed subtotal cystic adrenal lesion, and 9.7 cm tumor size with about 1cm wall thickness. Pre-operative diagnosis was complicated by adrenal cyst such as pseudocyst or infected cyst. We learned that pheochromocytoma should be included in the differential diagnosis for complicated or indetermined adrenal cystic lesion.<sup>10</sup> An additional biochemistry test for catecholamine-screening should be performed to rule out pheochromocytoma.

CT detected tiny or punctate calcification in 4 tumors (40%). Histopathological correlation revealed no calcification. The reason is related with the technique and plane of pathological section - the tiny calcifications were not included in the slice for pathological interpretation.

At present, differentiation between benign and malignant adrenal pheochromocytoma was depended on metastatic presentation. The limitations of our study were small sample size due to rare disease and non available CT imaging.

## CONCLUSION

CT findings of adrenal pheochromocytoma are typical heterogeneous soft tissue density mass with moderate enhancement. Tumors with cystic component and hemorrhage were common in our study. CT study was also useful for tumor characterization in patients with nonclassical clinical manifestation of pheochromocytoma and also for pre-operative management.

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