

Functional Adrenocortical Oncocytoma: A Case Report of Rare Neoplasm of Uncertain Malignant Potential

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Adrenocortical oncocytoma is a rare adrenal neoplasm with only 25 cases having been reported in the English medical literature, of which only seven were functional tumors. Since these adrenal tumors are usually nonfunctional, they are mostly incidentally detected, and most of them are benign. Herein, we report on a rare case of a functional adrenocortical oncocytoma of an uncertain malignant potential and this tumor was located in the left adrenal gland in a 59-year-old woman who presented with hypertension. The tumor size was large with foci of necrosis in the cut surface and it exclusively had oncocytic histologic features.

Key Words: Adrenal cortical neoplasm; Adenoma; Oxyphillic; Hypertension

Oncocytes are large epithelial cells and on electron microscopy they are noted to have abundant eosinophilic granular cytoplasm packed with numerous swollen mitochondria and inconspicuous numbers of other organelles and inclusions.¹ The term "oncocyte" was used for the first time by Hamperl, and the term refers to large, highly eosinophilic, granular cells associated with Hurthle cell tumor (a tumor of the thyroid gland).² Oncocytomas can arise in several anatomic organs, including the kidney, thyroid, salivary glands, parathyroid, lung, pituitary gland and ovaries.³ To date, only 25 cases and 4 cases of the adrenal gland have been reported in the English literature and domestic Korean literature, respectively.^{4,5} Most of the reported cases were benign and nonfunctional, except for seven cases of functional adrenal oncocytomas.⁴

Herein, we report on a rare case of functional adrenocortical oncocytoma of the adrenal gland with an uncertain malignant potential in a patient with hypertension.

CASE REPORT

A 59-year-old woman was admitted to our hospital for inju-

ries caused by falling down. She had experienced intra-cerebral hemorrhage and hypertension for the past three years and she was receiving regular treatment for hypertension. She had no history of smoking, hematuria, headaches or palpitation. On a physical examination, she had severe abdominal pain, but no palpable abdominal mass was found. Any features that suggested Cushing syndrome, such as petechiae or abdominal striae, were not noted. Her pre-operation blood pressure was 160/88 mmHg. The laboratory parameters were almost within the normal ranges. The serum cortisol and adrenocorticotrophic hormone (ACTH) were slightly increased to 25.43 µg/dL (normal, 4.3 to 22.4 µg/dL) and 70.09 pg/mL (normal, 5 to 60 pg/mL), respectively. Computed tomography (CT) showed splenic rupture with hemoperitoneum in the perisplenic and perihepatic spaces, the right paracolic gutter and the pelvic cavity. There was an incidentally found 16.5×14.3 cm mass with hemorrhage in the left retroperitoneal area (Fig. 1A, B). There were visible traumatic injuries to the liver, pancreas and both kidneys. The CT suggested hemorrhage with a left adrenal hypervascular tumor due to traumatic injury. A left adrenal adenoma or pheochromocytoma was suspected due to the origin of the tumor. An open surgical left adrenalectomy and a splenectomy were per-

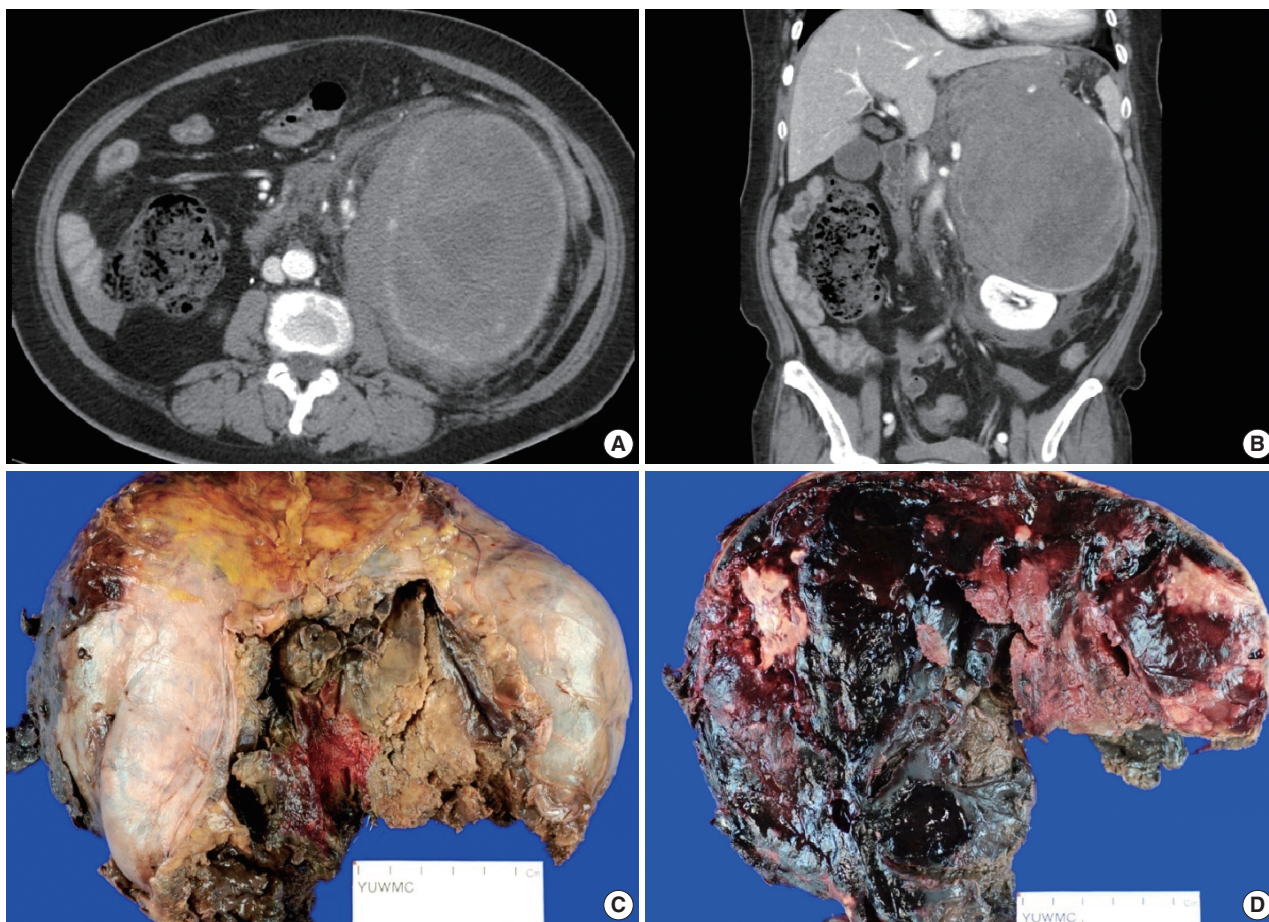


Fig. 1. (A, B) Abdominopelvic computed tomography shows a splenic rupture with hemoperitoneum in the perisplenic and perihepatic spaces, the right paracolic gutter and the pelvic cavity and there is a 16.5×14.3 cm mass in the left retroperitoneal area with hemorrhage. (C) The gross findings show that the external surface of the tumor is diffusely irregular and partly ruptured due to the traumatic injury. (D) The cut surface of the mass shows a diffusely hemorrhagic appearance with multifocal areas of necrosis and a golden-yellow colored peripheral rim.

formed. The operation findings showed a large mass of a left adrenal gland origin and splenic rupture.

During the pathologic examination, gross inspection showed the tumor to be diffusely irregular and partly ruptured due to the traumatic injury (Fig. 1C). The tumor was $21 \times 13 \times 7$ cm in size and it weighed 1.5 kg. The cut surface of the mass showed a diffusely hemorrhagic appearance with multifocal necrosis and a golden-yellow colored peripheral rim (Fig. 1D).

The microscopic findings of multiple tissue sections (eleven sections from all area of the tumor) showed that the tumor was surrounded by a thin fibrous pseudocapsule and a mildly atrophic adrenal cortex. The neoplasm was composed exclusively of polygonal oncocytes with abundant eosinophilic, granular cytoplasm (Fig. 2A). Occasional nuclear atypia with enlarged nuclei and prominent nucleoli were found (Fig. 2B). Mitosis and capsular or vascular invasion were absent, but there were multifocal necrotic areas (Fig. 2C). Immunohistochemically, the tumor

cells were positive for neuron specific enolase (Fig. 2D) and they were negative for S-100 protein, synaptophysin, chromogranin A, inhibin, ACTH, and neurofilament. Electron microscope examination revealed variable sized clusters of large polygonal cells separated by a scant stroma composed of compressed capillaries, extravasated red blood cells, occasional lymphocytes and collagen fibrils. The cytoplasm of all of the neoplastic cells was packed with elongated and round mitochondria and the nuclei varied in size and they contained multiple clumps of chromatin and one or two small nucleoli (Fig. 3).

On the basis of these findings, we made a final diagnosis of a functional adrenocortical oncocytoma of uncertain malignant potential according to the Bisceglia diagnostic system.⁶ The patient was discharged a few days after surgery. After four months follow up, the patient was asymptomatic with a normal blood pressure (132/77 mmHg) without having to use any anti-hypertensive medication and she had normal biochemical findings.

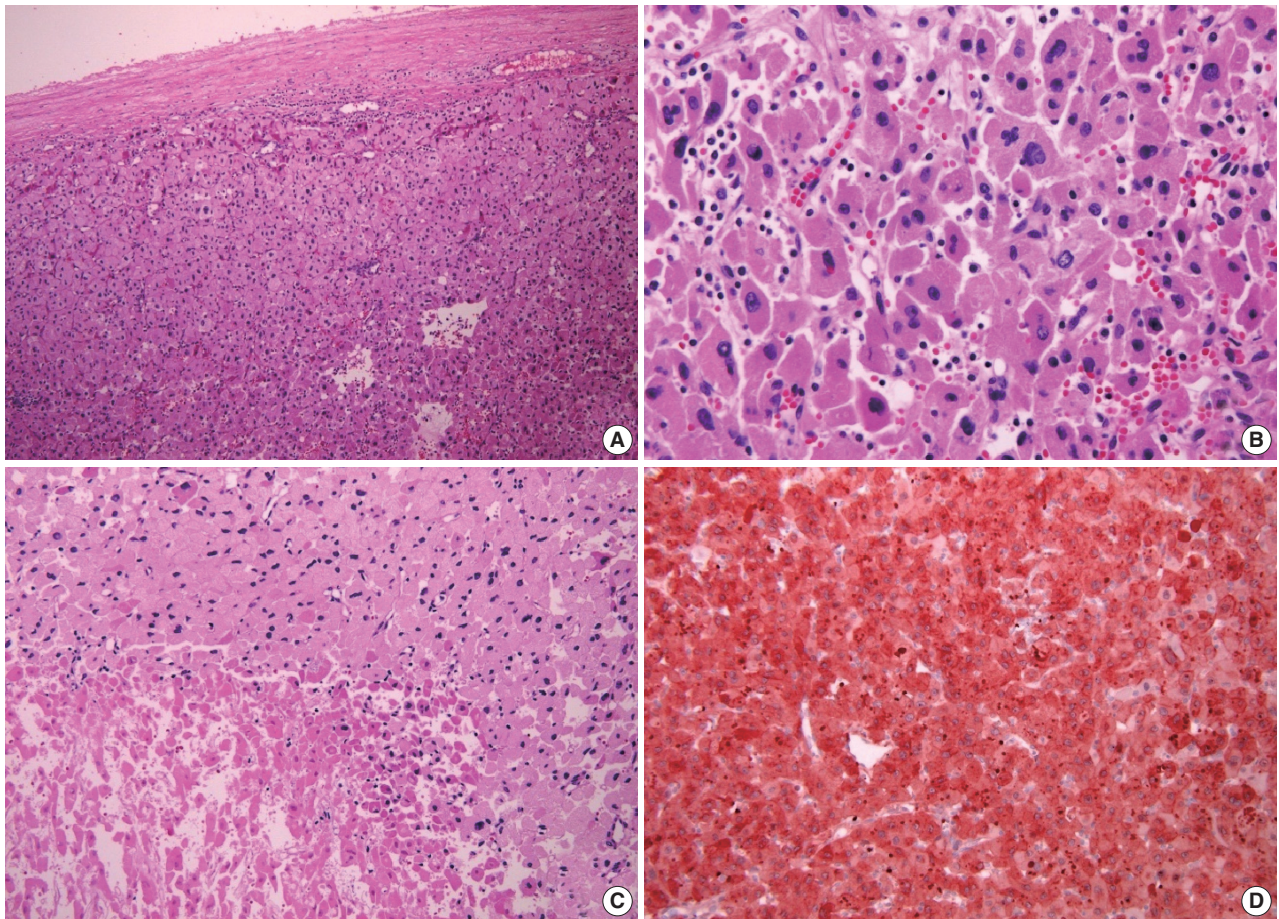


Fig. 2. (A) Microscopically, the tumor shows polygonal oncocytes with abundant eosinophilic and granular cytoplasm without capsular invasion. (B) Occasional nuclear atypia with enlarged nuclei and prominent nucleoli are found. (C) The tumor shows multifocal necrotic areas. (D) Immunohistochemically, the tumor cells are positive for neuron specific enolase.

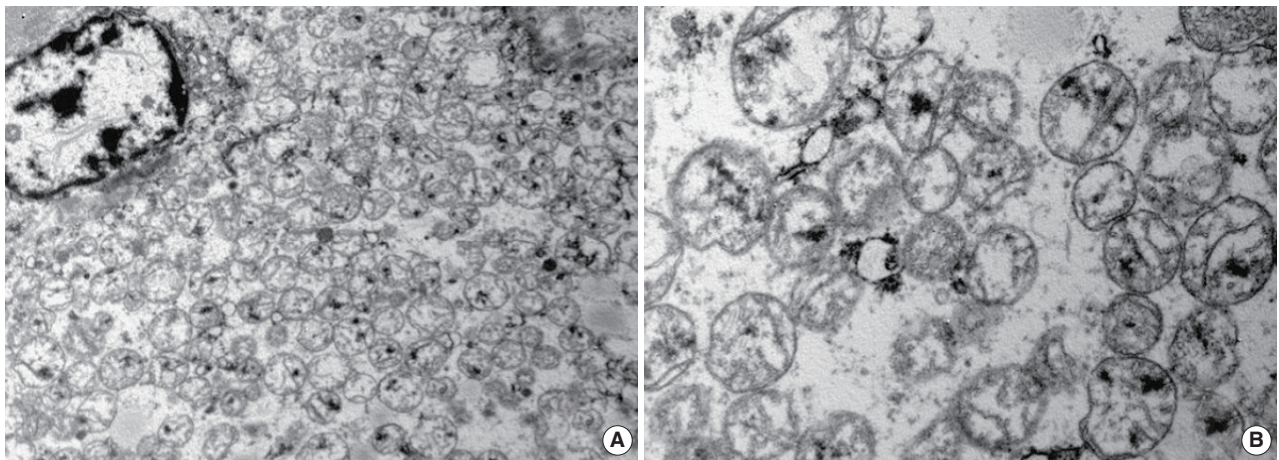


Fig. 3. (A) Ultrastructurally, the tumor cells show prominent nucleoli, perinuclear rough endoplasmic reticulum, numerous cytoplasmic mitochondria, and lipid droplets ($\times 8,000$). (B) The cytoplasm of tumor contains packed mitochondria with tubulovesicular cristae ($\times 20,000$).

Table 1. Functional adrenocortical oncocytoma cases

Case	Author	Age (yr)	Gender	Side	Size (cm)	Weight (g)	Diagnosis
1	Xiao <i>et al.</i> ⁸	53	Female	Right	2.2	8	Benign
2	Golkowski <i>et al.</i> ⁹	51	Male	Right	15.0×16.0×17.2	-	Malignant
3	Tahar <i>et al.</i> ¹⁰	6	Female	Right	3.5	30	Benign
4	Akatsu <i>et al.</i> ¹¹	38	Female	Right	4.5×3.5×2.5	-	Benign
5	Geramizadeh <i>et al.</i> ⁴	43	Female	Left	9.0	195	Benign
6	Sharma <i>et al.</i> ²	47	Female	Left	12.0×8.0×8.0	230	Benign
7	Oh <i>et al.</i> ⁵	49	Male	Left	10.0×7.5×4.7	260	Benign
8	Present case	59	Female	Left	21.0×13.0×7.0	1,500	Uncertain malignant potential

DISCUSSION

Oncocytic tumors arising from adrenal glands are very rare and most of them are found incidentally during the evaluation for unrelated problems.⁷ They are mostly non-functioning and benign. Only seven cases of functional adrenal oncocytomas have been reported in the English literature, with one additional case in the Korean literature (Table 1).^{2,4,5,8-11} It is often challenging to differentiate benign from malignant adrenal cortical tumors. The most widely used histologic criteria for the diagnostic categorization of adrenocortical tumors was proposed by Bisceglia, which were modified from Weiss's system for non-oncocytic adrenocortical tumors. The major criteria include a high mitotic rate (>5 mitosis/50 high power fields), atypical mitosis and venous invasion, while the minor criteria include increased size and weight (>10 cm and >200 g), necrosis, capsular invasion and sinusoidal invasion. The presence of one major criterion indicates malignancy, one to four minor criteria indicate an uncertain malignant potential (borderline) and the absence of all major and minor criteria indicates benignancy.^{6,10} A definite diagnosis of adrenocortical oncocytoma was made for our case by the electron-microscopic findings of numerous mitochondria in the tumor cell cytoplasm.

The cytoarchitectural features of adrenocortical oncocytomas may closely resemble the following tumors: 1) pheochromocytoma, which was excluded in this case by the negative chromogranin A immunoreactivity and the absence of neurosecretory granules on the electron microscopy, 2) adrenocortical adenoma and adrenocortical carcinoma, where the tumor cell's cytoplasm is not packed with mitochondria, and 3) renal oncocytoma and metastatic oncocytic carcinoma, both of which were excluded as no primary site was found in the right kidney or in other organs on the clinical or radiological examination.

For functioning adrenal cortical tumors, any evidence of hormone hypersecretion is an indication for surgical intervention. Most investigators also advocate removal of any adrenal tumor

greater than 6 cm in size.⁸

In this case, the patient had hypertension of an unknown origin prior to surgery. Among the reported cases of functional adrenocortical oncocytomas, hypertension was present in only one previous case² and according to the diagnostic criteria, our case showed two minor criteria (increased size and weight of 21 cm and 1.5 kg, respectively, and necrosis) and it should be classified as having an uncertain malignant potential (borderline). After four months of follow up, we found that the patient was asymptomatic and her blood pressure was 132/77 mmHg without having to use anti-hypertensive medication.

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