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Juxtaglomerular Cell Tumor of the Kidney : A Case Report

We report a case of renin-secreting juxtaglomerular cell tumor which developed in a hypertensive 47-yr-old Korean man. Presumptive clinical diagnosis was made before surgery based on the high level of plasma renin and the radiologic evidence of renal mass. Grossly, a round, bulging, well-encapsulated mass of 3×3 cm was located in the mid-portion of the right kidney. On microscopic examination, the tumor was composed of ovoid to polyhedral cells with bland nuclei, indistinct nucleoli and light eosinophilic cytoplasm. The immunostaining for renin showed strong positivity in the cytoplasm of tumor cells. The characteristic rhomboid shaped renin protogranules were observed in ultrastructural analysis.

Key Words: *Juxtaglomerular Apparatus; Renin; Hypertension*

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INTRODUCTION

Juxtaglomerular cell tumor of the kidney was first described in 1967 by Robertson et al. (1), and since then about 40 cases have been reported (2, 3). All patients presented high blood pressure usually associated with hypokalemia and hyperaldosteronism secondary to renin hyperproduction by the tumor (4-6) with sheets of tumor cells with numerous blood vessels. The typical histologic pattern often simulates hemangiopericytoma (7). Renin can be detected by immunohistochemistry and ultrastructurally characteristic rhomboid crystals are seen (8).

We report a juxtaglomerular cell tumor of the kidney as an unusual cause of hypertension in a man. To our knowledge, this is the first case report in Korean literature.

CASE REPORT

A 47-yr-old Korean man was treated for high blood pressure for 2 yr (range; 150 to 200/110 mmHg). He developed generalized edema, for which he was admitted to our hospital. On admission, hypokalemia was noted (potassium, 2.7 mEq/L; normal, 3.5 to 5.5 mEq/L). Urinalysis and other chemical and hematologic profiles showed no abnormality other than elevated plasma renin (7.33 ng/mL/hr; normal, 0.68 to 1.36 ng/mL/hr) and aldosterone levels (375.55 pg/mL; normal, 10 to 160 pg/mL). Selective blood sampling from renal veins to determine the plasma renin activity did not show any sign of lateralized renin production from his right kidney. Radiologic investigation with CT scan revealed a well-defined mass of 3×3 cm in the mid-portion of the right kidney (Fig. 1). Angiography revealed no obstruction or stenosis in the renal arteries.

Based on the clinical diagnosis of juxtaglomerular cell tumor in the right kidney, a right nephrectomy was performed. Grossly, a round, bulging, well-encapsulated mass of 3×3 cm was noted in the mid portion of the right kidney without extension beyond the capsule. This tumor was confined to the renal parenchyma. On section, the cut surface of this tumor was pale yellow to pale brown and solid.

Microscopic examination revealed a well-circumscribed tumor composed of large cells arranged in sheets and surrounded by fibrous septa. The cells were densely arranged and polygonal in shape, with well-defined cell membrane,

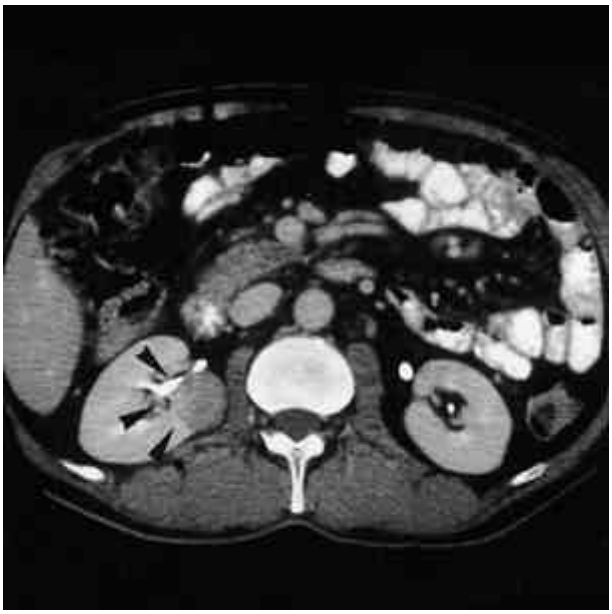

Fig. 1. Abdominal CT scan shows well- defined mass of 3×3 cm (arrow heads) in the mid portion of right kidney.

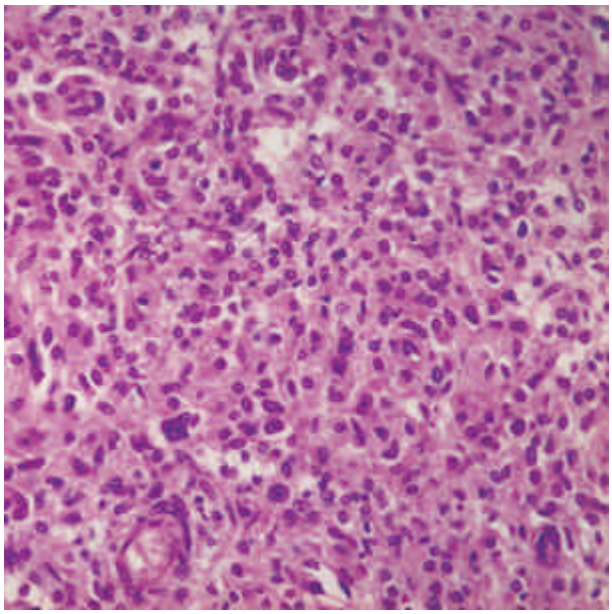

Fig. 2. The densely arranged polygonal tumor cells with abundant eosinophilic cytoplasm and uniform nuclei are noted in microscopic examination (H&E, ×100).

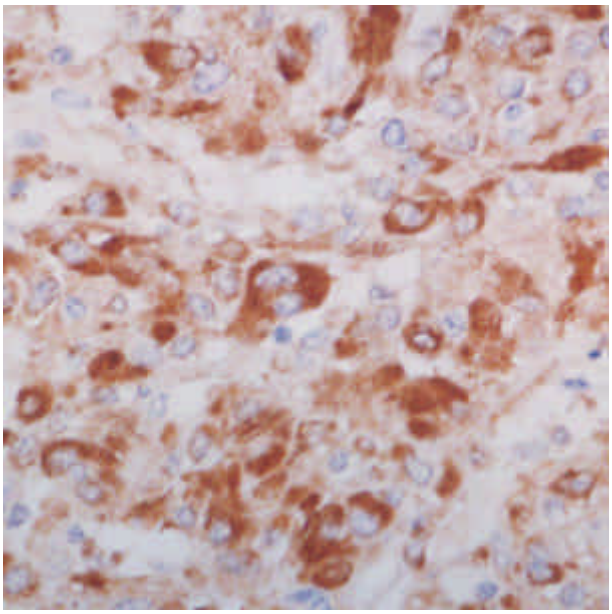

Fig. 3. The tumor cells show immunoreactive renin granules in the cytoplasm (×200).

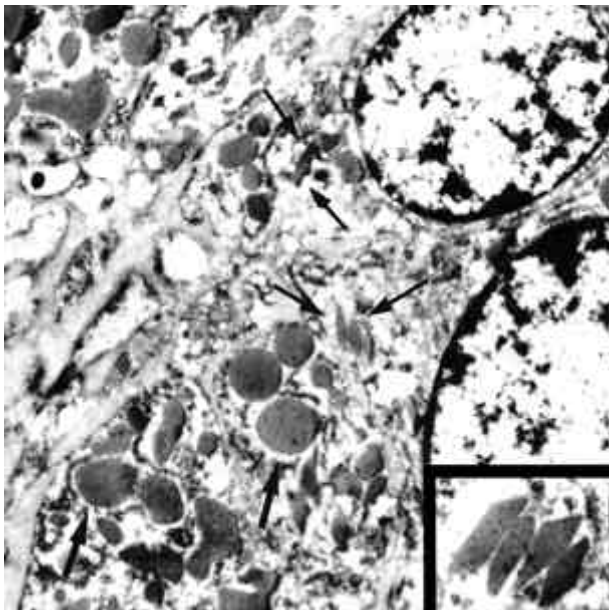

Fig. 4. Electron micrography of tumor cell shows electron dense bodies of different shapes (thick arrow) and typical rhomboidal renin secretory granules (thin arrow) (×8,000). Inset shows higher magnification of several membrane-limited rhomboid renin protogranules (×20,000).

pale eosinophilic or vacuolated cytoplasm, and uniformly round vesicular nucleus of fine chromatin pattern (Fig. 2). The periodic acid-Shiff (PAS) and methenamine silver stains showed positive granular cytoplasmic staining. Immunostaining for renin showed strong positivity in the cytoplasm of tumor cells (Fig. 3). Electron microscopic examination revealed that the cytoplasm of the tumor cells contained abundandant rough endoplasmic reticulum, Golgi apparatus, and varying numbers of large rhomboid or round, membrane-delimited renin granules (Fig. 4).

After surgery, the level of plasma renin activity in the patient decreased to normal range and his blood pressure was well controlled.

DISCUSSION

The renal juxtaglomerular apparatus located at the hilus of the glomerulus contains the granular modified arteriolar smooth muscle "juxtaglomerular cell" which produces renin enzyme. The renin functions in the regulation of blood pressure and volume and tissue hydration (9).

Juxtaglomerular cell tumor is a rare benign renal cortical neoplasm of patients primarily in the second and third decade life (6, 10); however, juxtaglomerular cell tumors have been reported in individuals as young as 6 yr (11) and as old as 69 yr (8). There was a female predominance (approximately 2:1). In all reported cases, tumors have been unilateral and solitary. The majority of juxtaglomerular cell tumors were 2 cm to 3 cm in diameters, but tumors of less than 1 cm or more than 6 cm in diameter have been reported (11, 12).

Clinical symptoms include marked hypertension, headache, nocturia, occasionally blurred vision, nausea and hypertensive retinopathy (11, 13, 14).

Laboratory studies reveal increased plasma renin activity, hyperaldosteronemia, and hypokalemia (7, 11, 12, 13). In patients with elevated plasma renin level, the combination of hypovascular solid renal mass with absence of renal artery lesion is highly suggestive of juxtaglomerular cell tumor (14).

Primary hyperreninism is a clinical syndrome characterized by hypertension, hyperreninemia and secondary aldosteronism produced by the renin secreting tumor (15). It is known that several tumors besides juxtaglomerular cell tumors can produce renin (renin-producing tumor, or reninomas). These include renal tumors (e.g., Wilms' tumor, the clear-cell type of renal cell carcinoma, oncocytoma and mesoblastic nephroma) and extrarenal tumors (e.g., granulosa cell tumor, lung cancer and pancreatic cancer) (15-19). For accurate diagnosis of juxtaglomerular cell tumors such neoplasms must be excluded because the demonstration of renin alone does not absolutely define juxtaglomerular cell tumors. Renal angiography may be helpful in defining a mass lesion, but since juxtaglomerular cell tumors are usually small and peripheral in location, they may not always be diagnosed by this method (20). All patients are cured by either a partial or total nephrectomy (7).

Light microscopy shows cords or clusters of round or less commonly, spindle shaped cells with benign-appearing nuclei and eosinophilic cytoplasms that are separated by thin-walled blood vessels and variable numbers of mast cells (7, 11-13). Cytoplasmic granules are visualized by PAS and Bowie method (toluidine-azure II stain), which is specific for renin granules (20).

The diagnosis of juxtaglomerular cell tumors is usually confirmed by either positive immunostaining of renin (5, 7) or electron microscopic identification of renin granules (4-7).

The most characteristic finding from electron microscopic examination consists of two types of granules: rhomboid crystalline protogranules and amorphous homogeneous, round, electron-dense mature granules (5). These ultrastructural findings are considered to be of great diagnostic value (7, 11, 12). The protogranules can be easily recognized by their rhomboid or polygonal shape and are often associated with the Golgi complex. Other features such as well developed endoplasmic reticulum and discontinuous basement membrane can be noted in electron microscopic examination (8).

The pathogenesis of juxtaglomerular cell tumors remains controversial. Furusato et al. (21) suggested that juxtaglomerular cell tumors are biphagic tumors, while More et al. (11) and Schambelan et al. (14) refined to the their hamartomatous nature.

Camilleri et al. (8) suggested that the juxtaglomerular cell tumors arise from smooth-muscle cells, judging from the presence of transitional cells containing both secretory granules and myofilaments with attachment bodies. Such findings are in agreement with the fact that juxtaglomerular cells appear to be modified vascular smooth-muscle cells (22).

All reported cases were benign with no instances of recurrence or metastasis. In nearly all cases, surgical removal of the juxtaglomerular cell tumor has resulted in normal blood pressure, but some patients have remained hypertensive following nephrectomy (7).

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