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Ipsilateral Synchronous Renal Cell Carcinoma and Transitional Cell Carcinoma

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The simultaneous occurrence of renal cell carcinoma(RCC) and transitional cell carcinoma(TCC) in the same kidney is unusual. We report a 53-year-old man with ipsilateral synchronous renal adenocarcinoma and renal pelvic transitional cell carcinoma with severe hypercalcemia and a huge staghorn calculus in the opposite kidney. The patient was admitted to the hospital because of left flank pain and intermittent fever which he had had for 2 months. Computerized tomography revealed a huge stone in the right kidney and a mass in the upper pole with an irregular calcified pelvis in the left enlarged kidney. Left radical nephrectomy was done. A section of the specimen revealed a renal cell carcinoma located at the upper pole and a papillary transitional cell carcinoma arising from the renal pelvis. This is a rare case of combined renal malignancies.

Key Words : *Renal cell carcinoma, Transitional cell carcinoma, Hypercalcemia, Renal stone.*

INTRODUCTION

The presence of synchronous renal carcinomas of renal parenchymal and urothelial origin is rare (Balch, 1935 ; Gillis et al., 1971 ; Voneschenbach et al., 1977 ; Magaret et al., 1979 ; Yokohama et al., 1981). This pattern of tumor occurrence has not yet been reported in Korea. Renal cell carcinoma is a well-known tumor, accounting for approximately 3 percent of adult malignancy and approximately 85 percent of all primary renal neoplasms ; the tumors are usually adenocarcinomas. The second most common primary neoplasm is of the renal pelvis or ureter, accounting for 7 to 8 percent. The majority of these are transitional cell carcinomas (Borring et al., 1991). Herein we report a very rare case of ipsilateral synchronous renal cell carcinoma and renal pelvic transitional cell carcinoma with severe hypercalcemia and a huge staghorn calculus in the contralateral kidney.

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CASE REPORT

A 53-year-old man was admitted to our hospital in 1993 because of left flank pain and intermittent fever which he had suffered for 2 months. He also complained of fatigue, malaise, anorexia, and weight loss. There was no history of gross hematuria, dysuria, frequency, or other urological symptoms. Also there was no history of pulmonary tuberculosis, hypertension, and diabetes mellitus. He did have a history of smoking 1 pack of cigarettes a day for thirty years. Upon admission, his blood pressure was 90/60 mmHg, body temperature 38.4℃, pulse rate 88/min, respiratory rate 20/min. On examination the patient was lethargic but arousable. Physical examination revealed an ill-defined, palpable

mass in the abdomen and tenderness on the left costovertebral angle. Neurologic examination was negative. Laboratory tests showed leukocyte count of 35,400/mm^3, with 89% of neutrophils ; hemoglobin 14.1 gm/dl ; hematocrit 39.9% ; serum calcium 13.6 mg/dl ; phospohrus 2.6mg/dl ; alkaline phosphatase 348IU/L ; BUN 19.4 mg/dl ; creatinine 1.4mg/dl ; uric acid 7.5mg/dl ; sodium 138mmol/L ; and potassium 3.1mmol/L. Urinalysis showed many red and white cells, and 1+ albumin. A 24-hour urine collection for calcium was 598mg. Cytologic study of the urine disclosed benign transitional cells. The culture studies of blood and urine were negative. The serum $1,25(OH)_2D$ was 6.0 pg/ml and 25-OHD 6.0ng/ml. The parathyroid hormone and thyroid hormones were normal. An X-ray film of KUB demonstrated an impacted staghorn calculus in the right renal pelvis and multiple calcified densities in the lower pole of the left kidney (Fig. 1). Excretory urography revealed a diffusely enlarged contour of both kidneys on the nephrogram with filling defects in the left renal pelvis and a faint opacification of the bladder in the delayed film (3 hour). A computed tomographic (CT) scan of the abdomen showed an in-

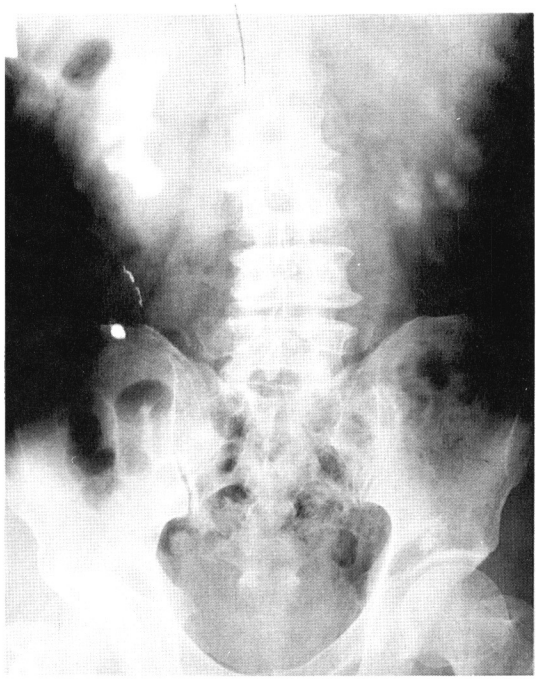

Fig. 1. KUB shows a staghorn calculus in the right kidney and multiple calcifications in the left kidney.

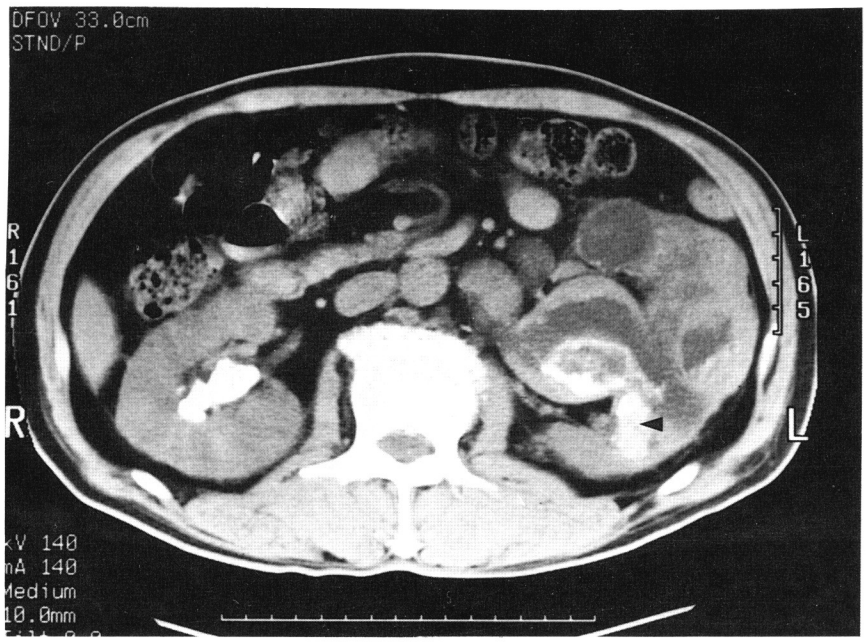

Fig. 2. Abdominal CT shows a mass in the upper pole of the left kidney. It also shows hydronephrotic changes and parenchymal calcifications(arrowhead) in the left kidney.

homogenous mass density in the suprarenal area and a suspicious mass density in the upper pole of the left kidney. It also showed a hydronephrotic change with parenchymal calcifications of the left kidney (Fig. 2). A bone scan disclosed no abnormal uptake on the skeletal system. Hydration therapy with intravenous furosemide and calcitonin therapy were given, but hypercalcemia did not improved. In order to confirm the diagnosis a left radical nephrectomy was tried but a tumor mass of suprarenal extension was not removed due to paraaortic invasion. Subsequently serum calcium decreased after surgery. Pathologically, the gross specimen consisted of a left kidney, measuring 20 X13X6 cm, with an attached ureter. On the transected specimen, the pelvis was dilated and revealed a friable papillary tumor growth and multiple small calcified stones. The renal parenchyma of the upper pole showed a yellowish solid tumor, measuring 6.5X5 cm. This tumor was sharply demarcated from the transitional cell carcinoma and ruptured during the operation (Fig. 3). Microscopic examination of the sections confirmed the presence of two separate and distinct malignant entities : a renal cell carcinoma, granular cell type, Fuhrman's grade 3, and a papillary transitional cell carcinoma, Ash grade 2 in the pelvis (Fig. 4). There was no transitional area between these two tumors in the kidney. These histologic findings were supported by the immunohistochemical staining. Both cytokeratin and vimentin were positive at the portion of renal cell carcinoma, and carcinoembryonic antigen and cytokeratin were positive with negative reaction for vimentin at the area of transitional cell carcinoma. Renal cell carcinoma extended to the perinephric fat and adipose tissue, but renal vein and lymphatics were free of the tumor (Robson's stage Ⅱ). An area of the transitional cell carcinoma was of stage B.

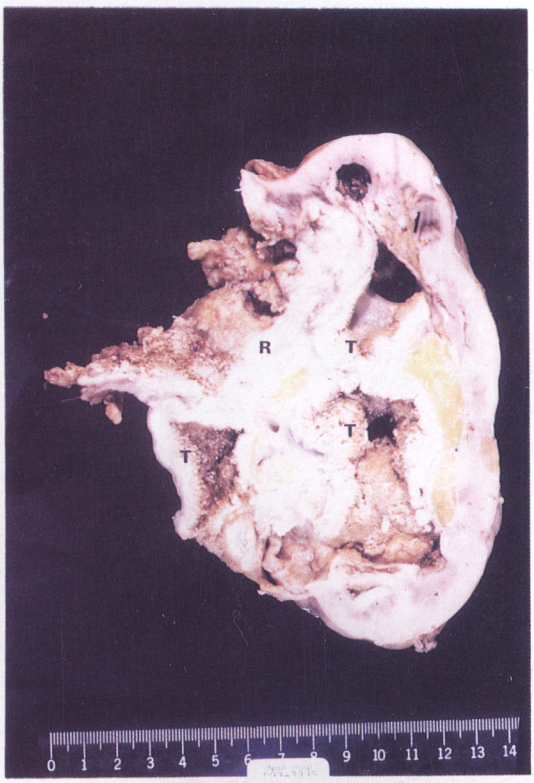

Fig. 3. The cut surface of the left kidney shows ruptured renal cell carcinoma(R) at the upper pole and papillary transitional cell carcinoma(T) at the pelvis. These two tumors have sharply defined borders.

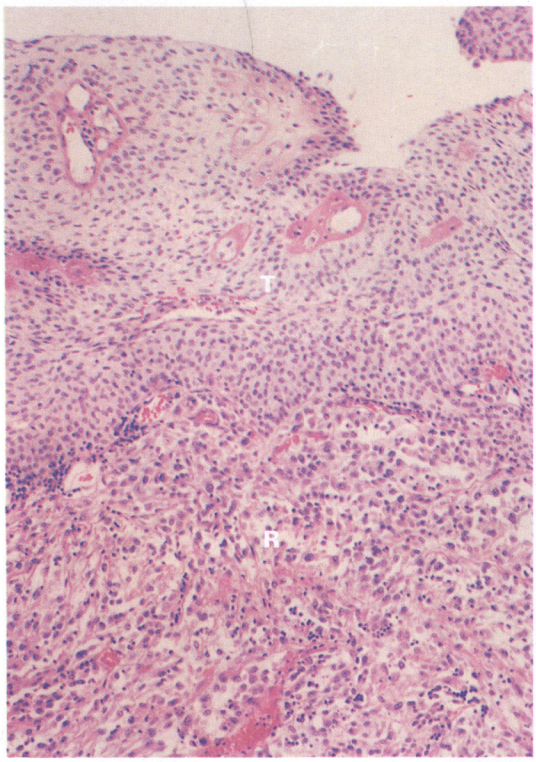

Fig. 4. Renal cell carcinoma(R), granular cell type and well-differentiated papillary transitional cell carcinoma(T) are colliding without transition.(H & E, X200)

DISCUSSION

Renal parenchymal and renal pelvic neoplasms may be primary or secondary in origin. Although mestastatic lesions are more common than primary lesions, these secondary lesions are usually asymptomatic, and most are discovered at postmortem examination. It is uncommon to have primary malignant tumors of dissimilar histogenesis in one kidney. Villegas (1967) reported two cases of bilateral primary renal carcinoma of dissimilar types. Simultaneous occurrence of renal cell carcinoma and transitional cell carcinoma of the ipsilateral ureter has only rarely been described (Richardson and Woodburn, 1963 ; Wilenius and Mattila, 1970). Synchronous discovery of renal cell carcinoma and urothelial (transitional cell) carcinoma of the pelvis in the same kidney is also rare. Graves and Templeton (1921) first reported a case with simultaneous occurrence of renal cell carcinoma and transitional cell carcinoma in the same kidney in 1921. Voneschenbach el al. (1977) reviewed 700 cases of renal cell carcinoma and found only one case (0.14% incidence) of this rare combination.

Several possible etiologic factors in primary renal cell carcinoma have been discussed in a recent review. Although the etiology of renal carcinoma remains uncertain, there is some evidence of an association between cigarette smoking and development of renal cell and urothelial carcinoma (Kantor, 1977). A familial form of the disease has also been described associated with chromosomal abnormalities (Cohen et al., 1979 ; Anderson and Lawson, 1992). Patients with von Hippel-Lindau's disease, acquired cystic disease, polycystic kidney disease, or horseshoe kidney appear to have a predisposition for development of the tumor (Chung-Park et al., 1983 ; Bernstein et al., 1987 ; Malek et al., 1987 ; Takagi and Kanai, 1992). Indeed, most signs and symptoms in patients with renal cell carcinoma arise from "remote humoral" effects of the cancer and these obscure problems include fever of unknown origin, leukemoid reaction, hypercalcemia as a result of the production of a PTH-like substance or some other substance, polycythemia secondary to the secretion of an erythropoietic stimulating substance, anemia, hepatic dysfunction, amyloidosis, polyneuromyopathy, hypertension caused by renin secretion, gynecomastia as a result of gonadotropin and placental lactogen, or Cushing's syndrome due to the secretion of an ACTH-like substance. The numerous systemic humoral manifestations of renal cell carcinoma have become known collectively as the paraneoplastic syndromes (Laski and Vugrin, 1987). Our patient had fever of unknown origin, leukemoid reaction, hypercalcemia, and hepatic dysfunction. Malignancy is the most frequent cause of hypercalcemia in hospitalized patients. The pathophysiology of hypercalcemia of malignancy is complex. While the existence of significant hypercalcemia in patients with cancer but no bony metastases has been known since the 1950's, the prediction that tumors might produce parathyroid hormone (PTH) or PTH-like substances had been predicted as early as 1948 by Allbright and Reifenstein. We could not estimate the serum level of PTHrP but the findings such as normal PTH, low $1,25(OH)_2D$, and low 25-OHD were suggestive of humoral hypercalcemia of malignancy.

Most transitional cell carcinomas of the renal pelvis occur in adults. The transitional cell carcinoma of the upper urinary tract has been associated with specific chemicals and may occur in the analgesic nephropathy. There is a history of analgesic abuse and/or co-existence of renal papillary necrosis in about one fourth of the cases (Johnason et al., 1974). These tumors have also been reported in horseshoe kidneys ; their incidence may actually be increased in this abnormality (Murphy and Zincke, 1982). Hematuria is the most common clinical presentation of this tumor. A case of transitional cell carcinoma of the kidney with hypercalcemia has also been reported (Tanaka et al., 1991). Synchronous or metachronous tumors elsewhere in the urinary tract are found in almost 40% of the patients ; exceptionally, an independent renal cell carcinoma may be found in the same kidney. The prognosis is largely determined by the stage of the lesion for both the pelvic and ureteral lesions (Akaza et al., 1987). Herein a patient with ipsilateral synchronous renal cell carcinoma and renal pelvic transitional cell carcinoma with severe hypercalcemia and a huge staghorn calculus in the contralateral kidney has been described. The finding of a staghorn calculus in the opposite kidney is interesting, although there is no known relationship with the humoral hypercalcemia of renal malignancy. Finally, it is noteworthy that this is a very rare case manifesting several combinations of disease occurrences.

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