

## Sarcomatoid acquired cystic disease-associated renal cell carcinoma

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**Summary.** In this article, we report a rare case of hitherto undescribed acquired cystic disease (ACD)-associated renal cell carcinoma (RCC) with sarcomatoid change. A 78-year-old woman had been receiving hemodialysis for fourteen years at the time when a renal tumor was encountered on the follow-up examination of the kidney. Microscopically, oncocyctic cuboidal cells proliferated with tubular, cribriform or papillary growth patterns, and atypical columnar cells with abundant cytoplasm proliferated with papillary configuration. Oxalate crystal deposition was observed in the stroma and the tumor focally resembled translocation type (TFE3) RCC. Sarcomatous neoplastic cells were also seen. The cytoplasm of oncocyctic and sarcomatous neoplastic cells was diffusely positive for anti-mitochondrial antibody and the ultrastructural examination detected many mitochondria in the cytoplasm of oncocyctic carcinoma cells and sarcomatous neoplastic cells. The loss of chromosomes 1p, 2q11-22, 9 and 14 was observed using comparative genomic hybridization analysis. We thus report here a case of hitherto undescribed ACD-associated RCC intermingled with oncocyctic cells, translocation type RCC-like area and sarcomatoid change. This is the sixth case of sarcomatoid RCC arising in end-stage kidney disease.

**Key words:** Acquired cystic disease, Renal cell carcinoma, Sarcomatoid change

### Introduction

It is well known that end-stage kidney may be associated with acquired cystic disease (ACD) together with or without a renal neoplasm. Previously, papillary renal cell carcinoma (RCC) most frequently occurring in patients receiving hemodialysis because of chronic renal failure has been reported (Ishikawa and Kovacs, 1993; Ishikawa et al., 1993; Ishikawa, 1999). Recently, Tickoo et al. (2006) have found that ACD-associated RCC, which is characterized by calcium oxalate crystal deposition and clear to eosinophilic cells, most frequently occurs in these patients. On the other hand, only five cases of sarcomatoid RCC arising in the end-stage kidney have been reported so far in the literature (Suvama et al., 1994; Harada et al., 2001; Aita et al., 2003; Tickoo et al., 2006). We report a case of hitherto undescribed ACD-associated RCC with a sarcomatoid change with immunohistochemical, ultrastructural and comparative genomic hybridization (CGH) analysis.

### Materials and methods

A 78-year-old woman received hemodialysis for fourteen years because of chronic glomerulonephritis, which was not confirmed histologically. The follow-up examination of the kidney disclosed a renal tumor. A radical nephrectomy was performed. Her clinical course was uneventful four months after the operation.

Kidney tissue obtained by nephrectomy was fixed in 10% formalin and embedded in paraffin. Three-micron thick sections were stained with hematoxylin-eosin. Additionally, immunohistochemical staining was performed using a Histofine Simple stain-PO (multi) kit (Nichirei, Tokyo, Japan). Antibodies against antimitochondrial antigen (MIA) (113-1, 1:800, BioGenex, San Ramon, CA, USA), AMACR (13H4, 1:150, Abcam Cambridge, UK), CD117 (c-kit)

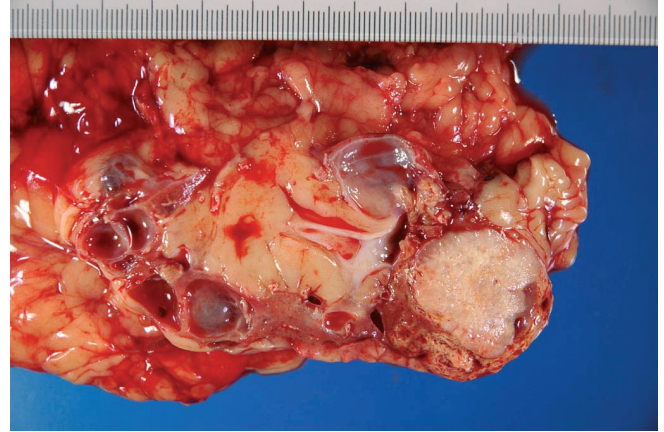
(polyclonal, 1:600, DAKO, Glostrup, Denmark), cytokeratin 7 (OV-TL 12/30, 1:100, DAKO, Glostrup, Denmark), RCC Ma (66.4.C2, 1:50, Novocastra Laboratories Ltd, Newcastle, UK), TFE3 (P-16, 1:600, Santa Cruz, CA, USA) were used in the present study. Fresh, small tumor sections were fixed with 2.5% glutaraldehyde and postfixed with 0.8% osmium tetroxide in phosphate buffer for 1h at room temperature. After dehydration in graded ethanol, they were embedded in Epon 812. The ultrathin sections were cut with a Reichert microtome, stained with uranyl acetate and lead citrate, and examined with an electron microscope (JEM-100S; JEOL Ltd, Tokyo, Japan).

CGH analysis was performed as previously described (Kasahara et al., 2005). DNA was extracted from fresh tissue.

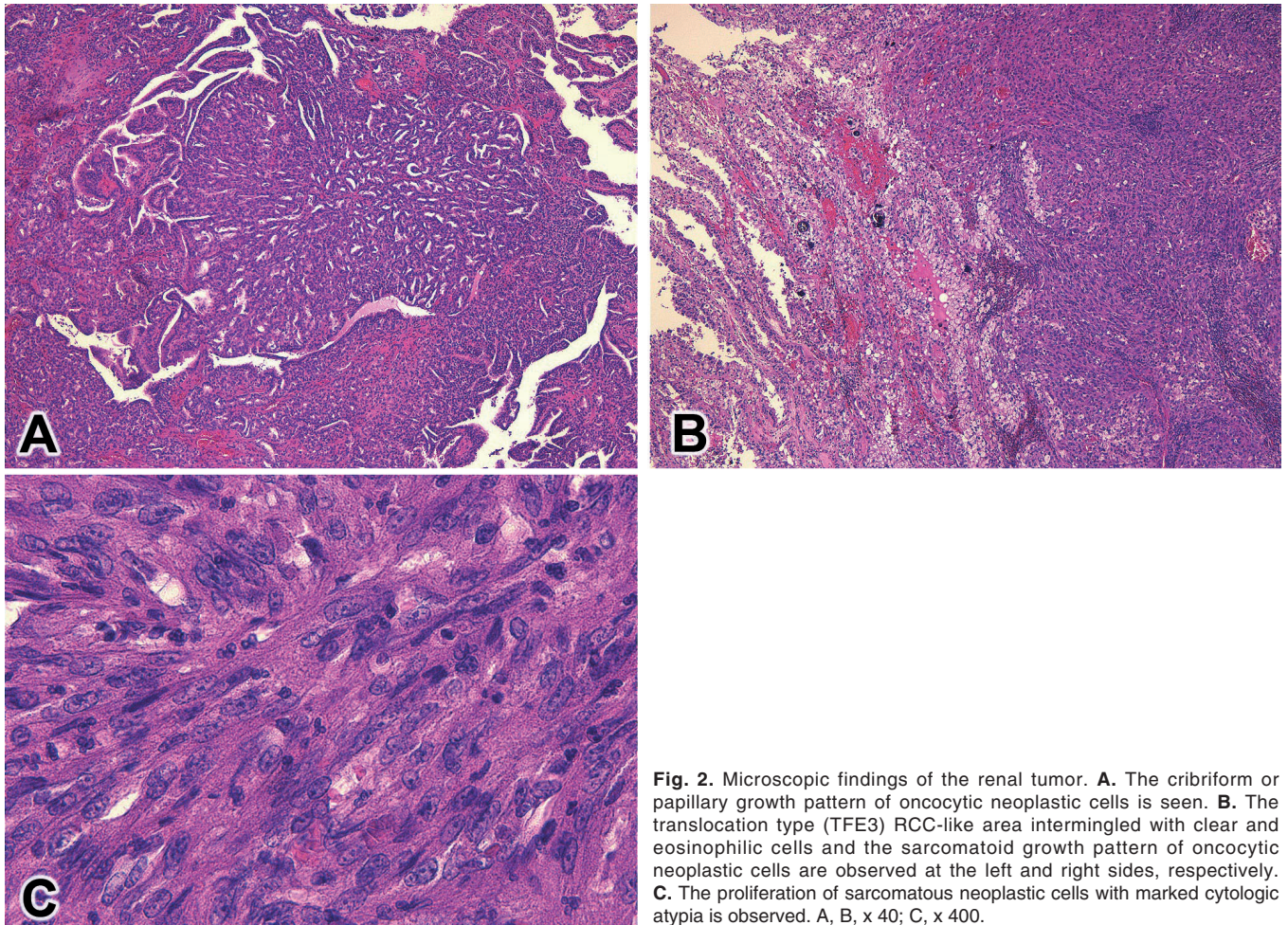
## Results

### Macroscopic findings

The cut surface of the kidney showed a multicystic



**Fig. 1.** Macroscopic finding of the renal tumor. The well-defined whitish tumor is observed.



**Fig. 2.** Microscopic findings of the renal tumor. **A.** The cribriform or papillary growth pattern of oncocytic neoplastic cells is seen. **B.** The translocation type (TFE3) RCC-like area intermingled with clear and eosinophilic cells and the sarcomatoid growth pattern of oncocytic neoplastic cells are observed at the left and right sides, respectively. **C.** The proliferation of sarcomatous neoplastic cells with marked cytologic atypia is observed. A, B, x 40; C, x 400.

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lesion. The whitish solid tumor which measured 3.5x3.4x2.7 cm was observed in the upper pole (Fig. 1).

#### Microscopic findings

Microscopically, cuboidal cells with so-called “oncocytic” cells were arranged in tubular, cribriform or papillary growth patterns. These patterns formed 30% of the total neoplasm (Fig. 2a). Additionally, atypical columnar cells with abundant cytoplasm proliferated with papillary configuration. This component was intermingled with clear and eosinophilic cells and resembled translocation type (TFE3) RCC (Fig. 2b). Calcifications were occasionally observed in this area. This component accounted for 20% of the total tumorous mass. About 50% of remaining tumor cells showed the proliferation of atypical spindle cells (Fig. 2b,c). The focal deposition of calcium oxalate crystal was confirmed under polarized light.

#### Immunohistochemical findings

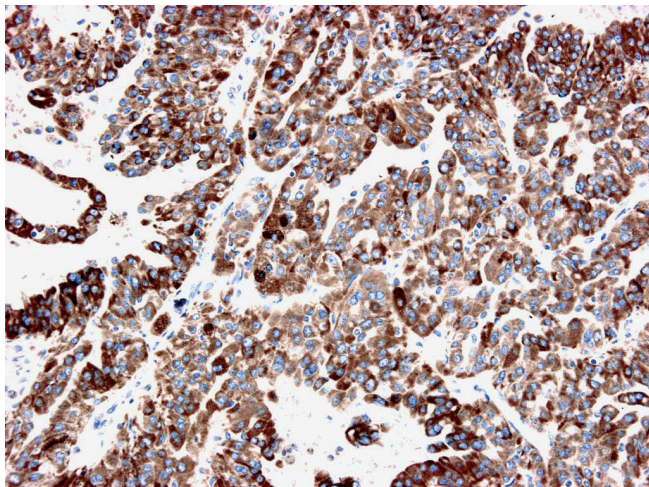
The cytoplasm of oncocytic cells and sarcomatous neoplastic cells was diffusely positive for MIA (Fig. 3). Neoplastic cells were completely negative for CD117, cytokeratin 7, RCC Ma and TFE3. AMACR was expressed only in papillary growth pattern.

#### Ultrastructural findings

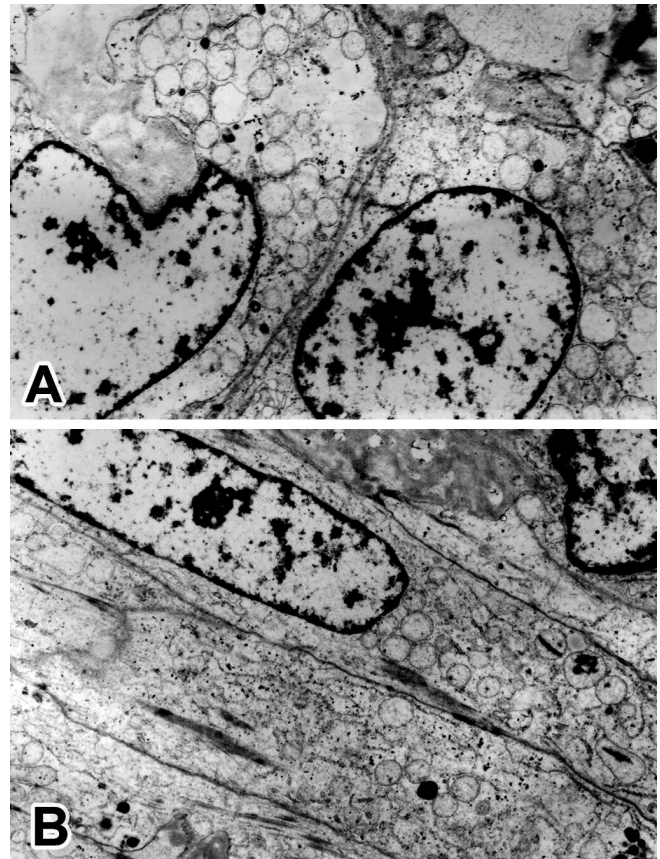
Ultrastructurally, the cytoplasm of oncocytic cells and sarcomatous neoplastic cells contained many mitochondria (Fig. 4a,b).

#### CGH findings

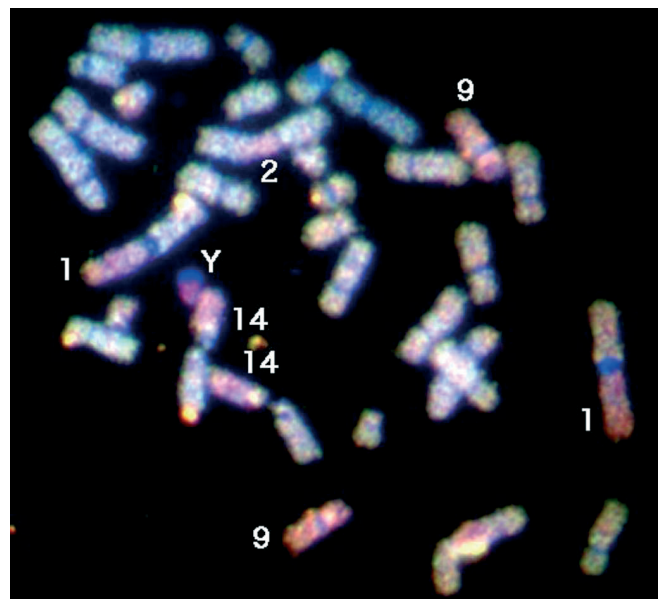
The loss of chromosomes 1p, 2q11-22, 9 and 14 was



**Fig. 3.** Immunohistochemical results of the renal tumor. Neoplastic cells with oncocytic cytoplasm are diffusely positive for antimitochondrial antigen (113-1) with granular pattern. x 100



**Fig. 4.** Ultrastructural findings of the renal tumor. Epithelial (A) and sarcomatous (B) neoplastic cells contain a lot of mitochondria in the cytoplasm. x 4,000



**Fig. 5.** Comparative genomic hybridization result. The loss of chromosomes 1p, 2q11-22, 9 and 14 is observed.

observed (Fig. 5).

## Discussion

The prevalence of RCC in dialysis patients is 40 to 50 times higher than that in the general population (Ishikawa, 1993; Troung et al., 1995). ACD is found in about 80% of RCC in chronic hemodialysis or end-stage kidney disease (Ishikawa, 1993; Tickoo et al., 2006). RCC arising in ACD is predominantly in males, and is frequently bilateral and multicentric (Ishikawa, 1993; Tickoo et al., 2006). In ACD kidney, papillary tuft, cribriform lesion, atypical cyst and adenoma are frequently observed, and these lesions are considered to be early neoplastic lesions in both morphological and genetic aspects (Hughson et al., 1980, 1986; Cheuk et al., 2002; Troung et al., 2003). RCC arising in ACD may show the deposition of calcium oxalate crystals (Dry and Renshaw, 1998; Rioux-Leclercq and Epstein, 2003; Sule et al., 2005; Tickoo et al., 2006). Many investigators have previously reported that RCCs arising in chronic dialysis patients may show the histological type of sporadic tumors, including papillary and clear RCCs (Hughson et al., 1986; Ishikawa, 1993; Ishikawa and Kovacs, 1993). However, some investigators have reported the histological patterns that differed from those of the sporadic tumors. Sule et al. (2005) have reported RCC with oxalate phenotype, which is characterized by ill-defined cell membrane, abundant eosinophilic granular cytoplasm, large nuclei and prominent nucleoli. This tumor may exhibit papillary, microcystic growth patterns. This tumor generally shows the proximal tubular phenotype. Tickoo et al. (2006) have reported two histological subtypes of ACD-associated RCC and papillary RCC consisting of clear cells. In the present case, we confirmed the presence of oxalate crystal depositions, but our case does not seem to fit into their categories because of the presence of oncocyctic area and mixed clear and eosinophilic cells resembling translocation type (TFE3) RCC (Argani and Ladanyi, 2004; Sule et al., 2005; Tickoo et al., 2006). Nagy et al. (2003) have reported the mutation of mtDNA in renal tumors in end-stage renal disease. Therefore, we cannot completely rule out the possibility that oncocyctic cells with abundant mitochondria in the present case may be associated with mtDNA alteration.

On the other hand, five RCCs with sarcomatoid change arising in end-stage kidney have been reported to date (Suvama et al., 1994; Harada et al., 2001; Aita et al., 2003; Tickoo et al., 2006). The histological type of the primary carcinoma contains collecting duct carcinoma and ACD-associated RCC. Our case is the sixth case with sarcomatoid RCC arising in ACD.

In chromosomal analysis, RCCs arising in ACD may show chromosomal abnormalities both similar to and different from those seen in sporadic tumors (Gronwald et al., 1999; Hughson et al., 1999). Therefore, it is likely that some hitherto unknown new tumors may arise within ACD-associated RCCs, particularly in those

neoplasms that morphologically differ from the sporadic tumors. On the other hand, Jiang et al. (1998) have reported that the inactivation of a tumor suppressor gene at chromosomes 13q and 4q may be important for sarcomatoid change of RCC using CGH analysis. However, sarcomatoid RCC in the present case showed no abnormalities of 13q and 4p. In contrast, the loss of chromosomes 9 and 14, which were identified in the present tumor, has been previously observed in clear cell RCC (Junker et al., 2003). Further examinations will be required in order to elucidate the pathogenesis of ACD-associated RCC with sarcomatoid change.

In summary, we report here a case of hitherto undescribed ACD-associated RCC intermingled with oncocyctic cells, translocation type (TFE3) RCC-like area and sarcomatoid change. This is the sixth case of sarcomatoid RCC arising in end-stage kidney disease.

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