Sarcomatoid renal cell carcinoma (SRCC) is an uncommon but particularly aggressive variant of renal cell carcinoma, accounting for 1% to 5% of all renal malignant neoplasms. Until recently, SRCC was thought to represent a primary renal sarcoma, but since these tumors coexpress both epithelial and stromal markers, they are now believed to represent a form of dedifferentiated carcinoma. Most sarcomatoid carcinomas are found in association with conventional (clear cell) renal carcinoma, but there are occasional descriptions of sarcomatoid transformation of chromophobe carcinoma, collecting duct carcinoma, and papillary carcinoma.

The classification of renal cell carcinoma has been significantly improved with the introduction of cytogenetic markers specific to each tumor subtype. There is, however, limited information regarding the genetic alterations in SRCC. Occasionally, association of non–clear cell tumors with sarcomatoid carcinoma has led to the presumption that the former dedifferentiates to form the latter. Genetic studies designed to trace the origin of SRCC in association with papillary tumors are limited to 3 case reports, with 2 reports suggesting a clear cell origin and all 3 failing to confirm a papillary derivation. In these 3 cases, the 2 tumors (papillary and SRCC) were not separately sampled; hence, comparative cytogenetic analysis between the tumor subtypes could not be performed.

The genetic composition of SRCC is highly variable, and most analyses have shown complex chromosomal rearrangements, suggesting the alteration of multiple genes in this transformation. The role of p53 gene mutation is unclear but has been observed in more than 80% of SRCC cases, including a single case report of SRCC in association with papillary carcinoma, which was believed to be of clear cell origin.

We present a detailed histologic, molecular biological, and cytogenetic evaluation of a papillary renal cell carcinoma with associated SRCC, where each tumor type was separately assessed and where the SRCC was clearly evolved directly from the papillary tumor.

**REPORT OF A CASE**

A 78-year-old man with chronic obstructive airway disease was admitted to hospital with an acute respiratory tract infection. Computed tomography of the chest revealed an incidental 5-cm tumor mass in the upper pole of the right kidney. Medical history was noncontributory, and the patient underwent radical nephrectomy. The patient remains well and apparently free of disease 12 months after surgery.

**Pathologic Findings**

A tumor mass within the kidney extended from the medulla to the cortex and macroscopically penetrated the renal capsule, extending into the surrounding fat (Figure 1). Toward the renal medulla, the tumor was friable and cystic, whereas in the outer cortex, it was more solid and uniform. The central tumor mass measured 25 × 30 × 20 mm, whereas the more solid perimeter tumor measured 20 × 25 × 18 mm. Fresh tissue from both tumor areas was submitted separately for cytogenetic analysis.

**Histologic Findings and Immunostains**

Sections of the central portion of the tumor confirmed a classic papillary renal cell carcinoma (Figure 2) composed of fine vascular cords lined by bland neoplastic cells with grooved nuclei. By contrast, the solid tumor area was composed of anaplastic.
spindle cells with a high mitotic rate, including atypical mitoses (Figure 2). The interface area between the 2 was composed of part papillary and part solid tumor that showed both significant pleomorphism and anaplasia and areas of coagulative necrosis. Immunostains for cytokeratin (AE1/3, Dako Corporation, Glostrup, Denmark) were positive in both tumors, whereas stains for vimentin (Dako) were only positive in the sarcomatoid region. The interface region was variably stained for both markers.

Cytogenetic Analysis

Cytogenetic analysis of 6 cell metaphases from the papillary tumor (central) produced a composite karyotype, 49,X[5]+3, +7,+7,+17 (Figure 3), which is consistent with the diagnosis of papillary renal carcinoma.18-20 No loss of 17p was detected, a feature associated with progression of papillary carcinoma to high-grade carcinomas.16 Analysis of 12 metaphases from the solid sarcomatous region gave a composite karyotype of between 114 and 116 chromosomes (ie, based on a triploid karyotype): 114±116,XX,+X,−1,−1,+del(1p)x2,+der(2)t(2;3)[3],+5,+5[4],+6[4]+7,+7,+7,+7,+8[5],+9,+13, +14[5],+17,+17, +18[5],+19[2],+20[3],+21, +21[5],−22[5]c[12] (Figure 3). There was no loss of 3p, and multiple copies of 7 and 17 are consistent with the tumor’s papillary origin.

Loss of Heterozygosity Analysis

DNA was isolated from neoplastic and normal kidney tissue; 20-µm sections were cut from paraffin-embedded tissue samples, each dewaxed in xylene, and DNA prepared as previously described.15 Loss of heterozygosity for chromosome 3p was determined by polymerase chain reaction amplification of polymorphic microsatellite markers and gel electrophoresis as previously described.20 Markers used in this study were D3S1297 (3pter–3p22.5), D3S1539 (3pter–3p22.5), D3S1514 (3p21–3p14.2), and D3S1478 (3p21.3–3p21.2). No loss of heterozygosity was observed at D3S1297, D3S1514, or D3S1478. The patient was homozygous at D3S1359. These results indicate retention of heterozygosity of chromosome 3p with no deletion of this chromosome fragment.

p53 Mutation

p53 mutations within exons 4 to 8 were screened using a polymerase chain reaction–single-stranded conformational polymorphism detection system.21 Both sarcomatous and papillary regions were separately assessed and showed no p53 mutations. Further, immunostains with anti-p53 (D-7, Dako) were negative in both tumor subtypes.

COMMENT

Sarcomatoid renal cell carcinoma is considered a late and almost invariably fatal cancer, with a mean survival time of less than 6 months.2 It usually evolves from conventional (clear cell) renal cell carcinoma. Although it is acknowledged that SRCC may be associated with multiple renal tumor subtypes of differing biological behavior, direct evolution from non-clear cell tumors has not previously been proven, and SRCC remains classified as a single pathological entity with a uniformly poor prognosis.22 This case represents the first cytogenetic evidence of direct progression of papillary renal carcinoma (non-clear cell) to SRCC as determined by cytogenetic analysis.

Using standard cytogenetics, loss of chromosome 3p, a specific genetic change associated with the clear cell subtype, was not detected in 12 metaphases from the sarcomatoid component. As has been previously indicated,15 discrepancies between metaphases of primary cultures are not uncommon. Therefore, we assessed 12 separate metaphases in conjunction with whole tissue loss of heterozygosity to exclude possible error. The loss of heterozygosity method further excludes minor deletions in the 3p region that may not be evident with standard cytogenetic evaluation.

A previous description of SRCC associated with papillary renal cell carcinoma cited multiple defects in chromosomes 1q, 12q, 16p, and 19p that are not seen in our case. This previous analysis was performed on a metastatic tumor site, and cytogenetic evaluation of the primary “mixed glandular-papillary-sarcomatoid” lesion was not performed.

In the current case, multiple and complex genetic changes have occurred in the transformation of papillary car-
evaluation of all SRCC in addition to routine histologic testing so that the biological behavior can ultimately be defined. Since preoperative diagnosis and distinction from other forms of renal carcinoma are rare, use of loss of heterozygosity techniques and p53 estimation on formalin-fixed tissues may be sufficient to identify SRCC of non-clear cell origin so that follow-up data can be assessed.

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References