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Synchronus renal cell carcinoma and Bellini duct carcinoma: a case report on a rare coincidence

Abstract Bellini duct carcinoma or collecting duct carcinoma (CDC) is a rare but aggressive primary renal neoplasm. The coexistence of two synchronous neoplasms in the same kidney is highly infrequent. As a result, it is hardly surprising that there are no references to renal cell carcinoma (RCC) combined with CDC of the same kidney in the literature. Histology and immunohistochemistry are important tools for differentiating between the two types of tumors involved. We present the first case of a synchronous occurrence of RCC and CDC of the same kidney.

Key words Renal cell carcinoma · Collecting duct carcinoma · Synchronous

Renal cell carcinoma (RCC) and transitional cell carcinoma (TCC) account for approximately 80% and 7% of primary renal malignant tumors, respectively. Collecting duct carcinoma (CDC), a distinct and rare variant of RCC, represents only about 1–2% of all renal primary malignancies. It arises from the epithelium of the collecting duct (the Bellini duct) and definitive diagnosis is only established by complete histological study.

The coexistence of multiple and synchronous primary neoplasms in the same organ has only rarely been described in the literature. The kidney is no exception. Some cases of rare synchronous occurrence of TCC and RCC in the same kidney have occasionally been reported. RCC has also been associated with adenocarcinoma of the ureter and upper urinary tract, and TCC with fibrosarcoma. However, to date there are no descriptions of the coexistence of RCC and CDC in the same kidney.

We present the first report of this condition and emphasize the importance of histological studies in the differential diagnosis between RCC and CDC. The prognosis and treatment depend on accurate identification of the neoplasm.

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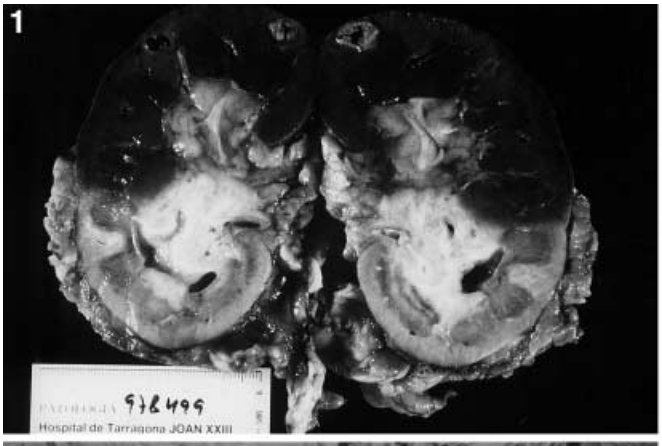
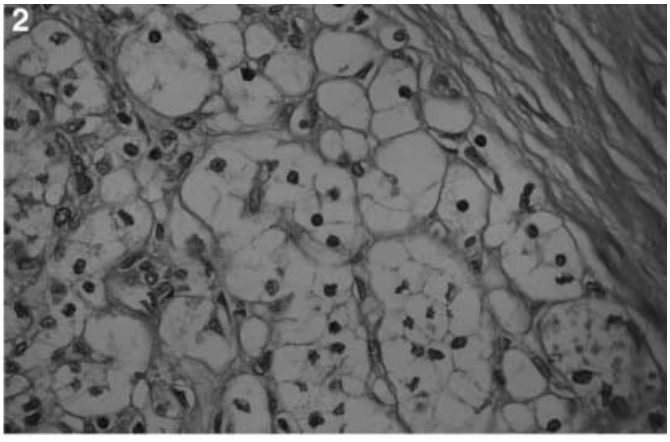
Case report

A 73-year-old man was admitted for microscopic hematuria found in the course of annual prostatic evaluation. Medical history was unremarkable. Physical examination and analytical studies were normal. The cytologies of urine obtained were negative. Intravenous urography and abdominal CT revealed a 13-mm solid mass in the upper portion of the right kidney without renal vein involvement. There were no lymph node, lung, or liver metastases, so the patient underwent a radical right nephrectomy. The resected right kidney weighed 180 g and measured $95 \times 60 \times 60$ mm. Macroscopic pathological study showed a yellow tumor of 13 mm in the upper renal pole, with focal areas of hemorrhage. In the inferior pole, there was a 6-cm gray-white consistent tissue with tumoral appearance, which produced distortion of the pelvicalyceal system The tumor was infiltrative but it did not invade the cortical (Fig. 1).

Microscopically, the first nodule was a RCC, clear cell type. The neoplastic cells had larger pleomorphic nuclei and prominent nucleoli (Grade II) (Fig. 2).

The microscopic examination of the second tumor revealed atypical hyperplastic changes in the epithelium of the collecting ducts in the adjacent renal medulla. These atypical collecting duct epithelial cells were columnar or cuboidal with eosinophilic cytoplasm, increased nuclear size, and hyperchromasia. Mitotic figures were also present. The tumor extended into the adjacent renal parenchyma. Anastomosing tubules, lined by cuboidal or columnar cells with pronounced pleomorphism and a high mitotic rate, were infiltrating the renal parenchyma. There was a marked peritubular desmoplastic reaction (Fig. 3). The immunohistochemical study demonstrated high molecular weight cytokeratins (34BE12, Dako), epithelial membrane antigen (Dako), and Vimentin (Bio-Genex). The nuclear grade according to the criteria of Fuhrman et al. [4] was grade III.





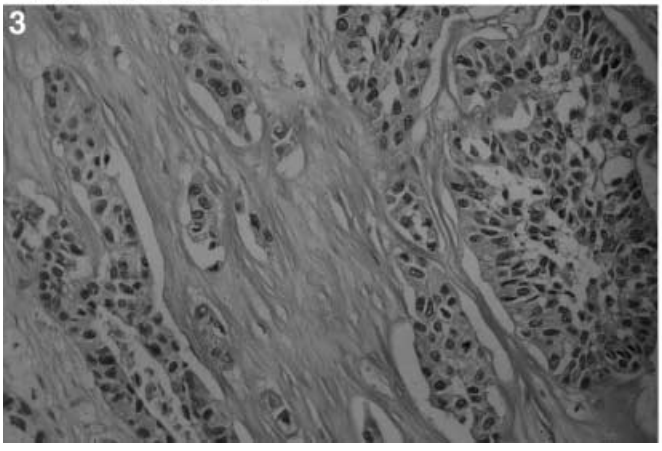


Fig. 1 Kidney macroscopic study: yellow tumor 13 mm in diameter in the upper renal pole. In the inferior pole, a gray-white consistent tissue with tumoral aspect

Fig. 2 Microscopic study of small nodule: renal cell carcinoma, clear cell type

Fig. 3 Microscopic examination of second tumoral tissue: atypical hyperplastic changes in the epithelium of the collecting ducts; cells were columnar or cuboidal with eosinophilic cytoplasm, increased nuclear size and hyperchromasia. Mitotic figures were present. Marked peritubular desmoplastic reaction

The patient was asymptomatic for 8 months postsurgery. After 8 months, he presented inflammatory chest pain. A bone scan revealed dense isotope uptake at both sixth ribs, suggesting bone metastases.

Discussion

The coexistence of multiple and synchronous primary neoplasms in the same kidney has been scarcely described in the literature. The most frequent tumor combination is RCC and transitional cell carcinoma (TCC) [6]. RCC has also been associated with adenocarcinoma of the ureter and upper urinary tract [5]. One case of TCC of the renal pelvis has been reported in association with CDC of the same kidney [4]. However, no cases of RCC combined with CDC have been reported to date, very probably because the second tumor is so infrequent.

CDC, or Bellini duct carcinoma, is a very rare, aggressive renal neoplasm which originates in the epithelium of the Bellini ducts in the distal tubule. Most CDC patients are younger than those classical RCC patients. CDC affects males more than females (ratio 4:1) and the patients affected have a strong family history of associated malignancies. The most common symptoms, similar to those of RCC, are hematuria (as in our case) and flank pain. Patients with CDC usually present advanced-stage disease and, therefore, the overall prognosis is poor. This rapid metastatic spread may be due to its central location, close to the renal hilus [1, 2]. However, McLennan et al. have described a series of unusual low-grade tubulocystic renal cancer with good prognosis [9].

The definitive diagnosis of CDC is only established by complete histological study, especially if it coexists with a RCC in the same kidney, as in our case.

For CDC diagnosis, both gross and microscopic criteria are required: the presence of a medial tumor (in the renal medulla), the resemblance of the neoplastic cells to those cells lining the collecting ducts, and dysplasia in the collecting ducts adjacent to the tumor. Identification of markers of collecting duct epithelium by immunostaining with peanut lectin, high-molecular-weight keratins, and epithelial membrane antigen support the histological diagnosis [3, 8].

Therefore, in some cases immunohistochemical staining is necessary to demonstrate the origin of the tumor. Tumor positivity for antigens that are normally expressed in distal tubules and collecting ducts, but not in the proximal tubular epithelium, distinguishes between Bellini duct carcinoma and RCC. CDC shows high-molecular-weight cytokeratin expression, indicating the origin of the tumor in the lower nephron, as occurs in our case. In contrast, RCC expresses pancytokeratin but is negative to high-molecular-weight cytokeratin [7].

In spite of complex immunohistochemical studies, differential diagnosis may continue to pose problems. Several authors have tried to define the cytogenic aberrations of the different renal tumors. Tumors arising from the renal collecting tube are frequently characterized by loss of chromosome 1, whereas in tumors of the proximal tubule origin, the loss of 3p is the most common molecular finding. However, further study will be required in this direction [11].

Histological, immunohistochemical, and genetic studies lead us to believe that RCC and CDC are histogenetically distinct tumor entities: CDC originates in the medullar collecting duct, which arises from the mesonephron. In contrast, the tubular structures of the kidney, which can cause RCC, originate in the metanephronic blastema [8]. The coincidence of the two tumors is more rare if we take into account this embryogenic difference.

The treatment of choice for renal primary malignancies is radical nephrectomy. However, CDC is more aggressive. In view of the advanced stage at presentation and the non-curative role of surgery in CDC, effective systemic treatment is required [6].

As this tumor occurs so infrequently there is no standard treatment regimen. Radiotherapy has been used in local recurrences, with transient response. The most common coadjuvant chemotherapy regimen used is methotrexate, vinblastine, doxorubicin and cisplatin, but response is poor. Better results have been achieved with interferon-α and interleukin-2. However, studies with more patients are needed to validate these findings [6]. In spite of receiving radical nephrectomy and chemotherapy, our patient presented metastasis spread after 8 months.

In conclusion, the coexistence of multiple and synchronous renal primary malignancies is rare, but possible. When kidney tumors do not have the macroscopic/microscopic features of conventional RCC, the possibility of CDC must be borne in mind. Then, immunohistochemical and genetic studies are needed.

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