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COLLECTING DUCT CARCINOMA OF THE KIDNEY: REPORT OF THREE CASES*

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SUMMARY – Collecting duct carcinoma or Bellini duct carcinoma is a highly malignant neoplasm that arises from the collecting duct epithelium of the kidney and accounts for approximately 1% of renal neoplasms. Collecting duct carcinoma generally pursues a more aggressive course than conventional renal cell carcinoma. Metastases to regional lymph nodes, bone, adrenal glands, lung, skin and meninges have been reported. During the 1998-2000 period, 161 patients underwent nephrectomy due to renal cell carcinoma at our hospital. The patients' age ranged from 24 to 90 (mean 59.5) years. There were 50 female and 111 male patients. Collecting duct carcinoma was diagnosed in three (1.9%) male patients aged 79, 66 and 67 (mean age 71.0) years. The patients presented with hematuria associated with fever, weight loss, pain and palpable abdominal mass. On gross examination, the tumors were located in the medulla of the kidney and extended into the cortex and adjacent adipose tissue. Histologically, the tumors showed tubulopapillary, tubular or solid areas. Immunohistochemically, positive staining with cytokeratin, EMA and Ulex Europaeus agglutinin was observed. All patients had regional lymph node metastases, and two of them died within one month from surgery. The third patient was alive and without signs of recurrence six months from presentation.

Key words: *Kidney neoplasms, pathology; Kidney neoplasms, diagnosis*

Introduction

Collecting duct carcinoma (CDC) or Bellini duct carcinoma is a neoplasm that arises from the collecting duct epithelium of the kidney and accounts for 0.4% to 2.6% of all renal carcinomas[1-3]. This tumor is a histogenetically, morphologically and cytogenetically defined entity. CDC predominantly affects men, and a majority of patients are white[4]. The average age of reported patients is approximately 53 years[1,4,5]. Tumors are mainly located in the medulla or central part of the kidney. They are white and gray and histologically show a tubular and papillary pattern. CDC generally pursues a more aggressive course than conventional renal cell carcinoma[1,2]. The prognosis is poor, as more than 50% of the reported patients died within two years of presentation[2,5,6]. Metastases to regional lymph nodes, bone, adrenal glands, lung, skin and meninges have been reported[4-6].

We present the clinicopathologic features of three cases that were observed over the past three years.

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Patients and Methods

During a three-year period (1998-2000), 161 patients underwent surgery at our hospital for renal cell carcinoma. Tumors of the renal pelvis are not included. The patients were aged 24-90 (mean age 59.5) years. There were 50 (31.1%) female and 111 (68.9%) male patients.

CDC was diagnosed in three (1.9%) male patients aged 79, 66 and 67 (mean age 71.0) years. Clinical data were obtained from the patients' medical records. Follow-up data to the last clinical examination or death were available in all three cases.

Formalin fixed, paraffin embedded tumor tissue was cut at 5 μm sections, deparaffinized, and stained with hematoxylin and eosin. Immunohistochemistry was performed on paraffin embedded archival material using primary antibodies (cytokeratin, low molecular weight cytokeratin, high molecular weight cytokeratin, EMA and Ulex Europaeus agglutinin I) purchased from DAKO (Glostrup, Denmark). The peroxidase/antiperoxidase method was used with 3,3'-diaminobenzidine as a chromogen.

Case Reports

Case 1

A 79-year-old man with a history of left nephrectomy for tuberculosis presented with sudden abdominal pain and acute renal failure. Intraoperative findings showed a tumor and massive hemorrhage from the right kidney. The patient underwent radical nephrectomy. Enlarged retroperitoneal lymph nodes were observed. After surgery, the patient underwent hemodialysis. The patient died from renal failure three weeks after the surgery.

Case 2

A 66-year-old man presented with lumbar pain. Physical examination revealed a palpable left lumbar mass and left cervical lymphadenopathy. Fine needle aspiration indicated metastatic adenocarcinoma of cervical lymph node. X-ray showed two metastatic nodules in the lung. Computed tomography (CT) scan of the abdomen showed a large tumor in the left kidney and enlargement of the hilar lymph nodes. The patient underwent radical nephrectomy. Three weeks later, the patient died. Autopsy revealed multiple metastases of the lungs and pulmonary thromboembolism.

Case 3

A 67-year-old man presented with painless hematuria lasting for the past two months. Urine cytology suggested transitional cell carcinoma. CT scans of the abdomen showed a large tumor in the superior pole of the right kidney, spreading to the pelvis. Radical nephrectomy with dissection of regional lymph nodes was performed. The patient was free from recurrence six months after initial presentation.

Pathohistologic Findings

All tumors were located in the renal medulla and extended to the renal cortex. The tumors measured 8-10 cm in largest diameter. One tumor was partly cystic with a solid part in the medulla (case 1). The tumors had ill-defined borders and showed infiltrative spread into the renal and hilar tissues (Fig. 1). Renal capsule was touched in two tumors. Tumor tissue was white or gray. Two tumors showed necrotic areas. Two tumors had connection with the pelvic transitional epithelium, and one of them had papillary projections to the pelvis. There were no tumor thrombi in the main renal veins.

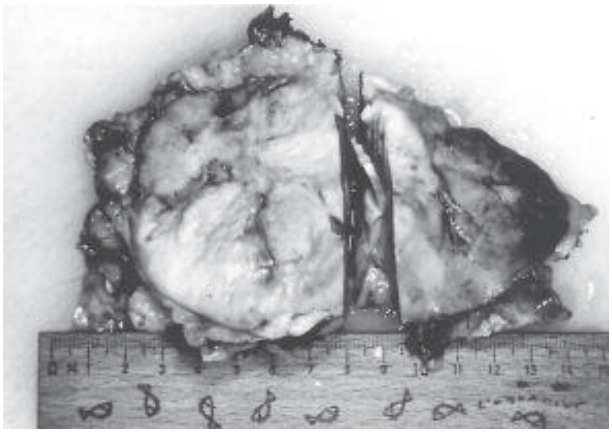

Fig. 1. Kidney with ill-circumscribed, infiltrative, white tumor extending from the renal pelvis to the renal capsule.

Tumor cells were relatively large with abundant, weakly eosinophilic cytoplasm. The nuclei were large and mainly vesicular with prominent eosinophilic nucleoli (Fig. 2). The cells showed medium to high cytologic atypia. The tumors showed cystic, papillary, tubular, solid and cribriform growth patterns (Fig. 3). In one tumor, there was intensive mononuclear stromal infiltration in papil-

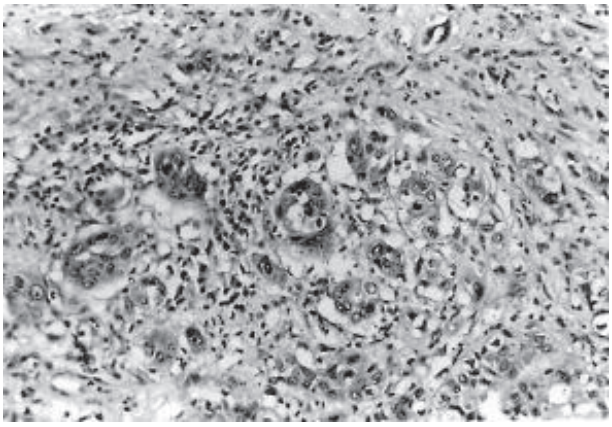

Fig. 2. Collecting duct carcinoma of the kidney composed of atypical epithelial cells with large vascular nuclei and prominent nucleoli (HE x200).

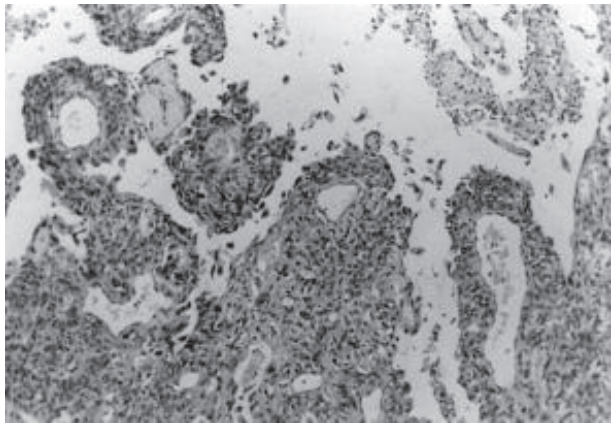

Fig. 3. Collecting duct carcinoma showing a tubular and papillary growth pattern (HE x100).

lary areas (case 2). In all tumors, desmoplastic stroma was observed. There were no dysplastic changes in the adjacent collecting tubuli. Immunohistochemical studies yielded positive results for CK, EMA and Ulex Europaeus agglutinin.

All patients had regional node metastases. In one patient, cervical lymph node and pulmonary metastases were also present (case 2). Histology of the regional lymph node metastases was similar to the primary tumor pattern. Two patients died within one month from surgery.

Discussion

To our knowledge, there are about 100 cases of CDC reported in the English literature[1-11]. In 1974, Mancilla-Jimenez et al.[12] reported on a series of 34 papillary renal cell carcinomas. They observed atypical and hyperplastic changes in adjacent collecting tubuli in three tumors, and hypothesized on their collecting duct origin. In 1979, Cromie et al.[13] described a renal tumor composed of papillary, transitional and tubular cell component, and suggested a collecting duct origin. However, according to Kennedy et al.[6], one of the first descriptions of CDC was given by Pierre Masson in his classical paper about human tumors, published in 1955 in French. Many case reports appeared in the meantime in the literature[6,8,9,10,14,15]. The largest series comprised 12 cases[5]. CDC has recently been recognized as a separate entity, and the latest World Health Organization (WHO) classification designates it as a distinct type[16]. In the previous WHO classification, this tumor was grouped with renal cell carcinoma, with a subdesignation 'Bellini duct carcinoma'.

The average age of all patients reported in the literature is 54 (range 13-83) years. However, the tumor is frequently seen in the second and third decade of life, in a much younger age group than conventional renal cell carcinoma[4]. The youngest patient was a 13-year-old girl reported by O'Brien and Bedard[14]. The patient was followed for 5 years without clinical evidence of recurrence after nephrectomy. The mean age of our patients was 71 years.

CDC shows a male predominance, with a male-to-female ratio of approximately 2:1[4,5]. All patients in our series were men.

The proximal tubular cell is generally considered a cell type giving rise to renal cell carcinoma. CDC arises from the collecting duct epithelium of the kidney and shares a common embryonic origin with renal pelvis and minor and major calyces (mesonephros) rather than with proximal nephron (metanephros).

Histologically, CDC is characterized by papillary structures suggesting transitional cell carcinoma, and glandular areas suggesting renal cell carcinoma. However, a sarcomatoid type of Bellini carcinoma has also been described[5,17]. A panel of four immunohistochemical markers including CK 19, CK 13, vimentin and UEA-1 were found to be useful in differentiating typical renal cell, CDC and urothelial carcinomas[2-4,18]. The collecting duct carcinoma cells share a similar phenotype (CK 19, UEA-1, CK 13) with the collecting duct cells. CDC is also positive for Ulex Europaeus and peanut lectin agglutinin[4,18]. In contrast to typical renal cell carcinoma, CDC is frequently mucicarmine positive[3,4,18]. Urothelial carcinomas express cytokeratin 13 and fail to express vimentin, while in CDC the reactivity to vimentin is weak. Renal cell carcinoma is usually positive for Leu-M1 (a proximal

tubule marker), low molecular weight cytokeratin and vimentin[4,18], but does not react with UEA-1. A panel of antibodies could be used to differentiate this tumor from conventional renal cell carcinoma and transitional cell carcinoma.

The patients with CDC usually present with a widely disseminated disease, while those having classic renal cell carcinoma more commonly present with a localized disease[2,5,18]. Metastases to different organs have been reported, including bone and leptomeninges[4,5,18]. Bone metastases usually are osteoblastic[5].

The majority of reported patients were treated by nephrectomy and regional lymph node dissection. However, seven of 12 patients reported by Dimopoulos et al.[5] were administered chemotherapy consisting of various combinations of chemotherapeutic agents, mostly MVAC (methotrexate, vinblastine, doxorubicin and cisplatin). Four of these seven patients were initially diagnosed as atypical papillary transitional cell carcinoma of the pelvis. No response was achieved by this combination chemotherapy. Six patients were treated with interleukin-2 and interferon-α, and one of these patients showed no evidence of the disease at 30 months from surgery[5].

At present, the number of reported cases of CDC is too small and with a short follow-up to make any real survival assessment. However, the cases reported in this series as well as those described elsewhere point to poor prognosis. Unfortunately, at present there does not seem to be any efficacious systemic treatment for CDC.

References

1. RUMPELT HJ, STÖRKEL S, MOLL R, SCHÄRFE T, THOENES W. Bellini duct carcinoma: further evidence for this rare variant of renal cell carcinoma. Histopathology 1991;18:115-22.
2. ZAMBRANO NR, LUBENSKY IA, MARINO MJ, LINEHAN WM, WALTHER MM. Histopathology and molecular genetics of renal tumors: toward unification of a classification system. J Urol 1998;162:1246-58.
3. STÖRKEL S, EBLE JN, ADLINHA K, AMIN M, BLUTE ML, BOSTWICK DG, DAVSON M, DELAHUNT B, ICZKOWSKI K. Classification of renal cell carcinoma. Workgroup No. 1. Union Internationale Contre de Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer 1997;80:987.
4. OLIVERE JW, CINA SJ, RASTOGI P, RO YJ. Collecting duct meningeal carcinomatosis. Arch Pathol Lab Med 1999;123:638-41.
5. DIMOPOULOS MA, LOGOTHETIS CJ, MARKOWITZ A, SELLA A, AMATO R, RO J. Collecting duct carcinoma of the kidney. Br J Urol 1993;71:388-91.
6. KENNEDY SM, MARINO MJ, LINEHAN WM, ROBERTS JR, ROBERTSON CN, NEUMANN RD. Collecting duct carcinoma of the kidney. Hum Pathol 1990;21:449-56.
7. SRIGLEY JR, EBLE JN. Collecting duct carcinoma of the kidney. Semin Diagn Pathol 1998;15:54-67.
8. KIRKALI Z, CELEBI I, AKAN G, YORUKOGLU K. Bellini duct (collecting duct) carcinoma of the kidney. Urology 1996;47:921-3.
9. MATZ LR, NATHAN BI, FABIAN VA, VIVIAN JB. Collecting duct carcinoma of the kidney: a report of three cases and review of the literature. Pathology 1997;29:354-9.
10. PRATI GF, DEAN P, FIRPO M, MOSCATELLI P, SAGGIN P, MUOLO A. Bellini duct (collecting duct) carcinoma of the kidney. Int Urol Nephrol 1998;30:677-80.
11. ONO K, NISHINO E, NAKAMINE H. Renal collecting duct carcinoma. Report of a case with cytologic findings of fine needle aspiration. Acta Cytol 2000;44:380-4.
12. MANCILLA-JIMENEZ R, STANLEY RJ, BLATH RA. Papillary renal cell carcinoma: a clinical, radiological and pathologic study of 34 cases. Cancer 1976;38:2469-80.
13. CROMIE WJ, DAVIS CJ, DeTURE FA. Atypical carcinoma of kidney, possibly originating from collecting duct epithelium. Urology 1979;13:315-7.
14. O'BRIEN PK, BEDARD YC. A papillary carcinoma of the renal pelvis in a young girl. A light and electron microscopic study. Am J Clin Pathol 1980;73:427-33.
15. CARTER MD, THA S, McLOUGHLIN MG, OWEN DA. Collecting duct carcinoma of the kidney: a case report and review of the literature. J Urol 1992;147:1096-8.
16. MOSTOFI FK, DAVIS CJ, SOBIN LH. Histologic typing of kidney tumours. International Histologic Classification of Tumours. No. 25. Geneva: World Health Organization, 1998.
17. FUKUNAGA M. Sarcomatoid collecting duct carcinoma. Arch Pathol Lab Med 1999;123:338-41.
18. ROSAI J. Ackerman's surgical pathology. Philadelphia: WB Saunders, 1996.

Sažetak

KARCINOM BUBREŽNOG SABIRNOG KANALA: PRIKAZ TRIJU SLUČAJEVA

B. Krušlin, I. Glumbić, A. Reljić, H. Čupić, B. Ružić, G. Štimac i M. Belicza

Karcinom sabirnog kanala ili karcinom Bellinijeva kanala je visoko maligna neoplazma koja nastaje iz epitela bubrežnoga sabirnog kanala i čini otprilike 1% bubrežnih neoplazma. Karcinom sabirnoga kanala uglavnom ima agresivniji tijek od konvencionalnog karcinoma bubrežnih stanica. Opisane su metastaze u regionalne limfne čvorove, kosti, nadbubrežne žlijezde, pluća, kožu i meninge. U razdoblju od 1998. do 2000. godine u našoj je bolnici 161 bolesnik podvrgnut nefrektomiji zbog karcinoma bubrežnih stanica. Bolesnici su bili u dobi od 24 do 90 godina (srednja dob 59,5 godina), a bilo je 50 žena i 111 muškaraca. Karcinom sabirnog kanala dijagnosticiran je u trojice (1,9%) muških bolesnika u dobi od 79, 66 i 67 godina (srednja dob 71,0 godina). Bolesnici su došli s hematurijom udruženom s groznicom, gubitkom težine, bolovima i opipljivom masom u trbušnoj šupljini. Makroskopskim pregledom su tumori locirani u bubrežnoj meduli, a protezali su se u koru i obližnje masno tkivo. Histološki su tumori pokazivali tubulopapilarna, tubularna ili kruta područja. Imunohistokemijski je zabilježeno pozitivno bojenje citokeratinom, EMA i Ulex Europaeus aglutininom. Svi su bolesnici imali metastaze regionalnih limfnih čvorova, a dvojica su umrla kroz mjesec dana nakon operacije. Treći je bolesnik bio živ i bez znakova ponovljene bolesti šest mjeseci nakon dolaska u bolnicu.

Ključne riječi: *Neoplazme bubrega, patologija; Neoplazme bubrega, dijagnostika*