Micropapillary Carcinoma of the Renal Pelvis and Ureter

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Purpose: MPC located in the upper urinary tract is rare with only 2 cases reported to date. We report clinical and histopathological data on 26 patients to increase the knowledge of this rare entity.

Materials and Methods: A clinical and histopathological review was performed in 943 patients with a neoplasm in the renal pelvis or ureter, diagnosed between 1971 and 1998. We identified 26 patients with MPC. No patients were alive at the end of the study.

Results: Of the patients 11 had greater than 50% MPC and 15 had focal MPC (at least 10%). The incidence was 2.8%. Median patient age at diagnosis was 69 years (range 54 to 88) and the male-to-female ratio was 17:9. All except 4 patients had stage T3 disease or higher. Carcinoma in situ was identified in 64% of cases and vascular invasion was present in 81%. A total of 20 patients (77%) died of disease and only 7 survived longer than 5 years.

Conclusions: The prognosis is poor since most patients with MPC of the renal pelvis and ureter initially present with advanced disease. Stage for stage the prognosis is not different from that in nonMPC urothelial cell carcinoma. Surgery is curative in less advanced cases. However, radiotherapy and systemic chemotherapy appear to be ineffective.

Key Words: kidney, ureter, carcinoma, prognosis

MPC has been described in the breast, lungs, ovary, salivary glands and bladder.[1] Amin et al were the first to report urothelial tumors with MPC features in the bladder and they found these features to be associated with CIS, vascular invasion and a poor prognosis.[2] MPC is considered a variant of urothelial carcinoma because all reported cases have areas of traditional TCC in addition to MPC.[2] The MPCs described include slender, delicate filiform processes or tight papillary clusters of neoplastic cells surrounded by clear spaces resembling small, dilated lymphatic channels, which are in fact retraction artifact. This characteristic morphology is believed to be due to a reverse in the polarity of cancer cells, in which the stromal facing (basal) surface of the cells acquires apical secretory properties.[1]

To date 68 patients with bladder MPC have been reported, making the incidence less than 0.7% of all bladder tumors.[2–7] There are only 2 patients reported with transitional cell cancer with MPC in the ureter.[8,9] To our knowledge there are no reports of similar tumors in the renal pelvis. We report a series of 26 patients with the goal of increasing our understanding of this rare entity.

PATIENTS AND METHODS

Since 1958, all Swedish patients with malignant tumors have been reported to the Swedish Cancer Registry. We identified 943 patients from western Sweden with malignant ureteral and renal pelvic tumors diagnosed between 1971 and 1998. This area comprises the city of Göteborg, the counties of Älvsborg, Skaraborg and Bohuslän, and the northern part of Halland. The reported population of this area in 1998 was 1.65 million. Patients with UUTTs underwent surgery at 18 hospitals in the region. The initial histopathological examination was performed at 6 pathology departments.

Clinical records were reviewed by one of us (SH) at the hospitals where the patients were treated and followed. A histopathological review of the UUTTs was performed by one of us (SLJ). Recuts were made from the paraffin embedded blocks and stained with hematoxylin and eosin if the original slides were unavailable or unreadable. Approximately 99% of clinical records and 94% of histopathology records were available for review. Tumors were restaged according to the TNM system and graded according to the 1999 WHO classification system and the 1998 WHO/International Society of Urological Pathologists Consensus Classification, which is identical to the 2004 WHO classification system.[10–13] We identified 26 patients with focal areas of MPC (at least 10%) or with MPC as the predominant pattern.

RESULTS

Table 1 lists the results. The incidence of MPC (predominant pattern and focal) was 2.8% (26 of 943 patients). MPC was not seen in patients with noninvasive tumors (stage pTa). The incidence of MPC in patients with invasive UUTT was 4.4% (fig. 1). There was scant information in the clinical records on possible etiological factors. Four patients were or had been tobacco smokers but information was lacking on the others. Histopathological examination showed renal

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TABLE 1. *Clinical and histopathological data*

No. MPC:	
Predonminant	11
Focal	15
Median age (range)	69 (54–88)
No. men/women	17/9
No. tumor side:	
Rt	15
Lt	11
No. site:	
Renal pelvis	19
Ureter	6
Renal pelvis + ureter	1
No. tumors:	
1	20
Multiple	6
Median mm tumor size (range)	30 (5–95)
No. stage:	
T1	3
T2	1
T3	18
T4	4
No. associated CIS	16
No. vascular invasion	21
No. tumor configuration:	
Solid	2
Papillary	9
Mixed	14
No. surgery:	
Nephrectomy or nephroureterectomy	20
Partial ureteral resection	3
None	3
No. other treatment:	
External beam radiotherapy	4
Systemic chemotherapy	2
No. bladder Ca	4
No. cause of death:	
Urothelial Ca	20
Other disease	6

papillary necrosis in 2 patients, which in Sweden was most often caused by the abuse of analgesics containing phenacetin. One patient had been treated with external beam radiation for ovarian carcinoma 15 years previously.

The presenting symptom was macroscopic hematuria in 20 patients, flank pain in 2 and an enlarged cervical lymph node in 1. Three patients had no symptoms but radiological imaging was done due to microhematuria in 1, bladder cancer followup in 1 and as followup after pneumonia in 1. A total of 20 patients were treated with nephrectomy or nephroureterectomy and 3 underwent partial resection. The diagnosis was established at autopsy in 3 patients who did not undergo surgery. Two of these patients had macrohematuria and were in poor general condition, while the third presented with cervical lymph node metastases at initial diagnosis.

One patient had associated urothelial low grade tumor (WHO 1). The other 25 patients had high grade tumors, which were grades 2 and 3 in 3 and 22, respectively. Urothelial carcinoma was identified in all patients and it was the predominant tumor type in all except 2 who had squamous cell carcinoma. Mucin producing adenocarcinoma was focally present in 2 patients.

Two patients had biopsy or computerized tomography verified local recurrences after external beam radiotherapy to the renal bed. Another 2 patients were treated with external beam radiotherapy for local recurrence but their general condition deteriorated and the outcome response for this treatment could not be evaluated. One of 2 patients treated with systemic chemotherapy was treated with modern agents. This patient, who had pulmonary and vertebral metastases, was treated with 4 courses of methotrexate, vinblastine, doxorubicin and cisplatin, followed by 5 courses of gemcitabine. He had a partial response but ultimately died of lung metastases 17 months after the start of chemotherapy. He had focal MPC in a renal pelvic tumor. The metastases were not biopsied.

Seven patients survived beyond 5 years (tables 2 and 3). Of particular interest is patient 2, who underwent extensive lymph node dissection, including multiple positive nodes with perinodal extension of MPC. He died of intercurrent disease 78 months later. Also of interest is patient 5, who was diagnosed with local recurrence 74 months after nephroureterectomy. Of patients with MPC who had stage T3 at initial diagnosis 23% survived beyond 5 years compared to 18% with stage T3 urothelial carcinoma and without MPC. The prognosis in patients with stage T3 squamous cell carcinoma was even worse, in that only 7% survived 5 years or more.

In 4 patients associated, recurrent bladder cancer was treated with repeat transurethral resections. Three of these patients died of advanced bladder cancer. Early cystectomy at the time when bladder cancer was organ confined could possibly have changed the outcome.

The 2 patients with solid tumors and 12 of the 14 (86%) with mixed papillary and solid tumors died of disease compared to 5 of 9 (56%) with papillary tumors. Vascular invasion was also associated with an adverse outcome (fig. 2). Of 21 patients with vascular invasion 19 (91%) died of disease compared to 1 of 5 (20%) without vascular invasion. Metastases were confirmed by radiological imaging in 14 patients. The most frequent sites were the regional lymph nodes, liver, lung and bone system (fig. 3).

DISCUSSION

In this report to our knowledge we present the first 19 patients with MPC of the renal pelvis and 7 with MPC of the ureter. There are only 2 earlier reported cases of MPC of the ureter.

We have previously reported a 0.7% incidence of MPC in the bladder.[3] The percent would be 1.5% if stage Ta tumors were excluded from that report. Actually there is only 1 reported patient with noninvasive bladder MPC of the total

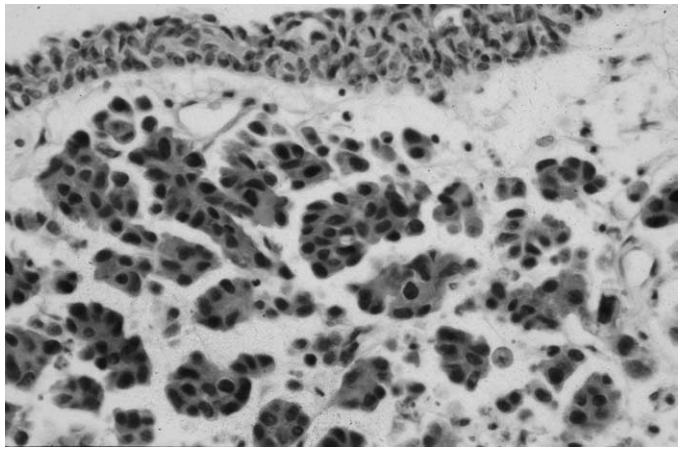

FIG. 1. MPC with tight atypical tumor nests surrounded by empty spaces reminiscent of ovarian papillary serous carcinoma. Note severely dysplastic surface urothelium.