Micropapillary urothelial carcinoma of the ureter

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SUMMARY
Micropapillary urothelial carcinoma (MPUC) is a rare aggressive variant of urothelial carcinoma, associated with advanced tumor stage, high tendency to invade lymphovascular spaces, and metastasize to lymph nodes and other organs. Therefore, it has a poor prognosis. One of the most prominent histological features is the presence of small, round empty spaces surrounding infiltrating tumor nests. If detected, even a small focus of micropapillary pattern may be therapeutically significant; the higher proportion of micropapillary component, the worse the prognosis. Radical nephroureterectomy is the treatment of choice even in the setting of superficially invasive disease. Although, MPUC has been well studied in urinary bladder, only a few cases of MPUC in upper urinary tract have been described. We are describing a case of a 79-year old woman with micropapillary urothelial carcinoma involving ureter and review the literature of this rare entity.

Keywords: transitional cell carcinoma – micropapillary carcinoma – ureter – urinary bladder

Mikropapilární uroteliální karcinom ureteru

SOUHRN
Mikropapilární uroteliální karcinom (MPUC) je vzácná agresivní varianta uroteliálního karcinomu, asociovaná s pokročilým klinickým nádorovým stadiem, s vysokou tendencí k lymfovaskulární invazi a k metastázám do lymfatických uzlin a dalších orgánů. Proto má špatnou prognózu. Jedním z nejvýraznějších histologických znaků je přítomnost malých okrouhlých opticky prázdných prostorů kolem infiltrujících skupin nádorových buněk. Identifikace i malé oblasti mikropapilárního růstu může být terapeuticky významná - čím větší je mikropapilární komponenta, tím horší je prognóza. Radikální nefroureterektomie je léčnou volby dokonce i u povrchově invazivních nádorů. Ačkoli je MPUC dobře známý v močovém měchýři, v horních vývodných močových cestách bylo zaznamenáno jen několik případů. Naše kazuistika přináší popis případu 79-ti leté ženy s MPUC v ureteru s přehledem literatury.

Klíčová slova: uroteliální karcinom – mikropapilární karcinom – uteter – močový měchýř

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Micropapillary urothelial carcinoma (MPUC) is a rare aggressive variant of urothelial carcinoma usually occurring in urinary bladder, while minority of tumors arises from urinary pelvis and ureter. Because of their low incidence, most studies associate MPUC of pelvis and ureter aligning them as micropapillary carcinoma of upper urinary tract. Several studies have confirmed that MPUC is associated with advanced tumor stage at time of diagnosis. It has high tendency to invade lymphovascular spaces, and metastasize to lymph nodes and other organs (1–4). Micropapillary carcinoma is a unique histological variant occurring in several other organs including the breast, lung, salivary gland and colon with high stage at time of diagnosis and poor prognosis compared to conventional carcinomas arising in the same organ (5). Although, MPUC has been well studied in urinary bladder, only few cases of MPUC in upper urinary tract have been described (7–13). We report a case of MPUC of ureter and review the literature.

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CASE REPORT

A 79-year old woman was admitted to our hospital because of left lumbar pain and haematuria. Intravenous urography disclosed small organic filling defect in upper part of left ureter. Diagnostic ureteroscopy with biopsy of small, sessile tumor was performed. Pathohistologic examination on small biopsy showed small clusters and cords of atypical cells displaying hyperchromatic nuclei. Left radical nephroureterectomy was performed one week afterwards.

Grossly, the kidney showed no remarkable changes. Ureteral lumen was obstructed by gray-white, poorly circumscribed tumor spreading to the ureteral wall (Fig. 1).

Microscopically, tumor found in ureter consisted of small nests of tightly cohesive tumor cells displaying hyperchromatic nuclei with scant rim of lightly eosinophilic cytoplasm. The tumor was composed entirely of micropapillary component and showed invasive growth pattern affecting inner part of muscular layer of the ureter (Fig. 2, 3). The tumor nests showed distinctive retraction artifacts from the surrounding stroma. No spread beyond muscularis was observed, mul-

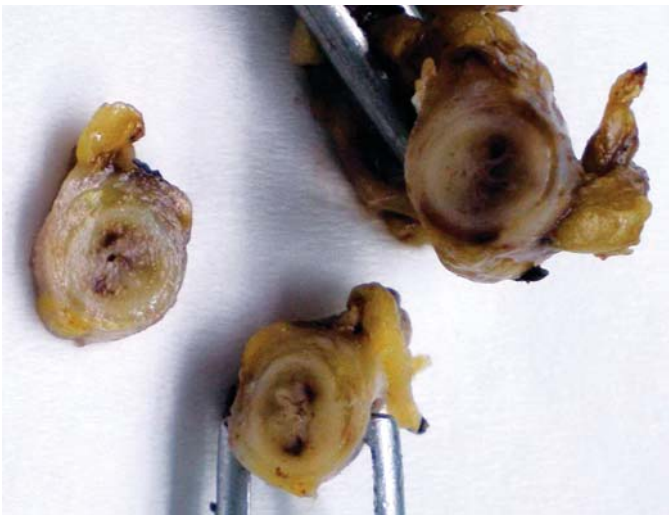

Fig. 1. Ureteral lumen obstructed by gray-white poorly circumscribed tumor, spreading to the ureteral wall.

tiple perirenal lymph nodes showed only reactive changes (i.e. T2N0Mx).

Carcinoma in situ of urinary bladder was found 30 months later during follow up and treated endoscopically. Routine clinical and pathohistological examination, three years after the initial resection showed no signs of recurrent tumor or metastatic spread.

DISCUSSION

The micropapillary pattern of urothelial carcinoma (MPUC) is a rare type of growth pattern first described by Amin et al., generally associated with high-grade urothelial carcinoma (1). MPUC is more common in urinary bladder (12,14). To our knowledge, 50 cases have been described in upper urinary tract. Most of them were diagnosed at a high tumor stage (T2–T4). Patients' mean age was 68.7 years with overall male predominance (M/F = 2.06/1) (7–13).

Preoperative urine smear finding of tightly bound papillary/spherical clusters comprised of highly atypical cancer cells is the most specific cytological finding in the urine of patients with MPUC (15).

Two different patterns of MPUC have been described in the urinary tract (16–18). More common is the invasive pattern showing micropapillary structures surrounded by clear spaces resulting from retraction artifact. Noninvasive pattern is composed of small, slender, finger-like projections lined by atypical cells with or without central fibrovascular cores. Recent studies have shown that there are no immunohistochemical markers that may be reliable in the distinction between invasive micropapillary carcinoma from typical invasive urothelial carcinoma (19). On the other hand, Sangoi et al. have found that invasive micropapillary carcinoma more commonly showed immunoreactivity for MUC1, CA125 and HER2/Neu compared to invasive urothelial carcinoma with retraction artifact, where only MUC1 reached statistical significance (19). Ching et al. found that HER2 gene amplification occurs frequently in the micropapillary variant of urothelial carcinoma and is significantly associated with immunohistochemically positive protein expression. They also found that 53 % of samples had aneusomy of chromosome 17, suggesting inherent genomic instability in this variant of urothelial carcinoma (20).

Most of studies have confirmed that MPUC is associated with advanced tumor stage at the time of diagnosis, characterized by aggressive behaviour and poor prognosis. Samaratunga and Khoo (5) noted that the higher proportion of micropapillary component, the worse the prognosis. If detected, even a small focus of micropapillary pattern, may be therapeutically significant and radical surgical therapy should be offered to patients because even in the absence of muscularis propria invasion in the biopsy, muscle invasion is often assumed (18,19).

Because conservative intravesical therapy with Bacillus Calmette-Guerin has shown poor success in micropapillary urinary bladder carcinoma patients, some authors have proposed early radical cystectomy for patients with surgically resectable disease in the absence of muscularis propria invasion on the initial biopsy (21). Guo et al. suggest that nephroureterectomy may be curative in some patients in whom MPUC of the upper urinary tract is identified at an early stage (11). Radiotherapy and chemotherapy have been reported to yield poor response, and should be applied only for salvage treatment. Holmang et al. reported that out of 26 patients who had MPUC of the upper urinary tract, 20 patients (77 %) died of the disease and only 7 survived for longer than 5 years (10). In our case radical nephroureterectomy was performed and on a 3-years follow-up there is no sign of recurrent tumor or metastatic disease. The importance of an early diagnosis for the prognosis of micropapillary carcinomas is obvious.

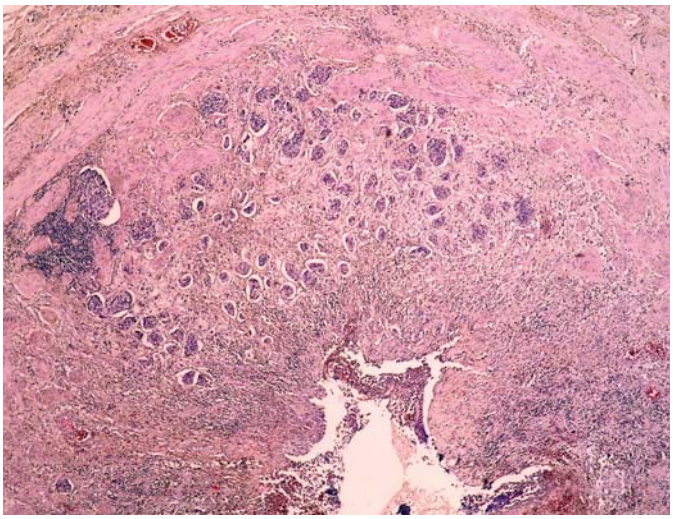

Fig. 2. Micropapillary urothelial carcinoma with invasive growth pattern affecting muscular layer of the ureter. HE, 40x.

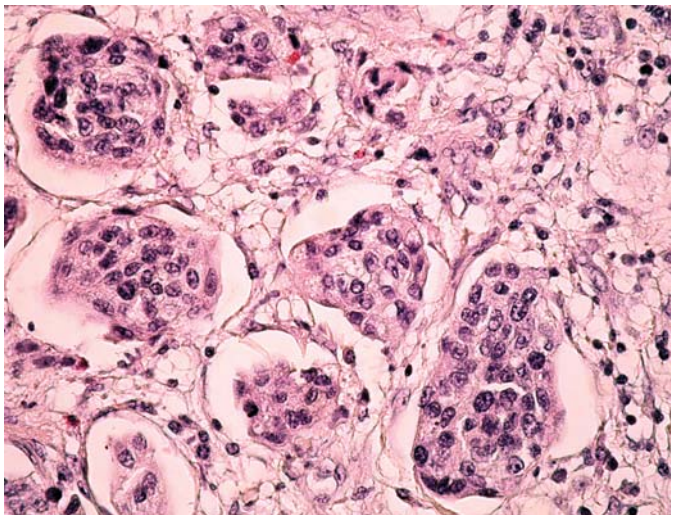

Fig. 3. Micropapillary structures surrounded by clear spaces resulting from retraction artifact. HE, 400x.

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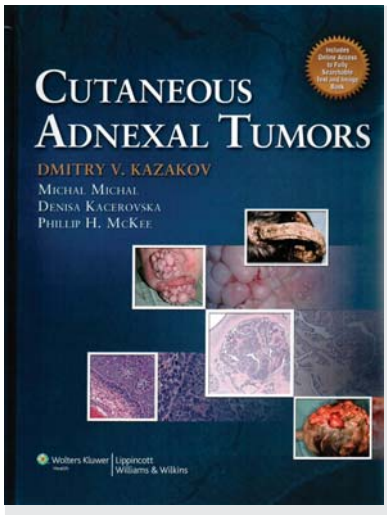

Cutaneous Adnexal Tumors

RECENZE

Kazakov D, Michal M, Kacerovská D, McKee PH

Wolters Kluwer / Lippincott Wiliams &Wilkins (Philadelphia, PA); 2012: 814 stran.

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Predovšetkým, jedná sa o mimoriadne kvalitnú monografiu, ktorá by nemala chýbať na stole žiadneho patológa ktorý sa v praxi stretáva s nádormi kože. Adnexálne kožné nádory sú vo všeobecnosti pomerne vzácne a ich diagnostika je náročná. Štandardné učebnice dermatopatológie (s výnimkou niekoľko málo monografií) sa téme venujú pomerne stručne, ilustrácie jednotlivých jednotiek ani zďaleka nepokrývajú celé spektrum histopatologických variácií a časopisecká literatúra s neprehľadným množstvom synoným je pre všeobecných patológov skôr mätúca ako nápomocná.

Predkladaná monografia je prehľadne didakticky členená do deviatich kapitol: 1. Lézie s predominantne apokrinnou a ekrinnou diferenciáciou, 2. Lézie s predominantne folikulovou diferenciáciou, 3. Lézie s predominantne sebaceóznou diferenciáciou, 4. Lézie s myoepitelovou diferenciáciou, 5. Lézie s multilineárnou diferenciáciou, 6. Adnexálne nádory na špecifických miestach, 7. Rôzne lézie, ktoré môžu adnexálne tumory napodobovať, 8. Tumory skin-adnexálneho typu v iných orgánoch a 9. Syndrómy sprevádzané kožnými adnexálnymi tumormi. Kapitoly 6-8 sú v takejto publikácii unikátom, integrujú problematiku do kontextu všeobecnej patológie a umožňujú patológom bez dermatopatologického tréningu lepšie pochopenie morfológie adnexálnych nádorov. Adnexálne nádory (benígne, menej často malígne) môžu byť indikátorom niektorého z hereditárnych syndrómov, preto je kapitola 9 povinným čítaním pre všetkých patológov. Veľkým bonusom je, že okrem kožných lézií je pri jednotlivých syndrómoch pomerne podrobne opísaná a ilustrovaná aj extrakutánna patológia. Pre štúdiachtivých čitateľov je k dispozícii viac ako tri tisíc najdôležitejších referencií.

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- M. Švajdler ml. -