Urothelial carcinoma of the bladder with adamantinoid (ameloblastoma-like) features. Case report

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An unusual case of bladder urothelial carcinoma that showed areas of adamantinoid (ameloblastoma-like) morphology is described. The tumor occurred in 69-ys-old patient. It was a recurrence of non-invasive low-grade urothelial carcinoma which had been resected 3 years ago. Currently, two transurethral resections were performed (to ensure the tumor removal was complete). The tissue from both resections contained urothelial carcinoma without invasion in lamina propria. Histologically, besides of conventional morphology of low- and high-grade papillary urothelial carcinoma, numerous foci of the tumor showed inverted growth with ameloblastoma-like features such as reversed polarization of basal cells and loose network-like arrangement of the cells in the lobules. At present, the patient is well one month after the resection, and he will receive intravesical BCG treatment. We suppose that adamantinoid (ameloblastoma-like) urothelial carcinoma can be regarded as a variant of inverted urothelial carcinoma.
Keywords: urothelial carcinoma, urinary bladder, transurethral resection, ameloblastoma, adamantinoid

Urotelový karcinóm močového mechúra s adamantinoidnou morfológiou. Kazuistika
Prezentujeme prípad urotelového papilokarcinómu s neobvyklou morfológiou, ktorá je podobná ameloblastómu (adamantinómu). Išlo o rekurenciu low-grade noninvazívneho karcinómu močového mechúra u 69-ročného muža. Tumor bol odstránený transuretrálnou resekciou v dvoch etapách. Histologicky šlo o urotelový karcinóm, high-grade, bez invázie do strómy. Okrem tradičnej papilárnej a invertovanej morfológie obsahoval tumor invertované lobuly s polarizáciou bazálnych buniek a dehiscenciou, resp. retikuláciou epitelu vnútri lobulov. Stav pacienta je mesiac po resekcii primeraný a je u neho plánovaná BCG terapia. Predpokladáme, že urotelový karcinóm s adamantinoidnou morfológiou možno považovať za podtyp urotelového karcinómu s invertovaným rastom.
Kľúčové slová: urotelový karcinóm, močový mechúr, transuretrálna resekcia, ameloblastóm, adamantinoidný

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Introduction

Common urothelial carcinomas (UC) consist of stratified urothelial epithelium with nuclear atypia and mitoses[(1)]. Histological diagnosis of these cases is usually straightforward and their biological behavior is well-known. However, there exist variants of UC which show unusual histological and immunohistochemical features. These tumor can cause difficulties, regarding both histological diagnosis and subsequent treatment. Spectrum of variant types includes squamous, glandular, micropapillary, nested, microcystic, inverted, villous-like, basaloid, sarcomatoid and lymphoepithelioma-like[(1-3)]. Recently, we have seen in our practice a case of UC with papillary and inverted pattern[(4)] which, moreover, showed ameloblastoma-like (adamantinoid) morphology with reversed polarization of basal cells and loose, network-like arrangement of cell islands[(5-7)]. We would like to briefly present this unusual case here.

Case report

A 69-ys-old male was admitted for recurrence of non-invasive low-grade UC that had been resected 3 years ago, without subsequent chemotherapy or BCG therapy. Otherwise, his medical history includes stage 1 hypertension, type 2 diabetes mellitus, obesity, metabolic syndrome, combined hyperlipoproteinemia, and hyperuricemia. Recent control cystoscopy revealed 4 polypoid tumors in the posterior wall of the bladder, measuring 5 cm x 4 cm, 3 cm x 2 cm, 2 cm x 2 cm, and 1 cm x 1 cm, respectively. The lesions were removed by two subsequent transurethral resections (TUR). The tissue fragments were examined histologically and immunohistochemically. In both TUR specimens, we have found common papillary UC with areas of both high- and low-grade and with focal inverted growth pattern. Invasion into the lamina propria was not present, and numerous pieces of muscularis propria did not contain tumor infiltration as well. In addition to common histological features of UC, we have seen areas with adamantinoid (ameloblastoma-like) morphology (**figures 1-4**). They were found in approximately one third of the tumor tissue. These areas included islands and cords of the basaloid appearing epithelium, with reversed polarization of the nuclei of the basal cells (**figures 3 and 4**). The cells inside the islands and cords showed loss of cohesion, resembling reticulated change seen typically in ameloblastoma[(5-7)]. In addition, numerous lobules contained round hyalin-

Figure 1. *Low-power shows adamantinoid lobules (right) and conventional UC (left).*

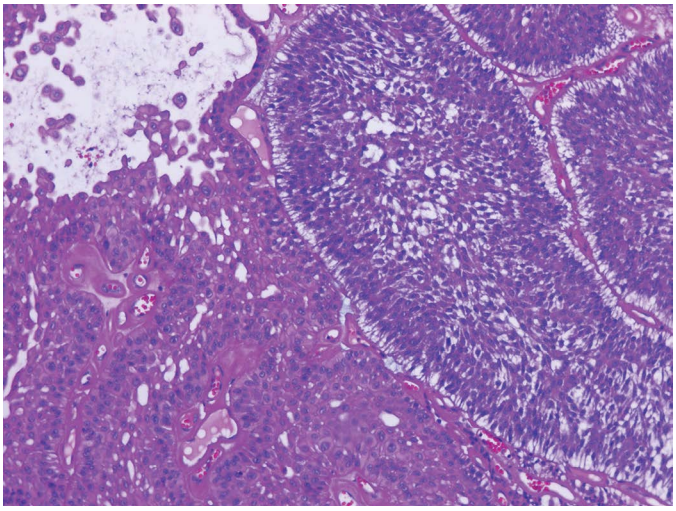


Figure 2. *Superficial papillae show reversed polarity of the basal cells.*

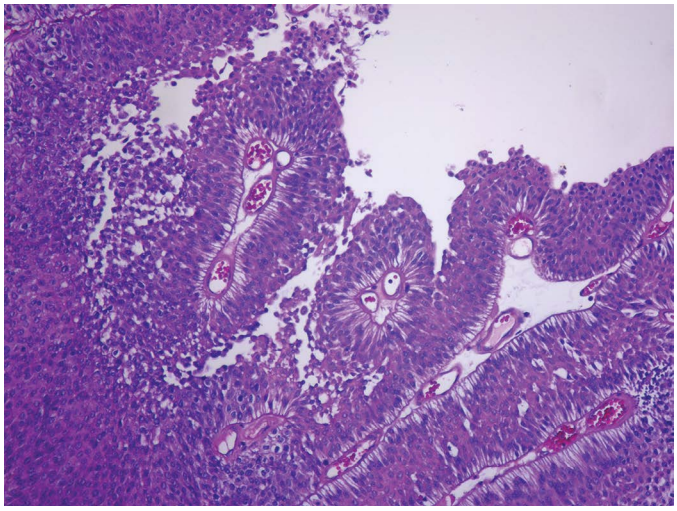


Figure 3. *Some of the lobules contain gland-like spaces (right and bottom).*

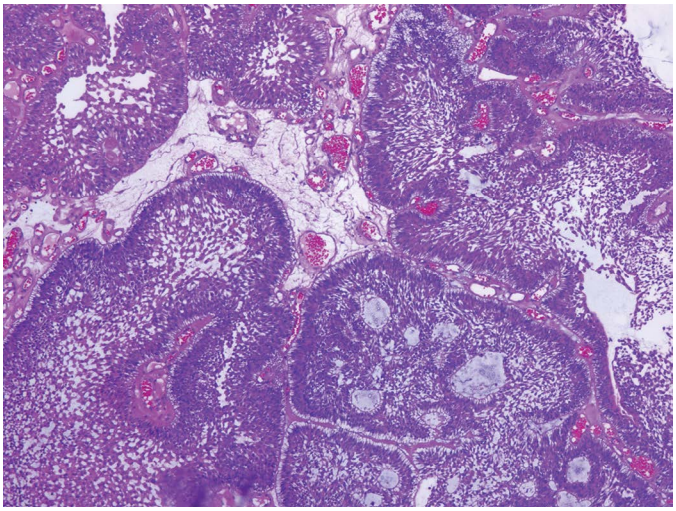


Figure 4. *Gland-like spaces are clearly developed due to inclusion of stroma into the lobule (creating "solid papillary" appearance). Arrow indicates direct transition between perilobular and hyalinized intralobular stroma.*

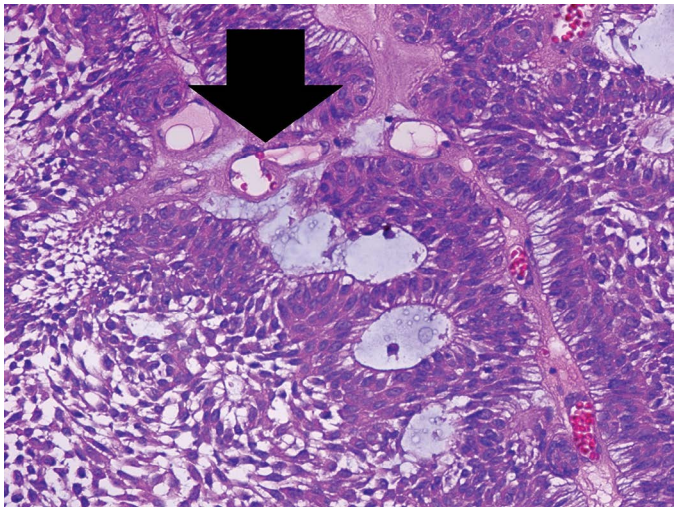
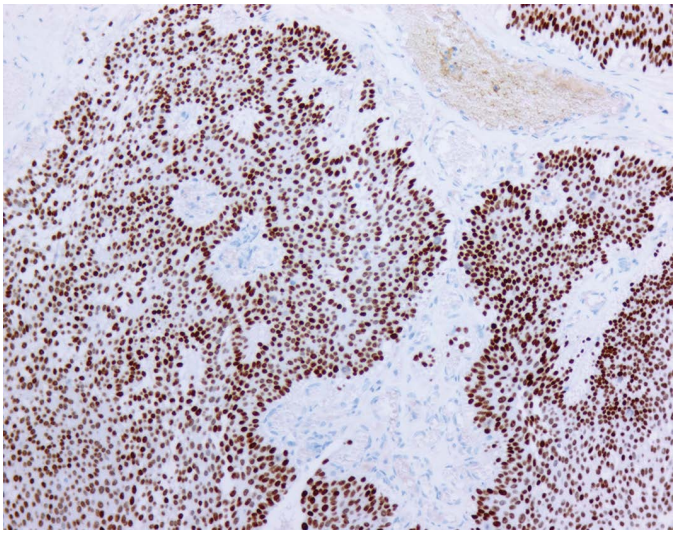


Figure 5. *Expression of GATA3 in the tumor.*



ized and edematous cores of papillae that mimicked glands. These pseudoglands showed, however, polarized basal cells indicating their stromal (non-glandular) nature (**figure 4**), and they were negative for mucicarmine. In addition, we reviewed slides from the tumor removed three years ago. We have found only focal reversed polarity of the basal cells in some papillae (as depicted in **figure 2**), without apparent adamantinoid lolules.

For immunohistochemistry, following antibodies were used: CK20 (clone Ks20.8), GATA3 (L50-823), p53 (DO-7), CK HMW (34BE12), p63 (DAK-P63), p40 (poly), CK5/6 (D5/16B4), CK19 (RCK108), HER2 (4B5), glypican 3 (GC33), alpha-fetoprotein (poly), CDX2 (DAK-CDX2), beta-catenin (14) calretinin (DAK-Calret 1), alpha-smooth muscle actin (1A4), and CD56 (123C3). The tumor cell were positive for GATA3 (**figure 5**), p63, p40, CK19, CK-HMW, CK20 and CK5/6. P53 was positive in 30% of tumor cells. Neoplastic cells were negative for CDX2, alpha-fetoprotein, beta-catenin, calretinin, glypican 3,

CD56, alpha-smooth muscle actin, and HER2. Currently, the patient is well one month after the tumor resection, and he will receive intravesical BCG treatment.

Discussion

The present tumor shows focal unusual features that resembled ameloblastoma (adamantinoma), such as reversed polarization of basal cells and loose and network-like arrangement of the cells in the lobules[5-7]. To our knowledge, this morphology was not explicitly described in UC before. Regarding reverse cell polarity in urothelial lesions, we have found in the literature one case of inverted glandular papilloma[8]. Sundaram et al. shows in their Fig. 1 the reversed polarity of the glandular epithelium. In common UC, one can sometimes see subtle reversed polarity with subnuclear clearing of the cytoplasm, as depicted for example in Figure 2 in study by Comperat et al.[9]. However, these features are so mild that they do not resemble ameloblastoma. So-called adamantinoid morphology, typical of ameloblastoma, was rarely reported in non-odontogenic tumors. Well known are adamantinoid basal cell carcinoma[10], adamantomatous craniopharyngioma[7], and adamantinoid trichoblastoma[11]. Differential diagnosis in our case included UC with glandular differentiation and rare yolk sac tumor with glandular and reticular pattern[1-3,12,13]. As mentioned previously, true glands in UC contain epithelial mucin positive secretion, and this contrasts with stromal features in gland-like spaces seen in our case[1-3]. Yolk sac tumor of the bladder or UC with yolk sac tumor differentiation can contain primitive endodermal cells with subnuclear vacuoles and with reticular pattern[12,13]. However, our tumor was negative for markers of yolk sac tumor, such as alpha-fetoprotein, glypican and CDX2.

Estimation of biological aggressiveness of presented UC is difficult, and observation of additional cases is needed. Currently, it seems that among UCs with variant histology, only micropapillary, sarcomatoid, squamous cell and basaloid types indicate worse prognosis, although knowledge is still limited[2]. In our case, the tumor showed features of high-grade UC with both exo- and endophytic inverted growth and without stromal invasion. Therefore, we suppose that behavior of the tumor will be similar to common high-grade non-invasive UC and that management of the patient should be in accord with current guidelines for such tumors.

In sum, we described unusual case of UC with adamantinoid (ameloblastoma-like) morphological features seen in substantial part of the lesion. The tumor showed both high- and low-grade areas, and it was non-invasive. Additional similar cases are needed for better knowledge of these tumors.

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