Adenocarcinoma of the urinary bladder, mesonephroid type: a rare case

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Abstract

Primary adenocarcinoma of the urinary bladder is a rare disease. It occurs in 0.5-2% of all bladder cancers and is discussed as the malignant counterpart of nephrogenic adenomas. We report a 46-year-old white female presented with gross hematuria for clinical examination. Histopathology revealed pT2, Pn1, L1, G2 adenocarcinoma of the bladder and carcinoma *in situ* according to the TNM classification. Computed tomography scan diagnostic was unremarkable. Patients with adenocarcinoma of the urinary bladder should be treated vigorously and without time delay. Only 7 cases of adenocarcinoma in the urinary bladder (mesonephroid) have been described until now. We present a case of clear cell adenocarcinoma of the urinary bladder, mesonephroid type that early diagnosed and till now 3 months after the cystectomy without symptoms and without complications.

Introduction

Primary adenocarcinoma of the urinary bladder is a rare disease. It occurs in 0.5-2% of all bladder cancers and is discussed as the malignant counterpart of nephrogenic adenomas. Clear cell adenocarcinoma (CCA) or mesonephroid adenocarcinoma is a variant of primary adenocarcinoma of the bladder and is an extremely rare neoplasm. Data on incidence are lacking. Only 7 cases of adenocarcinoma in the urinary bladder (mesonephroid) have been described until now. Mesonephroid adenocarcinomas occur in the ovaries and in congenital diverticula of the urinary bladder and are very common in women.[1,2] The first case of a mesonephroid adenocarcinoma was described in 1968 by Dow and Young.[3] Similar reports have been published since then by various authors.[4-9] The exact histogenesis was under discussion. Hematuria with any accompanying dysuria is the predominant clinical symptom, while women are diagnosed twice as often as men.

Case Report

A 46-year-old white female presented with gross hematuria for clinical examination. Her past medical history was, apart from hypothyroidism, unremarkable. Initial cystoscopy indicated multifocal bladder tumor (>3 cm) with papillary and solid aspects. The tumor was completely resected by bipolar transurethral resection (TURBt).

Histopathology revealed pT2, Pn1, L1, G2 adenocarcinoma of the bladder and carcinoma in situ according to the TNM classification. CT-scan diagnostic was unremarkable. Four weeks after initial diagnosis the patient was scheduled for radical cystectomy and Mainz I pouch. Final histopathology showed no remaining adenocarcinoma, but still carcinoma in situ. One of 39 lymph nodes were positive [pTis, pN1 (1/39), L0, V0, R0]. The perioperative course of the patient was unremarkable. For voiding the patient has learned to perform self-catheterization.

Results

The histological examination of tissue samples after transurethral resection of the tumor revealed a papillary urothelial carcinoma with muscle invasion and concomitant chronic cystitis. To exclude metastases a CT-scan of abdomen and thorax was performed, which showed a wide circular bladder wall thickening without evidence of organ-border growth. A lymphatic or organ metastasis was not detected. The skeletal Scintigraphy showed no evidence of metastasis. Histologically, an invasive, moderately differentiated clear cell adenocarcinoma, which corresponded to mesonephroid carcinoma histologically and immunohistochemically was found. The neoplastic cells express strong cell membrane positivity in staining for CK7 and for CD-10 and CA-125 with a weak positivity in staining for CK20 and focal positivity in staining for Ck-19 and Ck8/18. Nuclear positivity for S-100-P and for GATA-3. Cytoplasmic positivity is evident in the staining for β-HCG with negativity in the staining for CD117, BerEp4, TTF-1, estrogenic receptor, Progestron receptor, CDX-2, PSA, AFP, and S-100 (Figures 1 and 2). The immunomarkers S-100-P und GATA-3 are specific for cells in the urinary tract.

Discussion

Bladder cancer is the second most common malignant tumor of the urogenital tract. Primary malignant epithelial bladder cancers derives from the urothelium in 90%, less frequent are the squamous cell (3-5%) and adenocarcinomas (0.2-2%) as well as sarcomas or metastases from other primary tumors. The primary CCA of the urinary bladder is different from those of the urachus or metastases from other organs, which show features of adenocarcinomas (stomach, colon/rectum, endometrium, prostate, breast), Table 1.

Men are affected three times as often as women with urothelial bladder cancer whereas women show a higher incidence for clear cell adenocarcinoma of the bladder. In general, bladder cancer is a disease of the elderly. Primary adenocarcinoma commonly appear at the trigonum, the lateral bladder walls and the bladder dom, while the urachale carcinoma is common in the bladder roof and rarely found in front of the bladder wall.[10-14] Among the five histopathological variants of primary urinary bladder adenocarcinoma including the glandular carcinomas, papillary adenocarcinomas of the colloidal, the Signet ring cell cancer and ultimately the mesonephroid or clear cell carcinoma.[10,11,13,15,16] These can be histologically as a single structure or as a combination of several variants exist.[12] In cases of adenocarcinoma (mesonephroid) the female/male ratio is of 2:1.

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Mesonephroid adenocarcinoma may also occur in the urethra, and these are described frequently in adult females.[17]

Very difficult - because of the great histological similarity - is the distinction of benign nephrogenic metaplasia to mesonephroid adenocarcinoma.[6,10,17] The nephrogenic metaplasia is a rare lesion, which is confined to the lamina propria of the lower urinary tract.[18] They can result from traumatic injury to the urothelial mucosa. Another explanation is mesonephritischic remnants in the lower urinary tract, especially in the area of the trigone of the bladder or the urethra. A common presence of a nephrogenic metaplasia is possible in the transitional cell carcinoma.

The lesion was initially described by Davis in 1949 as a hamartoma. In 1950 Freidman and Kuhlenbeck published eight additional cases as nephrogenic adenomas due to their characteristic formation of epithelial tubules, comparable to renal collecting ducts.[19] Characteristically epithelial cells of nephrogenic adenomas show clear cell cytoplasm with vacuoles and uniform nuclei without mitoses in the benign form. The malignant form is characterized by mitotic figures and/or invasion into the muscle. In superficial tumors is difficult to make a distinction between nephrogenic adenomas and mesonephroid adenocarcinomas.[6]

Sorensen *et al.*[18] reported that nearly all cases of nephrogenic metaplasia derive from preceding traumatic lesions of the urothelium. The interval until the formation of metaplasia can vary from one month to several years. Possible mechanisms are usually responsible such as traumatic injury, infection, instrumental manipulation, catheterizations, and stones, congenital malformations of the urogenital tract, immune suppression or immunotherapy using BCG instillations made.[18]

Mesonephroid tumors with clear cell and papillary morphology as well as tubular structures emanating from the ovary or the female genital tract are described frequently. They arise from remnants of mesonephritic tissues, most notably the Mullerian duct for men and women. Similar tumors have been described in the seminal vesicles and the prostatic urethra.[5] Differential diagnosis is clear cell variants of urothelial carcinoma but differs from these by the absence of pathognomonic tubular growth.[17] Mesonephroid adenocarcinoma may show an extremely aggressive and invasive growth behavior resulting in an early indication for radical surgery.[4,6] Superficial tumors can be controlled by complete

Table 1. World Health Organization histological classification of tumours of the urinary tract (2004).

Infiltrating urothelial carcinoma 8120/31	With squamous differentiation With glandular differentiation With trophoblastic differentiation Nested Microcystic Micropapillary 8131/3 Lymphoepithelioma-like 8082/3 Lymphoma-like Plasmacytoid Sarcomatoid 8122/3 Giant cell 8031/3 Undifferentiated 8020/3
Non-invasive urothelial neoplasias	Urothelial carcinoma in situ 8120/2 Non-invasive papillary urothelial carcinoma, high grade 8130/23 Non-invasive papillary urothelial carcinoma, low grade 8130/21 Non-invasive papillary urothelial neoplasm of low malignant potential 8130/1 Urothelial papilloma 8120/0 Inverted urothelial papilloma 8121/0
Squamous neoplasms	Squamous cell carcinoma 8070/3 Verrucous carcinoma 8051/3 Squamous cell papilloma 8052/0
Glandular neoplasms	Adenocarcinoma 8140/3 Enteric Mucinous 8480/3 Signet-ring cell 8490/3 Clear cell (mesonephric carcinoma) 8310/3 Villous adenoma 8261/0
Neuroendocrine tumours	Small cell carcinoma 8041/3 Carcinoid 8240/3 Paraganglioma 8680/1
Melanocytic tumours	Malignant melanoma 8720/3 Nevus
Mesenchymal tumours	Rhabdomyosarcoma 8900/3 Leiomyosarcoma 8890/3 Angiosarcoma 9120/3 Osteosarcoma 9180/3 Malignant fibrous histiocytoma 8830/3 Leiomyoma 8890/0 Haemangioma 9120/0 Other
Haematopoietic and lymphoid tumours	Lymphoma Plasmacytoma 9731/3
Miscellaneous tumours	Carcinoma of skene, cowper and littre glands Metastatic tumours and tumours extending from other organs

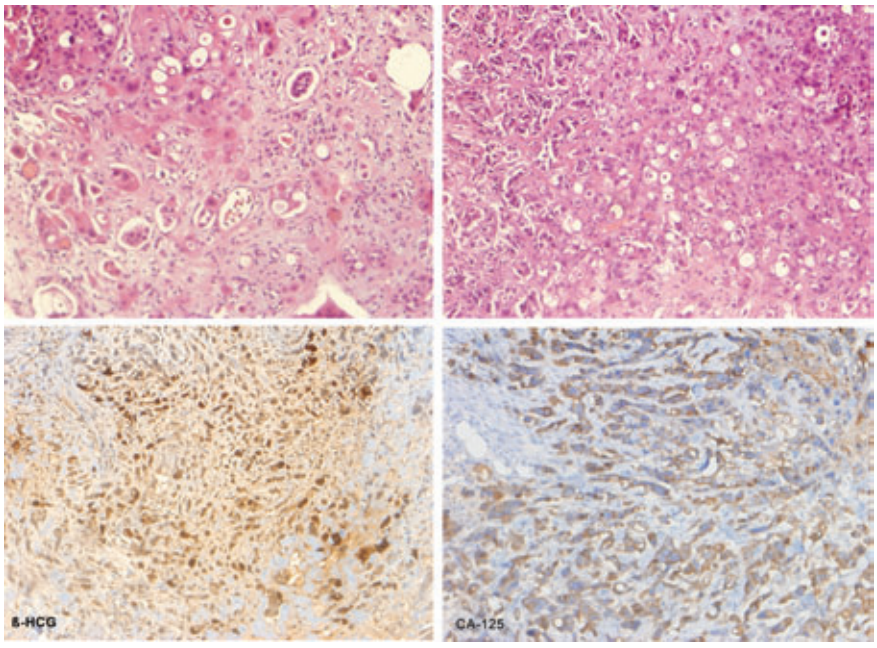

Figure 1. Haematoxylin & Eosin that showed the acinar differentiation of the tumor with signet ring cells. Immunohistochemical markers (CA-125, β-HCG) which are common positive in these tumors.

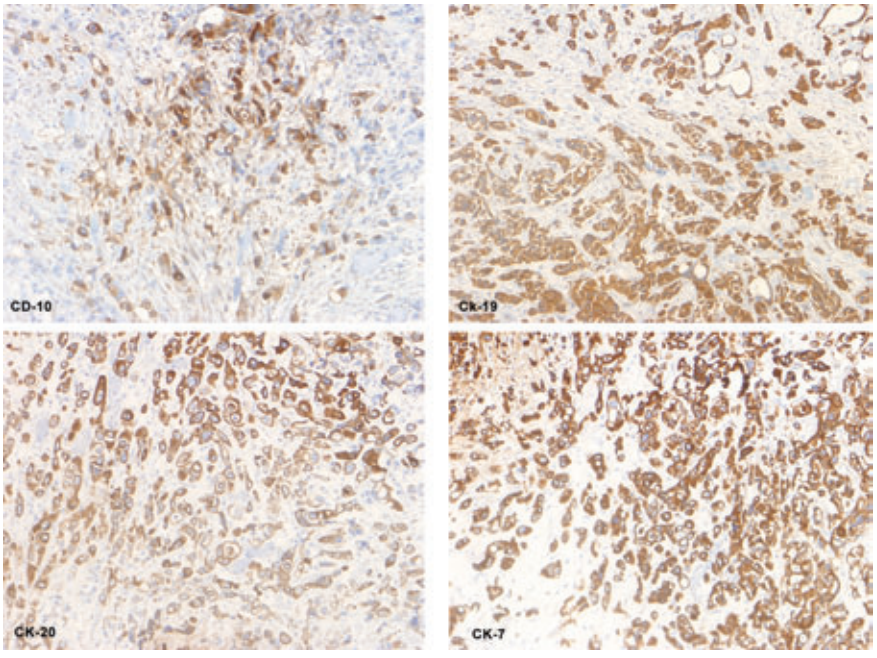

Figure 2. Variable immunomarkers (CK7, Ck20, CK19 and CD-10) which are common positive in urothelial carcinoma.

transurethral resection. In one case, a mesonephroid adenocarcinoma was successfully applied to adjuvant systemic chemotherapy.[9] However, the long-term data is lacking. The radiosensitivity of this tumor entity is still unclear. The prognosis of all histological types of adenocarcinoma of the bladder, including the mesonephroid carcinoma is poor and depends primarily on the tumor stage (depth of invasion).[11] One possible explanation is a late diagnosis in many cases with advanced tumor stages as a consequence. Consequentely, the reported 5-year survival rate is low (18-55%).[11,13]

Conclusions

In conclusion, this case demonstrates the importance of early detection of these subtypes of urinary bladder carcinoma and the requirement of clinical data and long follow-up of patient after the operation to avoid relapse and metastasis which may give better outcome and prognosis. Our immunohistochemical findings support also an urothelial origin for most clear cell adenocarcinoma of the urinary bladder.

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