

Mucinous urothelial carcinoma of the renal pelvis

Kemal Behzatğlu, Ceren Boyacı, Oğuzhan Okçu, Ezgi Hacıhasanoğlu, Yasemin Çakır, Seher Darakçı

Department of Pathology, Istanbul Education and Research Hospital, Istanbul, Turkey

Abstract

Urothelial carcinoma with abundant myxoid stroma is a newly-described and extremely rare entity. Since only very few cases have been reported, there is no consensus on its nomenclature. Microscopic examination revealed invasive urothelial carcinoma with widespread low-grade noninvasive areas. There were focal invasive areas in the neighborhood of the renal parenchyma. Malignant urothelial tumor/cell groups localized in the stroma had abundant myxoid/mucinous background in the invasive areas. The cytoplasm of the tumoral cells was more eosinophilic in these areas and the cells formed small groups and cords. Histochemically, PAS and Alcian Blue were positive in the cytoplasm of the tumoral cells and in the stroma while negative in the non-mucinous areas. Immunohistochemically, the tumoral cells of the mucinous invasive areas diffusely expressed MUC1 and MUC2. We discuss the origin of the mucinous/myxoid stroma, the tumor's nature and its nomenclature with histochemical and immunohistochemical features.

Introduction

Urothelial carcinoma is a tumor with various patterns and variants.^{1,2} While the bladder is normally lined only by urothelium, it has several tumor variants involving different cells, similar to the way that variant cell types appear in lung or gastric tumors.

Urothelial carcinoma with abundant myxoid stroma is a newly defined entity that is not present in the WHO 2004 classification. After having been described in 2009, two series of 12 and 13 patients and a few individual cases have been reported.³⁻⁷ All cases have been localized in the bladder, and none in the renal pelvis.

Abundant myxoid stroma is a distinctive feature of diagnostic value and is frequently seen in soft tissue tumors. It is an important histological and diagnostic feature in myxoid liposarcoma, parachordoma, chordoma, and

many fibrohistiocytic tumors. The cause of the myxoid stroma in soft tissue tumors is controversial. In our opinion, probable reasons can be: secretion from stromal cells (such as fibroblasts), secretion from tumor cells or degenerative reaction of the stroma.

Unlike mesenchymal tumors, the source of the myxoid stroma in epithelial tumors is generally the epithelial cells. Mucinous carcinoma of the breast and gastrointestinal system are the best examples of this condition. Immunohistochemically, MUC2 protein is generally expressed in mucinous carcinoma. Mucin is easily detectable in the stroma and cytoplasm of the tumor cells with PAS, Alcian Blue and mucicarmine.

The term urothelial carcinoma with abundant myxoid stroma is still controversial. Gilg *et al.*⁵ showed histochemical reactivity in tumoral and stromal cells with PAS, Alcian Blue and mucicarmine; there was also MUC2 and MUC5AC immunoreactivity in the tumoral cells. They suggest that the term *mucinous urothelial carcinoma* could be more appropriate for these cases.

Here we report a case of invasive urothelial carcinoma with widespread low-grade areas in the renal pelvis. The tumor had invasive urothelial carcinoma cells embedded in abundant mucinous stroma, especially localized at the renal border. We discuss the origin of the mucinous/myxoid stroma, the tumor's nature and origins of its name, together with the histochemical and immunohistochemical features.

Case Report

A 71-year-old female presented at our urology clinic with hematuria. Cystoscopy and laboratory results were normal. Computerized tomography (CT) revealed a 3×2.5×1.5 cm mass localized to the renal pelvis. Surgery was planned according to the clinical and radiological findings and radical nephrectomy was performed. Macroscopic examination revealed a papillary tumor of 3.2 cm in the largest diameter, in the renal pelvis. The border between tumor and renal parenchyma was not discernable in the cut surface. Microscopic examination revealed invasive urothelial carcinoma with widespread low-grade noninvasive areas. There were focal invasive areas in the neighborhood of the renal parenchyma. Malignant urothelial tumor/cell groups localized in the stroma had abundant myxoid/mucinous background in the invasive areas (Figures 1 and 2). This appearance resembled mucinous carcinoma of the breast and gastrointestinal system. The cytoplasm of the tumoral cells was more eosinophilic in these areas and the cells formed small groups and cords (Figures 1 and

Correspondence: Kemal Behzatğlu, Kasap İlyas Mahallesi, Abdurrahman Nafiz Gurman Cad, Istanbul Eğitim ve Araştırma Hastanesi, Patoloji Servisi, Fatih, Istanbul, Turkey.
Tel.: +90.505.578.4122 - Fax: +90.212.589.3235.
E-mail: kbehatoglu@hotmail.com

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2). Mucinous material was detected in a few focal areas, localized on the surface of the non-invasive tumor.

Histochemically, PAS and Alcian Blue were positive in the cytoplasm of the tumoral cells and in the stroma while negative in the non-mucinous areas.

Immunohistochemically, the tumoral cells showed cytoplasmic MUC1 and MUC2 staining diffusely through the invasive and mucinous areas (Figure 2B). Interestingly, both markers were focal weak cytoplasmic positive in noninvasive and low-grade urothelial carcinoma areas. No expression of MUC5A or MUC6 was detected in any of the cells. There was no recurrence or metastasis during the 16-month follow-up.

Discussion and Conclusions

Urothelial carcinoma with abundant myxoid stroma is a newly described and extremely rare entity. Histologically the tumor has malignant epithelial cells with eosinophilic cytoplasm which form nests and cords within the myxoid stroma. These features make it appear similar to soft tissue tumors such as myoepithelioma and chordoma. The relationship between the myxoid stroma and malignant epithelial cells resembles mucinous carcinoma of the gastrointestinal system. When first described, it was called chordoid tumor due to the abundant

myxoid stroma and its similarity to soft tissue tumors.³ The term *urothelial carcinoma with abundant myxoid stroma* was preferred in the existence of myxoid stroma in noninvasive/low grade cases.⁴ Gigl *et al.*⁵ reported PAS and Alcian blue positivity and MUC2 and MUC5A immunoreactivity in tumoral cells. This presented a new aspect of the urothelial carcinoma variant.

Due to the general use of the term *muinous carcinoma* within the concept of the breast and gastrointestinal system, the term mucinous urothelial carcinoma could be controversial at first. Mucinous differentiation should not be a surprise, taking into account the embryological differentiation from various structures (cloaca, allantois, mesonephric duct) and the capacity to transform into glandular, squamous and nephrogenic cells.^{8,9} Cystitis glandularis with intestinal metaplasia in non-neoplastic processes supports the capacity for mucinous differentiation. Ninety percent of the sample was low grade/noninvasive urothelial carcinoma in our case. There was an invasive component interlaced with the noninvasive component at the periphery of the tumor-at the renal border. All invasive areas had prominent mucinous/myxoid lakes with malignant epithelial

groups forming nests, clusters and cords. The cytoplasm of the cells was eosinophilic, resembling the prototypical appearance of mucinous carcinoma of other parenchymal organs. Our case had MUC2 positivity and interestingly the MUC2 positive areas were also MUC1 positive while noninvasive areas were focal weak positive with MUC1 and MUC2. The MUC2- and MUC1-expressing cells had probably gained invasive capacity.¹⁰ MUC2 is expressed in Goblet cells, but it is also expressed in mucinous /colloidal carcinomas that are generally seen in the breast and GIS. Colloidal carcinoma of the breast, gastrointestinal system (GIS) and pancreas are less aggressive than typical not otherwise specified (NOS) adenocarcinomas. However, MUC1 expression, related to aggressive behavior, is generally seen in MUC2-negative- NOS adenocarcinomas.¹⁰⁻¹² The tumor interestingly expressed both of these markers in the same areas in our case. In contrast to the case of Gigl *et al.*,⁵ MUC5AC was not expressed in our case. As far as we know, our case is the first renal mucinous urothelial carcinoma in the literature. This was a rare and interesting case with MUC2 and MUC1 immunoreactivity. We believe our case will be helpful in finding the source of the tumor.

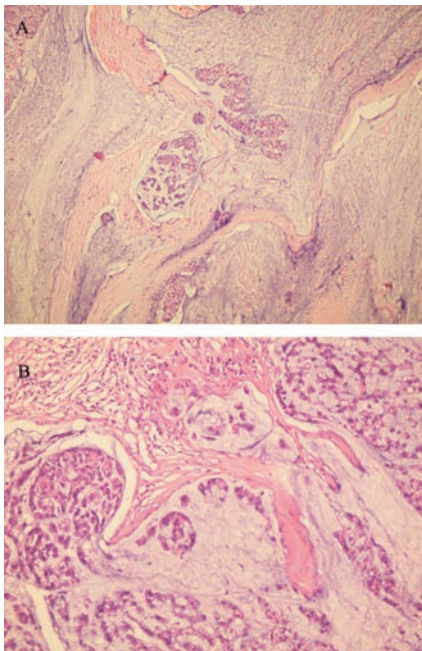


Figure 1. Tumor cells are present as clusters within large lakes of mucin (A), tumor with stromal invasion and mucin extravasation (B) (Hematoxylin and Eosin staining 100× for A and 300× B).

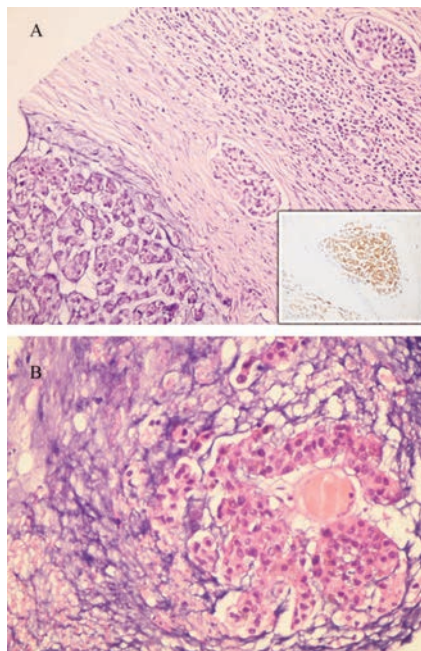


Figure 2. Tumor with renal parenchymal invasion (A), tumor has staining for MUC2 (insert), nests and clusters of tumor cells surrounded by pools of extracellular mucin (Hematoxylin and Eosin staining 200× for A and 300× B, immunohistochemical staining 200× for insert).

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