A Rare Concurrence: Villous Adenoma and Non-invasive Urothelial Carcinoma of the Bladder

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Abstract
Villous adenoma appearing in the urinary system is very rare. This tumor is common in the gastrointestinal tract and, as far as we know, villous adenoma of the gastrointestinal tract is premalignant. However, there is insufficient evidence about the malignancy potential of villous adenoma seen in the urinary tract and inadequate information about follow-up procedures. The aim of this report was to highlight a rare but important lesion: villous adenoma presenting with non-invasive urothelial carcinoma in the bladder.

Keywords: Urinary bladder; urothelial carcinoma; villous adenoma.

Case Report
A 61-year-old male patient had been admitted to the clinic with lower urinary tract symptoms about 3 years earlier. He was diagnosed with benign prostatic hyperplasia and was followed up with alpha-blocker therapy. No hematuria was present and this treatment relieved his complaints. The patient also had hypertension, diabetes mellitus, and coronary heart disease. A physical examination and rectal palpation revealed nothing significant. A prostate biopsy under transrectal ultrasound guidance due to an elevated total prostate-specific antigen (5.02 ng/mL) was reported as benign prostate tissue.

Two years later, a 17-mm mass on the right wall of the bladder was reported following a control abdominal ultrasound (US) (not present on previous US). Cystoscopy under general anesthesia revealed a 20-mm papillary tumor lesion on the right wall and 4 millimetric lesions in the periphery. The lesions were resected and sent to pathology. Histopathological examination indicated a positive result for cytokeratin 7, cytokeratin 20, and the carcinoembryonic antigen in the luminal focal areas. In addition, acid mucin positivity was seen in the specimen with an Al-
cian blue stain. The lesions were reported as villous adenoma and non-invasive urothelial carcinoma (Fig. 1, 2). During 1 year of follow-up of the patient, 3 control cystoscopies were performed and no recurrence was seen.

**Discussion**

Bladder neoplasms are categorized in 2 groups: epithelial and mesenchymal. Benign urothelial neoplasms are classified as papilloma, epithelial metaplasia, leucoplastic, inverted papilloma, nephrogenic adenoma, cystitis cystica, cystitis glandularis, or low malignant potential bladder neoplasm, and malignant urothelial neoplasms are classified as urothelial carcinoma, squamous cell carcinoma, adenocarcinoma, metastasis, small cell or neuroendocrine carcinoma, melanoma, or carcinoid. Benign mesenchymal tumors are classified as leiomyoma, fibroma, paraganglioma, plasmocytoma, hemangioma, solitary fibrous tumor, neurofibroma or lipoma; malignant tumors include rhabdomyosarcoma, leiomyosarcoma, lymphoma, osteosarcoma, angiosarcoma, and malignant fibrous histiocytoma [1].

Villous adenoma is defined as a premalignant polyp of the gastrointestinal tract. It is more commonly observed in the rectum than in the gastrointestinal tract. There is no difference between men and women in the distribution. The seventh and eighth decades of life are the peak periods of occurrence [2]. Recurrence may be up to 40%, despite complete excision [3].

Villous adenoma seen in the urinary system is rather rare. Morphologically, it is not different from gastrointestinal villous adenoma [4]. The differential diagnosis includes cystitis glandularis and well-differentiated adenocarcinoma.

Although the pathogenesis of a glandular lesion in the urinary system is not known precisely, embryologically, it is known that the Wolff duct opens to the cloaca and the urinary sac septum divides into the rectum and the urogenital sinus at approximately the seventh fetal month. It may be that villous adenoma originates from a remnant of cloacal epithelium left behind during this division. An alternative theory suggests that villous adenoma is a product of the chronic irritation-metaplasia-dysplasia-carcinoma sequence. Yet another possibility is that the 2 tumors may be coincidental pathologies.

A search of the literature for cases/case series about villous adenoma in the urinary tract, 62 cases were found. Among these cases, 34 were isolated villous adenoma, 24 were villous adenoma with bladder adenocarcinoma, 2 were villous adenoma with urethelial carcinoma, and 2 were a combination of adenocarcinoma, urethelial carcinoma and villous adenoma [5]. Characteristically, these lesions can cause hematuria and irritating lower urinary tract symptoms. A differential diagnosis for urothelial carcinoma using US, computed tomography, or magnetic resonance imaging is not easy. Therefore, villous adenoma of the bladder is primarily a histological diagnosis.

As this is a rare case, knowledge about the treatment is not sufficient, but the prognosis for isolated villous adenoma cases after transurethral resection treatment is excellent [6]. Nonetheless, a case in literature reported that isolated villous adenoma progressed to villous adenocarcinoma [7]. In cases of villous adenoma associated with bladder adenocarcinoma, the likelihood of recurrence and distant metastasis is greater and may require more aggressive treatment.
In conclusion, other lesions seen with villous adenoma should be differentiated. As macroscopic detection is not possible, thorough sampling is very important in the diagnosis and each sample should be reported individually, even if the surgeon thinks that it is a satellite lesion. Moreover, cases diagnosed with isolated villous adenoma should be followed up cystoscopically due to the potential of malignant transformation.

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**References**