A Nested Variant of Transitional Cell Carcinoma of the Urinary Bladder: a Case Report

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Nested variants of transitional cell carcinomas (TCC-NVs) are relatively rare neoplasms in the urinary bladder, but at least 25 cases have been described. This disease is characterized by the pathological finding of irregular nests and/or tubules of transitional carcinoma cells infiltrating the lamina propria without involvement of the mucosal layer. In our case, diagnosed by open biopsy, there were scattered tumor cells observed from the muscle layer to the subserosa, with a tendency toward increasing cellular anaplasia with the depth of invasion. Since the prognosis of TCC-NV is generally poor, comprehensive chemotherapy was performed. No changes were observed on computed tomography and the performance status (0) remained the same after 1 year, so the treatment was considered effective. We conclude that open biopsy should be carried out without hesitation when bladder cancer is suspected, even if there are negative findings of repeated urinary cytology examination and/or endoscopic cold cup biopsy. Immunohistochemical analysis may help in the diagnosis of TCC-NVs derived from epithelial cells. Diagnosis and treatment at an early stage should reduce the mortality of patients with TCC-NVs.

Key words: bladder carcinoma – transitional cell carcinoma – nested variant tumor

INTRODUCTION

Nested variants of transitional cell carcinomas (TCC-NVs) are relatively rare neoplasms in the urinary bladder, and so far 25 cases have been described (1–5). This disease is characterized by irregular nests and/or tubules of transitional carcinoma cells infiltrating the lamina propria without involvement of the mucosal layer (6). Our case demonstrated typical pathological features.

CASE REPORT

A 70-year-old man presented with urinary retention and appetite loss. In his past history, he had suffered a gastric carcinoma in 1995, histopathologically diagnosed as a mucosal cancer, a well-differentiated adenocarcinoma (Fig. 1). He visited a local clinic for medical advice on May 19, 1999, and serum biochemical values showed creatinine 6.9 mg/dl, BUN 60 mg/dl and potassium 6.0 mEq/dl. Moreover, abdominal ultrasonography yielded bilateral hydronephrosis. He was referred to our institute with postrenal failure on May 26, 1999.

Physical examination did not reveal any abnormalities. Chest and abdominal X-rays showed no abnormal findings. Cystoscopy revealed diffuse change in the bladder mucosa with an edematous and irregular erythematous lesion in the left lateral and posterior bladder wall (Fig. 2). No tumor was recognized and no atypical cells were identified on repeated urinary cytology examinations. Percutaneous right nephrostomy was performed on May 28, 1999. Computed tomographic (CT) scans showed a thickened left bladder wall with no evident lymph node swelling in the pelvis (Fig. 3) and bilateral hydronephrosis (not shown). On magnetic resonance imaging (MRI) with T1 weighting, the intensity was iso, and with T2 weighting, high- and isointensity areas were apparent in the left lateral and posterior bladder wall.

Based on these findings, bilateral ureterocutaneostomy and total cystectomy were planned. However, during the operation, the urinary bladder was unexpectedly adherent and could not be removed. Therefore, open urinary bladder total layer biopsy and bilateral ureterocutaneostomy were performed on June 21, 1999.

Grossly, the cut surface of the resected specimen revealed a stony hard, solid white tumor. Microscopically, no apparent neoplastic changes were observed in the mucosal lumen. Most
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...of the mucosal urothelium was denuded and the submucosa was severely edematous. The subserosa was thickened with fibrous tissue. No massive tumorous lesions were evident at lower magnification (Fig. 4a). For immunohistochemical analysis, anti-cytokeratin (AE1/AE3, Dako Japan, Kyoto, Japan), anti-S100 (Dako), anti-chromogranin A (LK2H10, Shandon Lipshaw, Pittsburgh, PA), anti-desmin (Dako), anti-vimentin (Dako) and anti-thrombomogulin (Dako) antibodies were employed at dilutions of 1:50, 400, 1, 50, 10 and 25, respectively. A Vectastain ABC Elite Kit (Vector Laboratories, Burlingame, MA) and DAB were applied for visualization of binding. Among these immunohistochemical parameters, only cytokeratin proved positive on tumor cells (Fig. 4b and d). Small nests of atypical cells, positive for cytokeratin, were seen scattered in the muscle layer and subserosa (Fig. 4b). Most of the tumor cells were small with eosinophilic or clear cytoplasm and rounded nuclei. The chromatin was finely granular and evenly distributed. They showed no apparent tubular or granular features (Fig. 4c). Cytokeratin-positive tumor cells were growing invasively in the muscle layer and fibrous subserosa with occasional lymphocyte infiltration (Fig. 4d).

From these histopathological findings, we diagnosed a transitional cell carcinoma of the urinary bladder, grade 3, INFγ, pT3b, N0, M0, stage ≥III according to the ‘General Rules for Clinical and Pathological Studies on Bladder Cancer’. Three cycles of methotrexate, etoposide and cisplatin combined general chemotherapy were performed. However, these drug doses had to be reduced by 25% because of chronic renal failure. Thereafter, no changes were observed on CT and the performance status (0) remained essentially the same 1 year after the operation.

**DISCUSSION**

To date 26 cases of TCC-NV, including this case, have been described (1–5). Table 1 summarizes the clinicopathological features. The average age at the time of diagnosis was 68.7 years (range, 45–97 years) and 25 of the cases were men, with only one woman. Symptoms were documented for 22 of the cases, gross hematuria being the most common presenting sign, with hydronephrosis, as in our case, the second most frequently encountered.

Our case was diffusely localized although the periureteral orifice is the major site for TCC-NVs. Previous lesions were variably described as ‘a small, peculiar, submucosal bump’, ‘an erythematous patch/plaque’, ‘a small, non papillary, non-sessile lesion’, ‘a wide-based tumor’ and ‘a slightly raised and gritty tumor’ (4).

These lesions must be histologically differentiated from proliferation of Brunn’s nests, cystitis granularis and proliferative cystitis, inverted papilloma, adenocarcinoma, nephrogenic metaplasia and paraganglioma (2). Immunohistochemical staining with PSA, neuron-specific enolase and chromogranin is useful for differential diagnosis. In our case, there were no obviously massive tumor cells. However, scattered epithelial cells, positive for cytokeratin were observed from the muscle layer to the subserosa. Furthermore, negative immunohist-o-...
chemical findings were observed with anti-S100 and anti-chromogranin A, generally positive in neuroendocrine tumor cells, and with the anti-thrombomogulin marker for mesodermal elements. Moreover, we did not obtain positive reactions for vimentin, typical of fibroblast cells or desmin of smooth muscle. We therefore concluded that the diagnosis was transitional cell carcinoma.

Murphy and Deana reported a tendency for increasing cellular anaplasia with increasing depth of invasion (3), although neither vascular nor lymphatic invasion (nor a combination of both) were commonly encountered and the prognosis was relatively poor (2–5). Most cases with extended survival were those diagnosed in early stages with no metastasis and with the treatment limited to transurethral resection of bladder tumors. Patients who died had peritoneal or other metastases and the treatment was total cystectomy (4). General chemotherapy for severe stage TCC-NV was performed and in our case it appeared relatively effective. In our case, exact diagnosis was impossible before surgery. During the operation the urinary bladder was unexpectedly adherent with surrounding fusion and could not be removed. Therefore, open urinary bladder total layer biopsy without removing the bladder and bilateral ureterocutaneostomy were performed. Our experience indicates that one should carry out open biopsy without hesitation when urinary diversion is performed under general anesthesia, even if there are negative findings of urinary cytology and/or endoscopic cold cup biopsy, to maximize the chance of survival with aggressive treatment when appropriate.

References