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Plasmacytoid Urothelial Carcinoma of the Urinary Bladder with HER2 Protein over Expression

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Case Report

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Abstract

A 58-year-old man presented with dysuria and microscopic hematuria. Biopsy revealed plasmacytoid urothelial carcinoma, a rare and aggressive form of bladder carcinoma with HER2 protein overexpression.

Keywords: Plasmacytoid Urothelial carcinoma ; HER2 protein

Abbrevations: TCC: Transitional Cell Carcinoma; PUC: Plasmacytoid Urothelial Carcinoma; WHO: World Health Organization; CT: Computed Tomography; EF: Ejection Fraction; TURBT: Transurethral Resection of the Bladder Tumor; HER2: Human Epidermal Growth Factor Receptor Type 2; GC Carboplatin Plus Gemcitabine; M-CAVI: Methotrexate / Carboplatin / Vinblastine.

Introduction

Bladder cancer mostly exists as an epithelial tumor and about 90% of cases are transitional cell carcinoma (TCC). Plasmacytoid urothelial carcinoma (PUC) has been recognized in the current World Health Organization (WHO) classification of urothelial neoplasms which is a rare variant of urothelial carcinomas with similar histology as plasmacells. We report a case of PUC with positive HER2 protein over expression from our institution.

Case Report

A 58-year-old former smoker man presented with a month history of dysuria and frequency in November 2015. There was no gross hematuria or abdominal pain. Urine analysis showed microscopic hematuria. Abdominal computed tomography (CT) demonstrated a thickening of the urinary bladder and bilateral hydronephrosis. Thorax CT showed a 12-mm-diameter nodule at the left upper lobe. Due to high levels of creatinine, left nephrostomy was performed in December 2015.

He underwent transurethral resection of the bladder and pathology revealed a high-grade PUC. Axial 18-FDG PET demonstrated an intensely hypermetabolic left upper lobe nodule with SUV max of 2,4 and thickening of the left lateral wall of the bladder with SUVmax of 5,4. He received 6 cycles of gemcitabine and carboplatin treatment.

In September 2016, he presented with abdominal distension and severe pain at right lower quadrant. Rectal examination indicated a narrowed rectal lumen, with an intact rectal mucosa. Colonoscopic findings revealed a narrow rectal lumen and edematous mucosa, suggesting extrinsic compression. The patient underwent colostomy and intraoperative exploration revealed a frozen pelvis. A biopsy was taken from the solid lesion on the pubic bone. The histopathological assessment revealed a tumor formed of loosely cohesive sheets of atypical cells with eccentrically located nuclei in the cytoplasm (Figure 1). Morphological patterns such as nested or papillary growth which are reminiscent of conventional urothelial carcinoma were observed. Tumor cells had plasmacytoid features with eccentrically located nuclei and dense eosinophilic cytoplasm. Mucin production was not observed in tumor cells on histochemical stains. Immuno histochemical analysis showed that tumor cells were PanCK, CK7 and thrombomodulin positive (Figure 2). LCA, p63, HCG, ER, PSA were negative in tumor cells. CD138 was partially expressed in the cytoplasm of neoplastic cells (Table 1). In addition C-erbB2(HER2) expression was 2 positive (Figure 3). The lesion was interpreted as “plasmacytoid urothelial carcinoma”. Weekly adriamycin regimen and radiotherapy (2 Gy/day for 5 days/week) were initiated. Adriamycin was administered at a dose of 20 mg/m^2 weekly. He had an ejection fraction (EF) of 69% by transthoracic echocardiogram prior to chemotherapy. However he developed progressively worsening dyspnea 3 days after the first dose. On his physical examination diffuserales and S3 gallop washeard at which time repeat echocardiogram showed an EF of 35%. Repeated doses of adriamycin could not be given, but radiotherapy was continued. Following radiotherapy improvement of pain was observed. After this, weekly paclitaxel was started as a maintenance treatment and continued for 6 months. Pelvic CT in March 2017 showed a decrease in tumor size (Figure 4). He is doing well without any evidence of distant metastasis at the present time.

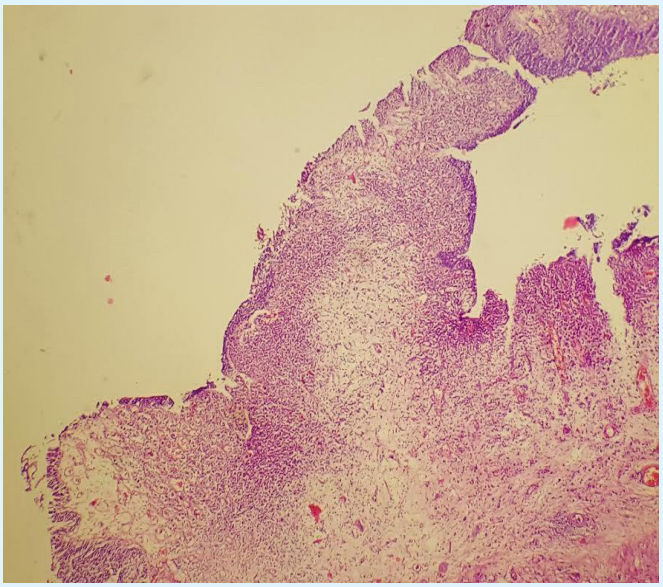

Figure 1: Low power magnification of bladder mucosa. Loose cohesive tumor cells are seen in laminapropria. This apprearence may mimic an inflammatory process (HE stained section, X20).

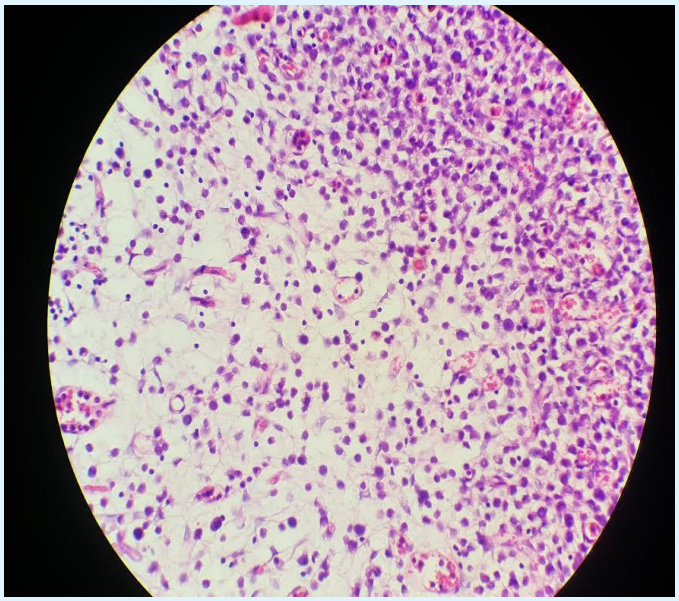

Figure 2: CK7 expression on tumor cells. CK7 expression is strong and extensive on tumor cells. (CK7, immuno histochemistry, X10).

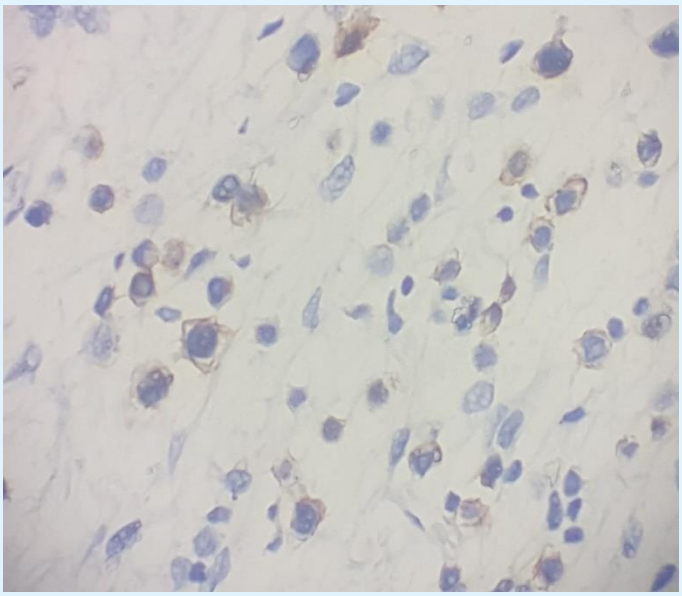

Figure 3: HER2 overexpression on tumor cells.

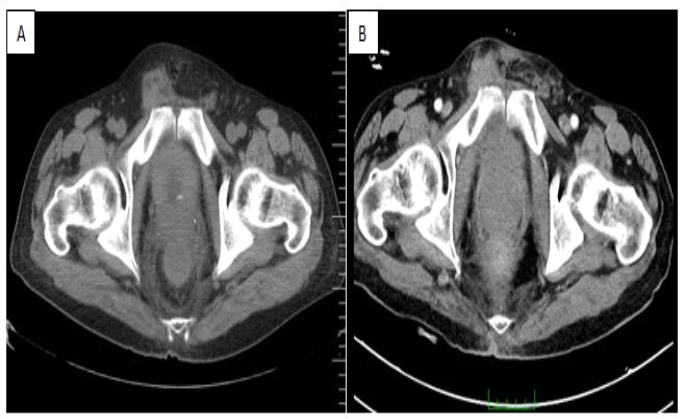

Figure 4: A: Pelvic CT in August 2016 B: Pelvic CT in March 2017 showed a decrease in tumor size.

CK	Cytokeratin
CD	cluster of differentiation
LCA	leukocyte common antigen
HCG	β-human chorionic gonadotropin
ER	estrogen receptor
PR	progesterone receptor
PSA	prostate-specific antigen

Table 1: Abbreviation of immunhistochemical terms.

Discussion

Bladder cancer is the most common cancer of the urinary system and the 9th most common cancer in all cancers [1]. Urothelial carcinoma is the most common cancer of the urinary bladder. As mentioned in our patient's history, the most important factor contributing to the incidence of urothelial cancer is smoking. [2]. The first urothelial carcinoma with plasmacytoid features was reported by Sahin et al in 1991 [3]. So far less than 100 cases have been published with a recent large series in the literature [4]. PUC is usually diagnosed at an advanced pathological stage due to the presentation similar to benign diseases such as urinary tract infection, interstitial cystitis, prostatitis [5].

The presence of unexplained hematuria in individuals over the age of 40 often points to urinarytract cancer until proven otherwise. Urinary cytology and flexible cystoscopy are important as the first step in the diagnosis. Transurethral resection of the bladder tumor (TURBT) is required as done in the present case in order to determine histology, depth of invasion, and potential involvement beyond the bladder [6].

PUC is a rare variant of urothelial carcinoma and it must be distinguished from plasmacytoma. Plasmacytoid morphological variation may be observed in primary urothelial tumors as well as other cell types involving bladder mucosa such as non-Hodgkin lymphomas, plasmacytoid lymphomas, malignant melanomas, tumors with rhabdoid features. Inaddition, such plasmacytoid differentiation may be encountered in metastatic lobular carcinomas of the breast and gastric carcinomas. Correct diagnosis of tumor type and origin may not always be difficult when a complete clinical information and sufficient tissue are available for pathological evaluation including immuno histochemical analysis.Cytokeratin reactivity in immuno histochemistry as observed in the present case, confirms the diagnosis of the malignant epithelial tumor. In addition, cell type and tissue specific protein panels may help to rule out other mimickers. Plasmacytoid urothelial carcinomas are commonly positive for CK7, CK20 and urothelial marker. CD138 which is commonly utilized to identify plasmacytoid differentiation, may be expressed in plasmacytoid urothelial carcinomas as well as other tumors. So CD138 expression should be evaluated along with other epithelial and lymphoid markers. Our case had panCK, CK7, CD138 (Figure 5) and HER2 positive tumor staining. Human epidermal growth factor receptor type 2 (HER2) is a transmembrane receptor tyrosine kinase. HER2 over

expression is associated with poor prognosis in various cancers and anti-HER2 therapy is a therapeutic target for HER2 over expressing breast cancer and gastric cancer [7,8]. HER2 over expression and gene amplification have been reported in urothelial carcinomas and prognostic significance of HER2 over expression has been demonstrated in such cancers [9]. Anti HER2 treatment as in breast and gastric cancers may be effective in PUC.

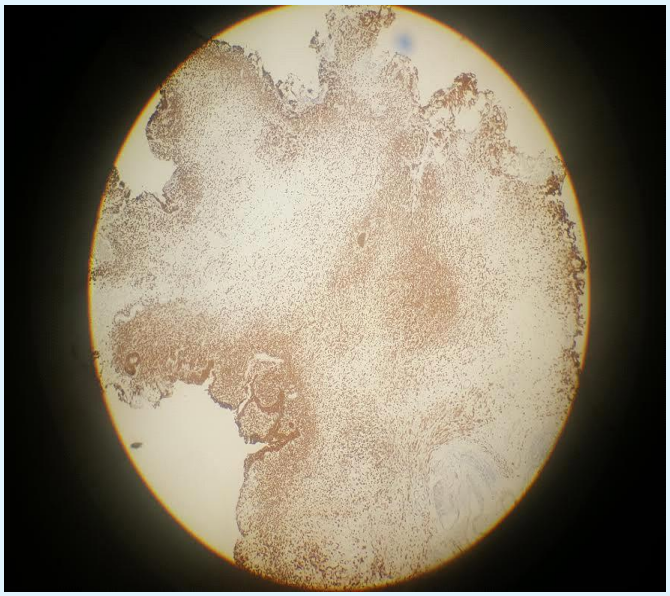

Figure 5: CD 138 expression on tumor cells. Expression are partially present on tumor cells (CD138, İmmuno histochemisty, X10)

Combined-modality approaches involving TURBT with radiotherapy and simultaneous chemotherapy can be performed in patients with muscle invasive urothelial bladder cancer for those who are not a candidate for radical cystectomy [10]. Platinum-based chemotherapy is the preferred initial approach for systemic therapy in patients with metastatic disease [11]. For patients who are unable to receive cisplatin due comorbidities such as chronic renal disease like our patient has, options include a carboplatin-based regimen such carboplatin plus gemcitabine.

In the EORTC 30986 study methotrexate / carboplatin / vinblastine (M-CAVI) treatment compared with carboplatin plus gemcitabine (GC). The trial suggests that GC has similar efficacy with M-CAVI. For having a better toxicity, GC can be preferred in patients with impaired renal function or a poor performance status (ECOG ≥2) for combination chemotherapy [12]. In patients with metastatic urothelial carcinoma single-agent chemotherapy such as adriamycin can be a treatment option either in the first-line or in previously treated patients. Our patient did not receive adriamycin because cardiac performance deteriorated after a single dose of adriamycin administration. Concurrent capecitabine and radiation therapy were shown to be well tolerated and effective in elderly patients with urothelial carcinoma [13]. Weekly paclitaxel was given for 6 months following radiotherapy which resulted in analmost complete response. Recently, C Messina et al published ametastatic PUC case who achieved remission following carboplatin and paclitexel combination [14]. Our patient is the second case responding to paclitaxel following chemoradiotherapy for the metastatic lesion of PUC. Patient's quality of life improved significantly. We thought chemotherapy responsiveness of this rare tumor is important and should be reported.

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