Case Report

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Rare Primary Signet Ring Cell Carcinoma of the Bladder Cancer

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Abstract

Primary signet ring cell carcinoma of the bladder is a rare tumor and it has a poor prognosis and is more mortal than the urothelial cell carnioma. However, most patients apply with painless macroscopic hematuria; rarely do they could apply with urinary tract infection or lower urinary tract symptoms. In this study; a 47-year-old male was referred to our clinic with dysuria, which was antibiotic therapy and symptomatic treatment. In ultrasonography, bladder wall thickening has been seen then patient underwent with cystoscopy. After atypical lesions were seen on the bladder mucosa, random punch biopsies were taken. A pathological examination revealed infiltrative urothelial carcinoma with a poorly differentiated signet ring cell component.

As in this case report, patients with signet ring cell bladder cancer, which is rare and has an aggressive course, might only present with non-specific complaints such as dysuria. If atypical lesions are observed during the diagnostic cystoscopy procedure, the threshold should be kept low to decide on biopsy.

Keywords: Adenocarcinoma, lower urinary tract symptoms, urinary bladder neoplasms

Introduction

Bladder adenocarcinoma; colloid, clear cell, colonic, signet ring cells and many unclassifiable histological subtypes, is an extremely rare carcinoma among bladder cancers. Primary signet ring cell carcinoma of the bladder is one of poor prognosis, mortal and treatment-resistant subtype of bladder adenocarcinoma (1). Most patients may present with painless macroscopic hematuria, but they can also be associated with lower urinary tract symptoms (2). These tumors are diagnosed with histological examination of biopsy which is performed with cystoscopy. Unfortunately, treatment options for this tumor are limited due to its rare occurrence among bladder cancers and its aggressive and poor prognosis. In this tumor, where radiotherapy and chemotherapy are not effective enough, the most effective treatment is radical cystectomy in the early stage (3). In this case report, we drew attention to the fact that dysuria may be the only symptom of signet ring cell bladder cancer and the necessity of biopsy in patients with atypical cystoscopy findings.

Case Report

A 47-year-old male patient presented with dysuria that has been continuing for 3-4 months without hematuria. It was learned that cystoscopy was performed in another urology clinic about 2 weeks ago; suspicious areas were evaluated as lokoplakia, fulgurization was performed, antibiotherapy and analgesic treatment was applied, and he was referred to our clinic because his complaints continued. In his medical history, smoking for 10 pack years and 2 cystolithotomy operations were performed 25 and 30 years ago. There was no abnormal sign in his genitourinary and rectal examinations. Other system examinations were evaluated as normal. In the biochemical evaluation of the patient, creatine was 1.5 mg/dL and other values were normal. In his urinalysis, there were 30 erythrocytes, 49 leukocytes and leukocyte esterase positivity were detected. Grade 2-3 pyelocalcial dilatation and increased diffuse bladder wall thickness were detected by urinary ultrasonography and computerized tomography (CT) (Figure 1). A diagnostic cystoscopy was performed. Cystoscopy revealed that; areas compatible with bladder trigonal leukoplakia, and bullous edematous areas on the posterior wall. The right

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ureteral orifice was not seen. The left ureteral orifice was seen, but the ureteral catheter could not be advanced through this orifice. After taking cold biopsies from the suspicious areas, the procedure was terminated. In the postoperative period, bilateral 8F nephrostomy catheter was inserted by the interventional radiology clinic. Pathological evaluation revealed that; atypical cells with narrow cytoplasm, prominent nucleoli, and hyperchromatic nuclei, individually and in small clusters, without a clear pattern. The pathology report of the patient was T1 high-grade signet ring cell component and poorly differentiated carcinoma (Figure 2). After the pathological evaluation, it was considered that the patient might have a primary gastrointestinal system malignancy. Gastrointestinal system was performed and no foci of malignancy were detected. Contrast-thoracoabdominal tomography was performed for staging, and 5x4 mm nodular lesions in the bilateral lungs and solid lesions of 18x16 mm and 52x43 mm in the right lobe of the liver were detected. Radiological images were evaluated and no other primary focus was detected in the gastrointestinal tract. Lesions detected in the liver were evaluated as hemangioma. Radical cystoprostatectomy, bilateral lymph node dissection (obturator and iliac) and ileal loop diversion were performed. The patient did not have any problems in the postoperative period; the right abdominal drain was removed on the 6th postoperative day, the pelvic drain was removed on the 9th postoperative day, and the left abdominal drain and bilateral nephrostomy catheters were removed on the postoperative 12th day. Pathology was reported during the same period and the tumor infiltrated the surrounding tissue of the bladder, there was lymphovascular and perineural invasion and involvement in bilateral iliac and obturatory lymph nodes is seen in the report. Also left ureter surgical margin was positive. The patient was clinically staged as T3N2M0. In the immunohistochemical examination, it was seen that the tumor cells were stained positively with CK7, panCK, and GATA-3 and partially stained positively with CK20. The patient was evaluated as having undifferentiated bladder carcinoma with a primary signet ring cell component (Figure 3). Adjuvant chemotherapy was planned and the patient was discharged on the postoperative 15th day. The patient died from neutropenic fever and pulmonary thromboembolism while receiving the 6th course of gemcitabine and cisplatin chemotherapy in the 6th postoperative month. Informed consent was obtained from the patient.

Discussion

Signet ring cell bladder cancer is a rare subtype of bladder cancer and it is diagnosed in 0.12-0.6% of bladder cancers (1,4). Signet ring cell cancers are mostly detected in geographic information systems (GIS) as the stomach, colon, gallbladder, or breast adenocarcinoma. Therefore, primary adenocarcinomas of these organs should be investigated and excluded before the diagnosis of primary bladder signet ring cell cancer. Signet ring cell cancer of the bladder has a progressive course and high mortality. It metastasized at a rate of 50%, at the time of diagnosis. It may also present with ureteral invasion (3).

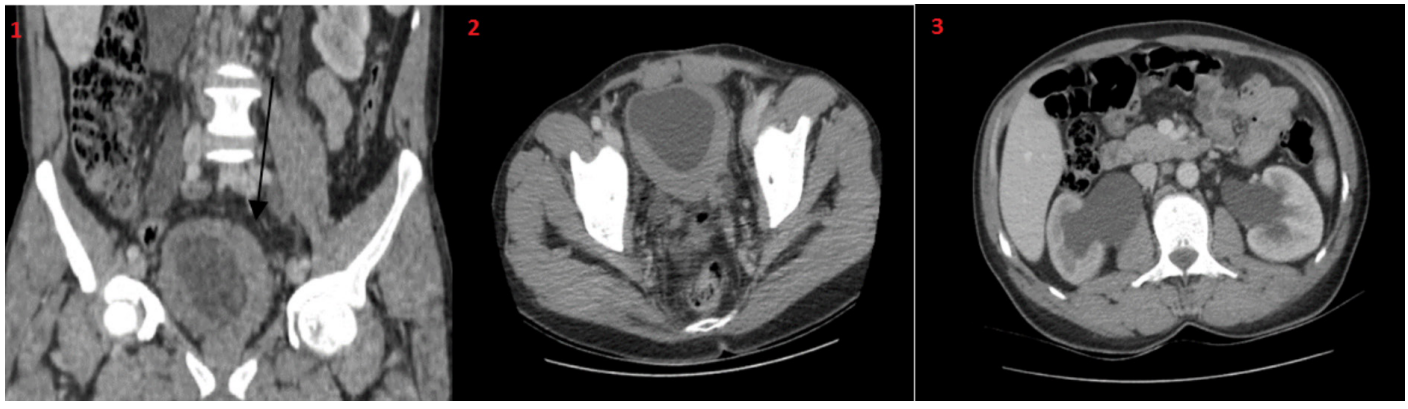

Figure 1. (1-2) Diffuse bladder wall thickness increase in preoperative computed tomography, (3) bilateral hydronephrosis view

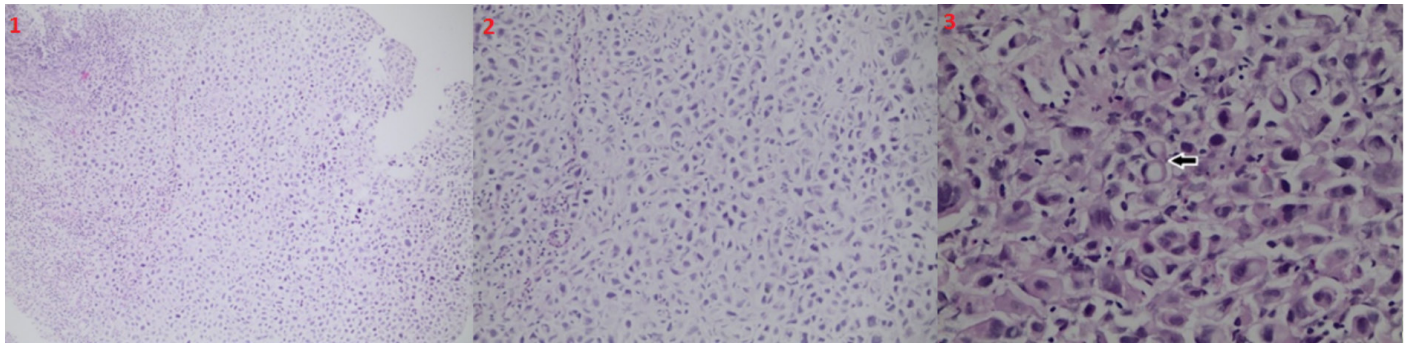

Figure 2. There are atypical cells and signet ring cells with a hyperchromatic nuclei with a narrow cytoplasm, prominent nucleoli, and individual and small clusters, which do not have a clear pattern (cold-cup biopsy) (signet ring cell) (1: HEX10, 2: HEX20, 3: HEX40)

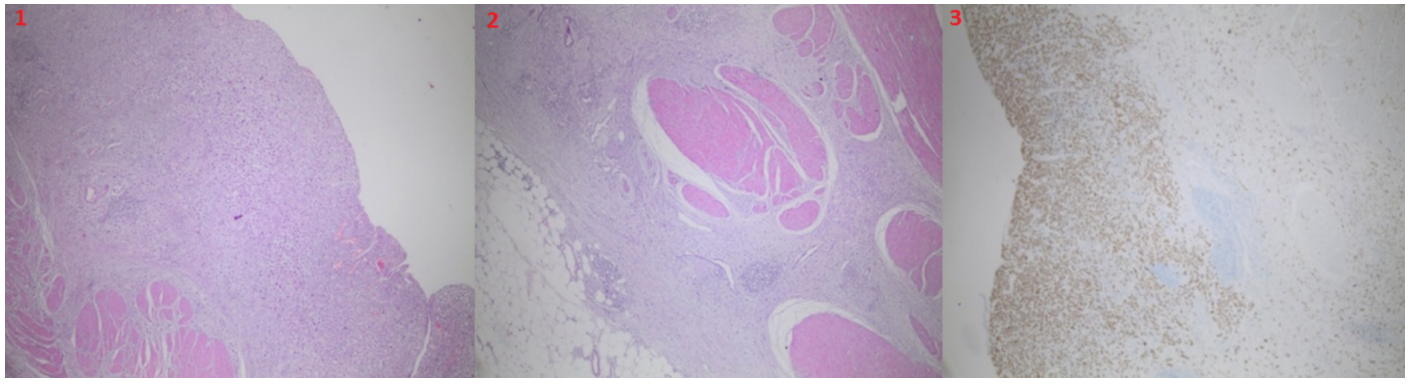

Figure 3. (1-2) Tumor cells appear to have crossed the muscularis propria and invaded the perivesical adipose tissue. Epithelial, muscular and perivesical adipose tissue invasion is seen in the same pathology preparation (1: HEX4, 2: HEX4, 3: panCKX4), (3) Tumor cells staining positive with panCK in radical cystectomy material

The disease is mostly seen in middle-aged men and it is usually accompanied by complaints of hematuria, dysuria and lower urinary tract symptoms. As in our case, there were findings resembling urinary tract infection or infravesical obstruction. Gaurav et al. (2) primary signet ring cell bladder cancer was detected in the patient whom they examined with the complaints of pollakiuria, nocturia, and incomplete urination without hematuria. Yamamota et al. (5) also detected signet ring cell bladder cancer in a patient who presented with oliguria and renal failure without the complaint of hematuria. These authors reported that signet ring cell bladder cancer may progress silently and asymptomatically, or may present with bladder irritation findings, flank pain, oliguria, and acute renal failure.

For staging of signet ring cell bladder carcinoma thoracic, abdominopelvic computed tomography could be performed and CT urography may be performed for the examination of the upper urinary tract. Upper gastrointestinal endoscopy, colonoscopy, mammography, and gynecological examination should be performed to exclude any other possible primary site. Our case was also evaluated according to the results of GIS endoscopy and imaging studies, and no other possible primary focus was found.

When cystoscopic findings are examined, there are no specific findings of signaling ring cell bladder cancer. It could be seen on cystoscopy as a prominent mass to the peduncle and ulceroinfiltrative lesions. Grignon et al. (6) In a study conducted, because of the cystoscopic examination of 34 primary signet ring cell bladder cases, no mass protruding into the lumen was seen in the bladder in 47.1% of the cases. The most prominent findings encountered in the cystoscopic examination of the cases were reported as mucosal edema, erythematous or granular mucosa (6). No significant mass formation was seen also in our case. Cystoscopy revealed trigonal leukoplakia and diffuse bullous mucosal edema. Cold-cup biopsies were taken from suspicious areas because no obvious solid mass or papillary formation detected. In signet ring cell bladder cancers, subepithelial invasion of the disease may cause full-thickness involvement of the bladder wall, ureter invasion, and bilateral hydronephrosis, as in our patient (6). Bladder wall irregularity, increased thickness, and/or hydronephrosis may be seen on computed tomography or intravenous pyelography. In our patient, a spread in the form of infiltrative and diffuse bladder wall thickness increase and bilateral hydronephrosis was seen.

Treatment options in primary signet-ring cell bladder cancer include surgical treatment such as transurethral resection, radical cystectomy and lymph node dissection, radiotherapy and chemotherapy and a combination of these. However, chemotherapy or radiotherapy is an option in treatment; its effectiveness is quite limited (3,5,6,7). Primary signet ring cell bladder cancer is usually diagnosed in advanced stages and a 5-year survival is 27-30% (8). For treating these patients, a multidisciplinary approach is required and urology, medical oncology, radiation oncology and pathology departments should work together. In non-metastatic and non-invasive cases, the most effective method of treatment is complete resection of the tumor. In cases with invasive, diffuse and intramural spread such as our case, radical cystectomy along with ileal loop diversion and lymph node dissection are considered the most effective treatment methods (3,5).

Conclusion

Primary signet ring cell bladder cancer is a rare disease and it has a high mortality. Asymptomatic and insidiously progressive, it may cause symptoms similar to urinary infection or infravesical obstruction and this could make it difficult to diagnose early. In cases with suspected signet ring cell carcinoma and non-specific cystoscopic findings, subepithelial infiltrative spread should be considered and biopsy should be performed.

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Ethics

Ethics Committee Approval: The University of Health Sciences Turkey, Diskapi Yildirim Beyazit Training and Research Hospital Clinical Research Ethics Committee approved the study protocol (decision number: 132/13, date: 07.03.2022).

Informed Consent: Informed consent was obtained from the patient.

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Authorship Contributions

Surgical and Medical Practices: S.B., S.Ç., Concept: H.S., S.Ç., Design: H.S., B.Y.E., M.A.İ., Data Collection or Processing: F.Ş.U., M.A.İ., Literature Search: F.Ş.U., S.B., Writing: H.S., B.Y.E.

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