Case Report

Adenocarcinoma of Urinary Bladder in 60 Years Old Female Patient- A Rare Case Report and Literature Review

Dr. M A Sameer¹, Dr. Rohit Mangal², Dr. Mansi Gulati²

¹Associate Professor, ²Resident,
Department of Pathology, Dr. Shankarrao Chavan Government Medical College (SCGMC) and Hospital - Vishnupuri, Nanded, Maharashtra

Corresponding Author: Dr. Rohit Mangal

ABSTRACT
Primary adenocarcinoma of the bladder is a very rare histological and pathological type of bladder cancer and so that here we present the case of a 60 years female patient who presented with chief complaints of bleeding per urethra since 10 days and diagnosed as adenocarcinoma of the urinary bladder. Because of no specific characteristics for symptoms, signs and accessory examinations compared with common urothelial carcinoma, adenocarcinoma of urinary bladder was diagnosed mainly based on histopathology. For recurrent tumor after transurethral resection of bladder tissue (TUR-BT), the patient should undergo total cystectomy or radical surgery.

Key words: Adenocarcinoma, Urinary bladder, Histopathology, cystectomy.

INTRODUCTION
Bladder cancer is a very common cancer of the urinary system and the ninth most common type of cancer worldwide, with a reported 386,000 new cases leading to 150,000 deaths worldwide in 2014. [1] The majority of bladder cancer cases (90-95%) are urothelial carcinomas, with squamous cell carcinoma and adenocarcinoma representing only 3 and 2% of the cases, respectively. [2,3] Adenocarcinoma of urinary bladder is an uncommon malignant tumour of all malignant tumors of the bladder. It affects adults with a peak incidence in the sixth decade of life and occurs more commonly in males than in females at about 2.6:1. The most common symptoms are hematuria, suprapubic pain, and dysuria. [4] Histologically, pure adenocarcinoma of the bladder may show different patterns of growth, these include: enteric (colonic) type, adenocarcinoma not otherwise specified (nos), signet ring cell, mucinous (colloid), clear cell, hepatoid, and mixed. In this report, we present a rare case of adenocarcinoma of the bladder not otherwise specified.

CASE PRESENTATION
A 60 year female patient admitted with chief complaints of bleeding per urethra since 10 days, which is painless, gross in nature, not relieved by medication. There was no history of loss of weight and appetite. She had past history of asthma and hypertension was stable on bronchodilator and tablet amlodipine respectively. Family and personal history was not significant and general and systemic examination also normal. On basic investigations, her haemoglobin was 9.4
gm% while TLC and PLT was 8300/cumm and 1,41000/cumm respectively, blood urea was 24, serum creatinine:0.83mg%, Her serum for HIV, HBs Ag were negative and renal function test, liver function test and random blood sugar level (83.11mg%), were within the reference range. On microscopic examination of urine showed plenty of red blood cells (RBCs). The urine cytology report showed chronic inflammatory lesion with developing malignancy, for typing and confirmation biopsy was done. On ultrasonography (USG), bladder mass measuring 30x17mm was seen (Photo 1). Few echogenic areas were seen within part of the lesion protruding in bladder lumen.

Under all aseptic precaution, pfannensteil incision was taken and partial cystectomy with intra abdominal drainage done under general anesthesia. The bladder mass was removed and specimen was send for histopathological examination. On gross examination we received single globular well circumscribed greyish white mass of 6x5cm (Photo 2).

Tumor tissue was fixed in 10% formalin solution and routinely processed. Sections from the paraffin block were cut with thickness of 5 micron and stained by hematoxylin and eosin (H & E) stain. Microscopic examination showed that the tumor cells predominantly arranged in glandular pattern with pools of mucin separating them, (Photo 3). Tumour cells were columnar with pleomorphic hyperchromatic nuclei with moderate amount of eosinophilic cytoplasm (Photo 4). Tumour tissue shows involvement into deep
mucosal epithelium, muscle and fibrofatty tissue in verning fibrocollagenous stroma with dilated congested blood vessels with muscle bundles and scanty inflammatory infiltrate (Photo 5). Final pathological diagnosis was given as adenocarcinoma of urinary bladder with involvement of all four margins and base is free of tumour tissue.

**DISCUSSION**

Urinary bladder cancer is the second most frequent tumor of the genitourinary tract. [5] Adenocarcinoma of the urinary bladder is classified according to its origin into 3 categories: primary, urachal and metastatic. [6,7] The primary mucinous adenocarcinoma of the bladder is an extremely rare urologic entity, which is found in less than 2% of all urinary bladder...
tumors and is often presented as metastatic. The incidence of this cancer increased with age with peaks in sixth, seventh and eight decades. The reported mean age at presentation was 62.2 and the median age was 63 (range, 35-80). There were more female cases than male which was different from TCC. The usual presenting symptoms included gross hematuria, dysuria, recurrent UTI and suprapubic pain. Patients rarely complained of local tumor effects or pain from local spread of the tumor. [8] Based on available data, the most common locations which tumours originated from were bladder neck and posterior wall, with incidence 31.6% and 26.3% respectively. Other common locations included trig one, lateral wall and urethra. Unlike urothelial carcinoma, most clear cell adenocarcinoma of bladder was large, solitary masses forming papillary or sessile structures. [9]

Some authors believe that it arises from mullerian elements in the bladder and are his to genetically identical to the female genital tract, because in some cases the neoplasms have been associated with vesical endometriosis or have arisen in mullerian duct cysts or remnants in the bladder. [10,11] This has also been considered an explanation for the observation that female incidence is dominant. However, a recent study presented evidence for urothelial origin in most adenocarcinoma of urinary tract, despite the morphologic resemblance to mullerian-derived tumors of the female genital tract. [12]

Cystitis glandularis present in invasive adenocarcinoma ranging from 14-67% of cases, [13,14] but its role in the pathogenesis of invasive adenocarcinoma is not clear. However, in patients with pelvic lipomatosis, which harbours cystitis glandularis, adenocarcinoma may occur. [15,16] Adenocarcinoma may also arise in conjunction with villous adenomas, S. haematobium infestation, and endometriosis of the bladder. Primary vesical adenocarcinoma represents the most common type of cancer in patients with bladder extrophy. In general, it is more malignant than common urothelial carcinoma, but more cases and longer follow-up periods are required to elucidate these points. Lymph nodes and bone seem to be the most common metastatic sites for this disease. [17]

The diagnosis of urinary bladder adenocarcinoma raises the question of whether the lesion is primary, urachal, or metastatic from a distant or adjacent organ. Primary adenocarcinoma is generally invasive at the time of diagnosis and is associated with a less favorable prognosis than TCC. [18] Unfortunately, when evaluated by the cytologic, histopathologic, histochemical, immunologic, and ultrastructural techniques currently available, primary adenocarcinomas have no distinctive features distinguishing them from those of secondary adenocarcinomas of gastrointestinal origin. [19,20] Most bladder cancers are detected because they produce hematuria; additionally, 10% of the patients with bladder cancer have asymptomatic microscopic hematuria and are positive for urine cytology. [21] Thus the mainstay for diagnosis of bladder cancer is combination of cystoscopy, biopsy and voided urine cytology. Among these, urine cytology is a non–invasive technique suitable for screening, diagnosis and follows up. [22] It can detect cases of carcinoma in situ, low grade non invasive tumor, and also the most aggressive neoplasm. An important diagnostic principle in urine cytology is that higher the grade of the tumor, the more accurate the diagnosis. [23,24] Also, it has been shown that patients with negative cytological findings have a very low risk of recurrence, while high–grade cytological abnormalities predict an aggressive tumor course. [25] Apart from these, urine cytology is also a better indicator of the presence of concomitant urothelial atypia, and indicator for bladder wash or mucosal biopsies. [26]

For the differentiation of various adenocarcinoma of the urinary bladder immunohistochemistry (IHC) is required. The immunohistochemical panel used to distinguish vesical from colorectal...
adenocarcinoma include CK 7, CK 20, CDX2, B-catenin. CK 7 and CK 20 positive in more than half of bladder adenocarcinoma but CK 7 negative and CK 20 positive in 29% of primary vesical adenocarcinoma thus it doesn’t discriminate between the two. Another marker of interest is β-catenin exhibits nuclear staining in 81% of primary colorectal adenocarcinoma while membranous staining in 88% of primary vesical adenocarcinoma. Hence it’s a good marker for distinguishing between the two entities.

The prognosis depends on the stage of disease; it is usually poor almost of the cases diagnosed at an advanced stage. 5 year survival of 70 -100% in patients with tumor confined to bladder, however less than 30% present at early stage. The diagnosis made on pathology, and exclude metastatic adenocarcinoma. Ultrasonography and CT are very important auxiliary examinations for adenocarcinomas of urinary bladder, which can indicate the size, range of the tumor and enlarged lymph nodes, and have positive significance for the diagnosis of urachal carcinoma. Surgery is the main stay of treatment.

**CONCLUSIONS**

Because of no specific characteristics for symptoms and signs, adenocarcinoma was diagnosed mainly based on histopathology. Once the diagnosis is confirmed, the radical surgery should be advised which abolish the risk of recurrence. The Post-TUR intra vesical therapy is of no help for preventing recurrence, although the TUR-BT has resected all visible tumors and even reached to the muscular layer of the bladder.

**ACKNOWLEDGEMENT**

The authors sincerely thanks the Department of Pathology, other staff and administration of Dr. Shankar Rao Chavan Government Medical College and Hospital - Vishnupuri, Nanded, Mahashatra, for permission to study and providing facility to carry out the work.

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How to cite this article: Sameer MA, Mangal R, Gulati M. Adenocarcinoma of urinary bladder in 60 years old female patient- a rare case report and literature review. Int J Health Sci Res. 2017; 7(9):332-337.