Original Article

Spectrum Of Urothelial Lesions with Clinical, Radiological and Histopathological Correlation in Tertiary Care Hospital

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DOI
10.21276/apalm.3549

Article History
Received: 12-03-2025
Revised: 30-08-2025
Accepted: 28-09-2025
Published: 20-11-2025

How to cite this article
Thumar M, Mulla F, Parmar Z, Gupta M. Spectrum Of Urothelial Lesions with Clinical, Radiological and Histopathological Correlation in Tertiary Care Hospital. Ann Pathol Lab Med. 2025;12(11):A396-A403.

Abstract

Background: Urothelial lesions, both neoplastic and non-neoplastic, commonly present with haematuria. Urinary bladder cancer, the 10th most common cancer globally, is 90% of urothelial origin. Cystoscopic biopsies and Trans Urethral Resection of Bladder Tumour remain the gold standards for diagnosis, staging, and prognostic evaluation.
Methods: This study analysed 100 cases (retrospective, prospective) of all urothelial lesions. Neoplastic cases were classified as per the 2022 World Health Organization classification of urothelial carcinoma and reported as per College of American Pathologists (CAP) protocol. Demographics, clinical history, and radiological data were collected from hospital databases. Descriptive statistics [Frequency, Mean, SD, P-value] was used to depict the baseline profile and clinical diagnosis of all the study participants. Statistical analysis was performed using STATA 14.2.
Results: Neoplastic lesions (65%) were more common than non-neoplastic ones (35%), with a male predominance (Male: Female = 5:1) and peak occurrence in the seventh decade (36.92%). Hematuria was the most frequent presentation (81.53%), with smoking being the leading risk factor (36.92%, P = 0.021). The most common non-neoplastic and neoplastic lesion were interstitial cystitis (71.43%) and invasive urothelial carcinoma (73.83%), respectively. Radiological and histopathological findings were concordant in 90% of cases.
Conclusion: Invasive urothelial carcinoma predominates among neoplastic lesions, occurring in older males with smoking as a significant risk factor. Hematuria remains the primary clinical symptom. Evaluating muscle invasion is critical for prognosis and treatment planning. Radiology and histopathology play a vital role in diagnosis, while immunohistochemistry and molecular studies are essential for precise classification and typing.

Keywords: Urothelial lesion; non-neoplastic urothelial lesion; Cystitis; Invasive urothelial carcinoma; Haematuria; TURBT

Introduction

Urothelium, a transitional epithelium lining the renal pelvis, ureters, bladder, and most of the urethra, is prone to both neoplastic and non-neoplastic lesions. Non-neoplastic conditions like cystitis, malacoplakia, urachal lesions, and tuberculosis are often debilitating but rarely fatal [2]. Cystitis, in particular, is a significant contributor to bladder-related symptoms. Neoplastic lesions are a major cause of illness as well as death [2].

Urothelial bladder cancer (UBC), comprising 3% of global cancer cases, is the 10th most prevalent cancer and the 13th leading cause of cancer mortality worldwide, with 573,278 new cases and 212,536 deaths reported in 2020 [3]. In India, UBC ranks 17th in prevalence and 21st in cancer mortality, with 21,096 cases and 11,154 deaths reported in 2020 [3].

The incidence of bladder cancer varies between countries, states, and urban and rural areas, indicating that social, occupational, environmental, or dietary factors may contribute to the development of bladder cancer [4].

Most UBC cases are non-muscle invasive, though 20% are muscle invasive, necessitating aggressive treatment [5, 6, 7]. Diagnostic and prognostic tools include cystoscopic biopsy and transurethral resection of bladder tumours (TURBT), with advanced imaging techniques like ultrasonography, CT, and MRI replacing excretory urography.

In order to enhance the treatment and results of urothelial lesions, this study analyses the histopathological spectrum of these lesions, correlates radiopathological and clinicopathological findings.

Materials and Methods

A retrospective and prospective observational study of 100 cases was conducted in the Surgical Pathology Section, Department of Pathology, Central Diagnostic Laboratory, Shantaben Suryakant Desai Diagnostic Centre, Bhaikaka University, Shree Krishna Hospital, Karamsad, from 2021 to 2024.

The study received approval from the Institutional Ethics Committee of Bhaikaka University, Shree Krishna Hospital, Karamsad (letter no.-IEC/BU/141/Faculty/38/24/2023). For retrospective data, patient confidentiality was strictly maintained, and the requirement for informed consent was waived by the ethics committee. For prospective data collection, written informed consent was obtained from all participants before their inclusion in the study.

The study considered TURBT specimens, cystectomy and nephreureterectomy specimens, cystoscopic biopsies, slides and blocks (for review) of the urinary bladder, urethra, ureter and renal pelvis that were received in the Surgical Pathology department, excluding inadequate bladder biopsies.

Patient data, including demographics, clinical, radiological findings, and histopathology, were collected from laboratory and hospital databases. Histopathological examination was performed using light microscopy, and the lesions were classified accordingly. Neoplastic lesions were categorized based on the 2022 WHO classification of epithelial tumors of the urothelial tract. Bladder tumours were staged as per the 8th edition of the AJCC staging guidelines.

Descriptive statistics, including frequency, mean, Standard Deviation (SD), and p-values, were analysed using STATA 14.2 to summarize the baseline profile and diagnoses of study participants.

Results

This study analysed 100 cases of urothelial lesions. Of the biopsies received, the majority were cystoscopic bladder biopsies (88%), followed by cystectomy specimens (6%), ureteric biopsies (3%), nephrectomy specimens (2%), and cystoscopic urethral biopsies (1%).

The distribution of urothelial lesions showed a predominance of neoplastic lesions (65%) compared to non-neoplastic lesions (35%). Gender analysis revealed an almost equal representation of males and females among non-neoplastic lesions, while neoplastic lesions exhibited a marked male predominance (Male: Female = 5:1). The age range for neoplastic lesions was 45–90 years, with the highest incidence (n=24) observed in the 54–60-year age group. Notably, all neoplastic lesions were diagnosed in patients aged 40 years or older. The mean age at diagnosis was 49.68 $\pm$ 15.00 years for non-neoplastic lesions and 63.23 $\pm$ 10.40 years for neoplastic lesions (Table 1).

Among the 35 cases of non-neoplastic lesions, interstitial cystitis was the most common diagnosis, followed by cystitis cystica, cystitis cystica with glandularis, granulomatous cystitis, and reactive atypia. Of the 65 cases (100%) of neoplastic lesions, 10 (15.38%) were non-invasive urothelial neoplasms, while 55 (84.61%) were invasive urothelial carcinomas. High-grade carcinomas constituted 50.77% of neoplastic cases, while low-grade carcinomas accounted for 23.08% (Table 2). Most neoplastic lesions originated in the urinary bladder (90.76%), followed by the ureter (4.61%), renal pelvis (3.07%), and urethra (1.53%).

Among the 65 cases of urothelial neoplasm, the predominant risk factor identified was smoking, present in 36.92% (n=24) of patients. This was followed by bladder stone (18.46%), radiation exposure (9.63%), and chemical or dye exposure (7.69%). 18 patients (27.69%) with neoplastic lesions were not associated with any above-mentioned risk factors.

Among 35 cases of non-neoplastic lesions, burning micturition was the most common symptom (62.85%, n=22), followed by increased frequency (51.42%) and abdominal/flank pain (37.14%). Other symptoms included haematuria, urgency, dysuria, and fever. Among 65 urothelial neoplasm cases, haematuria was the predominant symptom (81.53%, n=53), followed by dysuria (69.23%), burning micturition (32.30%), and abdominal/flank pain (18.46%). Additional symptoms included increased frequency, urgency, nocturia, incomplete voiding, and fever. These findings highlight the diverse clinical presentations of non-neoplastic lesions and urothelial neoplasms, with haematuria being the most prevalent symptom in neoplastic cases.

A diagnostic concordance of 90% was observed between clinical and histopathological findings, while 10% of cases exhibited discordance.

Table 1: Age and Gender-wise Distribution of Urothelial Lesions

Age	Non-neoplastic lesions, n=35 (100%)	Neoplastic lesions, n=65 (100%)
21-30	4 (11.43%)	0 (0.00%)
31-40	7 (20.00%)	0 (0.00%)
41-50	9 (25.71%)	6 (9.23%)
51-60	5 (14.29%)	24 (36.92%)
61-70	7 (20.00%)	21 (32.31%)
71-80	2 (5.71%)	9 (13.85%)
81-90	1 (2.86%)	5 (7.69%)
Gender	**Non-neoplastic Urothelial lesion**	**Neoplastic urothelial Lesion**
Female	18 (51.43%)	11 (16.92%)
Male	17 (48.57%)	54 (83.08%)

Table 2: Histopathological Classification of Non-neoplastic and Neoplastic Urothelial Lesions

Type of lesion	Number of cases	Percentage (%)
Non-Neoplastic Lesion, n=35 (100%)		
Interstitial cystitis	25	71.43%
Cystitis cystica	3	8.57%
Cystitis glandularis	3	8.57%
Reactive atypia/Metaplastic changes	1	2.86%
Granulomatous cystitis	3	8.57%
Neoplastic Lesion, n=65 (100%)		
Papillary urothelial neoplasm of low malignant potential (PUNLMP)	7	10.77%
Urothelial papilloma	2	3.08%
Inverted urothelial papilloma	1	1.54%
Invasive urothelial carcinoma, high grade	33	50.76%
Invasive urothelial carcinoma, low grade	15	23.07%
Urothelial carcinoma with squamous differentiation	3	4.62%
Pure Squamous Cell Carcinoma	3	4.62%
Sarcomatoid carcinoma	1	1.54%

Table 3: Association Between Risk Factors and Neoplastic Urothelial Lesions

Risk factor	Neoplastic urothelial lesion (n=65)		P value*
	Yes	No	
Smoking	24 (36.92%)	41 (63.08%)	0.021
Chemical exposure/Dye exposure/Driver/Painter	5 (7.69%)	60 (92.30%)	1.000
Radiation exposure	6 (9.23%)	59 (90.76%)	0.416
Bladder stone	12 (18.46%)	53 (81.53%)	0.247
No risk factor	18 (27.69%)		

*The association between various risk factors and neoplastic urothelial lesions was evaluated using the Chi-square test.

Table 4: Clinical Symptom Profile of Patients with Non-neoplastic and Neoplastic Urothelial Lesions

Symptoms	Non-neoplastic urothelial lesion (n=35)	Neoplastic urothelial lesion (n=65)
Hematuria	4 (11.42%)	53 (81.53%)
Burning micturition	22 (62.85%)	21 (32.30%)
Increase frequency	18 (51.42%)	7 (10.76%)
Urgency	3 (8.57%)	6 (9.23%)
Dysuria	3 (8.57%)	45 (69.23%)
Nocturia	0 (0.00%)	1 (1.53%)
Incomplete voiding	0 (0.00%)	2 (3.07%)
Abdominal/Flank pain	13 (37.14%)	12 (18.46%)
Fever	2 (5.71%)	0 (0.00%)

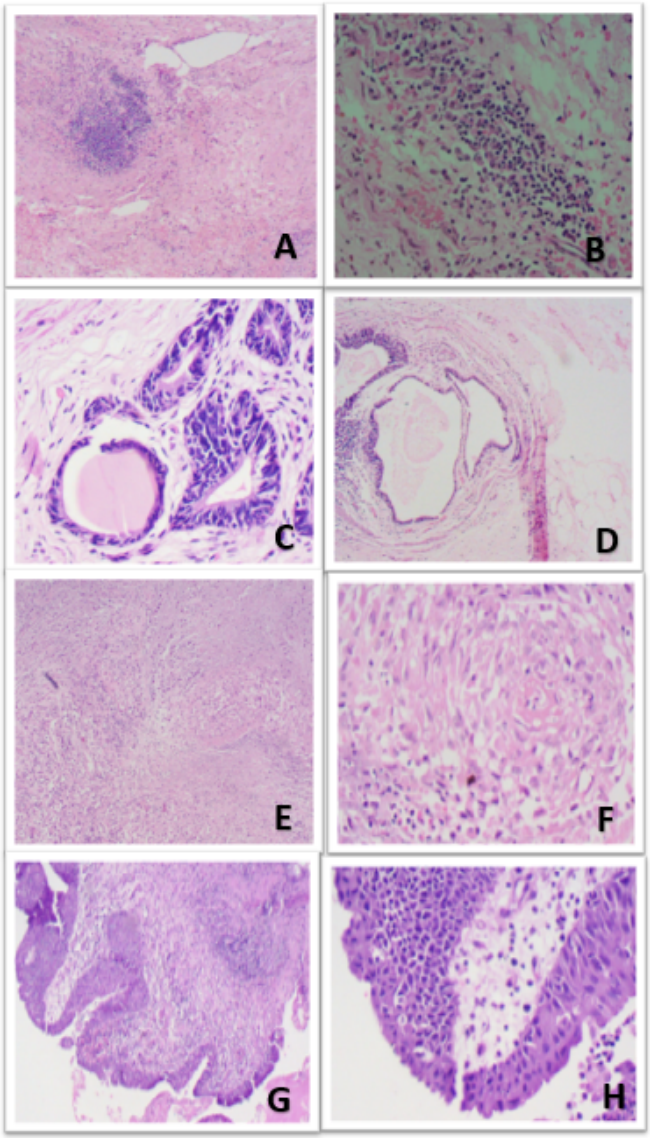

Figure 1: Non-neoplastic lesions. A, B: Non-specific Interstitial Cystitis (100X, 400X); C: Cystitis glandularis (400X); D: Cystitis cystica (100X); E, F: Chronic Granulomatous Cystitis (100X, 400X); G, H: Reactive atypia (100X, 400X)

Discussion

In the present study, 35% of cases were non-neoplastic and 65% were neoplastic. This closely aligns with findings by Aparna C et al. [8], who reported 31.5% non-neoplastic and 68.5% neoplastic lesions, and Pudasaini S et al. [9], with 31.9% non-neoplastic and 68.1% neoplastic lesions. However, Raghuveer CV et al. [10] observed an equal distribution, with 50% non-neoplastic and 50% neoplastic lesions. These differences may be due to varying biopsy practices, as neoplastic lesions are more likely to be sampled during cystoscopy, while non-neoplastic lesions are often managed conservatively.

The present study demonstrates a significant male predominance in neoplastic lesions, especially urothelial bladder carcinoma (Male:Female = 5:1), comparable to Matalka et al. [11] (9:1), Goyal et al. [1] (5.25:1), Joshi et al. [12] (3.66:1), and Agrawal et al. [13] (15.7:1). This disparity may be linked to higher rates of smoking, occupational exposure, and hormonal factors like androgen receptor (AR) activation [14, 1, 15]. Estrogen likely offers a protective effect, as studies report increased UBC risk in postmenopausal and nulliparous women [16, 17, 18], emphasizing the need for gender-specific preventive and therapeutic approaches.

In this study, non-neoplastic lesions were most frequent in the 41–50 years age group (25.71%) with a mean age of 50 years, indicating earlier presentation. Neoplastic lesions peaked in the 51–60 years group (36.92%) with a mean age of 63 years, aligning with Agrawal et al. [13] (40%) and other studies [10, 19]. Compared to Goyal et al. [1] and Vaidya et al. [20], who reported the highest incidence in the seventh decade (33%), our study shows a slightly earlier peak in the sixth decade.

In our study, interstitial cystitis was the most common non-neoplastic lesion, comprising 71.43% of cases, in line with

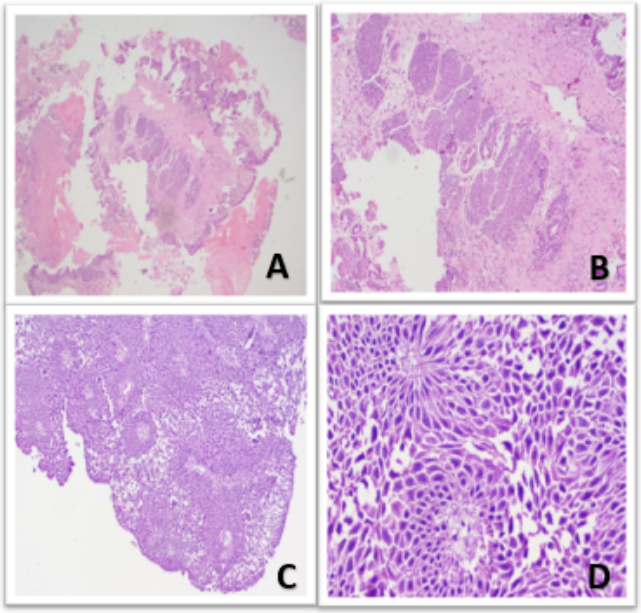

Figure 2: A, B: Inverted Papilloma (100X, 400X); C, D: Papillary Urothelial Neoplasm of Low Malignant Potential (400X)

findings from other studies [10, 21, 22]. This category included non-specific cystitis, acute on chronic cystitis, chronic cystitis, and acute cystitis. Similarly, Goyal VK et al. [1] reported chronic non-specific cystitis as the most frequent non-neoplastic lesion, along with a few cases of eosinophilic cystitis. Granulomatous cystitis accounted for 8.57% of cases in our study, consistent with observations by Srikousthubha et al. [21] and Shrestha M et al. [22], often linked to tuberculosis, especially in regions with a high prevalence of pulmonary tuberculosis [22, 23].

Non-neoplastic lesions showed an overall equal gender distribution, except in the 31–40 age group, where females were more affected—likely due to a higher incidence of UTIs in sexually active women [24]. In males aged 40–70, prostatic hyperplasia and bladder neck obstruction increased cystitis risk, as noted by Sharma DD et al. [23]. Cystitis cystica and glandularis each comprised 8.57% of cases. Histologically, glandularis showed gland-like lumens, while cystica displayed dilated lumens with eosinophilic fluid. Metaplastic changes (2.38%) were consistent with findings by Shrestha M et al. [22] and S. Devdhar et al. [25].

In our study, invasive urothelial carcinoma was the most common neoplastic lesion (73.83%), followed by PUNLMP (10.76%), consistent with findings by Agrawal S [13] and studies from China [26]. High-grade invasive carcinoma (50.76%) was more prevalent than low-grade (23.07%), aligning with Baidya et al. [19], and exhibited typical features described by Poudel S et al. [27]. Lamina propria invasion was noted in 46.15% of cases, similar to Agrawal S et al. [13] (41.67%). Muscle invasion occurred in 14 of 33 high-grade and 4 of 15 low-grade cases. Notably, detrusor muscle was absent in 62.5% of cystoscopy specimens—higher than the 33.3% reported by Pudasaini et al. [9]—potentially affecting accurate staging and subsequent treatment planning [28]. This is the limitation of our study.

In our study, urothelial carcinoma with squamous differentiation was the only variant observed, accounting for 4.61% of cases, whereas studies by Agrawal S et al. [13] and Goyal et al. [1] reported additional histological variants. No cases of non-invasive papillary urothelial carcinoma were identified, unlike Pudasaini et al. [9], who noted a higher proportion of low-grade cases. PUNLMP was seen in 10.76% (7 cases), comparable to Vaidya et al. [20] (10.28%) but higher than Agrawal S et al. [13] and Goyal et al. [11], who reported 4%. We also found two cases (3.07%) of urothelial papilloma and one case (1.53%) of inverted papilloma; in contrast, Thapa et al. [29] reported 8.9% papilloma cases, while other studies [8, 9, 21, 23] did not report any. Additionally, one rare case of sarcomatoid carcinoma was identified, with no similar reports in the cited literature [8, 13, 23].

The findings of this study align with existing literature [13, 25], demonstrating distinct symptom patterns between non-neoplastic and neoplastic urothelial lesions. Haematuria, commonly linked to neoplastic lesions, is a key clinical indicator necessitating cystoscopy and biopsy, while symptoms like burning micturition and increased frequency are more typical of non-neoplastic, inflammatory, or infectious conditions. Recognizing these differences is essential for accurate diagnosis and timely management.

Bladder cancer, which comprises 90–95% of urothelial neoplasms according to the American Cancer Society, was similarly predominant in our study, with bladder lesions accounting for 90.76% of cases. A significant association between smoking and neoplastic lesions was also observed: 36.92% of neoplastic cases had a smoking history ($P = 0.021$), supporting earlier

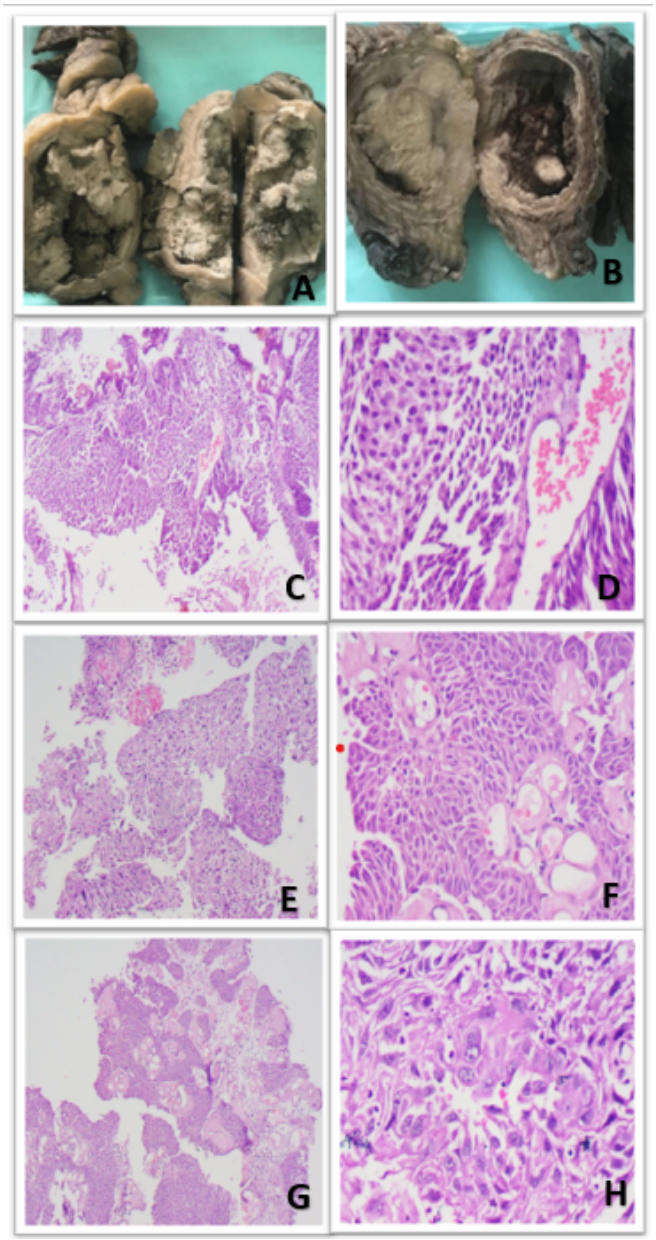

Figure 3: Invasive urothelial carcinoma. A, B: Radical cystectomy specimen: Infiltrating papillary urothelial carcinoma; C, D: Invasive urothelial carcinoma, High grade (100X, 400X); E, F: Invasive urothelial carcinoma, Low grade (100X, 400X); G, H: Pure Squamous Cell Carcinoma (100X, 400X)

studies by Agrawal S et al. [13] (74%) and Joshi et al. [12] (78%).

In our study, occupational exposure to chemical dyes was identified in 7.69% of neoplastic cases; however, no statistically significant association was found (P = 1.000), consistent with the findings of Agrawal et al. [13]. While literature acknowledges dye exposure as a significant risk factor for urothelial carcinoma [31], its limited impact in our study may be due to the low presence of dye industries in the Charotar region.

Histo-radiological concordance was observed in 90% of cases. Among the 10 discrepant cases, seven lesions initially appeared inflammatory on imaging but were later confirmed as malignant histologically, two radiologically normal cases revealed inflammatory changes on histopathology, and one case thought to be a hematoma was diagnosed as a high-grade invasive carcinoma. These discrepancies underscore the limitations of imaging alone and emphasize the essential role of histopathological evaluation in accurate diagnosis, which may be influenced by imaging resolution, sampling errors, or interpretive variability between radiologists and pathologists.

Conclusion

Urinary bladder biopsies reveal a spectrum of lesions, with a predominance of neoplastic cases. Neoplastic urothelial lesions are most common in the 6th decade and primarily affect males, while non-neoplastic lesions occur equally in both genders, except in the 31–40 age group, where females predominate due to higher infection rates. Hematuria is a key symptom, often indicating neoplastic processes. Smoking is a significant risk factor for bladder cancer, underscoring the need for smoking cessation and early detection programs. Cystitis is the most common non-neoplastic lesion, requiring preventive measures and targeted treatment. High-grade invasive urothelial carcinoma is the most frequent neoplastic lesion, with detrusor muscle invasion being a critical factor in prognosis and treatment. Rare cases of urothelial carcinoma with squamous differentiation, pure squamous cell carcinoma, and sarcomatoid carcinoma were also identified.

Acknowledgements: I would also like to give the warmest thanks to my teacher Dr. Monica Gupta (Professor and Head of Pathology Department) for constant encouragement for academic excellence and guidance. I also would like to thanks to all member of Pathology Department and Mrs. Mamata Patel (Statistician, Pramukhswami Medical College).

Funding: None

Competing Interests: None

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