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Original Research Article

A gamut of Histopathological Lesions of Carcinoma of Urinary Bladder- A study of 43 cases

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Abstract

Aims/Objective: Urinary bladder cancer is the 7th most common cancer seen worldwide, and is considerably more common in males than females worldwide. The present study was done to determine the age, sex incidence of the tumour occurrence and to study histopathological features of urinary bladder carcinoma with clinical background and to analyse the data descriptively.

Materials and Methods: This prospective study was done with the biopsy and resected specimen of the urinary bladder carcinoma during a period of two years (October 2012-June 2014) from Yenepoya Medical College hospital, Mangalore. The specimens were received in 10% formalin and subjected to macroscopic description and appropriate relevant clinical details were noted. Standard tissue sections were given. Microscopic features were studied with H&E stained tissue sections using the parameters described in the proforma.

Results: The present study was done on 43 cases of urinary bladder carcinomas. Cases occurred in age range of 42-91 years, peak incidence was seen in 6th decade of life, with a male to female ration of 3.1:1.No case was seen below 40 years of age. Haematuria was the most common presenting symptom, while lateral wall of urinary bladder was the commonest site of urinary bladder carcinoma with 58% of cases. Transitional cell carcinomas were the most common histological type found. 23 cases of non-invasive papillary urothelial carcinomas and 20 cases of invasive urothelial carcinomas were seen. Among non-invasive papillary urothelial carcinoma 15 cases were of low grade non-invasive carcinoma and 8 cases were of high grade non-invasive carcinoma.

Conclusion: Urinary bladder carcinoma patients present in advanced stages with an overall poor survival. Incidence and prognosis can be improved by reduction of risk factors and early detection. Few of the most promising patient approaches for improving patient prognosis focus on techniques that allow early diagnosis in their early stages.

Keywords: Urinary bladder carcinoma, Lateral wall of bladder, Haematuria, Invasion

1.Introduction

Bladder cancer is the 7th most common cancer seen worldwide, with higher incidence in the USA and Europe compared with Asian countries. According to the Delhi Cancer Registry[1], in 2003, bladder cancer was the 6th most common cancers, surpassed in frequency only by cancers of the lung, larynx, tongue, prostate, and oesophagus. Urinary bladder carcinoma is a disease of significant morbidity and mortality. Occupational risks, environmental risks, dietary habits and cigarette smoking are lifestyle factors known to influence the development of urothelial carcinoma.[2] It is important to understand the risk factors of this disease. Urinary bladder carcinoma is considerably more common in males than females (male: female ratio is seen 3.5:1) worldwide.[3] Localisation of bladder tumour on initial presentation provides a useful parameter for prediction of the behaviour and

prognosis of bladder carcinomas. Urinary bladder carcinomas are the heterogeneous group of neoplasms which show wide morphological variability of nonneoplastic lesions that may mimic neoplasms grossly and/or microscopically.[4]

1.1 Aims and Objectives

The aim of this study was to study malignant urinary bladder tumours histopathologically with clinical background, classify them according to WHO classification of tumours of urinary system and male genital organs and study the relationship between ages, sex incidence of the tumour occurrence and to correlate with site, type, grade and clinical behaviour of the tumour (metastasis) wherever possible.

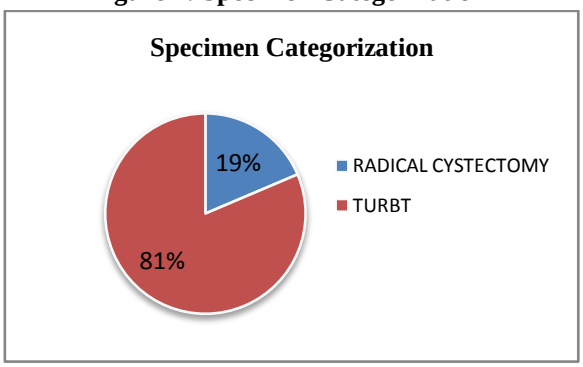
2.Materials and Methods

This study was done on endoscopic biopsies as well as the resected specimens clinically diagnosed as urinary bladder carcinomas. All cases received in the Department of pathology from Yenepoya Medical college Hospital are included in this study. The duration of this study period was from October 2012 to June 2014.The specimens were received in 10% formalin and subjected to macroscopic description and appropriate relevant clinical details were noted. Standard tissue sections were given. Haematoxylin and eosin (H&E) stained sections were prepared from the paraffin embedded blocks. The slides are studies and classified according to WHO histological classification of the tumours of urinary tract 2002. Special histochemical and Immunohistochemical methods were applied wherever applicable. The biopsy specimens who were diagnosed as inflammatory lesions, benign tumours as well as all non-epithelial tumours were excluded from the study. All urinary bladder carcinoma cases were included in the study.

3.Results

A total number of 43 cases were studies in the department of Pathology, Yenepoya Medical College Hospital. Clinical details and investigations of all the patients were recorded. The morphological features were studies in detail and findings were analysed. Out of 43 cases 8 cases were of radical cystectomy of the bladder and 35 cases were transurethral resection of bladder tumour (TURBT).

Figure 1: Specimen Categorization



The age of the patients in this study ranged from 40-91 years. Peak age of occurrence was in 6th decade with 14 cases, followed by 5th and 7th decade with 10 cases each. In this study we found that males had higher incidence of carcinomas than females. In males majority of the carcinomas found in 7th decade of life, while in females same numbers of cases were seen in 5th and 6th decade of life. No cases were found in younger age below 40 years.

Table 1: Age incidence of all urothelial carcinomas

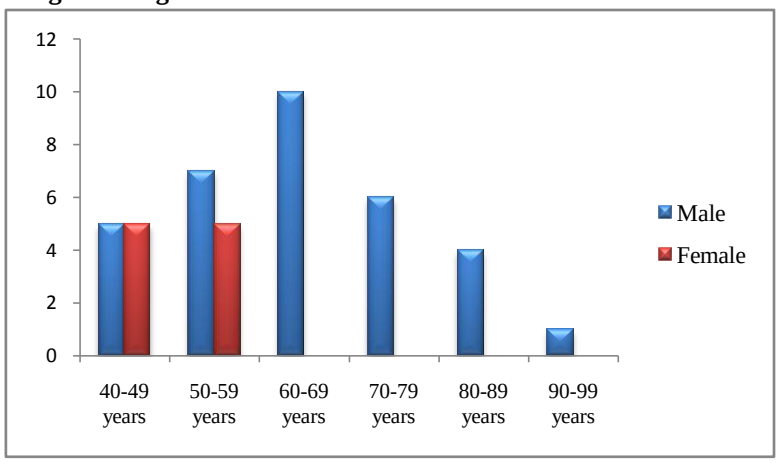
Age group	No of cases
40-49	10
50-59	12
60-69	10
70-79	6
80-89	4
90-99	1
Total	**43**

Figure 2: Age group distribution of urothelial carcinomas

Table 2: Age and gender distribution

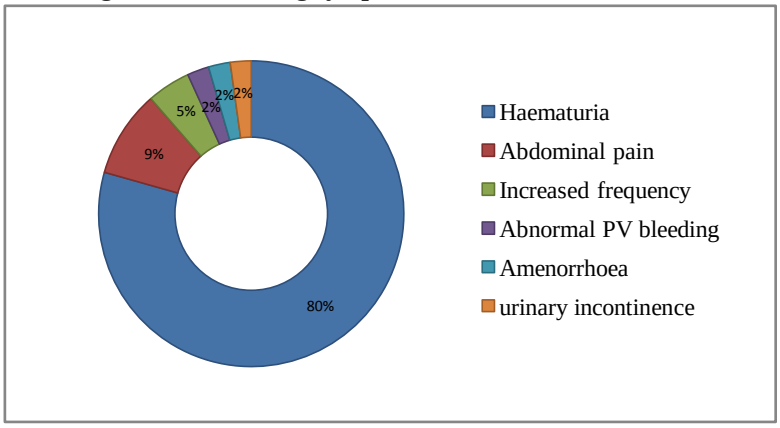
Age group	Male	Female
40-49	5	5
50-59	7	5
60-69	10	-
70-79	6	-
80-89	4	-
90-99	1	-
Total	**33**	**10**

Figure 3: Age and Gender incidence of all urothelial carcinomas



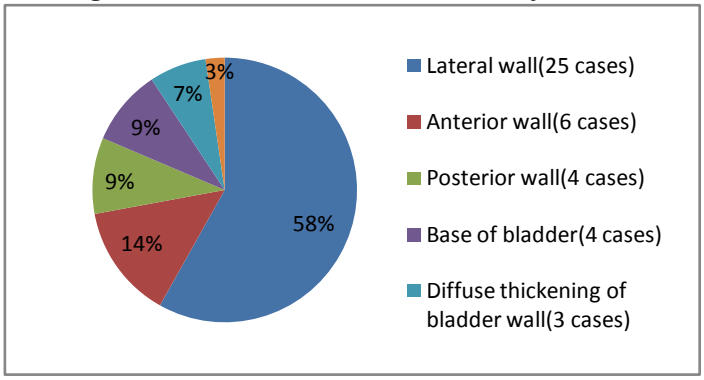
The most common presenting symptom of the patient was haematuria in 34 cases (79.3%) followed by abdominal pain in 4 cases (9.2%) increased frequency 2 cases (4.6%), abnormal bleeding per vagina, amenorrhoea, and urinary incontinency 1 case (2.3%) each as shown in figure 4.

Figure 4: Presenting symptoms of urothelial carcinoma



The commonest site of the carcinoma found by ultrasonography, CT scan, MRI scan or cystoscopy (whichever in done for the particular patient) was lateral wall of bladder in 25 cases (58%) followed by anterior wall in 6 cases (14%), posterior wall in 4 cases (9%), base of the bladder in 4 cases (9%) and fundus in 1 case (3%).Diffuse thickening of bladder wall was seen in 3 cases (7%). Above mentioned sites are shown in the figure 5.

Figure 5: Site of the carcinoma in Urinary bladder



All 43 cases were studied under light microscopy and were classified according to WHO histological classification of tumours of urinary tract 2004.Non-invasive papillary urothelial carcinomas were further subdivided in low grade and high grade, according to the microscopic findings mentioned below.

Low grade non-invasive papillary urothelial carcinoma are diagnosed by fused, slender papillary stalks with frequent branching but minimal fusion with few recognised variation in nuclear polarity, size, shape and chromatin pattern. Mitosis was very infrequent. 15 cases of low grade non-invasive papillary urothelial carcinoma were identified.

High grade non-invasive papillary urothelial carcinoma was diagnosed by frequently fused and branching papillae. As compared to low grade non-invasive papillary urothelial carcinoma high grade non-invasive papillary urothelial carcinoma has more variation in nuclear polarity, size, shape and chromatin pattern. The nuclei are moderately pleomorphic and show some irregularly distributed chromatin. Mitosis are frequent than low grade and they can be atypical. 8 cases of high grade non-invasive papillary urothelial carcinoma were identified. The results are shown in figures 6, 7 and 8.

Figure 6: Distribution of histological types of urothelial carcinomas

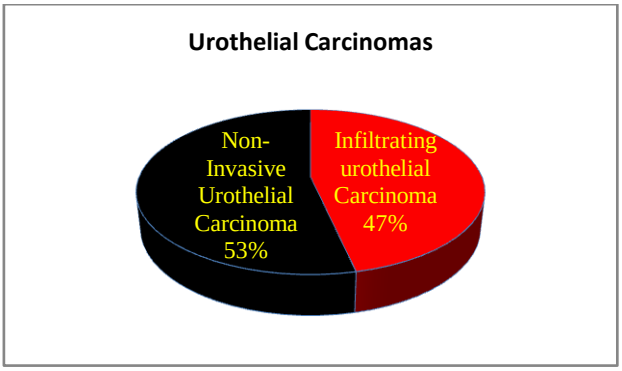
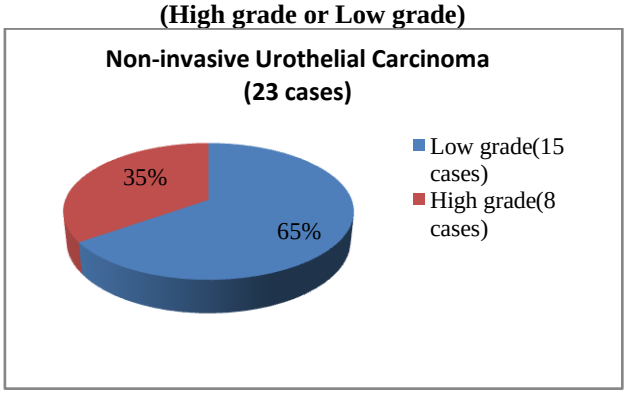


Figure 7: Distribution of Non-Invasive urothelial carcinomas according to grades (High grade or Low grade)



Among 15 non-invasive low grade urothelial carcinoma cases 4 were females while 11 are males. In most of the cases age group affected was 50-59 years(6^{th} decade) with mean age of 59.2 years. 11 out of 15 patients presented with complaints of haematuria while 9 out of 15 patients site affecting urinary bladder was lateral wall of bladder. In 14 out of 15 patients trans-urethral resection of bladder was performed.

Among 8 non-invasive high grade urothelial carcinoma cases 1 patient was a female while all other 7 cases were males. In most of the cases age group affected was 70-79 years (8^{th} decade) with mean age of 66.2 years. 7 out of 8 patients presented with haematuria while the only female patient presented with vaginal bleeding. Lateral wall of bladder was the most common site affected in 4 out of 8 pateints, while other sites affected are anterior wall, posterior wall, fundus and diffuse bladder wall thickening, one case each.

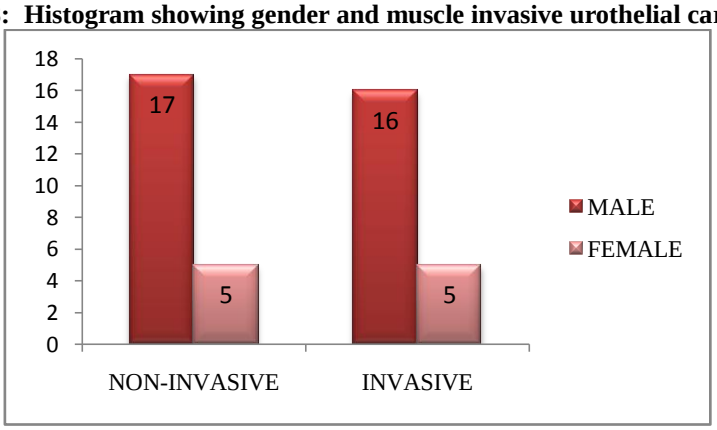
We found 20 cases of invasive urothelial carcinoma. All cases of invasive carcinoma in our study were transitional cell carcinoma. Four cases(20%) were of infiltrating urothelial carcinoma with squamous differentiation, two cases (10%) were of infiltrating urothelial carcinoma-clear cell variant, and one case(5%) each of sarcomatoid variant, plasmacytoid variant and infiltrating urothelial carcinoma with glandular differentiation.

We compared association of gender and muscle invasion in the cases of urothelial carcinoma of bladder. Cases were tabulated according to the gender and muscle invasion by tumour cells.

Table 3: Distribution of Gender and muscle invasion of the cases of urothelial carcinoma

	Non-invasive carcinoma cases	Invasive carcinoma cases
Male	17	16
Female	5	5

Figure 8: Histogram showing gender and muscle invasive urothelial carcinoma



The data was analysed with SPSS software 22.0 to find out the association between the gender and muscle invasion.

The analysis showed there is no significant association between the gender and the muscle invasion (p value=0.933) with degree of freedom is 1 and chi square value being 7.04.

Incidence of bladder carcinoma have marked geographic and clinopathological variation worldwide. The incidence of bladder carcinoma rises progressively with a peak incidence of 6th and 7th decade.[4][9] Males are affected more common than females.[5] In the present study of 45 cases of urinary bladder carcinoma, peak incidence of urinary bladder carcinoma was seen in 6th decade with a mean age of occurrence being 59.3 years. Lowest age incidence seen was 42 years, while highest age incidence was at 91 years. This result is being comparable to other studies as shown in table 4.

Table 4: Comparison of mean age, number of cases with other studies

Authors	Study Period	Total cases studied	Mean age(years)
Husain *et al*[6]	2004-2005	106	59.4
Zhang *et al*[7]	2006-2010	658	61.9
Gupta *et al*[8]	2001-2008	561	60.2
Laishram *et al*[9]	2001-2010	26	62
Biswas *et al*[10]	2007-2009	88	65
Present Study	2012-2014	45	59.3

As compared to other study series the present study also showed relatively higher male incidence. The gender incidence in our study was more in males than females with a sex ratio of 3.1:1 which is lower than the most of the studies[7][8][10] but higher than the study done by Laishram *et al*.[9]

Table 5: Comparison of gender incidence with other studies

Authors	Study Period	Sex incidence		Sex ratio
		Male	Female	
Zhang *et al*[7]	2006-2010	548	110	5:1
Gupta *et al*[8]	2001-2008	431	50	8.6:1
Laishram *et al*[9]	2001-2010	15	11	1.5:1
Biswas *et al*[10]	2007-2009	76	12	6.3:1
Present Study	2012-2014	34	11	3.1:1

In the present study we found that haematuria(80%) was the most common presenting symptom. Other symptoms abdominal pain (9%), increased frequency (5%) and urinary incontinence, vaginal bleeding and amenorrhea (2% each) were noted. Urinary urgency was seen as a presenting symptom in 5% of cases in our study, while it is seen in 15.7% of cases in the study done by Husain *et al*[6]. No study showed presenting symptom of vaginal bleeding and amenorrhea. Our findings were comparable to other studies as depicted in table 6.

Table 6: The comparison of clinical presentation with other studies

Clinical symptoms	Zhang *et al*[7]	Husain *et al*[6]	Rasool *et al*[11]	Present study
Haematuria	76%	84.3%	78%	80%
Abdominal pain	-	-	-	9%
Urgency	-	15.7%	-	5%
Others	-	-	-	6%

In studies done by Stephenson *et al*[12], and Husain *et al*[6] the most common site of urinary bladder carcinoma was lateral wall followed by posterior wall and anterior wall.

While study done by Biswas *et al*[10] most commonly found site was posterior wall (53%) followed by lateral wall (43%) and trigone (3%). The findings in the present study are comparable to above mentioned studies as shown in table 7.

Table 7: Comparison of site incidence with other studies

Site	Stephenson *et al*[12]		Husain *et al*[6]		Present study	
Lateral wall	339	37.1%	36	45%	25	58%
Posterior wall	164	17.9%	5	6.3%	5	9%
Anterior wall	35	3.8%	5	6.3%	6	14%
Sites other than above mentioned sites	556	41.2%	60	32.4%	8	19%

In our study, 23(56%) cases were Non-invasive urothelial carcinomas and 20(44%) cases were infiltrating urothelial carcinomas. Among non-invasive urothelial carcinomas, there were 15 cases of low grade non-invasive papillary urothelial carcinomas and 8 cases of high grade non-invasive papillary urothelial carcinomas. This finding is comparable to studies done by Gupta *et al*[8], Husain *et al*[6], Laishram *et al*[9], Biswas *et al*[10] and Rasool *et al*[11].

Table 8: Comparison of incidence of invasive, non-invasive (high grade and low grade) urothelial carcinoma with other studies.

Type of tumour	Zhang *et al*[7]	Husain *et al*[6]	Laishram *et al*[9]	Biswas *et al*[10]	Rasool *et al*[11]	Present study
Non invasive Low grade	-	-	14(53.9%)	51(58%)	-	15(33.3%)
Non invasive high grade	-	-	9(34.6%)	24(27%)	-	8(17.7%)
Invasive carcinoma low grade	328-49.9%	52.6%			51.4%	Nil
Invasive carcinoma high grade	330-50.1%	43.4%	-	-	21.4%	20(44.5%)

3.Discussion

Histopathological diagnosis is gold standard for all urinary bladder tumours. Though ultrasonography, computed tomography, Magnetic resonance imaging modalities has created a lot better understanding of urinary bladder lesions, still histopathological diagnosis has remained importance for the classification and management of urinary bladder lesions. As noted in various studies, Incidence of bladder carcinoma have marked geographic and clinopathological variation worldwide. The incidence of bladder carcinoma rises progressively with a peak incidence of 6th and 7th decade. Males are affected more common than females. These finding also confirmed in our study. Bladder carcinoma presents with variable clinical symptoms in which gross and microscopic hematuria are the main symptoms. Invasive carcinomas are graded as low grade and high grade depending upon the degree of nuclear anaplasia and some architectural abnormalities. Some cases may show relative bland cytology.

Laishram *et al*[9] found that majority of TCC were non-invasive and the invasion was seen in 50% of high grade tumours,98% of the carcinoma show invasion at the time of diagnosis and according to him the reason was patient has not seen doctor on time. Messing *et al*[13] reported 55-60% of tumours are of low histological grade, but majority of patient with invasion were high grade. In the present study majority of the invasive carcinomas (44.5%) were low grade, high grade tumours making up only 17% of invasive tumours. All cases of carcinoma in our study were transitional cell carcinoma. Four cases (20%) were of infiltrating urothelial carcinoma with squamous differentiation, two cases (10%) were of infiltrating urothelial carcinoma-clear cell variant, and one case(5%) each of sarcomatoid variant, plasmacytoid variant and infiltrating urothelial carcinoma with glandular differentiation. As of now, there is currently no standard reporting methodology with regards to the amount of variant histology(i.e. divergent differentiation) present within urothelial cancer.

Tumour grade showed a significant association with the outcome in the study done by Husain *et al*[6] this is closely related to study done by Messing *et al*[13] that of the high grade or invasive cases, the proportion of late stage tumours were significantly lower in the screening-detected bladder cancer compared to unscreened ones. In our study we found 44.5% of muscle invasive tumours which were of high grade

4. Conclusion

From this study it is concluded that, carcinoma of urinary bladder are not rare. They are rare before 40 years of age, but its incidence steadily climbs thereafter and peaks in 6th and 7th decade of life. The peak incidence was seen in 6th decade in the

present study. Urothelial carcinomas show male predominance. Worldwide urothelial carcinoma rates are almost twice in men as women. Urothelial carcinoma can present with variety of symptoms, where haematuria was the most common presenting symptom. Non-specific symptoms like increased frequency and urgency can also be seen as an alarming symptom. Urothelial carcinoma can arise in any part of urinary bladder; mostly it arises from the lateral wall of urinary bladder followed by anterior and posterior wall. Urothelial carcinomas were the only histological type observed. Focal differentiation is not seen frequently. Most of the tumours were non-invasive and low grade at the time of diagnosis. There is definite correlation between advancing tumour grade and invasion. Grading of urothelial carcinomas is important for optimizing the prognosis and the treatment of urinary bladder carcinomas. Therefore therapeutic strategies should be based on histological grading of the tumour.

Fig 9: Cut surface of bladder showing a papillary growth

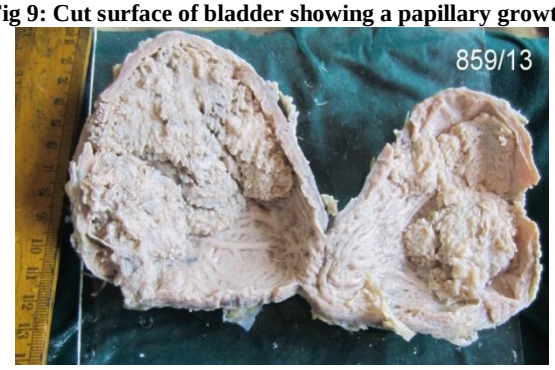


Fig. 10: Bits of transurethral resection of bladder

Fig 11: Non-invasive Low grade papillary urothelial urothelial carcinoma(x10,H&E)

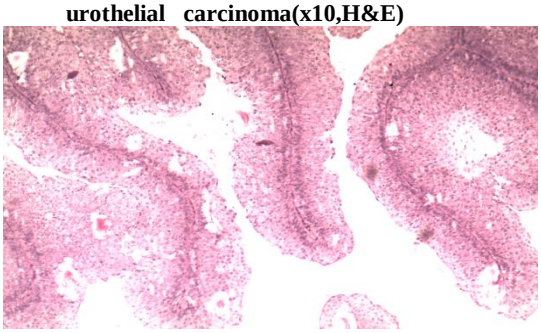


Fig. 12: Non-invasive high grade papillary carcinoma(x10,H&E)

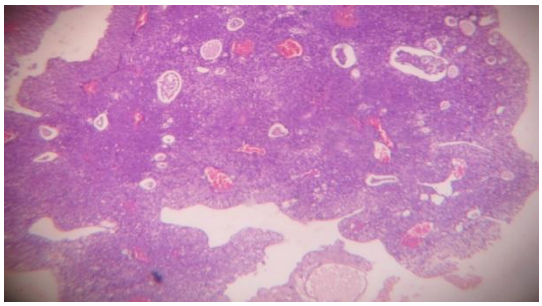


Fig 13: Invasive urothelial carcinoma with glandular differentiation

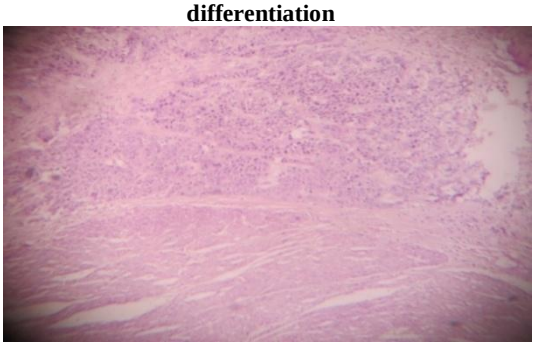


Fig 14: Invasive urothelial carcinoma with squamous differentiation

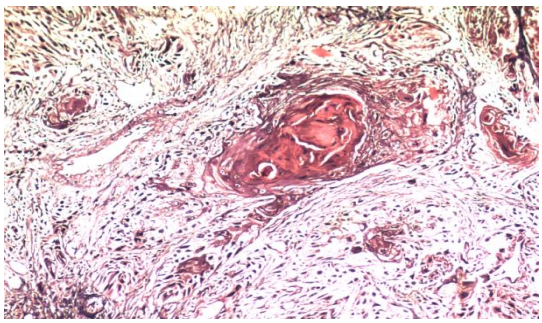


Fig 15: Invasive urothelial carcinoma-Sarcomatoid cell variant

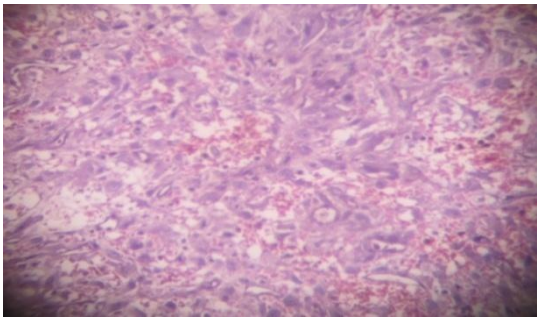
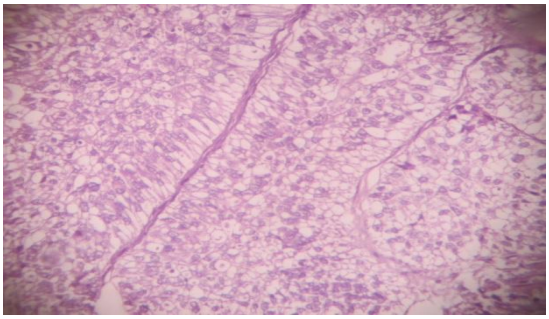


Fig 16: Invasive urothelial carcinoma-clear variant



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