นิพนธ์ต้นฉบับ

Primary adenocarcinoma of the urinary bladder and renal pelvis at King Chulalongkorn Memorial Hospital, from 1989 to 1998

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Somran J, Kittikowit W, Amornsirivat V. Primary adenocarcinoma of the urinary bladder and renal pelvis at King Chulalongkorn Memorial Hospital, from 1989 to 1998. Chula Med J 1999 Aug; 43(8): 533-43

Objective : *To study the pathology of primary adenocarcinoma in the renal pelvis and urinary bladder.*

Setting : *Department of Pathology, Faculty of Medicine, Chulalongkorn University*

Design : *Retrospective descriptive study*

Material : *All cases were pathologically diagnosed as primary adenocarcinoma of renal pelvis and urinary bladder in surgical pathology files during 1989 to 1998.*

Method : *Adenocarcinoma of renal pelvis and urinary bladder were collected from surgical pathology files of King Chulalongkorn Memorial hospital between 1989 to 1998. Metastatic adenocarcinoma, equivocal cases having tumor in more than one organ, and high-graded transitional cell carcinoma with glandular formation were excluded. Routine surgical slides (H & E) and Mayer's mucicarmine study in all case and immunohistochemical study in some cases were available. Histological types of primary adenocarcinoma were classified according to the criteria of Grignon et al. The tumors of the urinary bladder were also subclassified into urachal and non-urachal types by using the most practical criteria of Johnson et al.*

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Results : *Four cases of renal pelvis and eight cases of urinary bladder were primary adenocarcinoma. In the renal pelvis cases, most (75%) were males. The average age was 65.5 (54 to 79). Three of the four cases (75%) had renal stones and three cases (75%) were classified as mixed type. One case (25%) was of the clear cell type. For the urinary bladder, there was only one case, which was subclassified into urachal tumor. The remaining seven cases belong to the nonurachal subtype. Four (57%) of the seven cases presented with hematuria. The most common histologic feature was enteric type.*

Conclusions : *Primary adenocarcinoma of the renal pelvis and urinary bladder is a rare tumor. Average age and sexual preference are not significantly different between renal pelvis and urinary bladder cases. Primary adenocarcinoma of the renal pelvis is strongly associated with renal stones, obstruction of urine outflow, and intestinal metaplasia; except for the clear cell type for which the pathogenesis may be different. In our cases, there were limitations of bladder tissue received from TUR-BT. The associated pathological findings such as cystitis cystica, cystitis glandularis, and intestinal metaplasia were not observed in most cases. The frequencies of histiologic type of primary adenocarcinoma of the renal pelvis and urinary bladder were similar to the textbook.*

Key words : *Primary adenocarcinoma, Renal pelvis, Urinary bladder.*

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จุลินทร สำราญ, วิภาวี กิตติโกวิท, วินิจ อมรสิริวัฒน์. โรคมะเร็งปฐมภูมิของกรวยไตและกระเพาะปัสสาวะ ชนิด adenocarcinoma ที่พบในโรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2532 ถึง พ.ศ. 2541. จุฬาลงกรณ์เวชสาร 2542 ส.ค; 43(8): 533-43

วัตถุประสงค์ : *เพื่อศึกษาพยาธิสภาพ ของโรคมะเร็งปฐมภูมิ ชนิด adenocarcinoma ที่เกิดขึ้นในกรวยไต และกระเพาะปัสสาวะ.*

สถานที่ทำการศึกษา : *ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

รูปแบบการวิจัย : *เชิงพรรณาชนิดย้อนกลับ*

ตัวอย่างที่ทำการศึกษา : *ผู้ป่วยทุกคนที่ได้รับการวินิจฉัยว่าเป็นโรคมะเร็งปฐมภูมิ ชนิด adenocarcinoma จากผลชิ้นเนื้อทางพยาธิวิทยา ในช่วง 10 ปีระหว่าง พ.ศ.2532 ถึง พ.ศ. 2541*

วิธีการศึกษา : *รวบรวมผู้ป่วยที่ได้รับการวินิจฉัยเป็น โรคมะเร็งปฐมภูมิ ของกรวยไต และกระเพาะปัสสาวะ ชนิด adenocarcinoma จากแฟ้มข้อมูลของภาควิชาพยาธิวิทยา โรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2532 ถึง พ.ศ. 2541 โดยนำชิ้นเนื้อที่ผ่านกรรมวิธีการย้อมด้วยวิธีธรรมดาทางพยาธิวิทยา (H&E) และการตรวจพิเศษ Mayer's mucicarmine มาศึกษาโดยกล้องจุลทรรศน์ การตรวจพิเศษทาง immunohistochemistry ได้กระทำเพิ่มเติมในบางตัวอย่าง โรคมะเร็งปฐมภูมิ ชนิด adenocarcinoma ได้ถูกจำแนกลักษณะจุลกายวิภาคตามเกณฑ์ของ Grignon และคณะ นอกจากนั้นยังได้แบ่งย่อย adenocarcinoma ของกระเพาะปัสสาวะออกเป็นชนิด urachal และ non-urachal โดยใช้กฎเกณฑ์ของ Johnson และคณะ*

ผลการศึกษา : *จากการศึกษาพบว่าในช่วงเวลาสิบปีในโรงพยาบาลจุฬาลงกรณ์ มีอุบัติการณ์ของโรคมะเร็งปฐมภูมิชนิด adenocarcinoma เกิดขึ้นที่กรวยไต 4 ราย และกระเพาะปัสสาวะ 8 ราย ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งปฐมภูมิชนิด adenocarcinoma ของกรวยไตส่วนใหญ่เป็นเพศชาย (75 %) โดยมีอายุเฉลี่ย 65.5 ปี (54 ถึง 79 ปี) และสามในสี่ของผู้ป่วย (75 %) มีนิ่วในไต โดยที่ในจำนวนนี้สองราย พบมี intestinal metaplasia สามในสี่ของผู้ป่วยมีลักษณะทางจุลกายวิภาคของเนื้อเยื่อเป็นแบบ Mixed type ซึ่งมี mucinous*

component เป็นส่วนประกอบหลักทั้งสามราย ส่วนโรคมะเร็งปฐมภูมิชนิด adenocarcinoma ของกระเพาะปัสสาวะจำแนกตามต้นกำเนิดโดยเกณฑ์ของ Johnson และคณะพบว่าเป็นมะเร็งชนิด urachal (U) เพียง 1 ราย อีก 7 ราย จัดเป็นมะเร็งชนิด non- urachal (NU) ซึ่งมีอัตราส่วนระหว่างเพศชายต่อหญิงเท่ากับ 2.5 ต่อ 1 ราย มีอายุเฉลี่ยเท่ากับ 54 ปี (35 ถึง 68 ปี) สี่รายในเจ็ดราย (57%) ของมะเร็งชนิดนี้จะมีอาการปัสสาวะเป็นเลือด ส่วนมากของผู้ป่วยที่เป็นมะเร็งชนิด non-urachal (6 ใน 7 ราย, 86 %) เป็นชนิด enteric

สรุป : โรคมะเร็งปฐมภูมิชนิด adenocarcinoma ของกรวยไตและกระเพาะปัสสาวะเป็นเนื้องอกที่พบไม่บ่อย ในการศึกษาพบว่ายังขาดความสมบูรณ์ของข้อมูลทางคลินิกและข้อมูลบางอย่างทางพยาธิวิทยา อันเนื่องมาจากปริมาณเนื้อเยื่อที่ได้มาจาก TUR-BT ของกระเพาะปัสสาวะมีจำกัดเป็นต้น จากการศึกษาพบว่าอายุเฉลี่ย และสัดส่วนของเพศผู้ป่วยที่เป็นมะเร็งของทั้งกรวยไตและกระเพาะปัสสาวะนั้นไม่แตกต่างกันอย่างมีนัยสำคัญ โรคมะเร็งปฐมภูมิชนิด adenocarcinoma ของกรวยไตนั้นมีความสัมพันธ์อย่างมากกับนิ่วในไตและการอุดตันของทางเดินปัสสาวะ รวมทั้งการเปลี่ยนแปลงของเยื่อบุข้างเคียงชนิด intestinal metaplasia ซึ่งเชื่อกันว่ามีความสัมพันธ์กับการเกิดมะเร็งดังกล่าว ยกเว้น clear cell type ส่วนความสัมพันธ์ของการอักเสบและระคายเคืองเรื้อรังที่ทำให้เกิดการเปลี่ยนแปลงพยาธิสภาพของเยื่อบุใกล้เคียง เช่น cystitis cystica cystitis glandulalis และ intestinal metaplasia กับการเกิดมะเร็งชนิดนี้ของทั้ง urachal และ non - urachal นั้นสรุปไม่ได้เนื่องจากเหตุผลที่ได้กล่าวมาแล้ว อย่างไรก็ตามลักษณะย่อยทางจุลพยาธิวิทยาของมะเร็งชนิดนี้ที่พบบ่อยของกรวยไต และกระเพาะปัสสาวะ ทั้ง urachal และ non-urachal คล้ายคลึงกับในตำราอ้างอิง

Primary adenocarcinomas are uncommon epithelial tumors arising from urothelium and account for 0.5 to 2.0% of all bladder malignancies. [1,2] There are less than 50 cases of primary adenocarcinoma of the renal pelvis in the world literature. [3] Epithelial neoplasms arising in the ureter and renal pelvis do not differ pathologically from those of the urinary bladder. [4,5] In the renal pelvis, there was a strong association with urinary stones and urinary tract obstructions. [4] Chronic inflammation, obstructions, and irritations rendering intestinal metaplasia are considered to be the precursor lesions of primary adenocarcinoma of the renal pelvis and non-urachal type of urinary bladder. Adenocarcinoma arising in the urachus, which is a vestigeal structure deriving from the allantois that runs in the preperitoneal space from bladder apex towards the umbilicus, [6] do not associate with intestinal metaplasia, or chronic inflammation and irritation. [2] The separation of urachal from non-urachal cases requires correlation of clinical and pathological findings. There are no specific histologic features or immunohistochemistry that distinguish urachal from non- urachal adenocarcinoma. [1,2,7] The importance of differentiating urachal from non-urachal adenocarcinoma has not been designated. We present here a pathological study of primary adenocarcinoma of four renal pelvis cases and eight urinary bladder cases. All cases were reviewed from surgical pathology files of King Chulalongkorn Memorial Hospital between1989 and1998.

Methods and Materials

All patients with diagnosis of primary adenocarcinoma of the renal pelvis or urinary bladder between 1989 and 1998 were searched for in the surgical pathology files of King Chulalongkorn Memorial Hospital. All available pathologic materials were retrieved and reviewed by two of the authors (Somran J, Kittikowit W). Nine of seventeen urinary bladder cases were excluded, due to unavailable histologic slides, presence of transitional cell carcinoma, and presence of adenocarcinoma in the other organs.

Clinical data from examination request forms were obtained. This consisted of patient age, sex, and symptoms.

Surgical specimens of the tumor arising from renal pelvis and urinary bladder mostly were nephrectomy and TUR-BT, respectively. One case involving the urinary bladder had a partial cystectomy performed after being diagnosed by TUR-BT. Routine surgical slides (H&E) and Mayer's mucicarmine staining were available for most cases. Immunohistochemistry on formalin-fixed, paraffin–embedded tissue was done in some cases which were equivocal in nature and had primary sites such as PSA. Adenocarcinoma of both the renal pelvis and urinary bladder were divided into six histiologic variants according to Grignon et al : [1,7]

1. Adenocarcinoma of no specific type - the tumor did not resemble another recognized pattern.

2. Enteric - the cancer was composed of pseudostratified columnar cells forming a gland, often with central necrosis and resembling colonic adenocarcinoma.

3. Mucinous (colliod) - the tumors were single or in a nest appearing to float in extracellular mucin.

4. Signet ring cell - the tumor consisted of signet ring cells diffusely infiltrating the bladder wall.

5. Clear cell – the tumor was composed of papillary and tubular structures with cytologic features similar to mesonephric adenocarcinoma of the female genital system.

6. Mixed - two or more of the described patterns were found.

Other features evaluated were the presence or absence of cystitis cystica, cystitis glandulalis, and intestinal metaplasia. Cystitis cystica consists of von Brunn nests in which the central cells have degenerated to form small cystic cavities. Cystitis glandularis is defined by the presence of columnar epithelium or mucin–secreting epithelium in nests of cystitis cystica. Intestinal metaplasia is characterized by the presence of mucin-secreting epithelium on the mucosal surface. Adenocarcinoma of the urinary bladder was subclassified into urachal and non-urachal tumors by the Johnson et al criteria. [7] The urachal tumor should locate anteriorly or in the dome with a sharp demarcation between the tumor and normal epithelium. Primary tumor elsewhere must be excluded.

Results

Clinical and pathological findings of the primary adenocarcinoma of renal pelvis and urinary bladder are given in tables 1 and 2, respectively. One female and three male patients were diagnosed with primary adenocarcinoma of the renal pelvis. The average age was 65.5 (54 to 79). Most cases (3 in 4 cases or 75%) presented with renal calculi. Renal mass with hematuria was presented in other one case. Intestinal metaplasia was found in two of four cases (50%) which also had renal stones (Fig. 1A). Three cases (75%) were classified into mixed type and all of these had mucinous patterns (Fig.2A). Enteric pattern was also found in 2 cases of mixed type (Fig.1B). The remaining case had signet ring pattern (Fig.2B). Additionally, one case was of clear cell type (Fig.3) which presented with a mass, hematuria, and no renal stones.

Table 1. Summary of clinical data and pathological finding in adenocarcinoma of renal pelvic.

No.	Sex	Age	Presenting symptom	Histologic subtype	Associated intestinal metaplasia	Mucin study
1.	M	72	Mass and hematuria	Clear cell	-	Not available
2.	M	79	Left renal calculi	Mixed; enteric and mucinous	+	+
3.	F	57	Right renal stone	Mixed; signet and mucinous	+	+
4.	M	54	Right back pain with stone	Mixed; enteric and mucinous	-	+

Table 2. Summary clinical data and pathological finding of bladder adenocarcinoma.

No.	Sex	Age	Presenting symptom and sign	Histological subtype	Associated intestinal metaplasia	Mucin study
1.	F	35	Hematuria	Enteric	-*	+
2.	F	56	Paralysis (brain metastasis) and mass	Enteric	-*	+
3.	M	79	Mass at dome of urinary bladder	Mixed; enteric mucinous, NOS	-*	+
4.	M	62	Abdominal pain	Enteric	-*	+
5.	M	44	Hematuria	Enteric	-*	+
6.	M	59	Hematuria	Enteric	-*	+
7.	M	68	Hematuria and dysuria	NOS	-*	+
8.	M	55	Polyuria	Enteric	-*	+

* No associated feature present in all TUR-BT specimens.

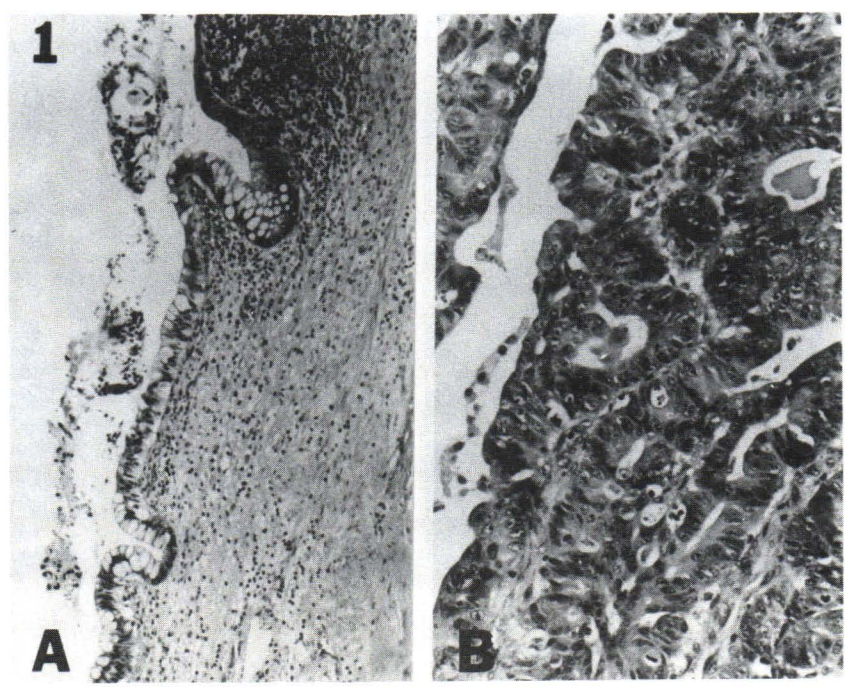

Figure 1. (A) Mucosa of renal pelvis shows intestinal metaplasia
(B) Adenocarcinoma, enteric subtype

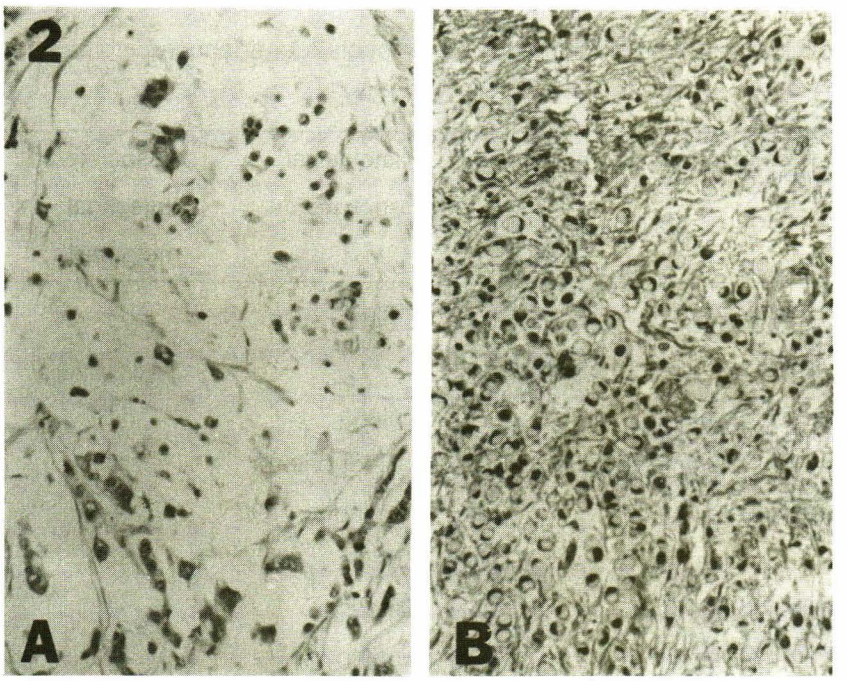

Figure 2. (A) Floating tumor cells in mucin-lake, mucinous subtype
(B) Signet ring cell subtype

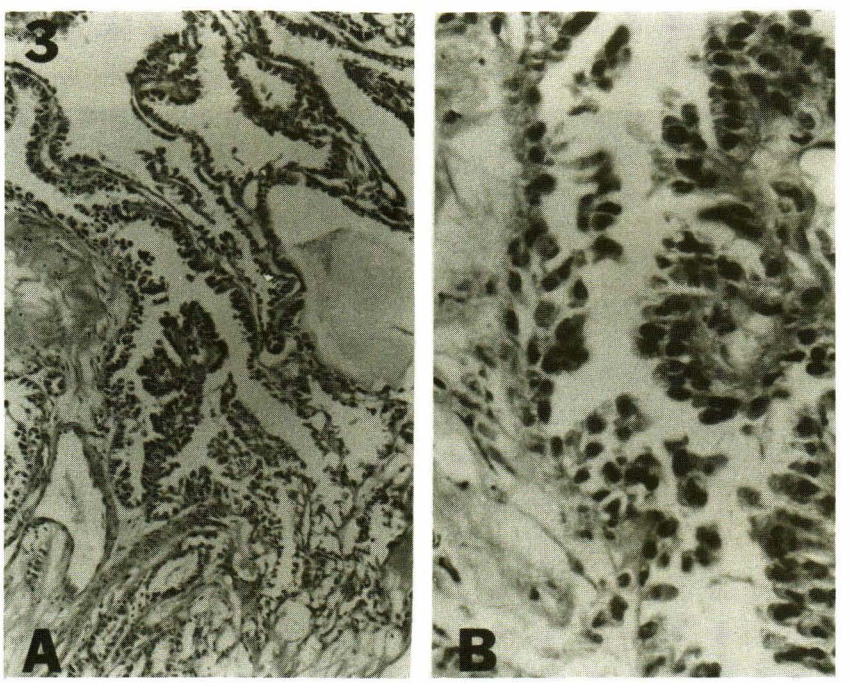

Figure 3. Clear cell subtype:
(A) Papillary structures in low magnification view
(B) Protruding nuclei of neoplastic cells. (Hobnail cells)

Primary adenocarcinoma of the urinary bladder was found in eight cases and one was considered to be urachal in origin according to the Johnson et al criteria. The case was a seventy-year-old male having a mass at the dome of the bladder. No signs of chronic irritation were found. The histologic type was mixed, composed of mucinous, enteric, and NOS patterns. Seven cases were of non-urachal origin. The male-to-female ratio of this non-urachal cancer was 2.5 to 1. The average age was 54 (35 to 68). Four cases (57%) presented with hematuria. The others had paralysis (14%) caused by brain metastasis, abdominal pain (14%), and polyuria (14%). Six cases (86%) belonged to the enteric type and the other was of NOS type (14%). All cases in our study were positive for mucicarmine with variable intensity except one case of the renal pelvis which was clear cell type.

Discussion

Primary adenocarcinomas of the renal pelvis (ARP) are also rare in King Chulalongkorn Memorial Hospital. There were four cases in a ten-year period (1989 to 1998). The incidence does not differ from elsewhere in the world according to literature. [3,4,8-12] A higher incidence of ARP in Kohn Kean Hospital, eleven cases in three and a half years, was recorded by Borwonpa-dungkitti et al. [3] In a five-year period in Ramathibodi Hospital nine cases were diagnosed as ARP. [8] Adenocarci-noma of the renal pelvis strongly associates with renal stones, obstruction of urine flow, and chronic inflammation. [3,4,8-10,12] Most ARP patient (3/4) at King Chulalongkorn Memorial Hospital had renal stones. Two third of the cases developed intestinal metaplasia of adjacent epithelium. Spire et al [10] reported that two third of their cases had stones. The incidence of urinary stones in Kohn Kean Hospital was higher than at others. Renal stones were found in all cases there. The higher incidence of ARP at Kohn Kaen Hospital can be explained. Chronic inflammation, with or without stones rendering intestinal metaplasia, which is suggested to be the precursor lesion of ARP, is the most likely pathogenesis. [3,4,7-10] In the clear cell type of ARP, histology resembling mesonephric adenocarcinoma of the female genital system is postulated differently. [13,14] Some authors believe that this originates from the duct of Bellini or collecting tubules. Thus the exact pathogenesis of ARP can not be concluded. [8] We found only one case which was considered to be clear cell type. That patient had no stones or intestinal metaplasia. In 59 cases of Spire et al [10] the most common histiologic types were tubulovillous or enteric (71.5%) and mucinous (21%). The different criteria we used was according to Grignon et al, [11] and in our small-sized study population we found mixed type in most cases (3/4) composed of mucinous and enteric (50%) or signet ring (25%) and the data such as average age and sex prevalence were different.

Many authors have reported different prognosis of urachal adenocarcinoma, compared with non-urachal adenocarcinoma. [7] In a study of 72 cases, Grignon et al [1] found no significant difference in crude survival rates between cases of adenocarcinoma of urachal and non-urachal origin. The urachus is the vestigeal remnant arising from the allantois. The lumen of the urachus communicates with the lumen of the urinary bladder in one third of general population. [6] Urachal tumors may be intramucosal, intramural or intravesical. Two reported cases of Na Ayudhya VC et al [5] were of non-urothelial origin, hence these

were unequivocal cases. The intravesical lesion is the problem. Separation of urachal and non-urachal origin requires more clinico-pathological correlation. No specific histological features or immunohistochemistry is useful. The most practical criteria belong to Johnson et al. [7] They consider only the location of the tumor, sharp demarcation of tumors, and absence of other primary sites. We have a case which was considered to be urachal adenocarcinoma. The pathogenesis of the urachal tumor has been addressed by two theories. First, the embryonic rest theory holds that sequestered and persistent glandular elements of the primitive cloaca undergo neoplastic degeneration. Second, the totipotential cell theory requires that the transitional cell lining the bladder and urachus retain the potentialities of the early cloacal cells to become elongated and cylindrical, or produce mucin with or without malignant degenerative change. Age, sex preference, and frequency of the histiologic type of nonurachal adenocarcinoma were similar to that reported in other literature [15] and textbooks. [7] The majority of patients are men. The male-to-female ratio is 2.1–3 to 1. [16,17] The most common presentation is hematuria. The average age fell in between the fifth and sixth decade. In our series, other pathological features associated with chronic inflammation and irritation were inaccessible because of limited specimens which were mostly received from TUR-BT. Most cases of primary non-urachal adenocarcinoma occurring in patients with longstanding diffuse intestinalization of the bladder mucosa are associated with a non-functioning bladder, chronic irritation, obstruction, and cystocele. [6,7,15,17,18]

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