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Follow-up criteria and cystoscopic classifications of bladder lesions: A retrospective analysis

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Abstract

Aim: To screen cystoscopically bladder cancer mimicking lesions and to present its clinical importance.

Material and Methods: After receiving anamnesis of patients, hematological, biochemical, microbiological, cytological, pathologic and radiological assessments were performed. Randomized cold cup bladder biopsy, transurethral resection or open surgical excision were performed. The lesions were classified according to their cystoscopy appearance. Practical approach criterias were compiled based on their treatments and follow-up, throughout 9 years.

Results: A total of 297 patients were reached .The mean age of all were 62±6 years. Almost all bladder lesions (95 %) were prediagnosed as bladder cancer according to the radiologic screening results like bladder wall thickening and irregularities. The precancerous /cancerous lesions were detected incidentally at a rate of 3.36 %. PAP (Papanicolaou) III urine cytology was observed at a rate of 3.4 %. Carcinoma in situ developed in the follow-ups and one converted to Grade I transitional cell cancer. Total cystectomy was required in a patient who was diagnosed with urinary tuberculosis.

Conclusions: There may be precancerous or cancerous lesions in the background of these lesions which do not respond to treatment or constantly recur. There may be changes in favor of malignancies in lesions. The study created a different perspective on these lesions with cystoscopy classification.

Keywords: Bladder neoplasm; cancer; cystoscopy; treatment

INTRODUCTION

Despite detection most frequently of epithelial malignant lesions of the urinary bladder in practice, bladder tissue carries the potential of converting into malignant and benign lesions. Among these, there are lesions that mimic cancer radiologically, pathologically and cystoscopically (1). As the clinical findings and radiological and endoscopic characteristics of such lesions may be confused with malignancies, definitive diagnosis requires pathological assessment. Yet, also the histological characteristics of these urothelial and non-urothelial lesions may mimic malignancies (1). This may pose a challenge in diagnosis for urologists, pathologists and radiologists. Differential diagnosis is required in lesions which mimic bladder cancer cystoscopically, radiologically and pathologically (1).Is there really an underlying cancer? Unveiling this is crucial for the patient (2). Treatments and followup criteria intended to differentiate cancer-mimicking benign or premalignant lesions. The cystoscopy images, pathological diagnoses and our follow-up approaches are presented regarding lesions mimicking bladder cancer cystoscopically within the past nine years.

MATERIAL and METHODS

Study population

Between 2006 and 2015, n = 297 patients were evaluated after archive scanning. Inclusion criteria were presence of patients with or without radiological pre-diagnosis of bladder cancer who were subjected to cystoscopy resulting in the appearance of bladder cancer. These mentioned patients underwent surgery and received pathological diagnosis.

Study design

As the study was based on the last two years of their 9-year follow-up, all data were recorded. Approval was received from the Necmettin Erbakan University Ethics Committee (Decision No. 2017/835, adopted in Session 1 on 17/03/2017 by the Ethics Committee).

Procedures and Evaluation

The hematological, biochemical, microbiological, cytological and radiological assessments of the patients were performed. Urine cytology samples were stained with the Papanicolaou (PAP) method. Hematoxylin-eosin staining was used in the lesions. Urinary cytological

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assessments were classified according to Koss LG and Murphy WM (3). Their immunohistochemical staining was performed with p53, as primary antibody (Immunogen, Novocastra Laboratories Ltd., United Kingdom) or p63 (Biogenex, Biogenex Laboratories Inc., USA)(4). Furthermore, COX-2 expression was used to investigate immuno-histochemically urothelial carcinoma and papillary tumors with low malignancy potential in the bladder (Abcam, UK)(5). The immunochemical stains for CK20 and CD44 were used for reactive atypia. Ultrasonography, conventional computerized tomography (CT-Scan) and magnetic resonance imaging (MRI) were used in radiological evaluations.

Surgical techniques

Light cystoscopy and randomized cold-cup bladder lesion biopsy, transurethral resection of the bladder (TURB) and open surgical excision were performed. The decision of cold cup biopsy, TUR or open surgery was made according to the width and size of the lesions detected, during the cystoscopic monitoring.

Established Follow-Up Criteria

The follow-up criteria were established according to the recurrence of symptoms and the detection of lesions in re-cystoscopic examinations. Generally, the lesions were followed up for a period of 3-48 months, while precancerous and cancerous lesions were followed up for up to 60 months. The median follow-up period was 18±6 months (Table 2).

Outcome assessment and perspective

The same cystoscopy definitions were used in different lesions in our classification. Thus, this led to a perception that all lesions have the same appearance. However, it was observed in the pathological evaluation that they were not the same. As we are more used to seeing typical (papillary) bladder cancer images in our practice of urology, all lesions were accepted as bladder cancer until proven otherwise. Thus, we tried to convey the message that mucosal hyperemia, edema, swelling and ulcer should be considered from all aspects. We noticed that there was a wider need for cystoscopy. This logic corresponds with the idea that it is bladder cancer in hematuria patients aged above 40 years, unless proven otherwise (1). We never concluded the diagnosis by considering only bladder-like lesions. It is not our goal to engage the readers in this direction. We prepared a joint table with the pathology department by making classifications under the main headings according to our cystoscopic images (Table 3). Our perspective and proposal are shown in Figure 1.

RESULTS

The mean age of males and females was 56 years and 68 years respectively. The lesions were detected in females at a rate of 38% and in males at a rate of 64 %. Particularly all patients diagnosed with *dysplasia*, *atypical cells* (*invasive papillary neoplasia*) were smokers and had been smoking for a long time (2 - 4 packs/day / 40 - 45 years).

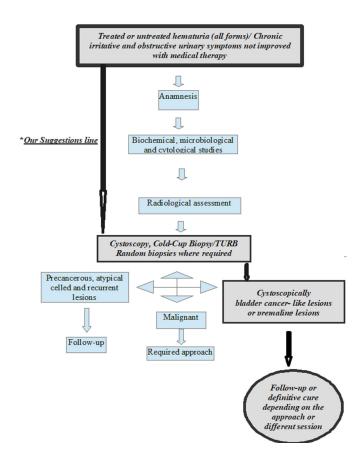


Figure 1. Flow diagram proposed in cystoscopic tumor-like lesions of the urinary bladder

While some patients having other lesions were not smokers, some patients differentiated itself from the others by smoking 0,5 - 3 packs/day/11 -34 years. There may be an impact of smoking in precancerous and cancerous lesions, but the fact that non-smokers were also included in the other lesions which did not fully reflect the impact of smoking in the ethiology. No clinical or laboratory finding specific to any lesion was observed. There was ongoing sterile pyuria only in the patient with mononuclear cell infiltration. The PAP III urine cytology was observed at a rate of 3.4% in a few patients with *chronic* cystitis, including those with dysplasia and atypical cells. The lesions mimicking bladder cancer cystoscopically were identified at a rate of only 15% in the radiological assessment (n = 44/297). Almost all of bladder lesions (95%) were pre-diagnosed with bladder cancer by the radiologist

Mucosal hyperemia, ulcers and nodules: It was attentiongrabbing to see that *dysplasia* as well as *invasive* papillary neoplasia were identified in this group. They were separately evaluated pathologically under the headings of precancerous and cancerous lesions at a rate of 3.36 %. One patient with early stage grade I transitional cell cancer (TCC) was detected in the follow-up of *dysplasia* patients.

The patient was treated without need for cystectomy. Carcinoma in situ (CIS) developed in four patients

suffering from chronic cystitis. Only one of them converted to grade I TCC. The patient began to be followed up after being treated with TURB. The antihistaminic and steroid treatment administered following the pathological diagnosis of eosinophylic cystitis exposed to antibiotics numerous times. The macroscopic hematuria of the patient was terminated following cauterization in mucosal hemangioma. Mucosal hemangioma diagnosis associated with the bladder tumor was made in the advanced age group. However, recurrences occurred and the conduct of TURB was sufficient in mucosal hemangioma . No recurrence was observed following TURB conducted on chronic inflammatory ulcer with a fully necrotized cancerous appearance associated with chronic infection. Following the pathological diagnosis of invasive papillary neoplasia, re-cystoscopy was planned and TURB was conducted upon catching the same lesions at different focal points in multiple bladder wall biopsies. The patient with mononuclear cell infiltration was diagnosed tuberculosis (tbc) with polymerase chain reaction (PCR). Urodynamic study was performed after anti-TBC treatment as a result of increased urinary complaints. Eventually, augmentation cystoplasty was performed because of contracted bladder development. Recurrences occurred at a few focal points following resection in a patient with *endometriosis*, but TURB was adequate (Tables 1, 2, 3) (Figures 2,3)

Mucosal swelling/hyperemia: Three patients with fibromuscular lesions were subjected to open partial cystectomy due to mass-forming recurrences and/or increasing bleedings following TURB. Squamous glandular metaplasia was seen in women with a rate of 61.5 %. As Hodgkin's lymphoma was considered in the diagnosis especially of the patient with chronic follicular cystitis, the diagnosis was confirmed with challenge upon conducting TURB. It became mandatory to perform cystectomy and ileal conduit surgery following the recurrences which exposed persistent gross lesions and complaints (Tables 1, 2, 3) (Figure 4).

Mucosal Hyperemia/Ulcer/Nodüles	Numbers	Age (means)	Symptoms	Smoke/year	Laboratory	History	Previous Surgery
Cystitis Cystica and Glandularis	16	61.8	F,D,N	20	Mic.H		TURB
Eosinophilic Cystitis	8	80	D,U	31	Mic.H		TURB
Dysplasia	9	52,2	U,F	40	Mic.H	BC	
Chronic Cystitis	174	63.8	D,U,F	33	Mic./Mac.H,L	BC,DM	
Mucosal hemangioma	1	74	D,U,F		Mac./Mic.H		
Chronic Inflammation Characterized with Ulcers	1	84	D,F	19	Mac.H		
Reactive urethelial atypia	12	74	D,U,F	22	Mic.H		CLT-O/P
Hyperplasia	3	61	F	34	L	BC	CCB
Endometriozis	1	34	D,U,F		Mac.H		
Mononuclear cell infiltration	1	68	D,U,F		L	TBC	
Atypical Cells(invazive papiller neoplazia)	1	80	D,U	45	Mic.H		
Intertisial Cytitis	3	69	D,U,F,P		Mic.H/L	BC,DM	
Mucosal Swelling /Hyperemia							
Squamous/Glandular Metaplasia	13	54	U,F	11	Mic.H	BC	OP+CLT
Chronic Follicular Cystitis	5	54.2	D,U		Mic.H		
Fibromuscular Tissue	38	63.6	U,F				
Mucosal Swelling/Papillary							
Leukoplakia	1	54	D		L		TURB
Inverted Papilloma	1	65	U				TURB
Pseudocarcinamotous proliferation	1	68	D,U	23	Mic./Mac.H,L		Colon resection
Papillary/Polypoidal Cystitis	5	65		14	Mic.H		
Mucosal Mass							
Xanthogranulomatous Cystitis	1	37	O,F,H		Mac.H		
Blood, fibrin, necrotic debridement	1	86	U,F		Mac.H		OP
Leiomyoma	1	82	O,F,H		Mic.H		TURB
TOTAL	297						

SSPS 26.0 PROGRAM Transurethral resection of the bladder:TURB, Cystolithotomy: CLT, Open prostatectomy:OP , Cold-cup biopsy:CCB, Benign Prostatic Hyperplasia:BPH, Prostate cancer:PCa, Tuberculosis:Tb, Bladder Cancer:BC, N:Nocturia, D:Dysuria, O:Obstruction ,H:Hesitency, F:Frequency, U:Urgency. Smoking :1-3 pack/daily/years, Mic.H:microscopic hematüria, Mac.H:macrsocopin hematüria, L: leucocyturia, DM: diabetes mellitus



Figure 2. a. Cystitis cystica and glandularis, b. Mucosal dsyplasia, c. Chronic cystitis, d. Eosinophilic cystitis, hyperplasia e. Mucosal hemangioma, f. Chronic mucosal ulcers

Figure 3. g. Reactive urothelial atypia, h. Mononuclear cell infiltration i. Mucosal endometriosis, i. Atypical cell (invasive papillary neoplasia), j. interstitial cystitis (glomerulation)

Table 2. The radiological images, cytology of the patients, diagnostic purposes, medical approaches, recorded recurrence months of complaints, follow-ups

Mucosal Hyperemia/Ulcer/Nodüles	USG/CT/MR	Our Surgery	Medical Treatments	Symptom recurrence months	Our Proposal
Cystitis Cystica and Glandularis	thickening	TURB	conservative follow-up	6,11,9,12	Annual cystoscopy
Eosinophilic Cystitis	thickening	TURB	conservative follow-up	6,5,6	6-month cystoscopy
Dysplasia	thickening	cold-cup biopsy+TURB		precancerous follow-up	3-month cystoscopy
Chronic Cystitis	thickening/ bulging	cold-cup biopsy+TURB	conservative follow-up	3,9,12	6-month cystoscopy
Mucosal hemangioma	thickening/ bulging	TURB	conservative follow-up	12,12,12	Annual cystoscopy
Chronic Inflammation Characterized with Ulcers	thickening/ bulging	TURB		no recurrence	
Reactive urethelial atypia	thickening/ irregularity	Cold-cup biopsy+TURB		no recurrence	
Hyperplasia	thickening/ bulging	TURB	conservative follow-up	3,6,6,6	6-month cystoscopy
Endometriozis	mass	TURB	conservative follow-up	3,6,6,6	6-month cystoscopy
Mononuclear cell infiltration	thickening/ ırregularity	Cold-cup biopsy, TURB	conservative follow-up	6,12,11,12,10	Annual cystoscopy
Atypical Cells(invazive papiller neoplazia)		TURB		cancerous follow-up	3-month cystoscopy
İntertisial Cytitis		Cold-cup biopsy	conservative follow-up	intermittent recurrence	maybe hydrodistension

Mucosal Swelling /Hyperemia								
Squamous/Glandular Metaplasia	thickening	TURB	conservative follow-up	12,10,8,13	Annual cystoscopy			
Chronic Follicular Cystitis	Thickening, ırregularity	TURB	cystectomy+ileal conduit	5,3,6,7,6	3-month cystoscopy			
Fibromuscular Tissue	thickening	TURB+open partial cystectomy	conservative follow-up	10,11,9,12	Annual cystoscopy			
Mucosal Swelling/Papillary								
Leukoplakia		TURB+cold cup biopsy	conservative follow-up	6,5,7,6	6-month cystoscopy			
Inverted Papilloma	mass	TURB	conservative follow-up	9,12	Annual cystoscopy			
Pseudocarcinamotous proliferation		TURB+cold-cup biopsy	conservative follow-up	6,6,8,4	6-month cystoscopy			
Papillary/Polypoidal Cystitis	mass	TURB	conservative follow-up	6,3,12,12	Annual cystoscopy			
Mucosal Mass								
Xanthogranulomatous Cystitis	mass	TURB+Open mass excision		no recurrence				
Blood, fibrin, necrotic debridement	mass	TURB+Open excision		no recurrence				
Leiomyoma	mass	TURB,Open Surgery	conservative follow-up	12	Annual cystoscopy			
SSPS 26.0 PROGRAM Transurethral resection of the bladder:TURB,								

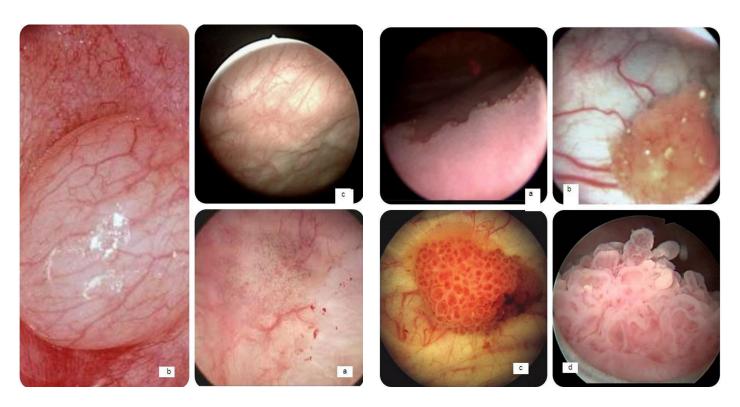


Figure 4. a. Squamous glandular metaplasia, b. Follicular cyst, c. Fibromuscular tissue

Figure 5. a. Mucosal leukoplakia, b. Inverted papilloma, c. Pseudocarcinomatous proliferation. d. Papillary/polypoidal lesion

Table 3. Our incidence rates and classification of cystoscopic cancer-like lesions and Arrangment of lesions with cystoscopic incidances according to 2004 WHO ISUP (The International Society of Urological Pathology) Classification. Comparison of tables

according to 2004 WHO ISUP (The International Socie	ty of Urological Pa	athology) Classification. Comparison of tables	
2004 WHO ISUP Classification %		Our cystoscopic cancer-like lesions classification-2019	%
Urothelial Neoplasia		Mucosal Hyperemia/Ulcer/Nodüles	78.06
Benign	0.33	Cystitis Cystica and Glandularis	5.38
Inverted Papilloma	0.33	Eosinophilic Cystitis	2.69
Inflammatory Reactive Pathologies	82.42	Dysplasia	3.03
Squamous/Glandular Metaplasia	4.37	Chronic Cystitis	58.58
Leukoplakia	0.33	Mucosal hemangioma	1
Cystitis Cystica and Glandularis	5.38	Chronic Inflammation Characterized with Ulcers	0.33
Eosinophilic Cystitis	2.69	Reactive urethelial atypia	4.04
Chronic Follicular Cystitis	1.68	Hyperplasia	1.01
Interstitial Cystitis	1.01	Endometriozis	0.33
Chronic Cystitis	58.58	Mononuclear cell infiltration	0.33
Papillary/Polypoidal Cystitis	1.68	Atypical Cells(invazive papiller neoplasia)	0.33
Chronic Inflammation with Ulcers	0.33	Intertisial Cytitis	1.01
Reactive urethelial atypia	4.04	Mucosal Swelling/Hyperemia	18.84
Hyperplasia	1.01	Squamous/Glandular Metaplasia	4.37
Endometriozis	0.33	Chronic Follicular Cystitis	1.68
Mononuclear cell infiltration	0.33	Fibromuscular Tissue	12.79
Xanthogranulomatous Cystitis	0.33	Mucosal Swelling/Papillary	2.67
Pseudocarcinamotous proliferation	0.33	Leukoplakia	0.33
Pre-Malignant	3.03	Inverted Papilloma	0.33
Dysplasia	3.03	Pseudocarcinamotous proliferation	0.33
Malignant	0.33	Papillary/Polypoidal Cystitis	1.68
Atypical Cells(invaziv papiller neoplazi)	0.33	Mucosal Mass	0.99
Non-Urothelial Neoplasia		Xanthogranulomatous Cystitis	0.33
Benign	1	Blood. fibrin. necrotic debridement	0.33
Mucosal hemangioma	1	Leiomyoma	0.33
Mesenchymal Tumours	0.33		
Leiomyoma	0.33		
Fibromuscular Tissue	12.79		
Blood, fibrin, necrotic debridement	0.33		

Mucosal swelling/hyperemia: Three patients with fibromuscular lesions were subjected to open partial cystectomy due to mass-forming recurrences and/or increasing bleedings following TURB. Squamous glandular metaplasia was seen in women with a rate of 61.5 %. As Hodgkin's lymphoma was considered in the diagnosis especially of the patient with chronic follicular cystitis, the diagnosis was confirmed with challenge upon conducting TURB. It became mandatory to perform cystectomy and ileal conduit surgery following the recurrences which exposed persistent gross lesions and complaints (Tables 1, 2, 3) (Figure 4).

Mucosal swelling/papillary: Continuous recurrences and complaints occurred despite TURB in *leukoplakia*. It was observed that the area and thickness of leukoplakia increased with every new recurrence. In case different

radiological images were seen only with leukoplakia in patients whose irritative complaints further increased following TURB or there were microscopic/macroscopic hematuria, re-cystoscopy+required intervention was performed. It was decided to propose palliative solutions instead of performing TURB. TURB was performed on the inverted papilloma with a size of 1x1.5 cm. Re-TURB was performed due to recurrence at 12th month in the follow-up of the patient. The pathological diagnosis was observed to be the same. It was learnt that the patient in whom pseudocarcinomatous proliferation was detected, used urethral catheter for a long time following a car accident. The patients with papillary-polypoidal cystitis diagnosis were approached with the preliminary diagnosis of pathological carcinoma in situ. Differential diagnosis was made at rebiopsy (Tables 1, 2, 3) (Figure 5).

Mucosal masses: Although mucosal masses were rarely seen lesions in our series, open surgery rate was high unlike other groups because TUR surgery was sometimes insufficient in fully extracting the lesion and diffuse hemorrhages were observed during TUR. The radiology department stated that there was definitive bladder cancer at tomography and that there was even perivesical involvement. Diagnosis was made primarily with TURB. Yet, frozen pathological assessment was performed at open surgery. The urology department still did not believe that the lesion was benign due to its macroscopic appearance. That's why, was performed at open surgery. Because of that, partial cystectomy was planned with frozen for achieving legality and re-confirming the diagnosis. TURB was performed primarily in the patient diagnosed with blood fibrin and necrotic debridement. It was understood that, prior to the formation occurring in the bladder dome. the patient underwent open prostatectomy. As TURB was sufficient in the second session, open excision was planned. Pathological diagnosis of the patient who had leiomyoma was made by TURB. This patient had bladder neck obstruction, experienced acute urinary retention numerous times, and was previously diagnosed with benign prostate hyperplasia. Open partial cystectomy was performed during re-TURB due to excessive bleeding (Tables 1, 2, 3) (Figure 6).



Figure 6. a. Xantogranulomatous cystitis, b. Blood fibrin necrotic debridement, c. Leiomyoma

According to the evaluation of all these lesions, it was observed that, none of them were considered to have definitive bladder cancer but based on their pathological diagnosis, 33.27 % of the lesions were malignant according to 2004 WHO ISUP classification. It was observed

that the recurrence periods in patients diagnosed with cystitis cystica and glandularis, chronic cystitis, hyperplasia, endometriosis, mononuclear cell infiltration, squamous/glandular metaplasia, chronic follicular cystitis, inverted papilloma and papillary/polypoidal cystitis were prolonged after TURB and the complaints were further reduced.

DISCUSSION

Lesions resembling cystoscopic bladder cancer were discussed repeatedly radiologically and pathologically and were presented mostly as urologic cases. When encountering such lesions with their pathological diagnoses, it was considered that our practice insufficient in terms of they should be treated and followed up. Particularly the presence of cancerous and precancerous lesions detected randomly among these lesions as well as the identification of CIS and Grade I TCC in the followup further enhanced the importance of the lesions and of the study. The patient who received continuous antibiotic treatment due to aseptic pyuria in the follow-up of the lesions was also worth nothing. Urodynamic studies were required in the follow-ups and it was even planned to perform neo-bladder surgery thus protecting the patient from the process of chronic renal failure and prevent and morbidities. Differences and new recommendations were presented upon taking into account limited clinical proposals suggested for the lesions in previous studies which mostly drew attention to pathological differential diagnosis.

Although cystoscopic follow-ups were recommended very rarely for these lesions in different articles in literature. the time interval for which the action would be required was not specified (2). Again, the recurrence periods of lesions which were not previously mentioned in literature are recorded (2). These recommendations were discussed for each lesion by making a comparison with our series. Our study suggested which surgical interventions were necessary at follow-up and the circumstances, when open surgery would be mandatory. Before, only the chaos in radiological and pathological diagnoses was described and effort was made to attract the attention of the specialist (2). Within the nine-year process, it was detected in the post-treatment follow-up of the lesions that, compared with the previous period, the conduct of surgeries prolonged the intervals between recurrences in the lesions compared to medical therapies, resulting in a significant relief in symptoms. Although the tables provide information on follow-up criteria and the approaches regarding all lesions, we will discuss those lesions resulting in different outcomes and with newly created follow-up criteria and treatment, about which no invasive approach was previously mentioned in literature.

A few cases of cystitis cystica and glandularis which converted to bladder adenocarcinoma in the past were reported (2,6). Although recurrences occurred afterwards, adenocarcinoma was not detected in the 38-month follow-up, but we still continue to conduct their six-

month radiological and annual cystoscopic follow-ups. Our treatment for eosinophilic cystitis was aligned with literature (7,8). Six-month follow-ups were established, based on the recurrence rate, unlike those in literature. One of the most important findings in this study was the detection and follow-up of the pre-cancerous lesion dysplasia. Considering also the recommendations on this topic, precancerous lesion follow-up was made in literature, regardless of the duration of recurrences (9). Chronic cystitis cannot be definitively differentiated from cancerous lesions based on sonography irrespective of its manifestation (10). Although follow-up was recommended in various occasions numerous times, following them up based on their recurrence rate differed from literature in our series (10). The detection of CIS in recurrences showed us how significant cystoscopy may be in case of recurrence. Although hemangiomas can occur in individuals of any age, they are seen most often in individuals under the age of 30 years and are slightly more common among males (11). They need to be differentiated from urinary bladder tumors (12). The hemangioma patient in our series was older than those mentioned in literature. Regarding chronic inflammation characterized with ulcer, such bladder pathologies were mostly defined after chemotherapy, in interstitial cystitis, stomach diversions and bladder cancers in literature (13). Such pathologies were not present in this patient's medical history. Probably, it was accepted as a manifestation of long-lasting chronic cystitis. Mononuclear cell infiltration, cystoscopy may be planned for its diagnosis (14). Although this was the way it was recommended in literature, recurrences were detected in the patient who experienced symptoms continuously. It was necessary to monitor especially sterile pyuria and consequently TBC. Multifocal cold-cup biopsy was performed and diagnosed as invasive papillary neoplasia atypic cells (15). After dysplasia, it was the second lesion which demonstrated how effective our approach was. In fact, no cystectomy was performed in the follow-ups. Squamous/ glandular metaplasia, while it was detected in 40% of women and 5% (16) of men due to trauma, infection and post-surgery, the lesions were identified in 61.5% of women in our series. Although rarely, pseudocarcinotamous proliferation may develop conditions leading to chronic irritation (17). Detection of PAP III initially and presence of dysplasia in repeated biopsies created a challenge in diagnosis. Thus, we applied a 3-month cystoscopic follow-up on these patients initially. Diagnosis was made after various pathologist consultations. Papillary/ Polypoidal cystitis should be considered in the differential diagnosis of TCC and a biopsy is required for a definitive diagnosis (18). CIS diagnosis was made initially, and this is the way follow-up was conducted. But annual follow-up began to be implemented after the change in recurrence rates, the diagnosis of Papillary/Polypoidal cystitis in at least three pathological diagnoses and the absence of complaints. Xanthogranulomatous cystitis, both cystoscopic and radiological images may be confusing with complete bladder cancer (19). Although histopathological diagnosis was made, action was taken by always taking into account the fact that this was cancer. What mostly challenged us was our lesion.

This series taught us that it is absolutely necessary to perform cystoscopic assessment on a wider scale in the anamnesis in long-lasting irritative, obstruction complaints. We do not believe that this approach is overtreatment. Because, we do not think that the costs to arise due to cystoscopy, cold-cup biopsy, TUR and pathological tests are higher than the medical treatment due to bladder cancer administered for a long period (> 10 years). In case of chronic urinary complaints which cannot be resolved with treatment and recur continuously, in addition to the need for bladder cystoscopy, the presence of any lesion detected or undetected radiologically within the bladder may be a sign of precancerous or cancerous onset. Our study tries to highlight and draw attention to lesions mimicking bladder cancer cystoscopically, which are generally never considered by urologists, and provides the opportunity for urologists to be more comfortable with more data for the cystoscopic evaluation of the urinary system. We have noted that differential diagnosis in cystoscopically detected tumor-like lesions reduced treatment costs and provided target-oriented and patient-specific treatment. Studies aimed at unveiling the etiological factors in these patients and further developing clinical perspective upon establishing guidelines may be conducted in the future.

CONCLUSION

In our urology practice, lesions that cause urinary symptoms and mimic bladder cancer cystoscopically, can very often cause recurrence and treatment failure. These lesions monitored at cystoscopy may contain precancerous or cancerous lesions inside. The current malignancy potential of many lesions may emerge at follow-up. We believe that this study will be helpful in reminding the urologists, for looking after these lesions mimicking bladder cancer cystoscopically, in a more careful manner.

Competing interests: The authors declare that they have no competing interest

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Ethical approval: Approval was received from the Necmettin Erbakan University Ethics Committee (Decision No.) 2017/835, adopted in Session 1 on 17/03/2017 by the Ethics Committee.

REFERENCES

- 1. Wein AJ, Kavoussi LR, Partin AW, et al. Bladder Lesions, Wein AJ, Kavoussi LR, Partin AW eds. Campbell-Walsh Urology Philadelphia: Elseveir 2016;3:2184-90.
- 2. Sauter G, Amin AF, Busch C, et al. Noninvasive urothelial neoplasias: WHO classification of noninvasive papillary urothelial tumors. In: Eble J, Epstein J, Sesterhenn I, eds. World Health Organization classification of tumors: pathology and genetics of tumors of the urinary system and male

- genital organs. Lyon (France): IARC Press 2004;110.
- Koss LG. Tumors of the urinary tract and prostate.
 In: Koss LG eds. Diagnostic Cytology and its histopathologic bases. 5th edition. Philadelphia: JB Lippincott 2005;810-6.
- 4. Tomkova K, Tomka M, Zajac V. Contribution of p53, p63, and p73 to Developmental Diseases and Cancer. Neoplasma 2008;55:177-81.
- Reddy Y, Hirose R, Lubet V, et al. Chemoprevention of colon cancer by specific cyclooxygenase-2 inhibitor, celecoxib, administered during different stages of carcinogenesis. Cancer Res 2000;293-7
- 6. Semins MJ, Schoenberg MP. A case of florid cystitis glandularis. Nat Clin Pract Urol 2007;4:341-5.
- Sparks S, Kaplan A, DeCambre M, et al. Eosinophilic cystitis in the pediatric population: a case series and review of the literature. J Pediatr Urol 2013;9:738-44.
- 8. Tsakiri A, Balslev I, Klarskov P. Eosinophilic cystitis induced by penicillin. Int Urol Nephrol 2004;36:159-61.
- Knüchel-Clarke R, Gaisa NT. Preneoplastic lesions and precursors of urothelial cancer. Pathologe 2016;37:33-9.
- Marcon J, Stief CG, Magistro G. Urinary tract infections: What has been confirmed in therapy? Internist (Berl) 2017;58:1242-9.
- 11. Stimac G, Dimanovski J, Katusic J, et al. A large cavernous hemangioma of the urinary bladder:

- imaging of possible spontaneous regression. Eur J Radiol Extra 2007;61:61-3.
- 12. De Sousa CSM, Viana IL, de Miranda CLVM, et al. Hemangioma of the urinary bladder:an atypical location. Radiol Bras 2017;50:271-2.
- 13. Hurst RE, Meerveld BG, Wisniewski AB, et al. Increased bladder permeability in interstitial cystitis/painful bladder syndrome. Transl Androl Urol 2015;4:563-71.
- 14. Altiparmak MR, Yalin SF, Denizli N, et al. Urinary tuberculosis: a cohort of 79 adult cases. Ren Fail 2015;37:1157-63.
- 15. Robert H Young. Tumor-like lesions of the urinary bladder. Modern Pathology 2009;22:37-52.
- 16. Ozbey I, Aksoy Y, Polat O, et al. Squamous metaplasia of the bladder: findings in 14 patients and review of the literature. Int Urol Nephrol 1999;31:457-61.
- 17. Harik LR, O'Toole KM. Nonneoplastic lesions of the prostate and bladder. Arch Pathol Lab Med 2012;136:721-34.
- Ong C, Lee VK, Mohamed Suphan N, et al. Xanthogranulomatous cystitis: A case report and clinicopathological review. Ann Acad Med Singapore 2013;42:301-3.
- Lane Z, Epstein JI. Polypoid/papillary cystitis: A series of 41 cases misdiagnosed as papillary urothelialneoplasia. Am J Surg Pathol 2008;32:758-64.