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Bladder histopathological changes secondary to double j stenting prospective selective study in patients of Upper Egypt

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Abstract
Objective: to evaluate the histopathological urinary bladder changes due to double J stenting and to correlate these changes with the period of the stenting in patients of Upper Egypt.
Material and Methods: This study includes 40 patients. The patients underwent Bladder cold cup biopsy in our Urology department, Alazhar University Hospital during removal of the double J stent from around the ureteric orifice and trigone of bladder. Stenting of the right ureter (57.5%) was slightly more common than of the left ureter (37.5%). The most common stent length and size used were 26 cm (95%) and 6 Fr (85%). The most common stent material was used in this study was Teflon (75%). These patients classified into 4 Groups according to duration of the stenting. Group 1 double J stenting for 2 weeks or less. Group 2 stenting for 2 to 6 weeks and Group 3 stenting for 6 to 12 weeks Group 4 stenting for more than 12 weeks. Then, the correlation between the histopathological changes and the period of the stenting determined.
Results: According to indication of stent placement the stents were fixed in 6 patients (15%) for two weeks or less, fixed in 17 patients (42.5%) for 4 to 6 weeks, fixed in 11 patients (27.5) for 6 to12 weeks, and fixed in 6 patients (15%) for period more than 12 weeks. the most common bladder histopathological changes due to double J stenting in patients of Upper Egypt for period 2 weeks or less are mild acute cystitis with mild edema and esinophilic infiltration and this found in (10%) of patients. While acute cystitis with sever edema and neutrophilic lymphocytic infiltration was found when fix double J stents for period from 2 to 6 weeks and this found in (37.5%) of patients. While brunn's nests was found when fix double J stents for period from 6 to 12 weeks and this found in (27.5%) of patients. While cystitis cystica was found when fix double J stents for period more than 12 weeks and this found in (10%) of patients.
Conclusion: We found that the urinary bladder inflammatory reactions increase as the stent duration increased, this reaction progresses from acute cystitis upto Brunn's nests and cystitis cystica with longstanding stents inside the ureter. So we suggest that the use of double J stents should be limited to highly indicated cases only.

Keywords: jj stent, ureter stent, bladder, histopathology

Introduction

Ureteric stents were first described by Zimskind *et al*. in 1967 [1]. The JJ ureteric stent has become an integral part of urological treatment options. The original indication for placing a ureteric stent was to treat a ureteric obstruction or fistula [2]. The characters of the ideal ureteric stent [3] include: easily inserted from any access; resistant to migration; optimal flow characteristics; well tolerated by the patient; biocompatible; bio-durable; resistant to encrustation; non-refluxing; radio-opaque or visible with ultrasonography; easily exchanged and removed; versatile; and affordable. However, different complications can occur with the short- or long-term use of indwelling stents [4]. These complications have varied from minor side-effects such as hematuria, dysuria, frequency, flank and suprapubic pain, to major complications such as vesico-ureteric reflux, migration, malposition, encrustation, stent fracture, UTI, pyuria, incontinence, inadequate relief of obstruction, ureteric erosion or fistulation, forgotten stent, necrosis and uretero-arterial fistula. Most complications require removal of the indwelling catheter [5].
Many studies reported the factors affecting the development of complications of DJ stenting and concluded that there is no correlation between the stent size and complication rates or better outcomes. However, they reported more complications with longer stents and poor outcomes with older patients after stenting [6]. Joshi *et al*, reported the evaluation of the symptoms associated with stents. They prospectively assessed lower urinary tract symptoms caused by DJ ureteric stents using validated questionnaires (International Prostatic Symptoms Score - IPSS, International Continence Society male questionnaire, Quality of Life questionnaires, and the Bristol Female Lower Urinary Tract Symptoms questionnaire - BFLUTS). They reported the association of urinary symptoms with stents and they showed the negative impact of these symptoms on patients' quality of life. The importance of their study is that they brought researchers attention to the need for the development of a stent-related symptoms score measurement [7].
A recent study by Aboutaleb and Gawish, reported the histopathological changes in the urinary bladder associated with double J (DJ) stenting over the time of 3 months, They concluded that when period of stenting increased, the reaction

changed from acute stage to be chronic especially when stents lasting more than three months [8].

Material and methods

This a prospective selective study was carried out at Urology department, AL-Azhar University Hospital from September 2017 to March 2018. This study includes 40 patients (30 male and 10 females) with fixed double J stents within six months. The mean age of the patients was 38.1±14.7 years (range 5–60 years). Stenting of the right ureter (57.5%) was slightly more common than of the left ureter (37.5%). The most common stent length and size used were 26 cm (95%) and 6 Fr (85%). The most common stent material was used in this study was Teflon (75%) table 1. Those patients underwent Bladder cold cup biopsy during removal of the double J stent from around the ureteric orifice and trigone of bladder. These patients will be classified into 4 Groups according to duration of the stenting. Group 1 double J stenting for 2 weeks or less. Group 2 double J stenting for 2 to 6 weeks and Group 3 double J stenting for 6 to 12 weeks Group 4 double J stenting for more than 12 weeks. Then, the correlation between the histopathological changes and the period of the stenting will be determined.

Patients with positive visible bladder pathological findings at the time of double J insertion, a history of bladder stones, specific and non-specific urinary tract infections, bilharziasis, bladder malignancies, intramural stone, migrated stents and patients with any history of allergy were excluded to avoid selection bias. The cases groups were selected according to criteria in which patients with no any visible pathological changes at ureteric orifice or trigone of bladder during insertion of ureteric stents detected by cystoscopy. Routine preoperative clinical evaluation in the form of full history taking, general and local examination, and routine laboratory investigation in the form of Prothrombin time and concentration, and complete urine analysis for infection or crystals and accordingly urine culture for microorganisms was needed to treat urinary tract infection prior to endoscopy, and other radiological investigation in the form of KUB film and pelviabdominal ultrasonography to exclude any bladder stones or growth were performed for all patients.

Technique

The patients were anesthetized in a spine lithotomy position and started with preliminary Cystourethroscopy to evaluate any urethral or intravesical pathological condition. Depending on the indication of stent placement, the stent was removed by 22 Fr cystoscope under local anesthesia. Bladder Cold cup biopsies were taken from bladder reaction around the ureteric orifices and sent for histopathological examination to assessment the type of reaction induced by the stents.

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 23.0 for windows. Data are presented as the Mean ± standard deviation (SD), frequency, and percentage. Categorical variables were compared using the Chi-square ($\chi 2$) and Fisher's exact tests (if required). The level of significance was accepted if the P value < 0.05.

Results

According to indication of stent placement the stents were fixed in 6 patients (15%) for two weeks or less, fixed in 17 patients (42.5%) for 4 to 6 weeks, fixed in 11 patients (27.5) for 6 to12 weeks, and fixed in 6 patients (15%) for period more than 12 weeks table 2.The most common indication of ureteral stenting in this study was post ureteroscopy for ureteral stones in 17 patients (42.5%), and the less common indication in study were post obstructive uropathy with elevated serum creatinine in 3 patients (7.5%) and pre extracorporeal shock wave lithotripsy in 2 patients (5%) table 2.

Table 1: Collecting data of Patients and stents

Parameters	**Total N=40**	
Age (years): Mean +SD	38.1±14.7	
Gender:	N	%
Male	30	75.0
Female	10	25.0
Laterality:	N	%
Rt side	23	57.5
Lt side	15	37.5
Bilateral	2	5.0
Material of stent	N	%
Teflon	30	75
Silicon	10	25
Stent diameter (Fr):	N	%
4.8	2	5.0
6	34	85.0
7	4	10.0
Stent length (cm):	N	%
18	2	5.0
26	38	95.0
Stent duration(days)	N	%
≤ 2 Weeks	6	15.0
2-6 Weeks	17	42.5
6- 12 Weeks	11	27.5
> 12 weeks	6	15.0

Table 2: Indications of ureteral stents insertion

Indications of ureteral stenting	**N**	**%**
Post URS	17	42.5
Open surgery	8	20.0
Stricture ureter	6	12.5
Post PCNL	4	10.0
Obstructive Uropathy with ↑ S.Cr	3	7.5
Pre ESWL	2	5.0

The most common complications in this study post double J insertion are dysuria and frequency and this found in 39 patients (97.5%). While other complication as urinary incontinence, hematuria, encrustation and stone formation are less common table 3.

Table 3: Complications post ureteral stents insertion

Parameters		Total N=40
Complications of ureteral stenting	N	%
Dysuria	39	97.5
Frequency	39	97.5
Nocturia	14	35.0
Urgency	9	22.5
Encrustation	4	10.0
Urinary incontinence	2	5.0
Gross hematuria	2	5.0
Stone formation	1	2.5

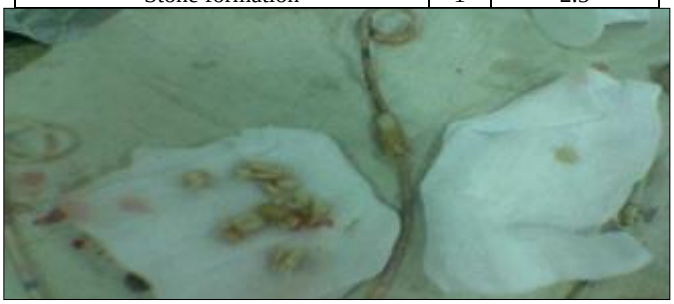

Fig 1: Picture showing encrustations on DJ missed for 6 months

Fig 2: Stent encrustration of proximal coil (aspect after stent removal).

The histopathological examination of bladder reaction that found at the bladder during removal of double J stents in patients with no any pathological finding during insertion of stents, we found that when we fix double J stents in 6 patients (15%) for 2 weeks or less, 4 patients the histopathological study of their biopsies showed mild acute cystitis with mild edema and esinophilic infiltration (10%). when we left double J stents in 17 patients (43%) for period from 2 to 6 weeks, 12 patients the histopathological study of their biopsies showed acute cystitis with sever edema and lymphocytic infiltration (37.5%). when we left double J stents in 11 patients (28%) for period from 6 to 12 weeks the histopathological study of their biopsies showed pathological feature of Von Brunn's nests (27.5%). when we left double J stents in 6 patients (15%) for period more than 12 weeks the histopathological study of their biopsies showed pathological feature of cystitis cystica (10%) table 4.

Table 4: Histopathological bladder changes with ureteral stents insertion

	Acute cystitis with sever edema and lymphocytic infiltration	Brun's nest	Cystitis cystica	Mild acute cystitis with mild edema and Esinophilic infiltration	
	N=15	N=11	N=4	N=4	
≥ 2 weeks	5.0%	0.0%	0.0%	10.7%	
2-6 Weeks	37.7%	2.5%	0.0%	10.0%	<0.001 HS
6- 12 Weeks	15.7%	27.7%	0.0%	3.0%	
> 12 weeks	4.0%	5.0%	10.0%	3.0%	

*Fisher's Exact test was used, statistically significant P<0.05.

Fig 3: Endoscopic view for the edema around the double J coil.

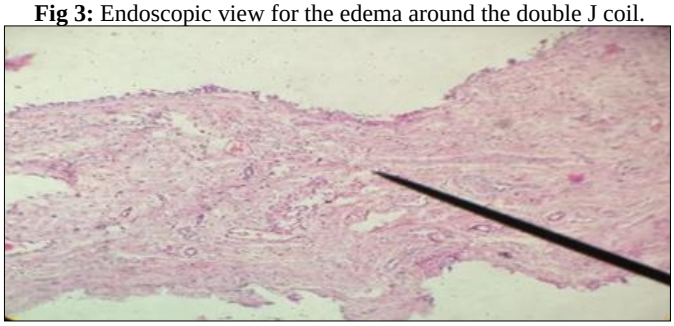

Fig 4: Mild acute inflammatory reaction at bladder showing: transitional epithelium with congested blood vessels and esinophilic infiltration with mild edema

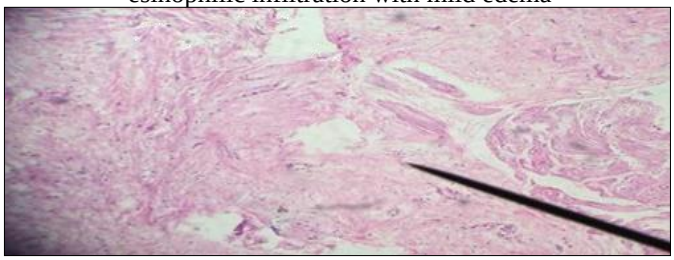

Fig 5: Acute inflammatory reaction at bladder showing: transitional epithelium with congested blood vessels and neutrophil and lymphocytic infiltration with sever edema.

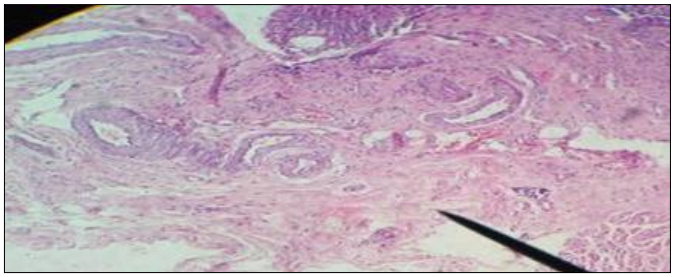

Fig 6: Brunn's nests: solid nests situated at superficial lamina propria with esinophilic and lymphocytic infiltration.

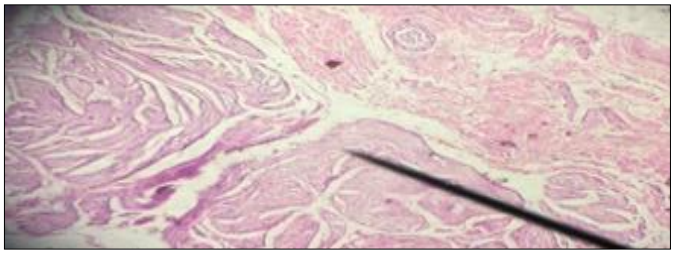

Fig 7: Cystitis cystica showing transitional epithelium with sub epithelial vesicles, and cystic dilatation of von Brunn's nest.

Discussion

The ureteral stents are commonly used in urological practice to bypass ureteral obstruction or after ureteral operations. Despite the frequent use of ureteral stents, they are still associated with morbidity in about 80% of cases [7]. There is no ideal ureteral stent up to now that can easy to insert and remove, drain the upper tract very well, free from side effects like irritative symptoms, resist encrustation, infection and migration, radio-opaque or visible with ultrasound, non-refluxing, durable and degradable if forgotten but still not available up till now [9].

In our study, we attempt to recognize the underlying histopathological changes in the urinary bladder due to the transient presence of Double J stent. There are infrequent studies to recognize bladder changes 2nd to jj stent.

Wishnow KI, *et al.* 1990 [10], reported that urothelium trauma caused by ureteroscopy would heals within 2-5 days, this Indicates that there is no relationship between the technique or procedure that used followed by Double J insertion will not affect the bladder reactions associated with double J stents. We should claim that the reactions documented are acute or chronic allergic cystitis which are linked to the bladder irritation due to presence of Double J stents in the ureter and the bladder.

Joshi R, *et al.* 2011 [11], reported that many studies are recorded about the patient's morbidity due to ureteral stents, Frequency and urgency are most commonly reported patient discomfort. Dysuria comes next in the order. Some patients report of suprapubic pain. Interestingly hematuria is not that common in all these studies. The prevalence of these symptoms (irrespective of the frequency of occurrence) is about a mean 50% when considered individually. The cumulated frequency is well over 80 - 90%.

In This study cold cup biopsies obtained from 40 patients (30 male and 10 females), patients were classified in to 4 groups that are similar to classification in study of Aboutaleb and Gawish (2017), From our results we found that classification in to 4 groups according to duration of the stenting lead to results similar to each other especially in group 3 and group 4, so that classification in to 3 groups could be more impacted.

The most common bladder histopathological changes due to double J stenting in patients of Upper Egypt for period 2 weeks or less are mild acute cystitis with mild edema and esinophilic infiltration and this found in (10%) of patients. While acute acute cystitis with sever edema and neutrophilic lymphocytic infiltration was found when fix double J stents for period from 2 to 6 weeks and this found in (37.5%) of patients. Brunn's nests was found when fix double J stents for period from 6 to 12 weeks and this found in (27.5%) of patients. Cystitis cystica was found when fix double J stents for period more than 12 weeks and this found in (10%) of patients. These results are similar to those reported by Aboutaleb and Gawish [8], who noted that in their study of 30 patients (28 male and 2 females), the stent duration was two weeks or less in 2 patients, 4 to 6 weeks in 18 patients, 6–12 weeks in 6 patients, and more than 12 weeks in 4 patients. Mild acute eosinophilic inflammatory reactions with mild edema were reported in patients who had stenting less than 14

days. Acute lymphocytic eosinophilic cystitis with edema was found in patients who had stents 48 to 6 weeks. Brunn's nests were reported in all patients with stents of more than six weeks.

Cystitis cystica was seen in all patients who had stents of more than 12 weeks.

In our study used three sizes of double J stent 4.8, 6, 7 Fr while in Aboutaleb and Gawish [8] reported used two sizes of Double J stents 4.7 and 6 Fr, and the same results will be reported, this Indicates that there is no correlation between the size of the stent to bladder histopathological changes, the size of the stent may aggravate the reaction but it will not change the type of the reaction from acute to chronic esinophylic lymphocytic cystitis. The material of stents used whatever Teflon or silicone, the same results were found, so that the material of stent has not impact on severity or aggravation of reaction, but the silicone stent has lower incidence of complication. In this study the most common complication are dysuria and frequency, but other side effects as nocturia, urgency, urinary incontinence, gross hematuria, encrustation and stone formation are less common.

Conclusion

We found that the urinary bladder inflammatory reactions increase and become sever as the stent duration increased, this reaction progresses from acute cystitis with lymphocytic eosinophilic reaction from time of 2–6 weeks up Brunn's nests and cystitis cystica with longstanding stents inside the ureter. So as our results suggest that the use of double J stents should be limited to highly indicated cases only to avoid these complications.

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