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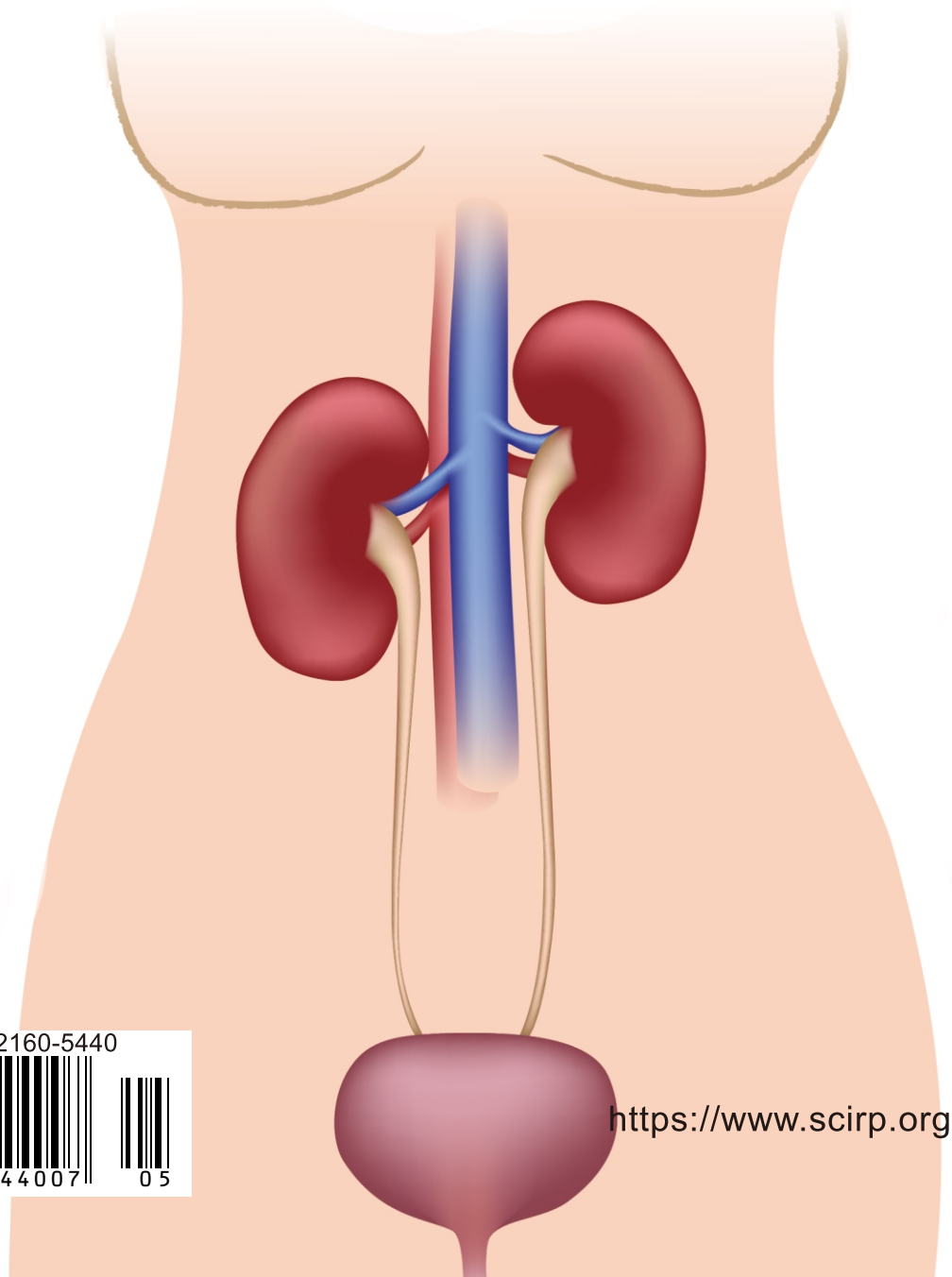

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Urological Cancers in Burkina Faso: Epidemiological and Anatomopathological Aspects of 2204 Cases

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Abstract

Purpose: To study the epidemiological and anatomopathological aspects of urological cancers in Burkina Faso from 1988 to 2018. **Patients and Methods:** A cross-sectional, retrospective and descriptive study of histologically confirmed cancers that are collected from pathological anatomy laboratory records. The aspects studied were age, sex, location and histological type. **Results:** A total of 2204 cases of urological cancer were collected. The predominance was male with a sex-ratio of 9.6. The average age was 63.32 years. We found 1602 cases of prostate cancer (72.68%), 361 cancers of the bladder and excretory tract (16.4%), 180 cancers of the kidney (8.16%), 33 testis cancers (1.5%) and 28 penile cancers (1.3%). The predominant histological type of prostate cancer was adenocarcinoma (96.4%) with a Gleason score 7 in 30.4% of cases. Bladder cancer consisted of 50% epidermoid carcinomas. Kidney cancer was mostly nephrotoblastomas with 42.2% of cases. We noted 42.4% of seminomas among testis cancers and 89.3% of epidermoid carcinomas within penile cancers. **Conclusion:** The incidence of urological cancers is increasing in Burkina Faso. These cancers occur at a relatively advanced age with male predominance. Prostate cancers are at the forefront of these urological cancers. The establishment of a cancer registry would allow better follow up of cancers in our countries.

Keywords

Urological Cancers, Epidemiology, Burkina Faso

1. Introduction

Urological cancers are increasingly common in urological pathology and constitute a real public health problem [1]. They include a series of malignant tumors affecting the organs, the urinary tract ducts and the male genital system in particular. Today, epidemiological and histological data on these urological cancers are available in developed countries, dominated by prostate cancers, which constituted, according to Globocan 2018, the first urological cancer and the fourth location in terms of frequency in the world. Bladder cancer, the second most common urological cancer in the world, has a specificity related to urogenital bilharziosis in our countries. In fact, bladder epidermoid carcinomas are more common in parts of the world where bilharziosis is endemic [2].

In Africa in general and Burkina Faso in particular, data on urological cancers are scarce due to the unavailability of effective collection tools, notably a operational cancer registry [3]. In recent years, we have seen an increase in the frequency of urological cancers in the various urology divisions in Burkina Faso [4].

In order to obtain an estimate of the epidemiology and to study the anatomopathological aspects of urological cancers at the national level, our work consisted in identifying all histologically diagnosed cancer cases from 1988 to December 2018 in the various pathological anatomy laboratories in Burkina Faso.

2. Patients and Methods

This was a descriptive and cross-sectional retrospective study of all the urological cancers cases diagnosed between 1988 and December 2018 (31 years) in all the six pathological anatomy departments in Burkina Faso. These were three public laboratories. They are those of Yalgado Ouédraogo hospital, Tengandogo hospital and Sanou Souro hospital. The other three are private. These are the laboratories of Sandof, Schiphra and Philadelphia. All cases of cancer have been collected from the registries of these different pathological anatomy laboratories. Then all the cases of urological cancers whose results could be analyzed were selected. The variables studied were frequency, sex, age, location and histological type. Data analysis was performed using Epi-info software version 7.0.8. Then an export was made on the SPSS 2.0 software to perform statistical tests. The curves were formed from an Excel 2010 spreadsheet.

3. Results

3.1. Epidemiological Results

3.1.1. Frequency of Urological Cancers Compared to Other Cancers

During our study, we collected 2204 cases of urological cancers from a total of 14,587 cases of cancers diagnosed in the pathological anatomy laboratories of Burkina Faso. These urological cancers accounted for 15.1% of the cases (**Table 1**).

The urogenital tract was the 3rd site of cancer localization in terms of frequency with 15.1% of the cancers diagnosed.

Table 1. Frequency of urological cancers compared to other cancers.

Apparatus or systems	Number	Percentage (%)
Gyneco-mammary apparatus	5595	38.4
Digestive system	2603	17.8
Urogenital apparatus	**2204**	**15.1**
Skin and skin appendage	1162	8.0
ENT-HN System	750	5.1
Musculoskeletal	710	4.9
Spleen and lymphatic system	520	3.5
Stomatological system	377	2.6
Respiratory system	290	2.0
Eye and annex	295	2.0
Nervous system	78	0.5
Endocrine system	3	0.1
General total	**14,587**	100.0

3.1.2. Evolution of Urological Cancers per Year

We collected 2204 cases of urological cancers over a 31-year period. There was an annual incidence of about 73 cases a year. There has been an increasing trend in urological cancers over the years. The largest number of cases was recorded in 2018 and 350 with a frequency of 15.9% (Figure 1).

3.1.3. Annual Incidence Rate of Urological Cancers

Table 2 shows the annual incidence rates of urological cancers collected in BURKINA FASO; according to the population estimates of the World Bank.

The results show abnormally increasing annual incidence rates of urological cancers. The highest incidences are recorded in 2018 with 1.77 per 100,000 inhabitants.

3.1.4. Age Distribution of Patients

Age was specified in 92.1% of cases. Figure 2 shows the representation of urological cancer cases according to age group (N = 2030).

The age group between 60 and 74 was the most represented with 1020 cases (50.24%). The average occurrence age of urological cancers was 63.32 years more or less 12.08 with 1 and 100 years.

3.1.5. Distribution of Prostate Cancers According to the Location

The distribution of urological cancers according to the location is shown in Figure 3.

In our study, we found 1602 cases of prostate or 72.68% of the cases of urological cancers collected. This cancer ranked first in terms of frequency compared to the other urological cancers and there was an annual incidence of about 53 cases per year.

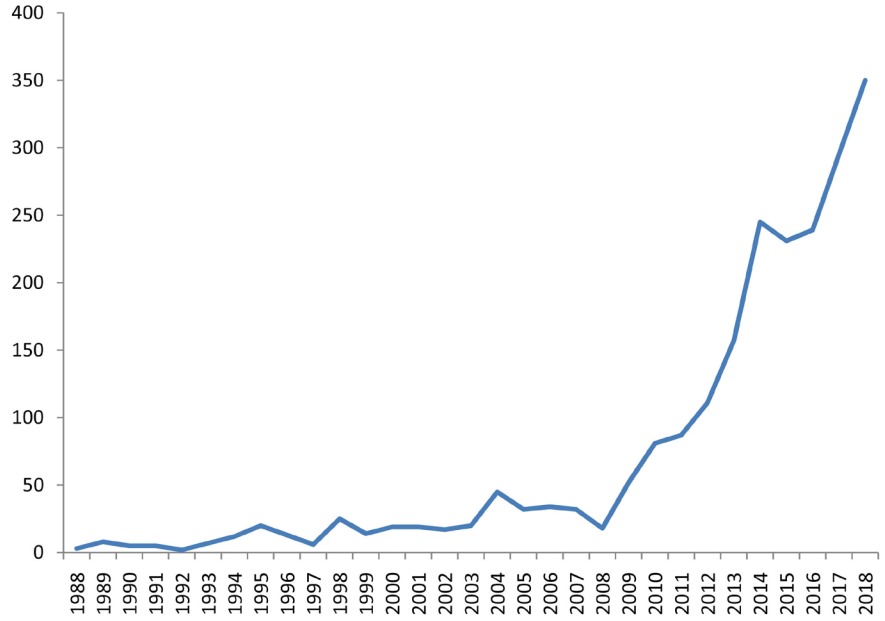

Figure 1. Dynamic evolution of urological cancers per year.

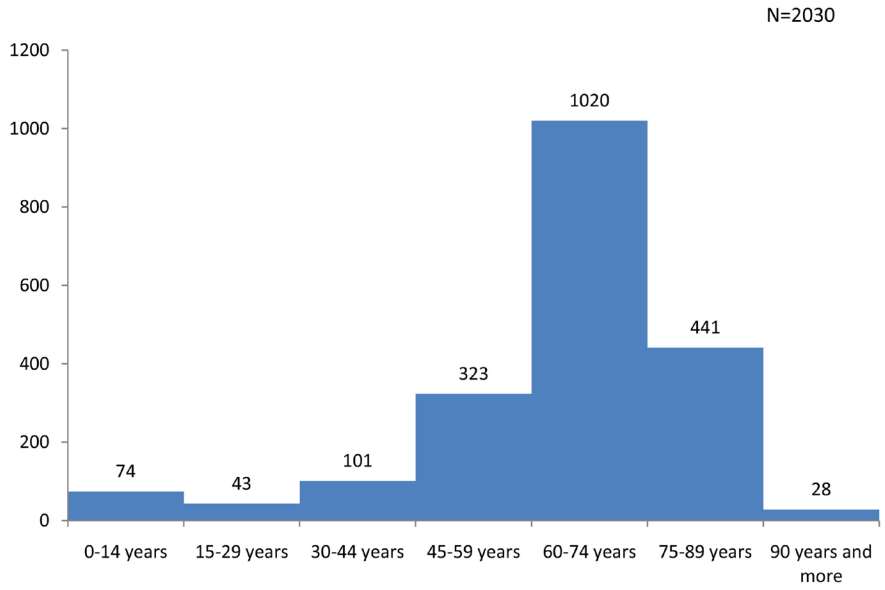

Figure 2. Distribution of patients according to age group.

Table 2. Annual incidence rate of urological cancers.

Year of diagnosis	Number of cases per year	Annual estimate of population	Ratio	Incidence rate per 100,000 inhabitants
1988	3	8,356,305	3.5901E−07	0.04
1989	8	8,579,823	9.3242E−07	0.09
1990	5	8,811,034	5.6747E−07	0.06
1991	5	9,050,084	5.5248E−07	0.06
1992	2	9,297,113	2.1512E−07	0.02
1993	7	9,552,476	7.3279E−07	0.07

Continued

1994	12	9,816,588	1.2224E−06	0.12
1995	20	10,089,878	1.9822E−06	0.20
1996	13	10,372,745	1.2533E−06	0.13
1997	6	10,665,546	5.6256E−07	0.06
1998	25	10,968,724	2.2792E−06	0.23
1999	14	11,282,701	1.2408E−06	0.12
2000	19	11,607,942	1.6368E−06	0.16
2001	19	11,944,587	1.5907E−06	0.16
2002	17	12,293,100	1.3829E−06	0.14
2003	20	12,654,621	1.5805E−06	0.16
2004	45	13,030,569	3.4534E−06	0.35
2005	32	13,421,930	2.3842E−06	0.24
2006	34	13,829,176	2.4586E−06	0.25
2007	32	14,252,021	2.2453E−06	0.22
2008	18	14,689,725	1.2253E−06	0.12
2009	52	15,141,098	3.4344E−06	0.34
2010	81	15,605,217	5.1906E−06	0.52
2011	87	16,081,9,911	5.4098E−06	0.54
2012	111	16,571,246	6.6983E−06	0.67
2013	157	17,072,775	9.1959E−06	0.92
2014	245	17,586,017	1.3932E−05	1.39
2015	231	18,110,624	1.2755E−05	1.28
2016	239	18,646,378	1.2818E−05	1.28
2017	295	19,193,284	1.537E−05	1.54
2018	350	19,751,535	1.772E−05	1.77

The highest incidences are recorded in 2018 at 1.38 per 100,000 inhabitants (N = 272).

3.1.6. Distribution of the Cases Prostate Cancers According to Age Group

Age was specified in 92.9% of the cases. Figure 4 shows the distribution of prostate cancers according to age group (N = 1488).

The age group between 60 and 74 years was the most represented by 867 cases (58.3%). The average age was 69.48 years with extremes of 18 and 100 years.

3.1.7. Distribution of Prostate Cancers According to Sex

Sex was specified in 2183 cases. The male sex was predominant with 91% of the cases and we found a sex-ratio (M/F) of 9.6.

3.2. Anatomopathological Results

3.2.1. Prostate Cancer

Gleason's score was specified in 85.95% of the cases. Table 3 shows a distribution of prostate cancers according to the Gleason score (N = 1377).

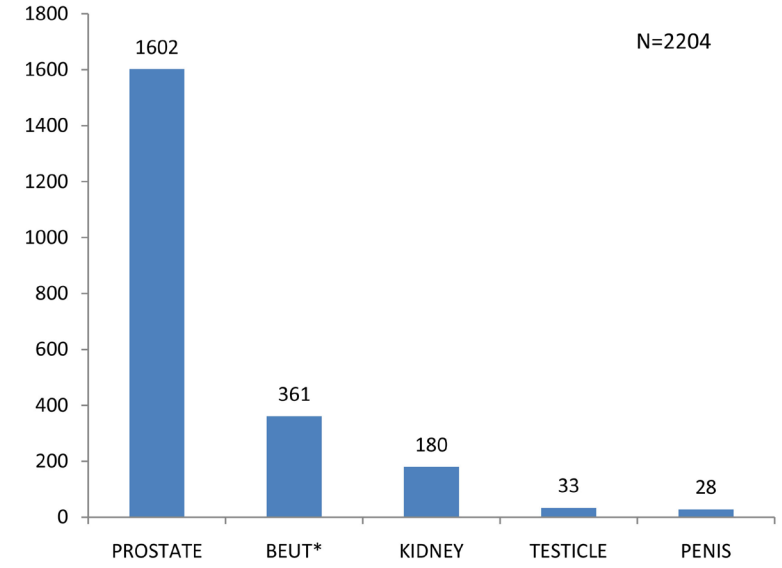

Figure 3. Distribution of prostate cancers according to the location. *BEUT. bladder-excretory urinary tract.

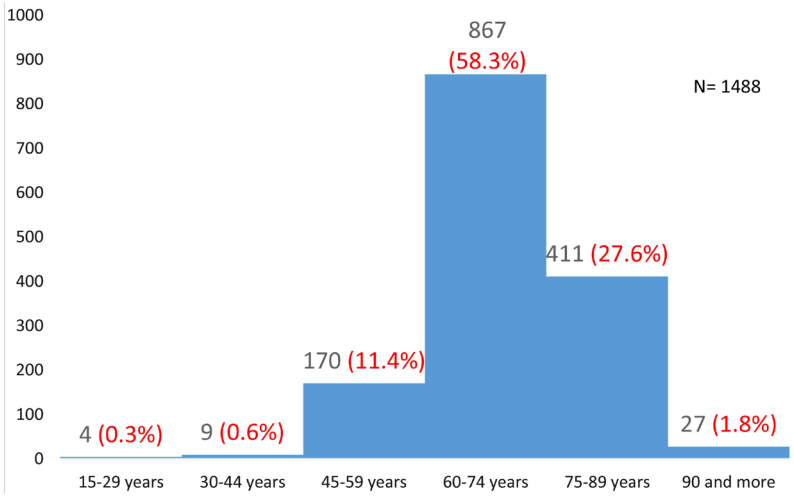

Figure 4. Distribution of prostate cancers according to age group.

Table 3. Distribution of prostate cancers according to Gleason score.

Gleason score	number	Percentage %
SCORE 2	69	5.0
SCORE 3	55	4.0
SCORE 4	108	7.8
SCORE 5	90	6.5
SCORE 6	408	29.6
SCORE 7	418	30.4
SCORE 8	183	13.3
SCORE 9	39	2.8
SCORE 10	7	0.5
Total	**1377**	100.0

The Gleason score 7 was the most represented by 30.4%.

Table 4 shows a distribution of prostate cancers according to the histological grade ISUP.

The grades 2 and 3 corresponding to Gleason score 7 were the most represented by 30.4% of the cases.

Table 5 shows a distribution of the cases according to the histological type (N = 1602).

Adenocarcinoma was the most represented by 96.4% of the cases.

We performed a statistical test on the distribution of the histological types of prostate cancer according to age. The results are shown in Table 6. Age was specified in 1488 cases.

There was a very significant statistical association of histological types and patients age. Adenocarcinoma was frequent in patients over 45 years especially in the 60 to 89 age group with 1244 cases or 86.4%.

3.2.2. Bladder and Excretory Tracts Cancer

In our series, we noted 361 (16.4%) cases of bladder and excretory cancer distributed in 357 cases of bladder cancer and 4 cases of urethral cancers.

Bladder cancer came in second place in terms of frequency with 16.2% of urological cancers. There was an annual frequency of 12 cases per year. Urethral cancer was scarce with 4 cases in 30 years. Table 7 shows the distribution of histological types of bladder cancers according to age. Age was specified in 321 cases.

There was a very significant statistical association of histological types and age of the patients. Epidermoid carcinoma was frequent in patients over 30 years

Table 4. Distribution of the cases of prostate cancers according to the ISUP grade.

Gleason score	Grade of ISUP	number	Percentage %
SCORE 6	grade 1	408	29.6
SCORE 7	grade 2 and 3	418	30.4
SCORE 8	grade 4	183	13.3
SCORE 9 et 10	grade 5	46	3.3

Table 5. Distribution of the cases of prostate cancers according to the histological type.

Histological types	Number	Percentage %
● Carcinoma	**1600**	**99.8**
Adenocarcinoma	1544	96.4
Epidermoid carcinoma	47	2.9
Urothelial carcinoma	9	0.5
● Sarcoma	**2**	**0.2**
Leiomyosarcoma	1	0.1
Rhabdomyosarcoma	1	0.1

Table 6. Distribution of histological types of prostate cancers according to age.

Histological types	15 - 29 years	30 - 44 years	45 - 59 years	60 - 74 years	75 - 89 years	90 years and more	TOTAL
● Carcinoma	**2**	**9**	**170**	**867**	**411**	**27**	**1486**
Adenocarcinoma	2	7	161	846	398	26	1440
Epidermoid Carcinoma	0	2	8	18	11	1	40
Urothelial Carcinoma	0	0	1	3	2	0	6
● Sarcoma	**2**	**0**	**0**	**0**	**0**	**0**	**2**
Leiomyosarcoma	1	0	0	0	0	0	1
Rhabdomyosarcoma	1	0	0	0	0	0	1

Statistical chi-2 test: P = 0.0001.

Table 7. Age distribution of histological types.

Histological types	0 - 14 years	15 - 29 years	30 - 44 years	45 - 59 years	60 - 74 years	75 - 89 years	90 years and more	TOTAL
● Carcinoma	**0**	**10**	**61**	**95**	**121**	**21**	**1**	**300**
Carcinoma Epidermoid	0	7	42	48	48	9	1	155
Carcinoma urothelial	0	3	16	40	61	12	0	132
Adenocarcinoma	0	0	3	7	12	0	0	22
● Sarcoma	**3**	**1**	**1**	**3**	**2**	**2**	**0**	**12**
Rhabdomyosarcoma	2	1	0	0	1	1	0	5
Fibrosarcoma	0	0	0	3	0	0	0	3
Leiomyosarcoma	1	0	1	0	0	1	0	3
Angiosarcoma	0	0	0	0	1	0	0	1

Statistic chi-2 test: P = 0.0001.

mostly in the age group of 45 to 74 years with 96 cases or 62.3%. Urethral carcinoma was mainly diagnosed in patients older than 45 years especially in the 60 to 74 years age group with 101 cases or 76.5%.

3.2.3. Other Urological Cancers

In our study, we found 180 cases of kidney cancer. This represented 8.16% of the cases of urological cancers collected. This cancer came in 3rd position in terms of frequency compared to the other urological cancers with an annual incidence of about 6 cases per year. The age group of 0 to 14 years was the most represented by 64 cases (38.3%). The average was 30.04 years with 1and 78 extremes. The female sex was the most represented by 55.4% of cases. The sex-ratio was 0.8. Nephroblastomas were represented by 42.2% of the cases. Nephroblastoma was frequent in the age group of 0 to 14 years with 62 cases or 88.6%. The epidermoid carcinoma was frequent in patients of more than 15 years, mostly in the age group of 45 to 59 years with 23 cases or 51.1%. The urethral carcinoma was mainly diagnosed in patients over the age of 15 and especially in the 15 to 74 age group with 6 cases or 60%. Neuroblastoma was present patients under 29 years

old with 3 cases in total including 2 cases in the age group of 0 to 14 years.

In our series, we had 33 cases of testis cancers. They consisted of 1.5% of the cases of urological cancers and ranked in the 4th place in terms of frequency compared to the other urological cancers with an annual incidence of about 1 case per year. The age group of 30 to 44 years was the most represented by 10 cases (33.3%). The average was 32.03 years with 1 and 70 years extremes. Seminomas (14 cases) and embryonic carcinomas (6 cases) were present in the under 59 years, especially in the age group of 30 to 44years. Non-Hodgkin's lymphoma was frequent in the under 14 years.

We totalled 28 cases of penile cancer or 1.3% of urological cancers. There was an annual incidence under one case per year. The age group of 45 to 59 years was the most represented by 9 (37.5%). The average was 58.5 years with 34 and 78 years extremes. The epidermoid carcinoma was the most represented by 89.3% of the cases.

4. Discussion

Urological cancers are a real public health problem [5] because of their worldwide frequency. Their frequency shows sensitive variations in the world. Indeed, data found in developed countries with high technical support center and functional cancer registries [6] [7] [8] are very difficult to compare with those in developing countries that do not have functional cancer registries [9] [10].

The continuous and exhaustive recording of all the cases of cancers (cancer registry) is a guarantee of the data quality and enables an approach to estimate the incidences as well as the different epidemiological parameters. In our series, we collected in 31 years; 2204 cases of urological cancer with a frequency of about 73 cases per year in average. These results are well above those observed by T. Darré *et al.* in Togo, of Ouattara A. *et al.* in Benin, R. Salah *et al.* in Algeria who obtained respectively in average, an annual frequency of 39.9 cases per year, 52.66 case per year and 29 cases per year [3] [10] [11]. This could be explained by our study period that was longer (31 years) therefore includes more cases, the different sensitizations campaigns to urological cancers, the improvement of the technical support centre within our laboratories and the increase in number of urologists. Throughout our study, we noted a growing trend over the years in urological cancers. The lower number was recorded between 1988 and 2008 with a slightly growing evolution curve. The highest number was recorded in 2018 or 350 (15.9%) cases of cancers. This is consistent with the literature. In fact, this increase was mentioned by Rébillard X. *et al.* in France [8] and Geolani Dy W. *et al.* in a study on the global burden of urological cancers [5]. Urological cancers may increase remarkably within an aging and increasing population. In Burkina Faso, according to the World Bank the population increased from 8.35 million in 1988 to 19.75 in 2018 and life expectancy from 49.55 years in 1988 to 60.77 in 2017. In our series, urological cancers were mainly present in the elderly. In fact, 89.3% of the patients were over 45 years. The average age in our series was 63.32

± 12.08 years and the most affected age group was the one between 60 and 70 with 1020 cases, or 50.24%. This is comparable to the results of many authors in the world. In the world T. Darré *et al.* in Togo, Ouattara A. *et al.* in Benin, R. Salah *et al.* in Algeria found respectively in their studies 62.89 ± 15.51 years; 65.53 years and 63.03 years [3] [10] [11]. In our study, there was a male predominance with a sex-ratio of 9.6, which is reported by several authors around the world including T. Darré *et al.* in Togo, Salah *et al.* in Algeria who found sex-ratio of 9.27 and 10.22 [3] [11].

Gleason's score gives a histoprognosis classification. It defines the degree of differentiation of the tumour and therefore its potential aggressiveness. In our context, a large proportion of patients were diagnosed at an advanced age. Gleason score was the most represented by 30.4% of the cases. There were 47% of patients with a prognosis higher or equal to 7. This result is slightly lower than the one observed in Côte d'Ivoire by E. Troh *et al.* that reported in their series 57.25% [12]. The Gleason score 7 gives fairly differentiated intermediate prognosis cancers of prostate and the scores 8 to 10 less differentiated cancers of poor prognosis. The ISUP (International Society of Urological Pathology) grade established through the correspondence with Gleason score, also gives a histoprognosis classification. In our series, the adenocarcinoma was the most represented histological type by 1544 (96.4%) cases followed by epidermoid carcinoma by 47 (2.9%) cases. These results are similar to those observed by NJP Engbang in the littoral region of Cameroon or 96.14% [9], T. Darré *et al.* in Togo and E. Troh *et al.* in Côte d'Ivoire with 94.86% and 93.67% [3] [12] respectively. The bladder cancer came in 2nd place in terms of frequency with 16.2% of urological cancers. There was an annual frequency of about 12 cases per year. The urethral cancer was scarce with 4 cases in 30 years. Our results are similar to those recorded by NJP Engbang In the littoral region of Cameroon in their study or 64 cases of bladder cancer in 10 years or 16.33% of urological 96 cases of bladder cancer in 20 years or 14.16% of urological cancers with an annual frequency of about 5 cases per year [3]. But in Algeria, R. Salah *et al.* in their study ranked bladder cancer in first place among urological cancers with 210 cases in 12 years or 60.3% [11]. Epidermoid carcinoma was the most represented in our study by 48.8% of the cases. These results are consistent with those recorded in Senegal by B. Diao *et al.* or 50.7%; in Cameroon by NJP Engbang or 40.63% [5] [9]. In our context this result could partially be justified by the fact we are in an endemic bilharzias area.

Bilharziasis is the main cause of squamous cell carcinoma of the bladder. B. Diao *et al.* in Senegal noted in series that Schistosoma haematobium eggs were found in 29.2% of the patients [5]. But our results contrasted with those obtained in Algeria by R Salah *et al.* who mostly gave urethral carcinoma (95.23%) [11]. The most represented histological types of kidney cancers were nephroblastoma with 42.2% and the epidermoid carcinoma with 26.7%. There was a distribution of the histological type of kidney cancers according to the age. Neph-

roblastoma, the most frequent histological type was present at paediatric age. Our results are similar to those observed in Cameroon and in Togo [3] [9].

Among testis cancers, germinal tumours were the most encountered histological types. There was 43.8% of seminoma, 18.75% of embryonic carcinoma. The distribution of histological types according to age showed significant results. In their series, R. Salah *et al.* in Algeria obtained similar results [4]. But T. Darré*et al.* in Togo and NJP Engbang in Cameroon obtained in their studies 5385% and 50% of lymphomas [3] [13].

Penile and scrotum cancers are known to be scarce in the literature, and the published series are sporadic [11]. Epidermoid carcinoma was the most represented by 89.3% of the cases. This is consistent with the literature. T. Darré *et al.* in Togo, Sow M. *et al.* in Cameroon and Gueyes M. *et al.* in Senegal reported in their series 100% of epidermoid carcinoma [3] [13] [14].

The weaknesses of our study are the lack of information on the age, sex, origin and occupation of some patients, as well as the retrospective nature of the study. Despite these limitations, these comments and discussions could be carried out.

5. Conclusion

Urological cancers were common in Burkina Faso and represented 15.1% of all cancers in the country. Urological cancers were common in elderly people. Prostate cancer was by far the most common. The establishment of a cancer registry would enable a better follow up of the evolution of cancers in our country.

Conflicts of Interest

The authors do not declare conflict of interest.

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Intravesical Infusion of Budesonide Foam Improves Symptoms in a Bladder Pain Syndrome/Interstitial Cystitis Rat Model

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Abstract

Purpose: Since intravesically administered steroid therapy may treat bladder pain syndrome/interstitial cystitis (BPS/IC) with fewer side effects than the current treatment of orally administered steroids, we investigated whether the intravesical infusion of budesonide foam can effectively treat BPS/IC symptoms in a rat model of tranilast-induced BPS/IC. **Methods:** There were 6 rat treatment groups (n = 8 per group): control + single or daily saline infusion, tranilast + single or daily saline infusion, and tranilast + single or daily budesonide infusion. All groups except for the controls were fed a tranilast supplemented diet for 5 weeks. Budesonide and saline were infused intravesically. After the BPS/IC rat model underwent single infusion treatments, we measured the paw pain threshold using the von Frey test and continuous cystometry was taken. After two weeks of daily intravesical infusions, we measured locomotor activity and serum cortisol levels; harvested bladders underwent histological analysis. **Results:** Both pain threshold and locomotor activity were significantly lower in the saline-infused groups receiving the tranilast diet, but there were no differences between the budesonide-infused groups and the controls. The interval between bladder contractions was significantly shorter in the tranilast group than the control or tranilast + budesonide infusion groups. The serum cortisol levels did not change. Hematoxylin-Eosin stainings of the bladder showed thickening of the bladder muscle layer and mucosal edema in the tranilast group, while the tranilast + budesonide infusion group showed only mild changes. **Conclusion:** Intravesical infusion of budesonide effectively treated BPS/IC symptoms in a rat model of BPS/IC.

Keywords

Bladder Pain, Budesonide, Interstitial Cystitis, Rats, Tranilast

1. Introduction

Bladder pain syndrome/interstitial cystitis (BPS/IC) is defined as suprapubic pain associated with bladder filling in the absence of urinary tract infections or other diseases and is typically accompanied by increased daytime and nighttime urination frequency, according to both the European Society for the Study of Interstitial Cystitis (ESSIC) and the European Association of Urology (EAU) [1] [2]. The etiology of BPS/IC is not fully understood yet, but there is evidence that indicates that BPS/IC is an autoimmune disease of the bladder because it is known to be associated with other autoimmune disorders such as systemic lupus erythematosus and allergies [3] [4].

When patients used tranilast to treat allergies, keloids, and hypertrophic scars, some of them sometimes developed BPS/IC [5] [6] [7]. Tranilast, N-(3,4-dimethyoxycinnamoyl) anthranilic acid, treats these diseases by suppressing the release of transforming growth factor (TGF)-β1 to inhibit collagen synthesis [8] [9]. We previously developed a BPS/IC rat model by administering high doses of tranilast to rats; our model closely resembles human BPS/IC because it has the typical signs and symptoms experienced by BPS/IC patients, such as increased urination frequency and decreased locomotor activity [10] [11]. Our BPS/IC rat model is also characterized by having an extended bladder that leads to inflammation, increased vascular permeability, and the presence of glomerulations in the bladder wall [10].

Although many systemic and intravesical agents have been investigated for treatment of BPS/IC, it remains a refractory disease. Oral administration of steroids is relatively effective for BPS/IC symptoms, but oral steroid therapy is associated with numerous adverse effects [12] [13]. As an alternative to oral administration, steroid enemas are used for the treatment of ulcerative colitis [14] [15]. Rectabul® (Kissei Pharmaceutical, Matsumoto, Japan) is a steroid enema foam containing 2 mg of budesonide per dose [16]. Since the drug is a foam preparation, it is retained in the rectum and sigmoid colon after infusion with minimal leakage [14] [15]. In addition, local administration of a steroid is expected to reduce systemic side effects.

Since intravesically administered steroid therapy may treat BPS/IC with fewer side effects than the current treatment of steroids administered orally, we investigated whether the intravesical infusion of budesonide foam can effectively control BPS/IC symptoms in a BPS/IC rat model induced by tranilast.

2. Methods

Animals

48 female Sprague Dawley rats weighing 200 to 240 g were used in this study. This study protocol was approved by the President of the University of the Ryukyus based on recommendations from the Institutional Animal Care and Use Committee (A2017182 and A2019002).

Treatment with a single intravesical infusion of budesonide

In the first experiment, 24 rats were randomly divided into 3 groups: control + single saline infusion group, tranilast + single saline infusion group, and tranilast + single budesonide infusion group (n = 8 for each group). For 5 weeks, all groups except for the controls were fed a powder diet containing 0.4% tranilast (Kissei Pharmaceutical, Matsumoto, Japan), and the controls were fed a standard powder diet (Clea Japan, Tokyo, Japan). After 5 weeks of the tranilast diets, rats were anesthetized using isoflurane and transurethral catheterizations were performed using a fine polyethylene catheter (PE50, Clay Adams, NJ, USA). Next, the tranilast + single budesonide infusion group received an intravesical infusion of 0.5 mL of budesonide foam (Rectabul®) that contains approximately 2 μg of budesonide, and both the tranilast + single saline infusion and control + single saline infusion groups received an intravesical infusion of 0.5 mL of physiological saline [16].

Von Frey testing

2 hours after the treatment infusions, the von Frey test was used to measure nociceptive paw pain (BIO-EVF5; PanLab, Holliston, MA, USA) in the three groups.

Continuous cystometry

We performed continuous cystometry on the single infusion-treated rat groups. The rats were anesthetized using urethane that was administered both subcutaneously (0.8 g/kg) and intraperitoneally (0.4 g/kg). Physiological saline was infused directly (0.05 ml/min) into the bladder using a PE50 catheter that was inserted transurethrally into the bladder and was connected to the infusion pump. We recorded bladder activity for a minimum of 90 min during cystometry. We also measured the residual volume after final voiding.

Treatment with multiple daily intravesical infusions of budesonide

The remaining 24 rats were randomly divided into 3 groups: control + daily saline infusion group, tranilast + daily saline infusion group, and tranilast + daily budesonide infusion group (n = 8 for each group). For 5 weeks, all groups except for the controls were fed a powder diet containing 0.4% tranilast, and the controls were fed a standard powder diet. After 3 weeks of the tranilast diets, all rats were given daily intravesical infusions for 2 weeks; the tranilast + daily budesonide infusion group received 0.5 mL budesonide foam, and both the tranilast + daily saline infusion and control + daily saline infusion groups received 0.5 mL physiological saline.

Locomotor activity testing

After 2 weeks of daily infused treatments, we measured locomotor activity to evaluate pelvic pain using previously described methods using a digital counter and an infrared sensor (NS-ASS01; Neuroscience Inc., Tokyo, Japan) [10].

Nighttime locomotor activity was measured from 8:00 P.M. to 8:00 A.M. with the lights off.

At the end of the experiment, rats were anesthetized for the collection of venous blood samples from the inferior vena cava to measure serum cortisol levels (BML Inc., Tokyo, Japan) and the excision of bladders for histological examination.

Histology

The bladders of the rats were harvested, visually inspected, fixed in 10% formalin buffer, processed, embedded, sectioned, Hematoxylin-Eosin stained, and analyzed for histological changes.

Statistical Analysis

Results are reported as the mean ± standard error of the mean (SEM). Student's unpaired *t*-test was used to determine significance. A $p < 0.05$ indicated significance.

3. Results

Nociceptive paw pain threshold

We used the von Frey test to determine that the mean threshold for nociceptive paw pain was 26.5 ± 2.2 g, 33.6 ± 2.1 g, and 35.3 ± 2.6 g for the tranilast + single saline infusion group, tranilast + single budesonide infusion group, and control + single saline infusion group, respectively (n = 8 for each group) (Figure 1). The mean threshold for nociceptive paw pain was significantly lower in the tranilast + single saline infusion group than in the control + single saline infusion group (n = 8, $p = 0.022$), and no significant differences were observed

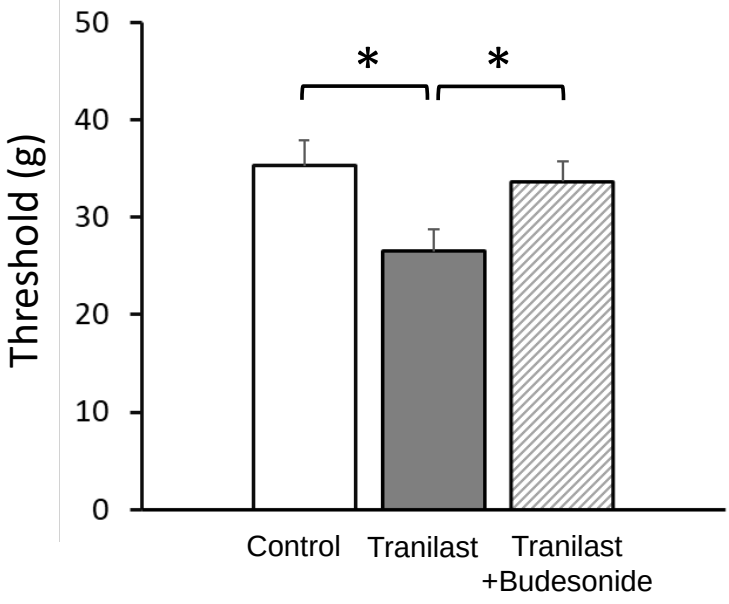

Figure 1. The von Frey test was used to determine the paw pain threshold in the BPS/IC rat model after treatment. Control: control + single saline infusion group, Tranilast: tranilast + single saline infusion group, Tranilast + Budesonide: tranilast + single budesonide infusion group. Mean ± SEM, n = 8 per group, $^{*}p < 0.05$, $^{**}p < 0.01$.

between the tranilast + single budesonide infusion group and the control + single saline infusion group. Therefore, we demonstrated that the significantly lower nociceptive paw pain threshold induced by tranilast was reversed by a single intravesical infusion of budesonide foam.

Continuous cystometry measurements

The mean interval between bladder contractions was 15.3 ± 1. min, 18.3 ± 1.7 min, and 18.9 ± 1.3 min for the tranilast + single saline infusion group, tranilast + single budesonide infusion group, and control + single saline infusion group, respectively (n = 8 for each group) (Figure 2). The interval between bladder contractions was significantly shorter in the tranilast + single saline infusion group than in the control + single saline infusion group ($p = 0.048$), but no significant differences were observed for the tranilast + single budesonide infusion group. The mean bladder pressure thresholds for inducing bladder contractions were 6.9 ± 0.5 cm H_2O, 8.3 ± 0.4 cm H_2O, and 8.1 ± 0.3 cm H_2O for the tranilast

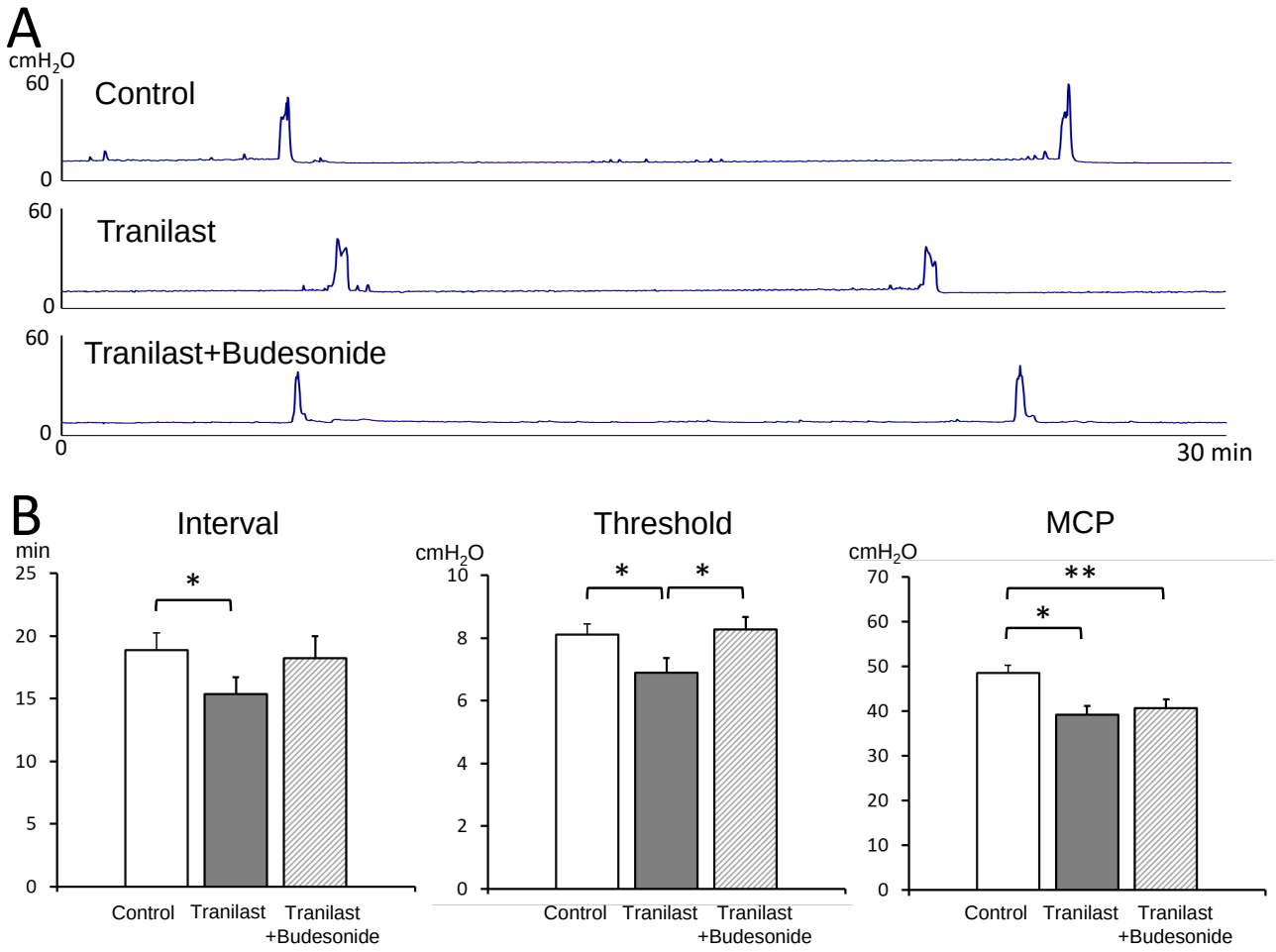

Figure 2. Comparison of continuous cystometry measurements the BPS/IC rat model after treatment. (A) Representative continuous cystometrograms are shown for the 3 treatment groups. (B) The graph shows the interval between bladder contractions (Interval), threshold bladder pressure that induced bladder contractions (Threshold), and the maximum bladder contraction pressure (MCP). Control: control + single saline infusion group, Tranilast: tranilast + single saline infusion group, Tranilast+Budesonide: tranilast + single budesonide infusion group. Mean ± SEM, n = 8 per group, $^*p < 0.05$, $^{**}p < 0.01$.

+ single saline infusion group, tranilast + single budesonide infusion group, and control + single saline infusion group, respectively (n = 8 for each group). The threshold bladder pressure for inducing bladder contractions was significantly lower in the tranilast + single saline infusion group than in the control + single saline infusion group (p = 0.039), but no significant differences were observed for the tranilast + single budesonide infusion group. The mean maximum bladder contraction pressure was 39.2 ± 2.0 cm H_2O, 40.0 ± 2.0 cm H_2O, and 48.5 ± 1.7 cm H_2O for the tranilast + single saline infusion group, tranilast + single budesonide infusion group, and control + single saline infusion group, respectively (n = 8 for each group). The mean maximum bladder contraction pressure was significantly lower in both the tranilast + single saline infusion group and the tranilast + single budesonide infusion group than in the control + single saline infusion group (p = 0.008). However, we did not observe any significant differences among the 3 groups for either the baseline bladder pressure that ranged from 3.8 to 7.1 cm H_2O or the residual volume that ranged from 0 to 0.2 mL. Thus, the shortened interval between bladder contractions induced by tranilast was reversed with a single intravesical infusion of budesonide foam.

Locomotor activity measurements

The mean nighttime locomotor activity was 14,510 ± 568 movements, 16,863 ± 1181 movements, and 16,719 ± 678 movements for the tranilast + daily saline infusion group, tranilast + daily budesonide infusion group, and control + daily saline infusion group, respectively (n = 8 for each group) (**Figure 3**). The tranilast + daily saline infusion group has significantly less movement than that of the control + daily saline infusion group (p = 0.023), but no significant differences were observed for the tranilast + daily budesonide infusion group. Thus, the lower locomotor activity induced by tranilast was reversed by intravesical infusion of budesonide foam.

Serum cortisol measurements

The mean serum cortisol level was 0.79 ± 0.04 μg/dL, 0.75 ± 0.08 μg/dL, and 0.79 ± 0.05 μg/dL for the tranilast + daily saline infusion group, tranilast + daily budesonide infusion group, and control + daily saline infusion group, respectively (n = 8 for each group). We found no significant differences in the serum cortisol levels among the three groups.

Histological findings of the bladder

The pathological examination of the excised bladders did not reveal any stones, drug foam, or residue. Thickening of the bladder muscle layer and edema in the bladder wall was observed in the Hematoxylin-Eosin stained sections of the bladder wall from the tranilast + daily saline infusion group, but these changes were less prominent in the tranilast + daily budesonide infusion group and control + daily saline infusion group (**Figure 4**). We also identified low levels of cellular infiltration into the mucosa in all 3 groups. Thus, the observed histological bladder wall changes induced by tranilast slightly improved after the treatment with budesonide foam.

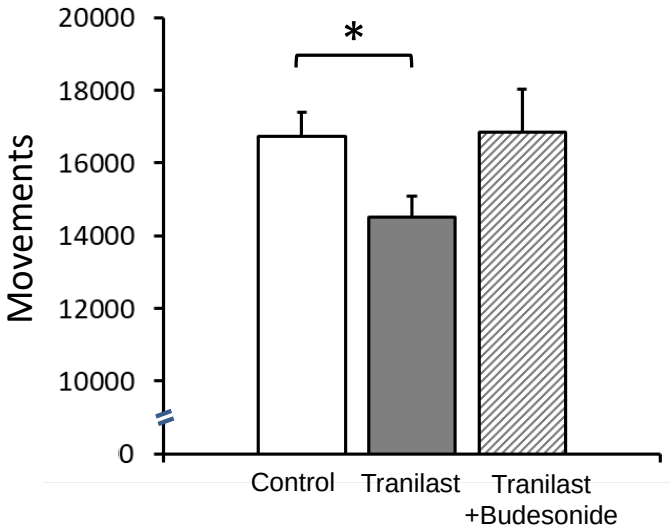

Figure 3. Comparison of nighttime locomotor activity in the BPS/IC rat model after treatment. Control: control + daily saline infusion group, Tranilast: tranilast + daily saline infusion group, Tranilast+Budesonide: tranilast + daily budesonide infusion group. Mean ± SEM, n = 8 per group, $^{*}p < 0.05$.

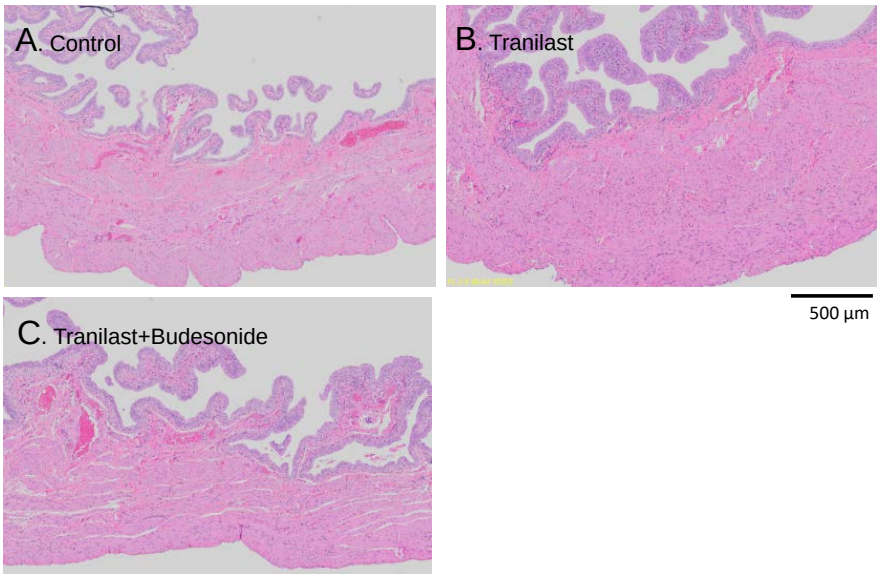

Figure 4. Histological examination of harvested bladders from BPS/IC rat model after treatment. Representative Hematoxylin-Eosin stainings of the bladder wall are shown for the (A) control + daily saline infusion group, (B) tranilast + daily saline infusion group that has thickening of the bladder muscle layer and mucosal edema, and (C) tranilast + daily budesonide infusion group that has only mild histological changes. Scale bar = 500 μm for (A), (B), and (C).

4. Discussion

In this study, we validated our previously established rat model of BPS/IC by measuring locomotor activity and urinary frequency [10] [11]. We found that rats in the tranilast + daily saline infusion group, who were treated with high doses of tranilast, had significantly less locomotor activity than the control rats.

Since reduced locomotor activity is an indicator of pelvic pain, this means that our BPS/IC rat model produces pelvic pain symptoms similar to the human version of BPS/IC. Furthermore, continuous cystometry performed on our BPS/IC rat model showed that the interval between bladder contractions was significantly shorter than that of the control group, indicating that our BPS/IC rat model has increased urinary frequency, which is another common symptom of BPS/IC. Therefore, we used our BPS/IC rat model to investigate whether the intravesical infusion of budesonide foam can effectively treat BPS/IC symptoms.

This study showed a lower pain threshold in the nociceptive paw of BPS/IC rats. Intravesical infusion of budesonide foam reversed the lower nociceptive paw pain threshold, reduced locomotor activity, and the shorter interval between bladder contractions that were all induced by the tranilast supplemented diet. Moreover, the histological changes in the bladder wall improved slightly, and no drug residue was observed in the bladders. However, serum cortisol levels were not affected by the intravesical infusion of budesonide foam. Thus, the intravesical infusion of budesonide foam ameliorated the tranilast-induced BPS/IC symptoms in our rat model without increasing serum cortisol levels or causing any adverse influences on the bladder.

In previous studies, we found that the BPS/IC rats had shorter intervals between bladder contractions and thinner bladder walls than control rats, but there were no changes to either the threshold bladder pressure or the maximum bladder contraction pressure [10] [11]. In this study, however, the BPS/IC rats had lower threshold bladder pressure, lower maximum bladder contraction pressure, and thicker bladder walls. These differences from previous studies may have been due to the influence of intravesical catheterization and saline infusion. Since our previous study identified slight inflammatory changes and an increase of bladder wall vascular permeability in the BPS/IC rats fed a tranilast supplemented diet [10], the bladders of these rats might be susceptible to the influence of catheterization and saline infusion. Therefore, it might be possible that intravesical catheterization and saline infusion under tranilast administration caused inflammation of the lower urinary tract, affected intravesical pressure, and thickened the bladder wall. Intravesical infusion of budesonide foam suppressed the bladder wall changes in the BPS/IC rats.

Even though orally-administration steroids can effectively treat BPS/IC, patients experience problematic side effects [12] [13]. Therefore, administering dimethyl sulfoxide (DMSO) [17] [18], heparin [19], hyaluronic acid [20], and bupivacaine with heparin and triamcinolone [18] by intravesical infusions for the treatment of BPS/IC has been investigated both experimentally and clinically, and were reported to be relatively effective with fewer side effects than oral steroids. Another effective BPS/IC treatment involving the endoscopic submucosal bladder injections of either botulinum toxin [21] or the steroid triamcinolone [22] [23] was reported. No major adverse events have been reported for any drugs that were administered by either intravesical infusions or endoscopic injections. However, multiple intravesical infusions and endoscopic submucosal

injections must be performed, which requires patients to visit clinics for each treatment. On the other hand, enemas can be done at home for the treatment of ulcerative colitis. In the urology field, patients with underactive bladders and large residual urine volumes perform intermittent self-catheterizations. Therefore, it is feasible for BPS/IC patients with severe bladder pain to perform intravesical infusions of steroids by self-catheterization at home.

There were several limitations in our study. The number of animals in each group was small. No data was acquired on possible urinary tract infections that may have occurred, and no data was acquired for possible injuries caused by daily catheterizations. For continuous cystometry, the single transurethral catheterization for the infusion treatment was relatively easy. However, the 2 weeks of daily transurethral catheterizations injured the urethra and caused bleeding that led to difficulties in performing the additional catheterization for cystometry. Therefore, we performed continuous cystometry after only 1 intravesical infusion of either physiological saline or budesonide foam to avoid injuring the urethra while inserting the transurethral catheter. In the future, we plan to investigate the long-term effects of bladder inflammation associated with intravesical steroid infusions performed by self-catheterization in patients with BPS/IC.

5. Conclusion

We demonstrated that intravesical infusions of steroid treatment using budesonide foam effectively reduced bladder pain, increased the interval between bladder contractions, and improved histopathological changes in the bladder wall of a BPS/IC rat model. Future clinical investigations on the impact of intravesical steroid treatments by self-catheterization in BPS/IC patients are planned.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendicular Mucosal Tube Implant with Dartos Wrap Operation for Hypospadias

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Abstract

Aims and Objective: To develop a better operation for hypospadias patients with poor and bad quality urethral plate and damaged urethral plate as in hypospadias cripples. **Materials and Methods:** I operated 21 cases of hypospadias with Appendicular mucosal tube implant with Dartos wrap operation from 17/04/2017 to 03/03/2019, in Jawale Institute of pediatric Surgery, and that group was labeled as group A. 27 cases of hypospadias were operated in same time span with conventional techniques such as extended Snodgrass operation and Byar's two-stage operation (group B), kept as control. 7 patients (33.33%) were cases of hypospadias cripples with multiple surgeries done in the past. 4 patients (9.52%) patients had congenital short urethra. Remaining 10 patients (50%) were fresh cases with no operation done in past but with bad and fibrotic urethral plate. The longest follow up was 3 years and the shortest of 1 year. **Technique of Operation:** Appendicectomy performed by open technique and the serosa of Appendix cut longitudinally and stripped off the mucosal tube. The proximal hypospadias opening sutured with the appendicular mucosal tube with 6 sutures of 5-0 Vicryl. Dartos fascia is raised from the scrotum wrapped over the tube and 8 - 10 interrupted stitches taken with 5-0 Vicryl. Glanuloplasty performed over it. Suprapubic diversion did and kept for 3 weeks postoperatively. **Results:** In group A, 3 patients developed fistula and only 1 (4.76%) required repair at the end of 6 weeks. 2 (9.52%) patients developed grade 3 infection and settled with conservative treatment. UFR was normal at the end of 12 weeks (12.85 Ml/sec. In group B, 11 patients developed fistula and 9 (33.33%) required repaired. 9 (33.33%) patients developed strictures and all of them required multiple urethral dilatation under GA. 7 (25.92%) patients developed meatal stenosis.UFR was badly reduced with average of 5.78 ML/Sec. **Conclusion:** The operation proves to be a much better option compared to the conventional for group A patients. We need a series with longer follow up and larger number of patients.

Keywords

Hypospadias, Hypospadias Cripples, Appendicular Mucosal Tube Implant, Appendicular Mucosal Tube Implant with Dartos Wrap

1. Introduction

The incidence of hypospadias [1] is generally 1 in 200 live births. There are a variety of operations described for hypospadias. Results of hypospadias surgery largely depend on quality of urethral plate. Generally, the variety of operations available for hypospadias has bad results when the quality of urethral plate is poor. There are a good number of cases done by less qualified doctors with multiples surgeries done which destroy the urethral plate, known as hypospadias cripples. Such patients also have poor results with the conventional operations. The conventional operations described in medical literature for above type of patients are Byar's two staged urethroplasty, extended Snodgrass operation, Buccal mucosa urethroplasty, bladder mucosa urethroplasty and Duckett's transverse island operation. All these operations are technically demanding and have a very high complication rate. I am describing an operation here which is technically less demanding and has much lower complication rates than the above options.

Aims and objectives: To develop a better operation for hypospadias with poor and bad quality urethral plate and damaged urethral plate as in hypospadias cripples

2. Materials and Methods

I operated 21 cases of hypospadias with Appendicular mucosal tube implant with Dartos wrap operation from 17/04/2017 to 03/03/2019, in Jawale Institute of pediatric Surgery, and that group was labeled as group A (Table 1). Age range for group A was 1 year to 13 years. 7 patients (33.33%) were cases of hypospadias cripples (Table 1) with multiple surgeries done in the past. 4 patients (9.52%) patients had congenital short urethra. Remaining 10 patients (50%) were fresh cases with no operation done in past but with bad and fibrotic urethral plate (Table 1). The appendicular mucosal tube implant with Dartos wrap operation involves using appendicular mucosal tube and implanting it in place of urethra and is wrapped by Dartos fascia. In the same time span, and 27 cases were operated with conventional techniques such as extended Snodgrass operation and Byar's two-stage operation and this group was labelled as group B which is kept as control. The extended Snodgrass operation involves taking a midline cut in the entire urethral plate and tabularizing it over a stent. In Byar's stage one operation, the urethral plate is excised and both skin flaps sutured in the midline to replace the urethral plate. In Byar's stage two operation, the urethra is made by tabularizing the skin. Age range for group B was 11 months to 12 years. The patients were distributed to both groups in a random manner. The variables to

Table 1. Group A patients operated by appendicular mucosal tube implant with Dartos wrap operation.

Sr. No.	Clinical Features	Age (Yr)	Degree of Chordee	Urethral plate	Position of meatus	Post-op cosmetic result	Follow up (Year)	UFR at 12 wksMl/Min	Complications
1	Hypospadias cripples with 3 operation in past	7	45	Badly damaged and fibrotic	Proximal	Average	5	15	Grade 3 infection
2	No operations in past, small penile size	7	90	Narrow and fibrotic	Proximal	Good	5	12	nil
3	Hypospadias cripples with 7 operation in past	12	30	Damaged urethral plate with fibrosis	Perineal	Poor	4	10	Fistula required surgical closure
4	No operations in past, small penile size	3	60	Narrow and fibrotic	Proximal	Good	4	15	nil
5	No operations in past, small penile size, congenital short urethra	7	90	Small and narrow	Subcoronal	Good	3.5	12	nil
6	No operations in past, small penile size	9	60	Narrow fibrotic	Proximal	Excellent	3	15	nil
7	Hypospadias cripples with 2 operation in past	5	30	Badly damaged and fibrotic	Proximal	Good	3	16	Grade 3 infection
8	No operations in past, small penile size	7	90	Narrow and fibrotic	Midpenile	Average	2.5	12	nil
9	No operations in past, small penile size, congenital short urethra	2	90	Small and narrow	Mid penile	Good	2.5	14	nil
10	Hypospadias cripples with 2 operation in past	7	30	Damaged urethral plate with fibrosis	Proximal	Excellent	2.5	15	Post op hematoma, drained successfully
11	No operations in past, small penile size	2	90	Narrow and fibrotic	Mid Penile	Good	2	12	nil
12	Hypospadias cripples with 3 operation in past	7	30	Fibrotic and scarred	Proximal	Average	2	15	nil
13	No operations in past, small penile size	2	60	Narrow and fibrotic	Mid penile	Excellent	2	12	nil
14	No operations in past, small penile size	5	90	Narrow and fibrotic	Perineal	Good	1.5	15	nil
15	No operations in past, small penile size, congenital short urethra	2	60	Small and narrow	Proximal	Average	1.5	15	Fistula healed on conservative treatment
16	Hypospadias cripples with 2 operation in past	5	30	Damaged and scarred	Mid penile	Good	1.5	12	nil
17	No operations in past, small penile size	13	90	Narrow, small penis	Perineal	Good	1.5	10	Post op hematoma, drained successfully
18	No operations in past, small penile size	11	60	Narrow and fibrotic	Mid penile	Excellent	1	12	nil
19	Hypospadias cripples with 5 operation in past	12	30	Badly damaged with scars	Proximal	Poor	1	16	Fistula healed on conservative treatment

Continued

20	No operations in past, small penile size, congenital short urethra	9	60	Small and narrow	Perineal	Excellent	1	14	nil
21	No operations in past, small penile size	8	90	Small and fibrotic	Proximal	Good	1	16	nil

be compared in two groups are fistula rates, redo operation rate, other complications, UFR at the end of 12 weeks and the cosmetic results. The variables in both groups were compared by calculating the percentage of each variable. Patients were followed up at monthly interval for first 3 months and 3 months till 3 years. The longest follow up was 3 years and the shortest of 1 year.

Technique of operation: Two days before the surgery, patient is subjected to mechanical bowel cleansing and antibiotics are given to reduce bacterial load in the colon. Under general anesthesia open appendicectomy is performed by the conventional open technique (Figure 1). Incision is taken at McBurney's point and deepened through muscles to open peritoneal cavity. The appendix is identified and held by atraumatic.

Babcock's forceps to avoid damage. Appendicular artery is divided between ligatures without damaging the appendix. The appendix is ligated at the base with 3-0 vicryl and distal appendix excised. The appendicular stump is cauterized with cautery and buried by 3-0 vicryl. The muscles closed by interrupted 3-0 vicryl. Skin closed by 3-0 vicryl subcuticular sutures. The appendicectomy can also be performed by laparoscopy, but my choice was open surgery.

A small cut is made in the terminal part of appendix. No.10 infant feeding tube coated with KY jelly passed through the appendix through and through. The serosa of appendix cut longitudinally and stripped off the mucosal tube (Figure 2) without creating a breach in it. Blunt and sharp dissection are needed to accomplish this step. Now the serosa is completely excised and only mucosal tube is left. The mucosal tube scrapped with a blunt scalpel to strip of any remaining part of submucosa and muscularis to keep only the mucosal tube (Figure 3). The tube is kept in Metronidazole solution (500 mg in 100 ml) for 10 minutes to disinfect it.

A glans stitch is taken by 4-0 vicryl on round body needle. The penile skin is degloved till the base of the penis. The urethral plate or its remnants are fully excised. Any chordee tissue around and below urethral plate is completely excised. Chordee test is performed by applying tourniquet at the base of penis and by injecting saline in corporal bodies through glans penis. Thus, it is confirmed that there is no residual chordee. The proximal hypospadias opening mobilized for 1 cm and any fibrous tissue around it excised. The 5 mm distal part of the opening is excised to have healthy tissue for anastomosis.

A midline incision is taken on median raphe of scrotum. Dartos fascia which is medial and inferior to the testis dissected off from the skin and testis on both sides (Figure 4). Dissection is performed and Dartos fascia separated from perineal

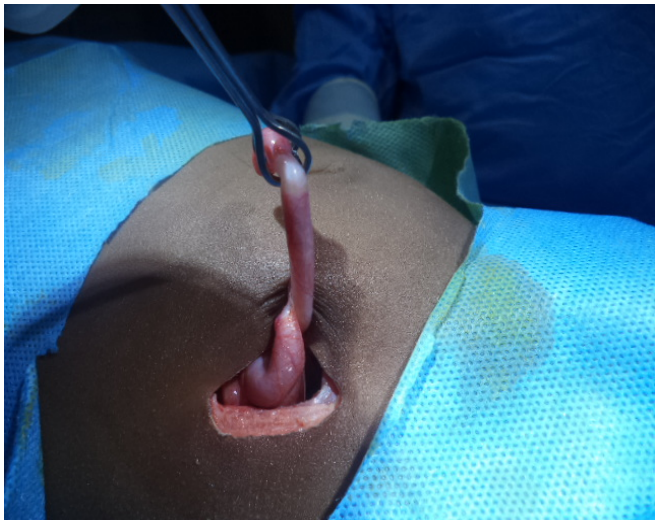

Figure 1. Appendicectomy performed by open technique.

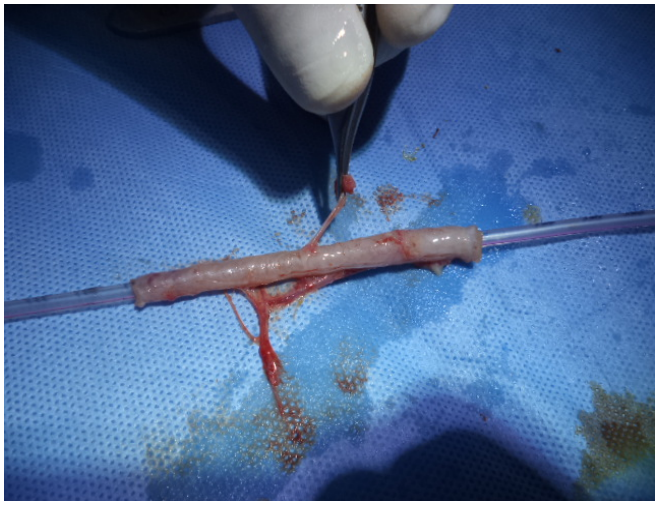

Figure 2. Serosa and muscularis stripped off the appendicular mucosal tube.

Figure 3. Appendicular mucosal tube ready for implantation.

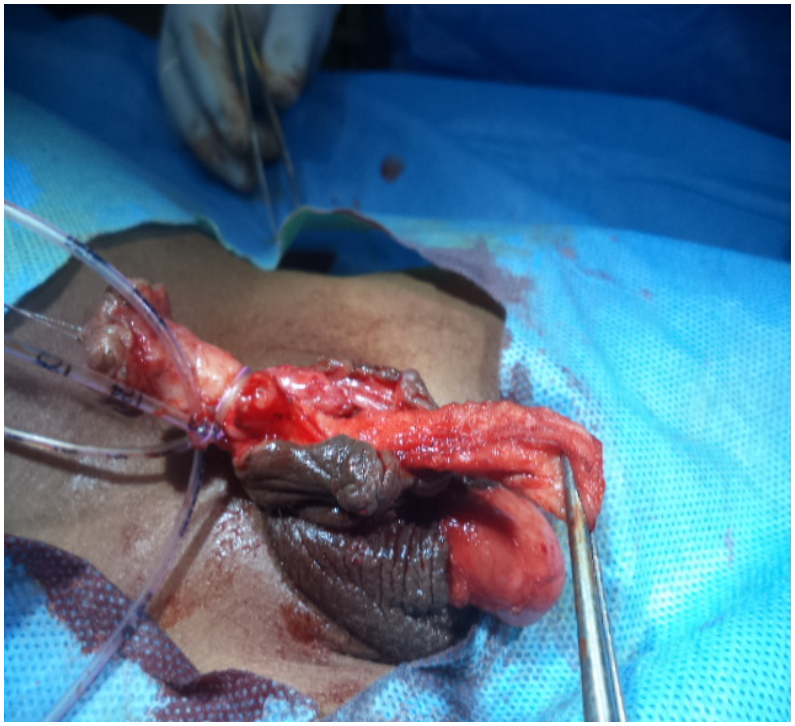

Figure 4. Dartos fascia raised from scrotum.

urethra. Dartos fascia lengthened till it comfortably reaches the tip of glans penis. Midline incision was taken ventrally on glans penis and glans wings raised on both sides. Dartos fascia now sutured to the tip of glans penis (Figure 5) in the midline by 5-0 Vicryl suture. The dartos fascia now forms a vascular bed (Figure 5) over the underlying Buck's fascia. A hole is made in Dartos fascia at the level of proximal opening of hypospadias that is already created. This opening is taken out through the hole in Dartos fascia.

The appendicular mucosal tube anastomosed with proximal urethral opening by 6 interrupted sutures of 5-0 Vicryl (Figure 6). The Dartos is wrapped over the appendicular mucosal tube and proximal anastomosis (Figure 7) by taking 8 - 10 interrupted stitches with 5-0 Vicryl. The distal end of the tube is passed through raised glans wings along with the Dartos wrapped around it. The pale mucosal tube immediately starts looking pink.

Glanuloplasty performed over it by 5-0 Vicryl horizontal mattress sutures. Penile skin cut vertically in the midline to raise Byar's skin flaps. Both the flaps moved ventrally forwards and sutures to each other as well as to the glans penis (Figure 8).

Penis is wrapped by Soffratulle and a gauze piece over it. A compression dressing gave over it by wrapping with Elastoplast bandage. A suprapubic diversion was done by putting No. 12 Foley's catheter into the urinary bladder by open technique. It is kept for 3 weeks postoperatively. Intravenous antibiotics are given in calculated dosages postoperatively for one week. The author's choice is Injection Ceftriaxone, Amikacin and Metronidazole.

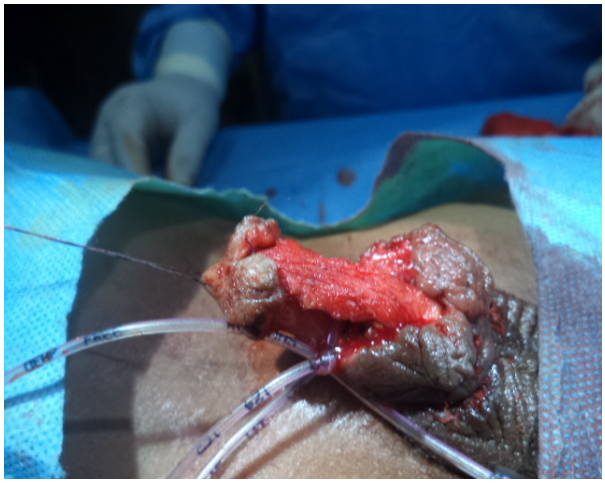

Figure 5. Dartos fascia anchored to the tip of glans penis to create a vascular bed.

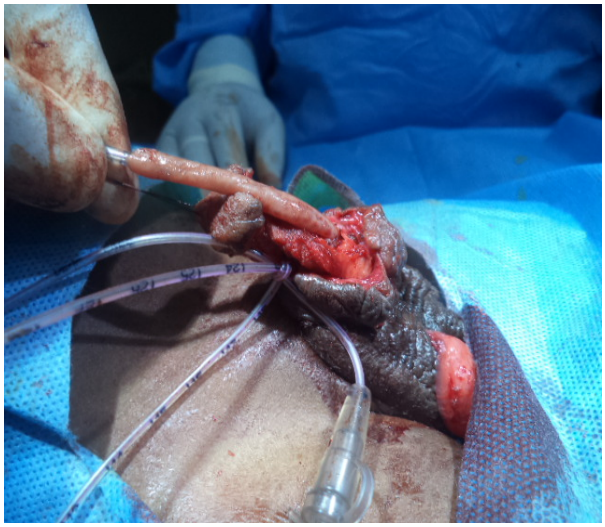

Figure 6. The appendicular mucosal tube anastomosed with proximal urethral opening.

Figure 7. The Dartos is wrapped over the appendicular mucosal tube.

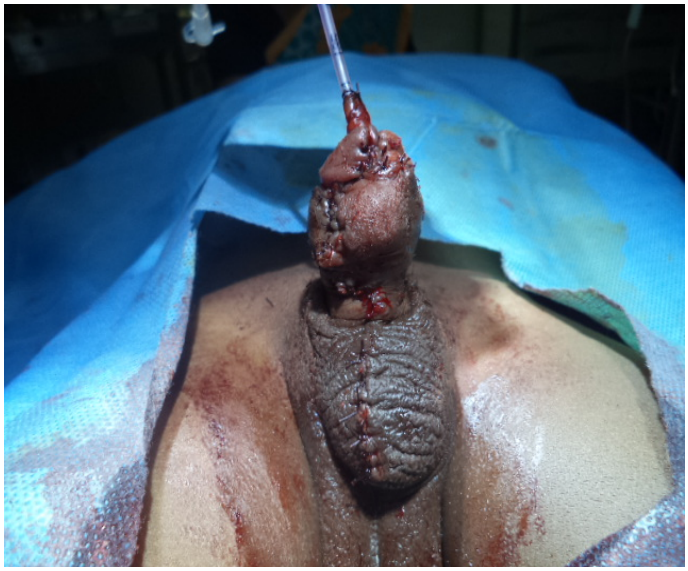

Figure 8. The end result.

3. Results

Patients were followed up weekly for 6 weeks and monthly thereafter. Longest follow up was 3 years and shortest of 1 year. In group A, 3 patients developed fistula and only 1 (4.76%) required repair at the end of 6 weeks. 2 (9.52%) patients developed grade 3 infection and settled with conservative treatment. 2 (9.52%) patients developed hematoma in postoperative period. It was drained successfully by taking a small skin incision and settled with conservative management. No patient developed stricture or stenosis. UFR was normal at the end of 12 weeks with average of 12.85 Ml/sec. The cosmetic result was measured on the scale of excellent, good average and poor. 5 patients (23.8%) had excellent cosmetic result, 10 patients (47.61%) had good result, 4 patients (19.04%) had average result and only 2 patients (9.52%) had poor result. In group B, 11 patients developed fistula and 9 (33.33%) required repaired. 9 (33.33%) patients developed strictures and all of them required multiple urethral dilatation under GA. 7 (25.92%) patients developed meatal stenosis. UFR was badly reduced with average of 5.78 ML/Sec.

4. Discussion

The use of whole appendix with pedicle graft [2] as a replacement of urethra is reported in the medical literature. But it is a complex and time-consuming operation. The appendicular vascular pedicle is short and such operation generally can only replace posterior urethra. Operation with appendix as a free graft [3] with anastomosing its vessels to the local vessels by microvascular technique is also reported. The vascular anastomosis is extremely challenging and prone to complications.

Buccal mucosal urethroplasty [4] and bladder mucosa urethroplasty [5] operations are also described in the literature of hypospadias surgery for hypospadias

with bad quality of urethral plate. The results of these operations are generally poor and are as follows. In a series of 50 cases of proximal hypospadias, treated with bladder mucosal urethroplasty [5] the long-term complications observed were, urethra-cutaneous fistula in nine patients (18%), urethral stricture in 15 patients (30%), meatal stricture in four patients (8%), and prolapse of meatus in seven patients (14%).

Early oral complications of buccal mucosal urethroplasty [6] in a series of 21 patients were as follows. Eighteen (85.7%) patients had mild pain, 13 (61.9%) had mild intraoral swelling, none of the patients had oral bleeding that needed extra procedure. Twelve (57.1%) of the 21 patients needed analgesic agents after the operation while 14 (66.7%) of them have remarked that perineal incision was more painful. Twenty (95.3%) of 21 patients stated that they could go under the same procedure again. None of our patients had speech disorders or intraoral numbness.

The penile complications in a series of buccal mucosa urethroplasty [7] was, wound dehiscence in 2 (1.9%) patients, re-stricture in 11 (10.5%), fistula in 6 (5.7%) patients, meatal stenosis in 3 (2.9%).

The results of my group B patients with 27 cases done by extended Snodgrass operation and Byar's two-stage operation were as follows. 11 patients developed fistula and 9 (33.33%) required repaired. 9 (33.33%) patients developed strictures and all of them required multiple urethral dilatation under GA. 7 (25.92%) patients developed meatal stenosis.UFR at the end of 12 weeks was badly reduced with average of 5.78 ML/Sec.

The results of my Appendicular mucosal tube implant with Dartos wrap operation (group A) were as follows. 3 patients developed fistula and only 1 (4.76%) required repair at the end of 6 weeks. 2 (9.52%) patients developed grade 3 infection and settled with conservative treatment. 2 (9.52%) patients developed hematoma in postoperative period. It was drained successfully by taking a small skin incision and settled with conservative management. No patient developed stricture or stenosis. UFR was normal at the end of 12 weeks with average of 12.85 Ml/sec. The cosmetic result was measured on the scale of excellent, good average and poor. 5 patients (23.8%) had excellent cosmetic result, 10 patients (47.61%) had good result, 4 patients (19.04%) had average result and only 2 patients (9.52%) had poor result. It is obvious that the results of this operation are far superior to group B patients and patients with bladder and buccal mucosa urethroplasty.

4 patients in my series (Group A) had congenital short urethra [8]. It is a rare congenital anomaly of urethra where skin forms the ventral wall of the urethra. The treatment of these cases is very challenging as generally entire urethra is to be sacrificed [8]. The treatment is generally done in a staged manner where first stage is done as Byar's stage one urethroplasty. After 6 months, Byar's second stage urethroplasty can be performed. This condition can also be treated as a primary operation by performing Duckett's Onlay flap or a Duckett's transverse island flap urethroplasty operation [8]. Both these operations are technically

challenging and have high rate of complications. All 4 cases in my series (Group A) were successfully operated as a primary operation by my technique.

According to me, the results of bladder and buccal mucosa urethroplasty are bad because the tubes are placed over Buck's fascia and wrapped by skin over it. The Buck's fascia and penile skin are both avascular tissues. They failed to vascularize the mucosal tube. I suggest that if the Dartos wrap technique is applied for Buccal and bladder mucosa urethroplasty, the results may be substantially superior as the vascular Dartos will vascularize the tubes very well.

Appendicular mucosal tube implant with Dartos wrap operation is superior to the bladder and buccal mucosal urethroplasty for the following reasons. The appendix is a vestigial organ. There are no ethical and moral issues for using it as a replacement of urethra. The bladder and oral mucosa are not vestigial organs. Bladder and buccal urethroplasties have a long suture line and chances of fistula formation are much higher. Contrary to that in my operation, the mucosal integrity of appendicular tube is intact, hence chances of a fistula formation are far less.

The use of appendicular mucosal tube as a replacement of urethra and Dartos wrap over it is reported for the first time in the medical literature. The appendicular mucosal tube being of same patient does not have graft Vs host reaction. The appendicular mucosal tube looks pale like a dead tissue in the bowl before implantation. After implantation and being wrapped by the vascular Dartos fascia, it starts looking pink immediately. The tube receives its early nutrients from the Dartos Fascia by the phenomenon of permeability. The tube acquires blood supply like a split skin graft from the Dartos wrap. The vascular Dartos fascia neovascularizes the tube rapidly. The tube has healthy mucosa, hence does not contract and leads to a stricture. The Dartos which is a tough fibro muscular tissue acts as Corpus Spongiosum which is absent in these patients.

5. Conclusion

The operation is an important addition to the armament of a hypospadiologist. The operation proves to be a much better option compared to the conventional for the said category of patients. We need an operative series with longer follow up and larger patient numbers.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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Urethral Stone: A Rare Cause of Acute Retention of Urine in Men

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Abstract

Urethral stones are a very rare form of urolithiasis, they most often originate from the upper urinary tract or bladder, and are rarely formed primarily in the urethra, it is formed on a urethral anatomical pathology in the majority of cases. The clinical symptomatology is very variable ranging from simple dysuria with penile pain to acute retention of urine. Smaller stones can be expelled spontaneously without intervention, but larger stones or complicated stones or those developed on an underlying urethral anatomical pathology require surgical treatment. The minimally invasive treatment should be the preferred route for the surgical treatment of this disease when feasible. We report the case of a young man with no particular pathological history who presented to the emergency department for acute retention of urine secondary to a primary fossa navicularis calculus, through this case, we discuss the different clinical aspects, etiology, pathogenesis, diagnosis and therapy of urethral stone in men.

Keywords

Urethral Stone, Meatotomy, Acute Urinary Retention, Penis

1. Introduction

Urethral stones are very rare localization of urinary stones, and they are in most cases located at the posterior urethra, most often secondary to the migration of bladder stones or upper urinary tract stones, and rarely formed primarily in the urethra, they are relatively more frequent in childhood and rare in females, its clinical manifestations vary widely, ranging from simple and progressive dysuria to acute retention of urine or even more serious complications [1] [2].

These stones are generally small and not very symptomatic, they can be single or multiple; however, very large stones are sometimes diagnosed, which represents a challenge for therapeutic management [2].

Their treatment remains poorly codified, it is discussed on a case by case basis and depends upon the form, size and location of the stones, as well as the existence or not of an underlying urethral pathology.

We report the case of a patient admitted to the emergency department for acute retention of urine due to impacted urethral calculus in the fossa navicularis, who benefited from a meatotomy with excellent postoperative results with 4-year follow-up.

2. Case Presentation

A 49-year-old man, with no specific medical history, including history of urolithiasis, urethritis or urethral trauma, who had consulted the emergency department for acute retention of urine, penile pain and foreign body sensation in the urethra.

The clinical history of his illness dates back to a year by the sensation of a mobile intraurethral foreign mass, which gradually increased in volume, with dysuria and sensation of incomplete urination which was complicated by an acute retention of urine justifying his consultation in the emergency department.

The physical examination of the penis revealed a hard intraurethral foreign body impacted in the fossa navicularis (**Figure 1**), the external urethra meatus was normal and the rest of the clinical examination was without abnormality.

The radiography of the pelvis centered on the external genitalia objectified the presence of a calculus at the penile urethra of 5 cm of the long axis (**Figure 2**), the radiological exploration of the upper urinary tract showed no other calculus localization. The bladder ultrasound had confirmed the presence of vesical globe with no suspicious bladder lesion or presence of bladder stones, the prostate was of normal size and consistency. The biological examination carried out in emergency did not objectify an anomaly.

After an initial urinary diversion in emergency by a suprapubic catheter, the surgical extraction of this calculus was carried out in a second step after eliminating a urinary tract infection by a small meatotomy because of the size and the distal localization of the calculus, this stone was removed after having blocked it at the distal urethra by applying a tight compress to the level of the root of the penis to prevent any migration into the bladder, the extraction of this stone was carried out by Bengolea forceps while ensuring do not damage the urethral mucosa to avoid any subsequent stenosis or fistula, the meatotomy was then sutured by two separate points of non-absorbable threads and a Foley catheter (18 Fr) was left in place at the end of the intervention (**Figures 3-5**).

The post-operative follow-ups were simple with the removal of the suprapubic catheter at the end of the intervention, and removal of surgical thread and the urethral catheter twelve days after intervention. After removal of the urethral catheter, the patient resumed normal urination without dysuria or pain.

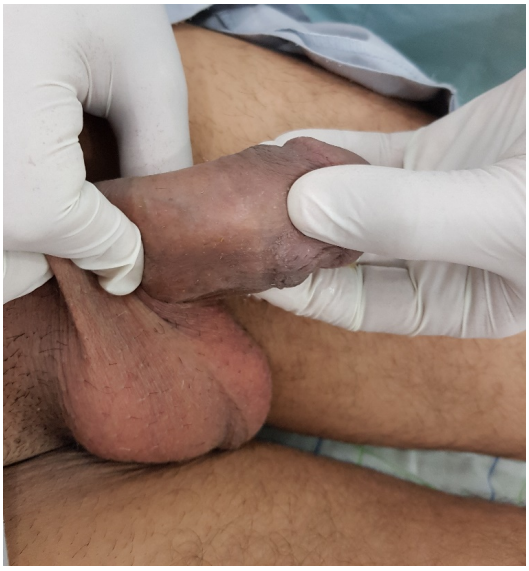

Figure 1. Physical exam showing location of stone.

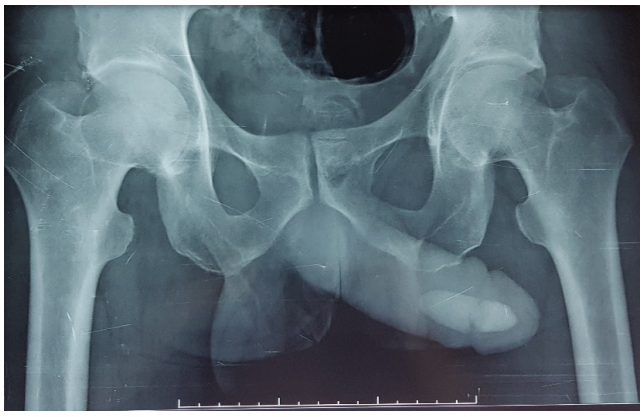

Figure 2. X-ray appearance of a primary fossa navicularis calculus.

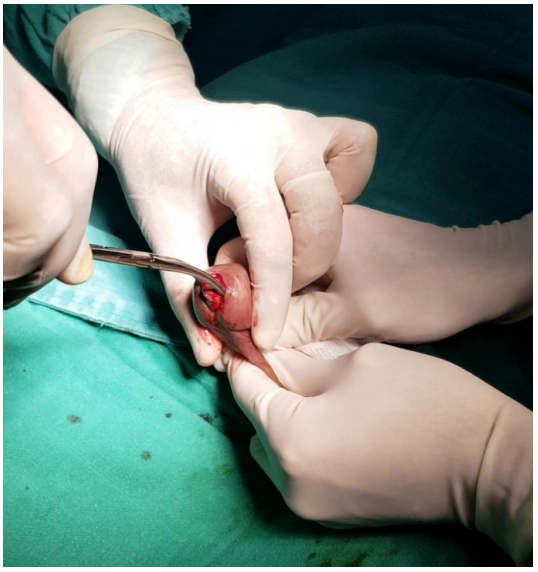

Figure 3. Urethral stone extraction by meatotomy.

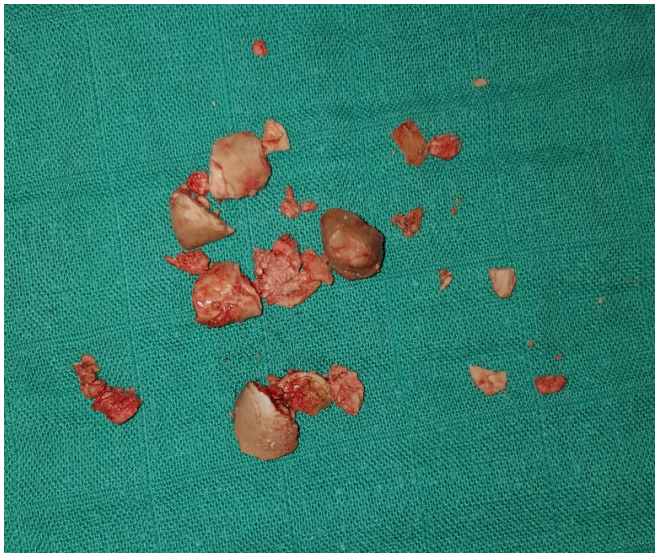

Figure 4. Aspects of extracted urethral stones.

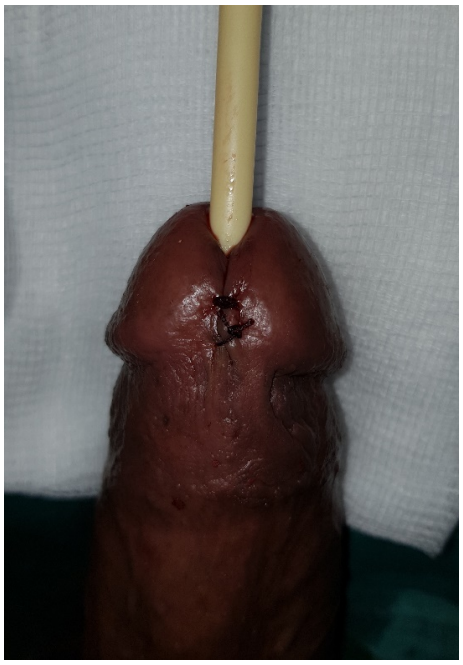

Figure 5. postoperative aspects with urethral catheter.

The results of infrared spectrophotometric analysis of the calculus showed that the stones were composed of ammonium magnesium phosphate.

The evolution with a 4-year follow-up was marked by the resumption of a good urinary stream with normal debimetry, without post-voiding residue and with a normal appearance of the external urethral meatus.

3. Discussion

Urethral calculus is a very rare pathological entity, with an incidence lower than 0.3% of all urinary lithiasis [3]. The frequency of urethral calculi differs accord-

ing to geographic areas, they are diagnosed individually in Western countries and endemically in the Middle East and Asia [4]. They are most often seen in children because of the high frequency of bladder stones, and rarely observed in women due to the anatomic peculiarities of the female urethra [1]. They are most often secondary to a urethral pathology such as a stenosis of the urethra, urethral diverticulum, hypospadias, tumor of the urethra or a meatal stenosis in young adults and exceptionally developed on a normal urethra, it is preferentially localized at the posterior urethra, and very rarely at the anterior urethra, they can be solitary or multiple [1] [4] [5].

The chemical composition of stones also varies according to geographic areas, in developing countries they generally consist of struvite and uric acid, while in industrialized societies calcium oxalate and cystine are dominant [1]. Calcium oxalate and cystine stones originate mainly from the kidneys, while struvite and uric acid stones originate from the bladder [1].

The clinical symptomatology is very variable ranging from simple penile pain with dysuria to complete urinary retention [6], these untreated or ignored stones may lead to serious complications such as the formation of an abscess and necrosis, urinary fistula or even penile gangrene [2] [6].

The diagnosis is most often easy by interrogation which seeks the history of urinary stones disease or emission of calculus, penile pain, and by the clinical examination which made it possible to palpate a mobile hard urethral mass when it is not impacted and located at the anterior urethra [6]. In other cases, the diagnosis can be confirmed by a simple radiography centered on the external genitalia or a penile ultrasound in the case of radiolucent stones which are not rare [7].

The treatment remains poorly codified, they depend on the size, the number, the localization of the calculus as well as the presence or not of an underlying urethral pathology and the existence or not of a complication modifying the surgical approach [1] [7]. Minimally invasive endoscopic approach by urethroscopy is to be preferred for small proximal calculi with the possibility of extracting them or fragments in situ or pushing them back into the bladder and fragmenting them by laser or lithotripsy with success rates close to 80% [1] [6] [7]. For a large, multiple, distal stones and stones encrusted in the urethra, conventional open surgery with a meatotomy or sometimes an urethrotomy with or without urethroplasty is an excellent therapeutic means [2] [7].

Regarding open surgical treatment, Mbouché [6] reported the case of three patients with obstructive and impacted urethral calculi successfully treated by an open urethrolithotomy. Agwu [7] also reported in a series of 39 patients the different surgical treatment methods depending on the location and size of the stones, as well as the existence or not of an underlying urethral pathology, a meatotomy was performed in 11 (27.5%) patients, an open urethrolithotomy in 6 (15%) patients, urethrolithotomy and urethroplasty in 2 (5%) patients, this series highlights the essential place that occupies open surgical treatment in the management of distal and impacted urethral calculi. Our choice of open surgical

procedures as the preferred approach for our patient was thus justified, and supported by the experience and perspective of these authors. Finally, this treatment must be part of a global approach where an etiological treatment must be considered if necessary to prevent recurrence and complications.

Our case highlighted that urethral calculi remains a very rare but not exceptional cause of acute retention of urine in men which remains dominated in the majority of cases by benign prostatic hyperplasia and stenosis of the urethra, our patient consulted immediately for acute retention of urine with impossibility of urethral catheterization because of the size and the distal localization of the calculus, the presence of the calculus of this size impacted at the fossa navicularis poses the problem of its etiology, especially that the exploration of the upper urinary tract did not reveal kidney or ureteral stones, and the lower urinary tract did not reveal a stenosis of the urethra nor bladder or prostatic pathologies or post-voiding residue, the chemical composition of the calculus agrees with its possible renal origin and which has gradually increased in size at the fossa navicularis given its anatomical particularity.

Considering the size and the distal localization of the calculus in the urethra, the open surgery by a simple meatotomy was selected after its discussion with the patient and his agreement, this surgery occupies a very important place particularly in developing countries where access to different endourological techniques is not always possible. Through this case, we hope to draw the attention of practitioners and especially emergency department doctors to this no exceptional etiology, especially in the case of urethral catheterization failure, and that a simple clinical examination and standard imaging will allow the diagnosis to be made in the majority of cases.

4. Conclusion

The urethral stone remains a rare cause of acute retention of urine in men, its presence does not exempt from a complete examination of the entire urinary tract in search of a calculus or underlying urethral pathology. The minimally invasive treatment is to be preferred whenever possible, and open surgery retains a major place in the management of large stones impacted or in distal localization.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Medical Expulsive Therapy (MET) for Large Distal Ureteral Stones: A Prospective Study Comparing Three Drugs

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Abstract

Introduction: One of the most common disorders of the urinary tract is Urolithiasis. Twenty percent of lithiasis are located in the ureter of which 68% are seen in the distal ureter. The concept of medical expulsive therapy (MET) has been developed with enough knowledge of the ureter physiology in order to make easier the spontaneous expulsion of the stone. The aim of this study was to evaluate the efficacy and safety of three different drugs for the treatment of pelvic ureteral stones. **Materiel and Methods:** Between October 2017 and November 2018, 90 adult patients presenting with low or non-obstructive pelvic ureteral stones sized 8 to 10 mm were included. They were prospectively randomized, using computer-based randomization charts, into three equal groups: treatment with ketoprofen 100 mg once daily (Group I), silodosin 8 mg once daily (Group II) and tadalafil 5 mg once daily (Group III). The aim was to compare spontaneous expulsion of stone between those drugs **Results:** The mean expulsion time from the start of MET was 11.5 ± 3.27 days for ketoprofen group, 10.71 ± 3.98 days for silodosin group and 10.57 ± 3.40 days for tadalafil group. But these differences were also not significant (P = 0.79). The use of analgesics (grade II) was higher in groups II and III compared to group I, but without significant difference (23.33% in group I, 33.33% in group II and 40% in group III, p = 0.38). **Discussion:** The overall chance of spontaneous passage is low when the stone diameter is sized more than 7 mm. A wide range of spontaneous passage rates have been reported in the literature, varying from 71% to 98% for distal ureteral stones less than 5 mm and 25% - 53% for stone sized 5 to 10 mm with a mean expulsion time of more than 10 days. **Conclusion:** The three drugs have a low expulsion rate

for 8, 9 and 10 mm pelvic ureteral stones with a higher adverse event rate for the NSAID group.

Keywords

Expulsive Therapy, Ureteral Stones, Drugs

1. Introduction

One of the most common disorders of the urinary tract is Urolithiasis. The world prevalence of stone disease has been estimated at 10% to 15% [1]. Twenty percent of lithiasis are located in the ureter of which 68% are seen in the distal ureter [2]. The most effective treatment modality depends on several factors such as size, location and composition of the stone, severity of obstruction, symptoms, and anatomy of the urinary system.

Proposed treatments for ureteral calculi are observation, medical expulsive therapy, extracorporeal shock wave and lithotripsy (ESWL), retrograde ureterorenoscopy, antegrade percutaneous ureterorenoscopy, and laparoscopic and open ureterolithotomy [3].

The possibility of spontaneous expulsion of the ureteral calculi depends on two factors: the size of the calculi and its anatomic location. According to a meta-analysis, the rate of spontaneous expulsion of the stones smaller than 5 mm is approximately 70% while it is 47% for the stones between 5 and 10 mm [4]. When we consider the anatomic location of the stone, we find that 71% of the distal ureteral calculi and 22% of the proximal ureteral calculi expulse spontaneously [5]. The concept of medical expulsive therapy (MET) has been developed with enough knowledge of the ureter physiology in order to make easier the spontaneous expulsion of the stone.

Several studies have been evaluated as MET, including: corticosteroid, non-steroidal anti-inflammatory drug (NSAID), calcium-channel blocker, α-adrenergic blockers and, more recently, the phosphodiesterase type 5 inhibitors (PDE5i). Moreover, MET may reduce medical costs and avoid unnecessary surgeries and they associated risks and complications. In current practice, MET has been shown to increase the stone passage rates of moderately sized ureteral stones. However, until now, the efficacy of MET in the expulsion of lower ureteral stones (LUS) larger than 7 mm has been evaluated in some studies and the results were discordant. For these reasons, we conducted a prospective randomized study to evaluate the efficacy and safety of three different drugs for the treatment of pelvic ureteral stones sized: 8, 9 and 10 mm.

2. Materiel and Methods

Between October 2017 and November 2018, 90 adult patients (>18 years of age) presenting with low or non-obstructive (grade I - II hydronephrosis) pelvic ure-

teral stones sized 8 to 10 mm were included. They were prospectively randomized, using computer-based randomization charts, into three equal groups: treatment with ketoprofen 100 mg once daily (Group I), silodosin 8 mg once daily (Group II) and tadalafil 5 mg once daily (Group III). An informed and written consent was taken from each patient before enrolment into the study. Ethical clearance was taken from the institutional ethics committee. Stone size (largest transverse diameter) was measured on non-contraste computed tomography scan.

The exclusion criteria were: patients with solitary kidney, history of previous surgery on same ureter, double J stent, deteriorating renal function, fever, grade III or IV hydronephrosis, acute or chronic renal failure, multiple ureteral stones, a location stone other than pelvic ureter, allergy to NSAID, silodosin or tadalafil, concomitant treatment with α-blockers, calcium antagonists, or nitrates, pregnant or lactating mothers, patients who demanded urgent stone removal.

Therapy was given for a maximum of 4 weeks. The primary end point was the expulsion rate. Time to stone expulsion, analgesic use, number of hospital visits for pain, and adverse effects of the drugs were noted. Statistical analyses were done using Fisher's exact test and Chi-square test. P-value < 0.05 was considered to be statistically significant.

3. Results

A total of 90 patients were included in the study and randomized into three equal groups of 30 patients each. All patients completed the study except three who presented acute pyelonephritis during the 4 weeks of evaluation: two patients from group I and one patient from group III (p = 0.463). No statistically significant differences were observed regarding the age, sex, and stone size distribution of patients between both groups (Table 1).

The expulsion rate was 22.22% overall and no significant difference was found for stone clearance rate between both groups (Group I—20%, Group II—23.33%, Group III—23.33%, P = 0.93) (Table 2).

The mean expulsion time from the start of MET was 11.5 ± 3.27 days for ketoprofen group, 10.71 ± 3.98 days for silodosin group and 10.57 ± 3.40 days for tadalafil group. But these differences were also not significant (P = 0.79) (Table 2).

Table 1. Patients and stone characteristics according to groups.

	Group I = Ketoprofen (n = 30)	Group II = Silodosin (n = 30)	Group III = Tadalafil (n = 30)	p-value
Age (mean± SD)	42.27 ± 10.66	43.03 ± 12.42	45.2 ± 12.94	0.772
Gender (male/female)	17/13	20/10	16/14	0.551
Stone size (mm) (mean ± SD)	8.76 ± 1.18	8.93 ± 1.07	9.14 ± 0.82	0.805
Side (right/left)	11/19	14/16	16/14	0.427

Table 2. Results of the three groups.

	Group I = Ketoprofen (n = 30)	Group II = Silodosin (n = 30)	Group III = Tadalafil (n = 30)	p-value
Expulsion rate (%)	20	23.33	23.33	0.93
Mean expulsion time ± SD (days)	11.5 ± 3.27	10.71 ± 3.98	10.57 ± 3.40	0.79
Use of grade II analgesics (%)	23.33	33.33	40	0.551

The use of analgesics (grade II) was higher in groups II and III compared to group I, but without significant difference (23.33% in group I, 33.33% in group II and 40% in group III, p = 0.38) (**Table 2**).

No serious side effects were noted, but a higher rate of adverse events was observed in the NSAID group (26.66% in group I, 13.33% in group II and 10% in group III, p = 0.18). Nausea and epigastralgia were the most common side effects in the ketoprofen group.

4. Discussion

Of all urinary tract stones, 20% are located in the ureter, of which 70% are located in its distal portion [2]. It is estimated that 95% of stones up to 4 mm pass spontaneously within 40 days [4]. A meta-analysis by the AUA guidelines panel showed that ureteral stones sized less than 5 mm will pass up to 98% of cases. The overall chance of spontaneous passage is low when the stone diameter is sized more than 7 mm [6] [7]. A wide range of spontaneous passage rates have been reported in the literature, varying from 71% to 98% for distal ureteral stones less than 5 mm and 25% - 53% for stone sized 5 to 10 mm with a mean expulsion time of more than 10 days [4] [5].

Due to the risk of renal damage, most authors recommend that stone passage should not exceed 4 - 6 weeks [7]. Patients with prolonged partial ureteral obstruction (>4 - 6 weeks), persisting pain or urinary tract infection are less eligible to conservative management. Therefore, observation is allowed only for informed patients without complications (infection, refractory pain, deterioration of renal function).

Many therapies have been tested as METs including NSAID, alpha blockers, calcium channel blockers, corticosteroids, and most recently PDE5i. But only the Alpha blockers are currently recommended for use as MET by the EAU [8].

The a-antagonist contraction inhibition of ureteral smooth muscle represents the pathophysiologic basis for medical expulsive therapy. It results in less severe ureterospasm, which eases the stone passage. The distal ureter has the highest density of a1-adrenergic receptors [9].

Thus, distal ureteral stones should benefit most from medical expulsive therapy. Due to the high probability of spontaneous passage of stones down to 5 mm, MET is less likely to increase the stone-free rate in these cases [10].

Actually, because of conflicting results from recent meta-analyses and large

randomized controlled trials, the efficacy of MET in large stones is unclear.

MET had been widely used until the release of the Spontaneous Urinary Stone Passage Enabled by Drugs (SUSPEND) trial. This large, multicenter, randomized controlled trial by Pickard *et al.* [11] revealed that tamsulosin was not superior to placebo in decreasing intervention rates to clear ureteral stone. The trial used the need for urologic intervention as the main outcome measure. Since that study, medical expulsive therapy has been compromised.

New multicenter, randomized, double blind, placebo-controlled trials were performed to elucidate the discrepancies between some meta-analyses of mostly small trials [12] [13] and a high-quality randomized controlled trial. A randomized controlled trial by Furyk *et al.* [14] including 403 patients, found no benefits of medical expulsive therapy with tamsulosin for patients with distal ureteral stones. However, the subgroup of patients with stones of 5 to 10 mm had an increased rate of expulsion.

Also, Meltzer *et al.* [15] in their randomized study including 512 patients with ureteral stones between 1 and 8 mm, didn't find a difference in stone passage rates between patients treated with tamsulosin compared with placebo (52% versus 49%).

More recent, large prospective randomized trial [16] had compared tamsulosin with placebo for 4 to 7 mm distal ureteral stones in greater in a population of 3200 patients. The results were similar to those of the Meltzer and al trial: there is no difference for stones 5 mm or less and an increase in stone passage in the group with 5.1- to 7-mm stones (87% versus 75%), with a small overall benefit when all sizes were considered (4 to 7 mm; 86% versus 79%).

In our study, although the number of patients was poor, we compared the three most used MET to treat large distal ureteral stones (8, 9 and 10 mm). The expulsion rate was globally low (22.22%) and no significant difference was found for stone clearance rate between both groups. Also, three of our patients (~4%) developed acute pyelonephritis during the four weeks of treatment.

Therefore, we decided to discontinue this study and to treat in a faster way using endoscopic procedure patients presenting this kind of stones.

5. Conclusion

The three drugs tried (tamsulosin, silodosin and tadalafil) have a low expulsion rate for 8, 9 and 10 mm pelvic ureteral stones with a higher adverse event rate for the NSAID group. More invasive intervention should be performed as early as possible for this type of calculi.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Cancer on Testicle Not Descended: Clinical and Therapeutic Aspects of 7 Cases

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Abstract

Objective: To study the clinics and therapeutics of testicular cancer not descended in Senegal. **Patients and Methods:** This is a retrospective study over a period of 15 years between January 1997 and January 2012. It focused on 07 patients. **Results:** The average hospital incidence was less than one case per year. The average age of patients was 30.7 years with a median of 28 (range, 21 years and 38 years). The reasons for consultation were dominated by the existence of an abdominal or pelvic mass associated with an emptiness of the stock market. Orchiectomy was the main therapeutic gesture. It was performed by transperitoneal route. CT-TAP was performed in all cases and revealed a tumor independent of the liver of the spleen or kidneys, developed on an undescended testicle. Four cases of lumbar-aortic lymph node metastasis were noted. Histologically, we noted four cases of embryonic carcinoma and three cases of seminoma. Four patients died within six months postoperatively. Two in an intestinal obstruction chart, one in a peritoneal carcinomatosis chart and one patient in a pulmonary embolism chart. Two had a 4-year survival without recurrence. One patient had a 7-year survival without recurrence. At the time of the counting, these three patients were lost sight off. **Conclusion:** Intra-abdominal or pelvic development of testicular cancer is rare. It constitutes a major subsequent risk of the undescended testicle.

Keywords

Cancer, Undescended Testicle, Embryonic Carcinoma, Seminoma

1. Introduction

Cancers of the testis are rare; they represent the first tumor in humans between 20 and 35 years. Their incidence is increasing, it is higher in the industrialized

countries, very low in Africa and Asia [1].

Worldwide, the incidence varies between 0.2 and 9.2 cases/100,000/year. The incidence has been increasing sharply over the past 25 years [2]. It is clearly above 0.1% in subjects with cryptorchid testicles. Up to 95% of testicular tumors originate in germ cells, the rest being mainly represented by lymphomas and certain tumors of the gonadal stroma [3].

The undescended testicle is correlated with a significant rate of degeneration. Intra-abdominal or pelvic development of testicular cancer is rare. It constitutes a major subsequent risk of the undescended testicle. The diagnosis and early lowering of undescended testes in the bursa remain the only way to fight this form of testicular cancer. These forms of testicular cancer are diagnosed at very advanced stages, making most of them inaccessible to any curative therapy [4].

Generally, in developing countries, cancers are a public health problem because of the absence of a national care policy.

The purpose of our work was to study the clinical and therapeutic aspects of undescended testicular cancer in Senegal.

2. Patient and Methods

This is a retrospective study over a period of 15 years between January 1, 1997 and December 31, 2012. We targeted all cases of testicular cancer diagnosed and managed in the department during the study period and from which we have extracted those from undescended testicular cancer.

We had included in our study, patients who were hospitalized for intra-abdominal or intra-pelvic testicular cancer, confirmed on pathological examination of the operating room.

Exclusion criteria were all patients who were hospitalized for an intra-abdominal or intra-pelvic testicular tumor without histological confirmation or for an intra-scrotal tumor.

The parameters studied were: age at the time of diagnosis, circumstances of discovery, physical examination data, results of complementary examinations (tumor markers, abdominal-pelvic ultrasound and thoraco-abdominopelvic computed tomography), treatment and the future of patients (healing, death, recurrence, progression).

The limits of this study relate to the difficulty of follow-up due to the fact that most of our patients came from the interior of the country, hence their inaccessibility for regular follow-up.

To this must be added the absence of additional treatment (chemotherapy, radiotherapy) which would have made it possible to better assess the outcome of the treatment.

3. Results

We collected 07 files of patients supported for undescended testicular cancer.

The average age of the patients was 30.7 years with a median of 28 years

Table 1. Distribution of patients by reason of consultation.

Reasons for consultation	Number of cases
Abdominal mass	5
Pelvic mass	2
Abdominal pain	3
Alteration of the general condition	4

(range 21 to 38 years).

Hospital incidence was less than one case every two years.

The reasons for consultation were dominated by the existence of an abdominal or pelvic mass (Table 1) associated with an empty purse.

A case of invasion of the peritoneum with presence of nodules perceptible subcutaneous was noted.

Tumor markers were assayed in five patients. The human gonadotropic hormone level assay performed in 4 patients was elevated in all cases. Alpha fetoprotein was elevated in 1 out of 4 patients. LDH was dosed in 1 case and was elevated 1.5 times normal.

An assay of carcinoembryonic antigen was performed in three patients. The rate was normal in all cases.

CT-TAP was performed in all cases and revealed a tumor independent of the liver, spleen or kidneys, developed on an undescended testicle (Figure 1 and Figure 2). Four cases of lumbar-aortic lymph node metastasis were noted.

Orchiectomy was the main therapeutic gesture. It was performed by transperitoneal route.

Histologically, we noted four cases of embryonic carcinoma and three cases of seminoma. No additional treatment (chemotherapy or radiotherapy) or ganglion dissection was performed.

The average patient follow-up was 27.7 months (range: 1 month and 84 months).

Four patients died within six months postoperatively. Two in an intestinal obstruction chart (Patients 1 and 3), one in a peritoneal carcinomatosis chart (Patient 2) and one patient in a pulmonary embolism chart (Patient 6).

Two patients had a 4-year survival without recurrence (Patients 4 and 5). One patient had a 7-year survival without recurrence (Patient 7). Table 2 summarizes the age, clinical stage, treatment and survival of patients.

4. Discussion

The undescended testicle is the most important risk factor for testicular cancer. Its intra-abdominal location is rare and poses a diagnostic problem. The absence of symptoms in case of undescended testis is responsible for its trivialization, while the consequences will be felt 15 to 20 years later.

In our study hospital incidence was less than one case every 2 years. This in

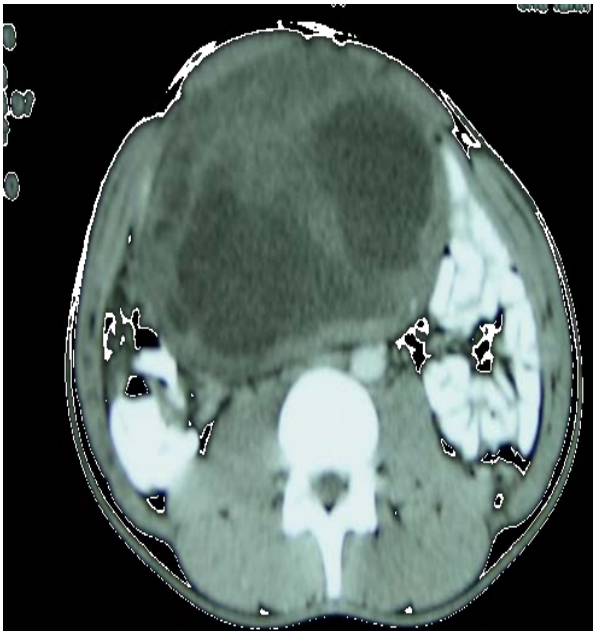

Figure 1. Testicular tumor of testicular origin with areas of necrosis.

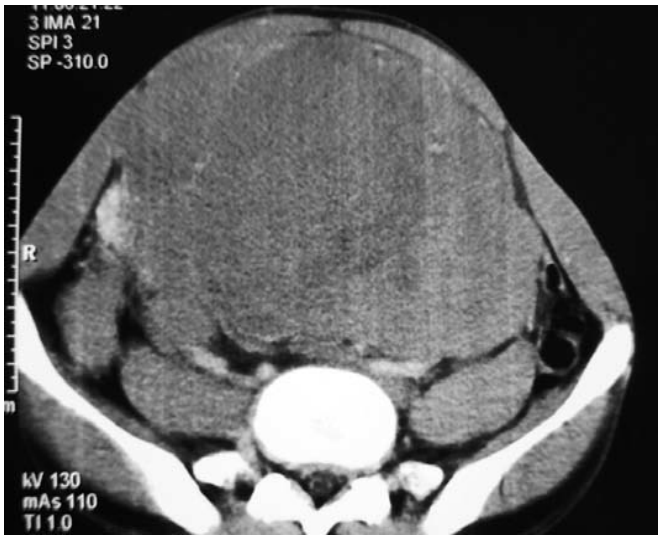

Figure 2. Pelvic tumor of testicular origin.

Table 2. Summary of data.

Patients	Age	Location	Histology	Stages	Complementary treatment	Patient monitoring
1	**23**	Pelvic	Embryonic carcinoma	N2M1bS1	No	Deceased 5 months after surgery
2	**38**	Abdominal	Embryonic carcinoma	N2M1bS1	No	Décédé un mois après chirurgie
3	**30**	Abdominal	Embryonic carcinoma	N2M1bS1	No	Deceased 6 months after surgery
4	**32**	Pelvic	Embryonic carcinoma	N0M0SX	No	Was alive 4 years after surgery
5	**34**	Abdominal	Anaplastic seminoma	N0M0Sx	No	Was alive 4 years after surgery
6	**37**	Abdominal	Pure seminoma	N3M1aS1	No	Deceased 2 months after surgery
7	**21**	Abdominal	Pure seminoma	N0M0Sx	No	Was alive 7 years after surgery

cidence is lower than that of the overall incidence of testicular cancer in West Africa. Ouattara *et al.* [4] in Cotonou, reported three cases of testicular cancer in three years with a frequency of 1.9% of all urologic cancers. In Burkina Faso, Goumbri *et al.* [5], over a 20-year study period, found 10 cases of testicular cancer and estimated the incidence at 0.25% of all cancers.

An increase in the incidence of testicular cancer has been observed in most countries of the world over the last 50 years with a greater increase in Europe [6] [7].

Testicular cancer is the most common cancer in men between the ages of 15 and 35 [8]. It is the second leading cause of cancer death in people under 50 years of age after leukemia [9].

Our results confirm the predominance of testicular tumors in young adults and their rarity at extreme ages. These results are consistent with those of the Sow *et al.* [10] from Goïta [11] and Niang [12] where the most affected age group was 30 - 40 years old.

The vacuity of the bursa associated with an abdominal or pelvic mass and the deterioration of the general state made it possible to suspect the diagnosis in the seven patients. The right testicle was the most affected in our series (Five times out of seven). The predominance is on the left for Valla *et al.* [13] as well as for Goïta [11].

For Niang [12] as well as in our series, the digestive symptomatology was in the foreground and misplaced the diagnosis. It is in this context that some of our patients stayed in internal medicine before being transferred to urology.

The undescended testicle is the major recognized risk factor for testicular cancer [8]. Any man who has had an undescended testicle at birth is four times more likely to develop a testicular tumor [14] [15].

The intra-abdominal location of the testis is correlated with a significant rate of degeneration and is a diagnostic problem. Hence the need for systematic palpation of the scrotum in front of any intra-abdominal mass in men.

In our series, tumor markers were measured in five (5) of our patients before the start of treatment. These markers were human gonadotropic hormone, α fetoprotein, L.D.H (lactate dehydrogenase) and A.C.E (Carcino-Embryonic Antigen).

The human gonadotropic hormone assay was high in four (4) of our patients, in whom the histology concluded embryonic carcinoma (3 cases) and seminoma (1 case). In seminomatous tumors, the increase in this rate was moderate (<100 IU). Human gonadotropic hormone is secreted mainly by embryonic choriocarcinomas and carcinomas and by 10% to 15% of seminomas [16].

Alpha fetoprotein was elevated in one patient with embryonic carcinoma and was normal in three others. According to the literature an elevation of alpha fetoprotein reflects the presence of a non-seminomatous germ cell tumor. A high level of α fetoprotein with seminoma diagnosis should encourage an anatomic-pathological study of the histological slide, in the absence of associated hepatic pathology [17].

L.D.H: It was dosed in one patient and was elevated (patient 6). It is increased in 50% of patients with seminoma at the time of diagnosis. It is not specific and is insensitive; but as for the other two tumor markers, it has a prognostic significance [16].

ACE: It was dosed in three (3) patients and was in the standards. The intra-abdominal development of tumors has been the origin of this marker which has no interest in the diagnosis and management of testicular tumors.

The abdominal and pelvic ultrasound was not able to specify in 4 cases out of 7, the organ at the expense of which the tumor has developed.

All patients had CT. She was more sensitive than ultrasound in the detection of intra-abdominal testicular tumors. It is the reference examination because it makes it possible to ask the diagnosis and to appreciate the tumor extension.

Abdominopelvic CT is routinely recommended in the initial assessment and follow-up of germ cell tumors [2].

Thoracic CT is the most sensitive examination for detecting lung metastases or mediastinal lymphadenopathy. It is systematically recommended in case of non-seminomatous germinal tumours (NGT) and is part of the initial balance sheet. In 10% of the NGT, small subpleural nodules are present and are invisible on a standard radiograph [2].

Embryonic carcinomas were more common. However, several studies have shown the predominance of seminomatous tumors in cases of undescended testicular cancer [18] [19].

Coupland [18] concluded that the risk of association between seminoma and undescended testis was greater than that of other tumors (odds ratio 5.3 vs. 3.0) and this association would be larger (odds ratio 11.9 vs. 5, 1) when the patient's age was greater than or equal to 32 years.

The main treatment in our study was surgery (orchiectomy). It was performed by laparotomy with tumor resection. No lymph node dissection or complementary treatment was administered in our series. It is the same in the 8 patients of Goïta [11] in Mali where orchiectomy was the only treatment.

The treatment of testicular cancers depends on the histological nature and stage of the tumor. In our study, we counted 4 patients who had a non-seminomatous tumor and 3 patients had a seminomatous tumor at different stages.

The patients (1; 2; 3; 4) had embryonic carcinoma on undescended testicle. They were ranked N2M1bS1 for the first three. A chemotherapy with 4 cycles every 21 days according to the recommendations of the AFU could have been carried out [17].

In our countries, the scarcity or even the exorbitant costs of chemotherapy products is a difficulty in the effective management of patients who have testicular cancer.

Three patients (5; 6; 7) had a seminomatous tumor classified N0M0SX, N0M0SX, N3M1aSX, could have had a para-aortic prophylactic radiotherapy at the dose of 20 to 24 Gy which remains the recommended standard [20] or chemotherapy (3 cures of BEP or 4 cures of EP according to the recommendations of the AFU) for

the patient who had the metastasized tumor.

The practice of radiotherapy in Senegal is based on obsolete means using cobalt. We noted the absence of conformal radiation therapy with intensity modulation which has the advantage of being more effective with fewer side effects. Sperm preservation has not been performed in our patients. To try to preserve the reproductive potential of cancer patients [21]; this preservation before a chemo or radiotherapeutic treatment has been proposed for more than 20 years. It is suggested systematically before orchiectomy for at least one sample.

In our study, no action was taken on the possibility of future procreation of patients. This would be related to the lack of structure for the management of these patients in the field of reproductive health.

In our series, the average follow-up was 27.7 months. As for the Goïta study [11] from the third month after the surgical treatment, none of the patients was seen again.

The specific mortality of testicular cancer in our study was high. This rate is comparable to that of Ouattara *et al.* [4] in Benin, who reported a mortality rate of 33.3%. This rate remains very high compared to that reported by Western series such as those of Miladi *et al.* [22] involving 60 patients with low testicular germ cell death rates (0% for HCWs and 4% for NERs at 7 years).

5. Conclusion

The undescended testicle is the most important risk factor for testicular cancer. Its intra-abdominal location is rare and poses a diagnostic problem. The absence of symptoms in the case of an undescended testicle is responsible for its trivialization, while the consequences will be felt 15 to 20 years later. In our countries, the scarcity or even exorbitant cost of chemotherapy products constitutes a difficulty in the effective management of patients with testicular cancer.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Calyceal Diverticula and Megacalycosis Urographic Diagnosis Complications and Treatment

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Abstract

Background: Calyceal diverticulae and megacalycosis are rare congenital anomalies. The majorities are asymptomatic but they can present with complications. **Objective:** The objective of this study is to describe the clinical presentations, complications, urographic diagnosis of calyceal diverticulae, megacalycosis, and their treatment. **Methods:** A descriptive study carried out over 8 years period from March 2012 to December 2019. In three big hospital of Aden province, we collect 15 patients aged from seven to 41 years (mean 13.5 years), our patients were 9 female (60%) and 6 male (40%). They diagnosed incidentally with calyceal diverticulae and megacalycosis by contrasted urography, describing the clinical manifestations, localization, complications, and type of treatment. **Results:** Sixty percent of patients with calyceal diverticulae and megacalycosis were women and (40%) were men. Clinical manifestations including, dull aching flank and abdominal pain in (40%), acute renal colic (20%), recurrent urinary tract infection (33%), and abdominal pain with a fever of unknown origin in (7%). Calyceal diverticula and megacalycosis were bilateral in (53%) and unilateral in (47%). In the right kidney were (57%), and in the left kidney (43%). In the upper pole of the kidney were (53.3%), middle pole (33.3%), and lower pole (13.3%). Complications occurred in (47%) of patients. They including, urinary stones in (71.4%), hypertension (14.3%), and delayed renal excretion (14.3%). Conservative treatment carried out in (73%) and surgically intervened in (27%). **Conclusions:** Calyceal diverticula and megacalycosis are rare anomalies. Dull aching flank pain and recurrent urinary tract infections are the most frequent clinical presentations. The most common complications are urinary stones. Conservative treatment is a common type of treatment.

Keywords

Calyceal Diverticulae and Megacalycosis, Diagnosis, Treatment

1. Introduction

Calyceal diverticula and megacalycosis are rare congenital anomalies. Calyceal diverticulae present as a cystic cavity of the renal calyceal system which communicates with it through a narrow fornical cannel, while megacalycosis is unilateral dilatation of the renal calyces in the presence of normal undilated renal pelvis and ureter. It results from abnormal budding of the ureteric bud with subsequent lack of parenchymal induction and resultant cystic cavity formation. Megacalycosis is a rare congenital malformation, characterized by homogenous dilatation of the renal calyces with non-obstructive and non-progressive evolution [1] [2]. Calyceal diverticulae were seen in 0.05% of patients out of 12,000 of examined excretory urography. In the majority of cases are asymptomatic, and incidentally diagnosed during imaging study but clinically can result in a variety of complications [3] [4]. Upright or right lateral decubitus plain abdominal radiography shows the half-moon shape of milky calcium appearance which is the pathogenic feature [5]. Ultrasound is the first investigation but is inconclusive because it resembles a simple cyst [6] [7]. The diagnosis is made by intravenous urography and computerized tomographic urography in complex cysts [8]. Stones in the pelvicalyceal diverticula occurred in up to 50% of patients and recurrent urinary tract infections in 25% of patients [9]. Historically open surgical procedures include excision, marsupialization, diverticulectomy or partial nephrectomy. Extracorporeal Shock wave Lithotripsy (SWL) is considered as the first line for treatment [10]. Percutaneous extraction and diverticulum fulguration with canal dilatation provide a good immediate success rate, and low morbidity, it is now accepted as the standard treatment [11]. The diagnosis of calyceal diverticula is a challenge, especially in children. They can result in various complications and diagnostic difficulties.

The objective of this study is to describe the diagnosis of calyceal diverticulae and megacalycosis and their treatment.

2. Methods

A descriptive study carried out over 8 years period from March 2012 to December 2019. In three big hospitals (Al-gamoriah teaching hospital, Al-Naquib and Almansorah Hospital) in Aden province, we collected 15 patients aged from seven to 41 years (mean 13.5 years), our patients were 9 female (60%) and 6 male (40%), Sixty percent of patients were children (60%) and (40%) were adults. They presented with nonspecific clinical manifestations, and incidentally diagnosed with calyceal diverticulae and megacalycosi by contrasted excretory urography.

Describing the clinical manifestations and localization whether unilateral or

bilateral, poles localization whether in the upper, middle, or lower pole of kidneys, the radiologic findings, complications, and type of treatment whether medical or surgical interventions. The data collection was retrieved from medical outpatients' registries and Hospitals' retained Medical documents.

Inclusion: We included those patients who attended these three Hospitals in Aden Governorate and diagnosed with calyceal diverticulae or megacalycosis.

Exclusion: The patients who had the acquired types, and those diagnosed as simple or complex renal cysts were excluded from the study.

Statistic: Statistics method carried out with frequencies and percentages, and confection of tables carried out manually using a summary measure. Data was processing and analyzed using Social Science Statistics software.

Ethical Approval and Consent for patients were not applicable, and patients' identifiers and organ exposure for patients are not involved.

3. Results

Of the total 15 patients included in our study nine patients (60%) with calyceal diverticulae and megacalycosis were women's and six patients (40%) were men. The clinical manifestations (Table 1) including dull flank and abdominal pain in six patients (40%), acute renal colic three (20%), recurrent urinary tract infection five (33%), and diffuse abdominal pain associated with fever of unknown origin one patient (7%). Calyceal diverticulae and megacalycosis were diagnosed by contrasted excretory urography. They were bilateral (Figure 1) in eight (53%) and unilateral (Figure 2) in seven (47%). Unilaterally localized in the right kidney four (57%), and in the left kidney three (43%). Localized in the upper pole of the kidney eight (53.3%), middle pole four (33.3%) and in lower pole two patients (13.3%) as shown in Table 2. Megacalycosis are localized in the central portion of the kidney, characterized by non-obstructive dilatation of pelvis and conserved renal function (Figure 3), and one patient (7%) of them presented with an associated right renal agenesis (Figure 4). Complications (Table 3) occurred in seven patients (47%) including, urinary stones in five patients (71.4%). Anemia and hypertension in one patient (14.3%), and delayed renal excretion in another one (14.3%), Bilateral multiple small renal stones in the lower pole (Figure 5) found in three patients (60%) and unilateral in two (40%) of patients with urinary stones. Conservative treatment carried out in 11 patients (73%) and surgically intervened four (27%). They including (Table 3) excision of the diverticulum

Table 1. Calyceal diverticula and megacalycosis regarding to the clinical presentations.

Clinical presentations	NO	%
Dull aching flank pain	6	40
Acute renal colic	3	20
Recurrent UTI	5	33
Abdominal pain with Fever of unknown origin	1	7%
Total	15	100

Table 2. Calyceal diverticula and megacalycosis regarding to the site and kidney poles localization.

Unilateral	7	47	Upper pole	8	53.3
Right	4	57	Middle pole	5	33.3
Left	3	43	Lower pole	2	13.3
Bilateral	8	53	Total	15	100
Total	15	100			

Table 3. Congenital calyceal diverticulae and megacalycosis according to complications and surgical procedures.

Complications	No	%	Surgical procedures	No	%
Urinary stones	5	71.4	ESWL	2	50
Hypertension	1	14.3	Excision	1	25
Delay of excretion	1	14.3	Diverticulutomy	1	25
Total	7	100	Total	4	100

ESWL = Extracorporeal shock wave lithotripsy.

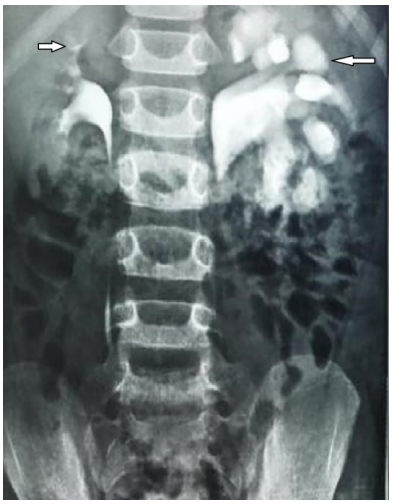

Figure 1. Intravenous urography (IVU) showing bilateral calyceal diverticula, more dilatation in the left side (bilateral arrows).

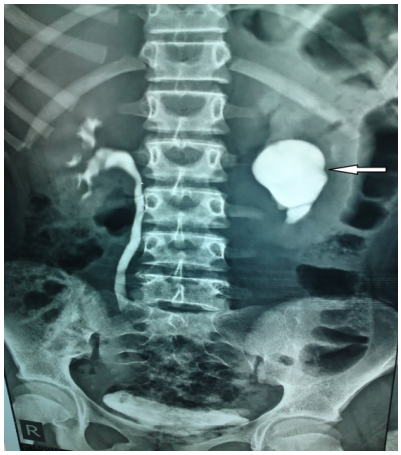

Figure 2. IVU Shows calyceal diverticula in the left pelvicalyceal system (arrow).

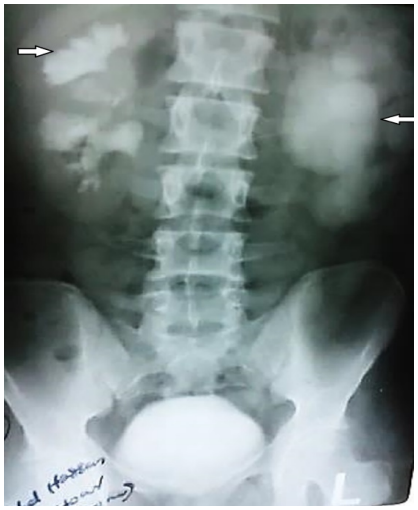

Figure 3. IVU showing bilateral megacalycosis, more calyceal dilatation in the left pelvicalyceal system (bilateral arrows).

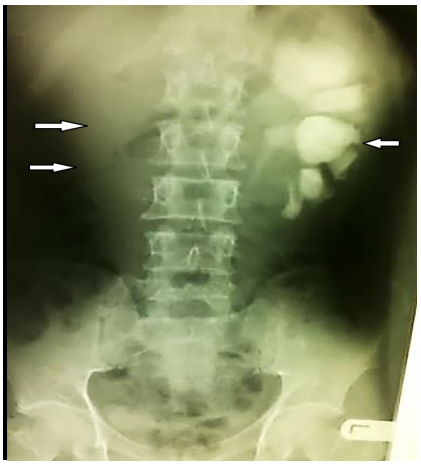

Figure 4. IVU showing left megalocalycosis (Single arrow) associated with right renal agenesis (Two arrows).

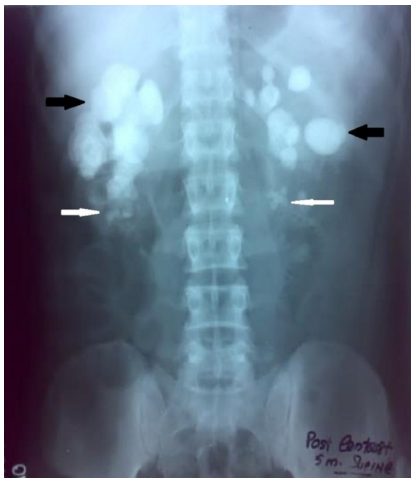

Figure 5. IVU showing bilateral megacalycosis (black arrows) with very small stones in both lower poles of kidneys (white arrows).

and marsupialization in one patient (25%), diverticulectomy in another one (25%), and two patients (50%) carried out extracorporeal shock wave lithotripsy (ESWL). Stones in the lower poles of kidneys in three patients were very small and treated medically. All patients were under continued follow up at our outpatient clinic and the outcome was excellent.

4. Discussion

Calyceal diverticula and megacalycosis are rare congenital anomalies; both represent dilatation of the collecting system but differ in their pathological and radiological features. Two types of calyceal diverticula are recognized. Type I: Calyceal diverticula is the most common, is related to a minor calyx [12]. Type II: It is an extremely rare renal anomaly; it communicates with the renal pelvis or major calyx. It is larger, and symptomatic in the majority of patients. Characterized by non-obstructive dilatation of calyces, the renal pelvis is not dilated, and the ureteropelvic junction is normal and conserved renal function [13]. Calyceal diverticula in the majority are asymptomatic. One-third to one-half of patients present with flank pain, urinary tract infection, and/or hematuria, and stones formation [14]. The calyceal diverticulae were bilateral in 53% and unilateral in 47% of patients, Calyceal diverticulae were commonly unilateral and less frequent bilaterally described by Jain *et al.* 2004 [15]. It is two times more often found in the right kidney than in the left one, and solitary calyceal diverticulae occurs in 90% of patients described by Surendrababu [16]. They should differentiated simple renal cysts, renal cortical abscess, papillary necrosis, and early stage of adult dominant polycystic kidney disease [17]. Clinical presentations and urographic findings are consistent with reported [18] by Stunnell *et al.* 2010. Megacalycosis is a rare congenital anomaly, mostly asymptomatic and discovered incidentally or by their complications. The renal pelvis, infundibulum, and ureter are not dilated [19]. Calyces in calyceal diverticulae present as a semilunar configuration rather than the triangular or conical form. Kaviani A. *et al.* 2010 [20]. Reported a huge extraordinary calyceal diverticulum. In this study stones size range from 3 mm to 18 mm. Touzani *et al.* 2015 [21] reported a giant stone of 28 mm complicating calyceal diverticula, localized in the upper pole of the kidney, treated by flexible uretero-renoscopy. In this study, the majority of patients were treated conservatively in 73% of patients.

Estrada *et al.* 2009 described a series of 22 children treated surgically in 43% of patients. Stones in this study presented in 20% of patients with calyceal diverticulae less than reported by Estrada *et al.* 2009 [22]. Waingankar *et al.* 2014 [23] in his review for a total of 497 patients with calyceal diverticulae determined that they were more common in women in 63% versus 37%. In men, located in the upper pole of the kidney in 48.9%, middle pole 29.7% and lower pole in 21.4%, Presented in the right kidney in 49% and left kidney in 51%, and stones in 96%. Most patients were treated by conservative treatment consistent with this study. Surgery carried out in patients with chronic pain, recurrent or persis-

tent urinary tract infections, obstructive stones, and renal damage. Surgical treatment is consistent with reported by Nerli R. B. *et al.* 2014 [24].

Different treatment modalities like percutaneous nephrolitottomy and flexible uretero-renoscopy. Urolithiasis was described by Baso *et al.* 2015 [25]. Recent study by Laura McGarry concludes that Laparoscopic ablation is the optimal treatment and has significantly higher success rates than the ureteroscopic approach [26]. Carcinoma in a calyceal diverticulum is largely uncommon but some cases were reported [27] this goes with our study no malignancy reported.

5. Conclusion

Calyceal diverticulae are rare congenital anomalies and megacalycosis is an extremely rare anomaly. The most common clinical manifestation is abdominal and flank pain in 60% followed by urinary tract infection. Urinary stones were the most common complications, 73% of patients treated conservatively and only 27 of patients need intervention.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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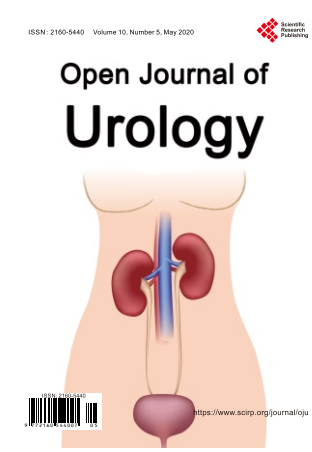

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