

Challenges in Management of Primary Urethral Carcinoma: Case Series and Literature Review

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Received: 24 July 2021

Accepted: 04 Aug 2021

Published: 09 Aug 2021

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Citation:

Mbwambo OJ. et al., Challenges in Management of Primary Urethral Carcinoma: Case Series and Literature Review. Clin Surg. 2021; 6(2): 1-5

Keywords:

Urethral carcinoma; Tanzania

1. Abstract

Primary urethral carcinoma is a rare disease globally and is much less commonly in African (< 20%). The knowledge of proper management for urethral cancer is limited due to lower prevalence of the disease. Furthermore, the consequences of the management of urethral carcinoma remains a challenge to both clinician and patients as it may result in removal of sexual organs and ending in long term catheters. Here we present case series of both 1 male and 2 females with challenges in the management from a tertiary hospital in Northern Tanzania.

2. Introduction

Urethral carcinoma is a rare disease globally, with majority (88%) of cases seen in whites and only 8% in African American [1, 2]. The disease is more prevalent in the 5th decade of life, with risk factors in males been chronic inflammation due to Sexually Transmitted Diseases (STD), urethritis, urethral stricture disease and human papilloma virus type [16, 3-5]. On the other end, urethral leukoplakia, chronic irritation, caruncles, polyps, parturition, human papillomavirus infection or other viral infections are some of the risk factors in female [6, 7].

The clinical presentation varies among patients and therefore a high index of clinical suspicion is required to diagnose urethral carcinoma. Symptoms may include hematuria, dysuria, urinary retention, urinary incontinence, weak stream, straining, perineal or

penile mass [8].

The commonest histological types in males are urothelial carcinoma (77.6%), squamous cell carcinoma (11.9%) and adenocarcinoma while in female's commonest histological types are squamous cell carcinoma (60%), followed by transitional cell carcinoma (20%), adenocarcinoma (10%), undifferentiated tumors (8%) and melanoma (2%) [9, 10].

Like any other cancers, the management of urethral cancer depends on the stage. Anatomical location of the disease also plays important role in management. Generally female sex carries a poor prognosis compared to males.

We report a case series of primary urethral cancer in both female and male and challenges associated with the management. The urethral cancer in a male patient was treated by radical penectomy followed by adjuvant radiotherapy. The two female cases were advanced cases and not amenable to surgery.

3. Case Series

3.1. Case Number 1

An 80 years old male presented with Lower Urinary Tract Symptoms (LUTS) for 1 year. During the course of this illness, he underwent direct vision urethrotomy for the diagnosis of urethral stricture at a peripheral hospital prior to attending at Kilimanjaro Christian Medical Centre (KCMC). However, the symptoms recurred few days after the surgery.

General examination and systemic examination was unremarkable on admission. Blood tests on admission were unremarkable. Urinalysis (U/A) showed > 50 RBC/Hpf and > 50 wbc/Hpf. Urine culture grew *Escheria coli* with sensitivity to amikacin and cefotaxime while demonstrating resistance to gentamicin, ciprofloxacin and amoxicillin-clavulanic acid. On ultrasound, kidneys were normal, bladder wall was irregular with outpouching suggesting diverticulum and there was insignificant residual urine volume (13/135cc). Retrograde urethrogram revealed a penobulbar urethral stricture of approx. 2.5 cm (Figure 1 and 2). After investigations, diagnosis of urethral stricture was reached and elective suprapubic catheterization (SPC) was done to be followed by either anastomotic or substitutional urethroplasty thereafter depending on length of stricture intraoperatively.



Figure 1: Retrograde urethrogram showing a narrowing (A) from mid to distal bulbous urethra with contrast extravasation. Basing



Figure 2: Antegrade urethrogram showing incomplete urethral stricture at mid bulbous

Two weeks after SPC the patient was scheduled for surgery and through midline longitudinal incision along median raphe on the perineum stricture site was identified and opened longitudinally where an incidental cauliflower like lesion was found on the stricture site. Excision of the stricture site containing cauliflower lesion was performed followed and end-to-end anastomosis of the urethral was done. Postoperative recovery was uneventful and the catheter was removed after 22 days. The patient was lost to follow up and re-appeared after 10 months.

The histology of the previously submitted urethral tissue (stricture site) showed dysplastic-thickened mucosa with large to oval cells, trabecular pattern which formed nests that invaded stroma. The conclusion was invasive squamous cell carcinoma of the urethra, grade 2.

Antegrade and retrograde urethrogram was done which revealed long incomplete penobulbar urethral narrowing. Metastatic work up was done by chest X-ray and abdominal pelvic ultrasound and they were all normal. The patient was counseled for radical penectomy and long term SPC and agreed.

Lambda incision was made on the perineum and circumscribed incision around penoscrotal junction. Tumour was found to extend from the area of proximal to distal bulbous urethra and infiltrating adjacent corpora carvenosa (Figure 3). Enblock mobilization of both corpora carvenosa and corpus spongiosum was done from penoscrotal junction up to the root of the penis (Figure 4). Transection of corpora carvenosa and corpus spongiosum was done at the root of penis with 1 cm of tumour free margin macroscopically and incision was closed in layers after achieving haemostasis (Figure 5). Postoperative histology report there was tumour free margins.

Postoperative the patient received adjuvant radiotherapy (66Gy/33) to penis, pelvic nodes and inguinal nodes for 2 months. One year after radical penectomy there was no evidence of recurrence (Figure 6 and 7).

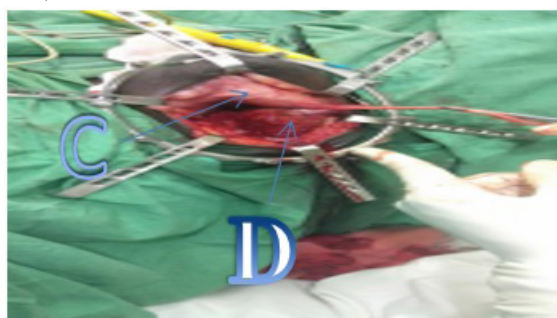


Figure 3: Normal part of bulbous urethra; D-tumour in bulbous urethra involving the corpus spongiosum



Figure 4: Tumour in bulbous urethra



Figure 5: Specimen of penis following total penectomy

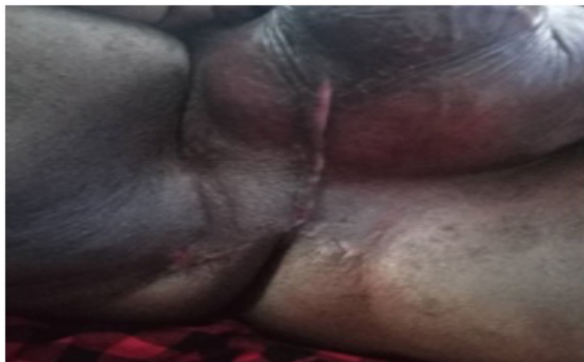


Figure 6: λ Incision scar 2-month post-operative



Figure 7: λ Incision scar 1-year post surgery

3.2. Case number 2

A 52 years old female known hypertensive for 2 years on regular medication presented with chief complain of voiding per urethral catheter for 3 weeks following acute urinary retention. However, there was no history of hematuria but the patient had lower back pain and numbness of lower limbs for 4 months. During the course of this illness she was treated several times with antibiotics for a diagnosis of urinary tract infection without relief.

She was 4 years postmenopausal and 20 years post appendectomy. She was a mother of 3 children, delivered through spontaneous vaginal delivery. There was no history of alcohol or tobacco use.

She was clinically stable. On abdominal examination she had Mac Burney's incision scar with other findings normal. However, on per vagina examination the introitus was normal on inspection, and there was hard and nodular mass on anterior vagina wall along the urethra with normal cervix and posterior vaginal wall.

Laboratory works up were normal. However; kidney, ureter and bladder ultrasound revealed thick bladder wall with bilateral mild hydronephrosis.

Urethrocystoscopy revealed rigid hard mass along the whole urethra with normal urinary bladder. Transurethral resection biopsy was performed followed by examination under anaesthesia that found a nodular hard mass with limited mobility on the anterior virginal wall. Postoperative period was uneventful and was allowed home with catheter on the second post op day to come for histology results after two weeks.

On day 9 post discharge, the patient was re-admitted after presenting with complaining of passing of shreads in urine, coughing, vomiting, nausea and blood in urine which started 3 days prior. Se-

rum creatinine was 687.28 μ mol/l, potassium 3,46 mEq/l, sodium 164.8 mEq/l and Cl 106.9 mEq/l . Chest X-ray showed bilateral pleural effusion > 50 %.

Chest tube was inserted and drained 1000mls of bloody stained fluid. After multidisciplinary discussion including the nephrology team the recommendation was palliative care with ant pain and less K as the disease was already very advanced. However, she succumb death on day five post admission for what was thought to be respiratory compromise as a result of metastasis.

3.3. Case number 3

A 70 years female who presented with chief complaint of recurrent urinary retention for 2 months which was preceded by LUTS. She also had one episode of hematuria. However, there was no history of schistomiasis or tobacco use. On examination, she was clinically stable with urethral catheter in situ, with normal vital signs and unremarkable abdominal examination. Per vagina examination revealed prolapsed uterus, other findings were normal.

Laboratory investigations and ultrasound were normal except for haemoglobin level which was 8,5 g/dl. Abdominal pelvic ultrasound was normal. The patient was planned for urethrocystoscopy and Examination Under Anaesthesia (EUA).

No tumour was palpable during EUA. On urethrocystoscopy, a finger like lesion was seen on the urethra about 1 cm distal to the bladder neck where a cold cup biopsy was taken. The urinary bladder mucosa was normal and postoperative period was uneventful. The patient was discharged 2 days' post-operative and was to attend the clinic after two weeks. However, she didn't turn up on time and instead he came 8 months later due to blood in urine. Follow up ultrasound reveled moderate right hydronephrosis with a huge bladder mass.

EUA noted the tumor to be palpable and fixed on the right pelvic sidewall. At urethrocystoscopy, there was papillary like lesion throughout the urethra with involvement of the trigone and right bladder wall. Ureteric orifices were not seen. Cold cup biopsy was performed on the urethral lesion and sent to the pathologist in a container containing 10% formalin. Pathological report revealed section of tissue fragment with atypical epithelium, evidence of nests and clusters of atypical epithelioid cells. Moreover, the Foci of tumor in the papillary pattern were also appreciated. The tumor cells showed marked atypia with high mitotic index. Hence, a conclusion of urothelial carcinoma of urethra, grade 2 was reached.

After tumor board discussion, the patient was planned for palliative chemo-radiation but she passed away by sudden death before initiation of the treatment.

4. Discussion

Primary urethral carcinoma is a rare condition in both sexes. In the past urethral carcinoma was more common in females than males but recent data shows that the trend has changed and currently it is

more common in males than females [11, 12]. It is common around the fifth and sixth decade in both sexes. In males, urethral carcinoma is more common in whites than in African-American 3 while recent studies have shown in females it is vice versa with 4.3 cases per million African-American women and 1.3 per million white women [12, 14].

A high index of suspicion is required in diagnosis of urethral cancer as there is no pathognomic features in both males and females. The most common manifestations in females include urethral bleeding, increased urinary frequency, dysuria, straining, focal tenderness and urinary tract infection¹⁵. In males most patients presents with symptoms and signs of urethral stricture disease (50%)¹⁶ as it was for our case. About quarter of patients have history of STD ¹⁶. In our case of a male patient, initially pre-operative diagnosis was thought to be a urethral stricture. However, intraoperative is when there was suspicious of cancer after seeing cauliflower lesions along the stricture site.

The histology of urethral carcinoma normally is consistent with the histologic features lining the particular anatomic part of urethra. The most common histologic types for both bulbomembranous (60% of urethral cancer) urethra and penile urethra (30% of urethral cancer) is SCC (80-90%) followed by TCC (10 %) with adenocarcinoma and other histologic types accounting for 10%⁴. The most common histologic type for prostatic urethra (10 % of urethral carcinoma) is TCC (90%) followed by SCC (10%). In our case report, the cancer was located in bulbous urethra and the histology was TCC-the second most common type. Urethral carcinoma usually spread by direct extension or through lymphatic system. Anterior urethra drain to superficial, deep inguinal and sometimes external iliac lymph nodes while posterior urethra drain to pelvic nodes.

The commonest histological types in females urethra also varies according to the site of the urethra. The proximal one-third is lined by transitional cell carcinoma with TCC the commonest histological type while the distal two-third is lined by SCC with SCC histological types being the most common¹⁵. However, overall the commonest histological types are squamous cell carcinoma (60%), followed by transitional cell carcinoma (20%), adenocarcinoma (10%), undifferentiated tumors (8%) and melanoma (2%) ¹⁵. Our female case had adenocarcinoma that is third most common histological type in this sex.

Because of the rarity of primary urethral cancer and heterogeneity of disease, appropriate treatment to urethral tumour is still debatable⁷. However, overall treatment depends on the stage and location of urethral tumour. Urethral cancer in the distal urethral (glanular and penile) may be treated with preservative surgeries such as distal urethrectomy and perineal urethrostomy, partial penectomy, transurethral resection and local excision [16, 17] while proximal urethral cancers require radical surgery which involve removal

of penis, urethra, scrotum, part of pubic bone, cystoprostatectomy and urinary diversion [18-21]. In our case of male patient, the cancer was located at mid bulbous urethra. The patient was treated with radical penectomy, followed by radiation. The bladder was closed and the patient was put on long term suprapubic catheter. One year post surgery, the patient was clinically stable with no evidence of local recurrence. He is still on six month follow up.

Female urethral cancer carries a poor prognosis and most cases present as advanced disease⁶. Five and 10-year survival rate is 32% to 51% and 31% to 42%, respectively, [12]. Lesions potential for cure in females should be < 2 cm where can be treated either surgically and/or radiotherapy. All of female's cancers presented at our institution were advanced and therefore not amenable for surgery.

5. Conclusion

Any patient presenting with symptoms of recurrent urinary tract infections or obstructive symptoms a differential diagnosis of urethral cancer should be considered. Primary urethral carcinoma in females present at advanced stage and carries a poor prognosis compared to males. Surgery followed by adjuvant radiation may be curative in urethral carcinoma.

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