CASE SERIES

LEIOMYOMA URINARY BLADDER, MIMICKING UROTHELIAL CANCER

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Leiomyoma of the urinary bladder is a rare bladder tumour, which is benign in nature. On presentation, it resembles urothelial cancer but it has an excellent prognosis. We reported two cases of urinary bladder leiomyoma. Both the patients presented with lower urinary tract symptoms (LUTS) and the patient in the second case also had painless haematuria. Bladder mass was detected initially on ultrasound and confirmed on contrast-enhanced computed tomography (CT). Transurethral resection of bladder tumour was performed in both cases and no recurrence was found on initial follow-up. But the second case had haematuria and recurrence on subsequent follow-up and managed by performing a partial cystectomy. Endoscopic management of bladder leiomyoma is a safe treatment option for bladder leiomyoma and if multiple recurrences noted with symptoms, then partial cystectomy can be considered. Histopathology is the only definitive way of establishing the diagnosis. These patients can be followed up initially with cystoscopy, and if no recurrence is detected, subsequent follow-up can be carried out with ultrasound.

Keywords: Urinary bladder leiomyoma; Benign bladder lesion; Transurethral resection of bladder tumour

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INTRODUCTION

Leiomyoma is a rare bladder tumour was usually seen in women in the latter half of the 4th decade of life. It is benign in nature, with approximately 250 cases reported in the literature, and constitutes less than 0.5% of all bladder lesions.[1] It can be found in any organ with smooth muscle. It is usually managed surgically and the tumour size and location in the bladder wall determine the ideal surgical approach. It has a very good prognosis as it's a benign lesion and has a very rare chance of malignant transformation.[2] The pathophysiology of occurrence of this tumour is still not explained and this might be due to an endocrine mechanism. The most common location in the genitourinary tract is the kidney and bladder, especially the bladder neck and trigone.[3] For many years leiomyoma remains asymptomatic, reaching considerable size unless the normal function of the lower urinary tract gets affected.[4] In 50% of the patients, the most common clinical presentation is urinary voiding symptoms.[5] On cystoscopy, it resembles a sub-mucosal tumour, sessile or pedunculated lesion covered by normal mucosa but if the tumour is intramural or sub-serosal, a normal-looking bladder wall can be seen.[6]

CASE-1

A 52-year-old female presented in the urology clinic with lower urinary tract symptoms (LUTS) and epigastric pain for the past 2 weeks. She had increased frequency, nocturia, urgency, and dysuria. She had no history of suprapubic pain, haematuria, weight loss, or tobacco use. Epigastric pain relieved by oral proton pump inhibitors. She was hypertensive for the past year and was taking amlodipine 5mg daily. She was a mother of four and post-menopausal for the past 6 years. Her daily fluid intake was around 1 litter per day. Her previous history was insignificant and normal abdomen and pelvis examination. Her basic haematological and biochemistry workup was normal. Urine culture grew Escherichia Coli for which antibiotics were given. An ultrasound scan was done which showed a hypo-echoic lesion along the anterior wall of the urinary bladder, measuring 32×13 mm. On post void examination the size of the lesion remained unchanged. No internal vascularity identified (Figure-1). Ultrasound pelvis and bladder were unremarkable. A contrast-enhanced CT urogram was performed which showed a non-enhancing lesion along the left anterior-lateral bladder wall measuring 32×16 mm. Bladder wall thickness was normal and there was no evidence of lymphadenopathy (Figure-1). No other abnormality was seen. At initial cystoscopy the bladder wall appearance was normal, showing a mass over the left anterolateral wall approximately 30×10 mm with normal-appearing overlying mucosa (Figure-2). Cystoscopy and transurethral resection of bladder tumour (TURBT) was performed as a day-care

procedure and administered a single dose of Mitomycin-C intravesically.

It was reported as leiomyoma bladder on histopathology (Figure-3,4,5). On gross examination of the specimen by the histopathologist, it consisted of multiple grey-brown to white irregular soft tissue fragments measuring 1.5×1.0 cm submitted entirely in a single block. On microscopy, the sections showed unremarkable bladder mucosa with fragments of muscularis propria (detrusor) exhibiting characteristic short bundles of smooth muscle cells. There were other fragments that show solid proliferation of spindle cells forming interlacing fascicles. These fragments were distinct from the normal muscularis propria tissue (Figure-5). The cells had abundant eosinophilic cytoplasm, bland-looking cigar-shaped nuclei with vesicular chromatin, and inconspicuous nucleoli (Figure-6). There was no significant cytological atypia, mitoses, or necrosis in the material examined. Based on these morphological features along with cystoscopy and radiological findings, leiomyoma was considered as the favoured diagnosis. Since smooth muscle tumours are relatively rare in the bladder, immuno-histo-chemical studies were carried out to confirm the morphological opinion and to rule out the other possibilities such as sarcomatoid carcinoma, peripheral nerve sheath tumour, and gastrointestinal stromal tumour (GIST). Immuno-histochemically the lesional cells showed diffuse staining for Smooth Muscle Actin (SMA) stain, confirming the smooth muscle nature of the tumour (Figure-7). Other immune-histochemical stains including CKAE1/AE3, S100 & DOG-1 were negative which ruled out other differentials.

Ultrasound bladder was normal on three months' follow-up. The patient remained well until 6 months of initial surgery and ultrasound performed at 6 months showed an echogenic lesion along the anterior wall of the urinary bladder which measures 33×16 mm. On post void examination the size of the lesion remains unchanged. No internal vascularity noted. Follow-up cystoscopy at 6 months showed approximately 30×20 mm, calcified, white-coloured lesion over the left anterolateral bladder wall. The rest of the bladder mucosa appeared normal. Re-TURBT was performed and biopsy reported as dystrophic calcification with reactive and regenerative changes, without any evidence of bladder tumour. The patient was followed up for 6 months after initial TURBT and redo-cystoscopy and biopsy confirmed benign pathology. The diagnosis was communicated to her and advised to follow up with an ultrasound scan. She is currently on 6 monthly ultrasound follow-ups and no recurrence of disease found on ultrasound after 2 years of the second TURBT.

CASE-2

A 42 years old female, known case of hypertension taking regular medications presented to our outpatient department with complaints of lower urinary tract symptoms for 1 year. Her LUTS include frequency 3–4 times per day, poor stream, the urgency with urge incontinence, and often she had to strain to empty her bladder. She also had painless haematuria without the passage of clots. Her past surgical history includes cystolitholapexy that was done 14 years back. She had no history of urogenital tract malignancy in the family but her father had renal stones. She was married having four kids. Her general and systemic physical examination was unremarkable. Also, per vaginal examination was normal. In this patient, haematological and biochemical workup was all normal. Urine culture and sensitivity were negative. An isoechoic lesion of around 30×30 mm at the left posterior-lateral wall of urinary bladder on ultrasound and both the kidneys were normal. Contrast-enhanced CT of the abdomen and pelvis supported the findings of extravesical extension of the lesion without any metastasis. (Figure-6, Figure-7). Cystoscopy showed a single mass with normal-appearing mucosa in the left lateral wall away from the left ureteric orifice but protruding into the bladder lumen. Cystoscopy and TURBT was performed and a single dose of Mitomycin-C was administered intravesically. Post-operatively she remained well and was discharged with a clinic follow-up given. Her histopathology report revealed a spindle cell lesion suggestive of a leiomyoma with nonspecific chronic inflammation and fragments of muscularis propria noted distinctly. The patient was kept on regular follow-up for surveillance. She remained well for two years, afterward, she had again painful haematuria and workup revealed recurrence of disease on the previously resected area. Partial cystectomy was done trans-peritoneally and around 2×3 cm tumour with free margins was resected. Later histopathology confirmed leiomyoma with clear surgical margins. The patient was kept on regular follow-up for surveillance. Currently, she is fine with no active complaints and no recurrence of disease on the first follow-up ultrasound after 6 months and 1 year. The appearance of lesion on ultrasound and contrast-enhanced CT scan mimics a urothelial carcinoma, although poor vascularity and non-enhancing nature of the lesions were unusual findings. Other differentials include leiomyosarcoma, lymphoma, squamous cell carcinoma, adenocarcinoma of the bladder, paraganglioma, and solitary fibrous tumour.

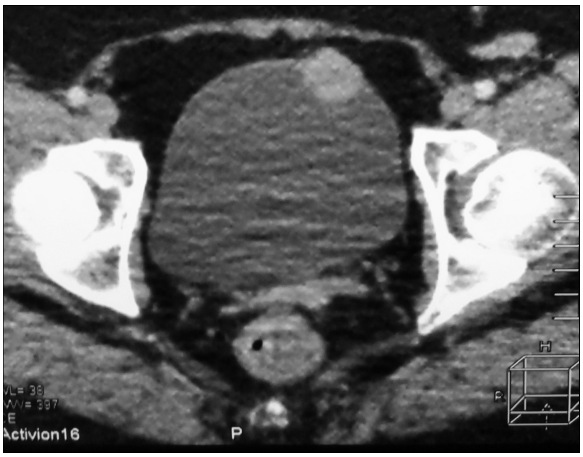

Figure-1: CT appearance of bladder Leiomyoma in case 1

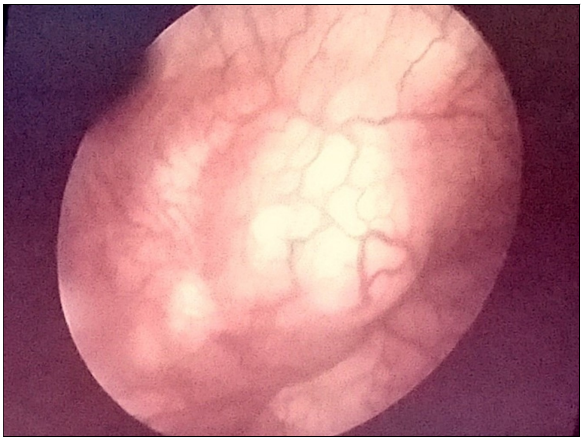

Figure-2: Cystoscopic appearance of bladder leiomyoma in case 1.

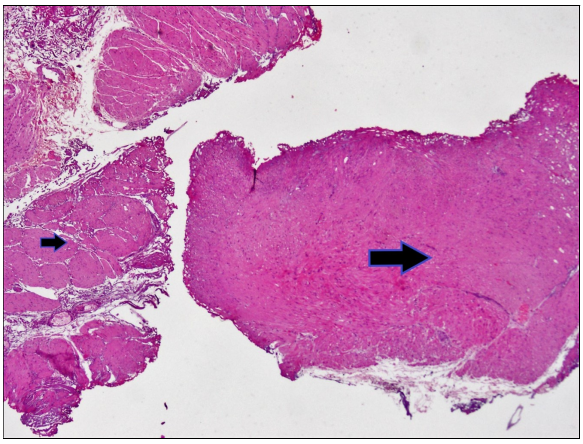

Figure-3: Histopathology slide of trans-urethral resection of bladder tumor specimen (case 1) showing normal muscularis propria on the left side (small arrow), composed of short thick bundles of smooth muscle with characteristic intervening clefts. Towards right (large arrow) the tissue shows sheets and long, compact fascicles of smooth muscle cells of leiomyoma. (H&E, 4X).

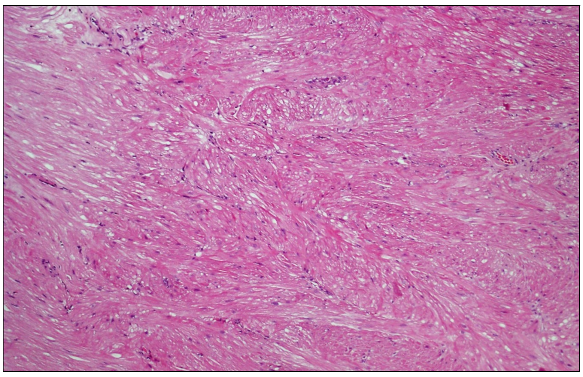

Figure-4: Bladder leiomyoma histologically (case 1) showing compact interlacing fascicles of smooth muscle cells with bland nuclei and no significant cytological atypia or mitoses. (H&E, 20X).

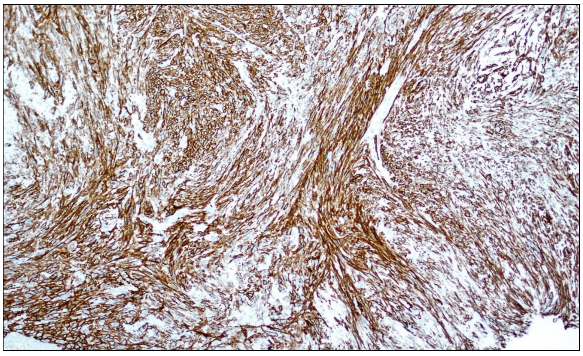

Figure-5: Bladder leiomyoma (case 1) showing strong diffuse positivity for the Smooth Muscle Actin (SMA) immune-histochemical stain (20X).

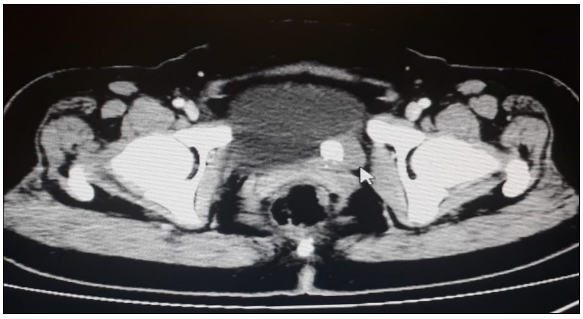

Figure-6: CT appearance of bladder Leiomyoma in case 2

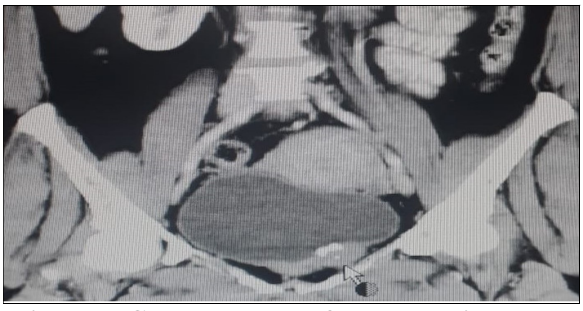

Figure-7: CT appearance of bladder Leiomyoma in case 2

DISCUSSION

It was first reported by Virchow in 1931.[7] Our cases had ages 52 and 42 years, which is similar to the median reported age of 44 years for leiomyoma of the bladder with a female predominance (76%).[8] The exact aetiology of this epidemiology is an enigma. However, oestrogen is thought to be associated with the growth of leiomyomas.[9–11] Both the cases in our report are female patients that can be explained by the oestrogen-dependent growth of these tumours. Grossly bladder leiomyomas may be intravesical, extra-vesical, or intramural and in our first case, the tumour was intramural with subtle protrusion into the bladder, while the second case had an intramural tumour with some extravesical extension. LUTS reported in our first case seem to be co-incidental as the tumour was small and localized, but the second case had the tumour located at the left posterior-lateral wall of the urinary bladder near the trigone which can explain the LUTS in the second case. The patient presents with LUTS or haematuria if the tumour protrudes into the bladder lumen.[12]

Endoscopically sub-mucosal tumours look like a pedunculated or sessile lesion covered by normal bladder mucosa, and if the tumour is intramural or sub-serosal then the mucosa may appear normal similar to findings observed in both our cases. These were pale appearing tumours and having minimal vascularity upon resection in both cases we described. Initially, ultrasound is done for evaluation of the urinary tract and pelvis as it's easily available and affordable. It appears as a mass attached to the bladder wall, which is typically iso- to hypoechoic on ultrasound.[13,14] In our cases, ultrasound showed a hypo-echoic lesion and an isoechoic lesion in case 1 and case 2 respectively. On Doppler, they may show some flow.[15] Ultrasound also defines the location of the lesion in the bladder, limits of the tumour, and adjacent structures. For females with posterior bladder wall tumours, transvaginal ultrasound is a very good option.[16] Contrast-enhanced CT images show the precise tumour features such as size, position, enhancement, and its relation with the bladder wall but benign tumours cannot be differentiated from malignant and other rare bladder tumour variants.[17] Contrast-enhanced CT showed non-enhancing lesions in both our cases and the second case also had some extravesical extension. Leiomyoma appears as an intermediate signal on T1 weighted images of magnetic resonance imaging (MRI), with a better difference of signal intensity between the tumour and the urine, as the tumour has a low signal intensity. T2 weighted images may differentiate leiomyoma from the bladder wall. Leiomyoma shows both high and low-intensity focus.[8] MRI was not performed in both our cases as US and Contrast-enhanced CT images are routinely helpful in establishing the radiological diagnosis of bladder tumour and making a decision regarding the management.

The benign nature of these lesions is pointed out by the presence of a well-circumscribed homogeneous lesion along with poor enhancement on contrast media. Definitive diagnosis is made on histopathology only, as no test can differentiate a leiomyoma from leiomyosarcoma.[18] In our first case, the cells had abundant eosinophilic cytoplasm, no significant cytological atypia, mitoses, or necrosis. In other studies, reported, the histopathology confirms a proliferation of smooth muscle fibres consisting of eosinophilic cytoplasm and less than two mitotic figures per high power field and are also bound by a variable volume of connective tissue with no necrosis or cellular atypia.[8,19]

The treatment depends upon the tumour size, location, and bladder wall-related configuration.[19,20] As these tumours have a growing capacity, surgery is indicated. However conservative management is an alternate acceptable option in cases confirmed by biopsy.[20] The only biopsy without TURBT was not a feasible alternative in our hospital setup due to cost concern but cystoscopy and biopsy may help in observing these masses for the nature of the lesion. Based upon history and investigations there was a high suspicion of urothelial cancer and after a detailed discussion with patients, a decision for cystoscopy and TURBT was taken.

These tumours are initially managed by transurethral resection and confirmation of histopathology, but sub-serosal and very large sub-mucosal tumours may eventually need partial cystectomy. Alternatively, these tumours can be enucleated trans-vaginally if located close to the urethra, and palpable through the vagina, however, this approach might increase the recurrence risk, as the limited operative field can hamper complete resection and it also depends upon the surgeon's experience.[17–19] In cases with symptomatic and recurrent leiomyoma, partial cystectomy with clear margins is recommended as a definitive procedure with routine follow-up. It has a good prognosis and recurrence is rare if adequately resected.[3,20] Most tumours can be managed easily with laparoscopy. If simultaneous cystoscopic control is used, normal bladder-wall edges can be easily identified.[21] Considering the benign behaviour of the lesions, treatment must be planned and kept as conservative as possible. As the malignant conversion of these tumours has not been documented, observation of asymptomatic lesions can be considered once the pathology is certain. Options for resection include

laparoscopic, robot-assisted, transurethral, and open surgery.[21–24]

CONCLUSION

Bladder leiomyoma is a rare bladder tumour that may cause lower urinary tract symptoms or may remain asymptomatic. Ultrasound can pick bladder leiomyoma easily as it is an initial investigation done for LUTS evaluation and contrast CT shows less enhancing bladder lesions but imaging alone cannot be reliably used for definitively differentiating it from urothelial cancer. These tumours have a normal overlying mucosa at cystoscopy and are fibrous upon resection with minimal vascularity. Treatments are surgical, with transurethral endoscopic removal providing confirm the diagnosis, a safe, and effective means of initial management. Partial cystectomy with clear margins is recommended for recurrent and symptomatic disease.

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