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# Leiomyosarcoma of the Urinary Bladder: A Review and Update of the Literature

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## Abstract

Less than 200 cases of Leiomyosarcoma of the Urinary Bladder (LUB) have been reported in the literature. LUB does affect both males and females. LUB has been reported mostly in adults, but sporadic cases of LUB have been reported in the younger age group, particularly in children who had previously undergone treatment for retinoblastoma by means of enucleation plus radiotherapy or chemotherapy. LUB may present as a de novo disease, or it may present many years pursuant to undergoing chemotherapy for example cyclophosphamide treatment of radiotherapy. LUB has been reported contemporaneously with urothelial carcinoma on one occasion and with chronic use of ketamine. LUB does manifest insidiously with visible haematuria, lower urinary tract symptoms, lower abdominal and or loin pain / discomfort. Radiology imaging, including ultrasound scan, computed tomography scan and magnetic resonance imaging scan would tend to show the lesion. Cystoscopy would tend to reveal majority of cases of LUB with the exception of extra-mural tumours. Diagnosis of LUB is established by pathological examination of biopsy specimens or excised specimens of the tumour showing spindled cell tumors usually associated with high mitotic figures and positive immunohistochemistry staining for smooth muscle actin (80%), h-Caldesmon, muscle specific-actin, desmin (<50%), calponin, and vimentin but negative staining for EMA, S-100, ALK-1, 34betaE12 and CK5/6. The majority of cases of LUB especially very large, high-grade, high-staged tumours with high mitotic activity tend to be very aggressive tumours and LUBS have traditionally been managed by radical cystectomy / cystoprostatectomy plus adjuvant chemotherapy plus / minus radiotherapy. Despite aggressive surgery and adjuvant combination chemotherapy some patients with LUB develop metastasis and death which would indicate that there is a need for the development and identification of new chemotherapy medicaments that would improve the prognosis. Nevertheless, there is evidence to suggest that partial cystectomy alone, or Trans-Urethral Resection of Bladder Tumour (TURBT) alone may be adequate treatment for some cases of small superficial low-grade and low-staged tumours. There is need to establish a multi-centre global trial to establish the best treatment options for LUBs. Clinicians should be aware that even after a recurrence-free interval of 12 years, LUB could still recur therefore a long period of follow-up would be required for LUB.

## Keywords

Leiomyosarcoma; Urinary Bladder; Smooth Muscle; Radical Cystoprostatectomy; Cystectomy; Partial Cystectomy; Trans-Urethral Resection of Bladder Tumour; Radiotherapy; Chemotherapy; Adjuvant; Smooth Muscle Actin, Desmin, H-Caldesmon; Desmin; Calponin; Vimentin; Cyclophosphamide; Retinoblastoma

## Introduction

Non epithelial tumours of the urinary bladder do account for less than 5% of all urinary bladder carcinomas and primary leiomyosarcomas do constitute 0.1% of all carcinomas of the urinary bladder. Less than 200 cases of primary leiomyosarcoma of the urinary bladder have been reported in the literature. Leiomyosarcomas of the urinary bladder do present with non-specific symptoms and because of the rarity of the malignancy majority of clinicians globally would not have encountered a case of leiomyosarcoma of the urinary bladder before and they would also tend not to be familiar with the manifestations and management of the disease. There are no global consensus guidelines related to the management of primary leiomyosarcomas of the urinary bladder (LUBs) in view of the small number of cases that have been reported sporadically. Leiomyosarcomas of the Urinary Bladder (LUBs) have been stated generally to be associated with poor prognosis especially if they are high-grade and high-stage tumours [1,2]. Because of the paucity of literature related to primary Leiomyosarcomas of the Urinary Bladder (LUBs), the natural history and biological behaviour of the malignancy is not well known and there is paucity of information related to the disease in majority of urology and general surgery text books. The ensuing article entailing a review and update of the literature on Primary Leiomyosarcoma of the Urinary Bladder (PLUB) is divided into two parts (A) Overview and (B) Miscellaneous

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narrations related to case reports, case series and studies related to Primary Leiomyosarcoma of the Urinary Bladder (PLUB).

## Aim

To review and update the literature on Primary Leiomyosarcoma of the Urinary Bladder (PLUB).

## Methods

Various internet databases were searched including: Yahoo; Google; Google scholar; and PUBMED. The search words that were used included: Leiomyosarcoma of urinary bladder, and leiomyosarcoma of bladder. Twenty nine references were identified as suitable to write the review and update of the literature on Leiomyosarcoma of the Urinary Bladder (LUB).

## Results

### Overview

#### Definition / General Comments

- Leiomyosarcoma of the urinary bladder is a sarcoma of smooth muscle origin, which is similar to its counterpart leiomyosarcoma smooth muscle tumours elsewhere in the body [3]
- Less than 200 cases of primary leiomyosarcomas of the urinary bladder have been reported in the literature therefore majority of clinicians would tend not to be familiar with the disease entity because they one not treated patients with the disease
- Leiomyosarcoma of the urinary bladder has been reported in males and females, in adults and children

#### Epidemiology

- It has been stated that leiomyosarcoma of the urinary bladder has usually been reported in men [3]; nevertheless, some studies have documented that leiomyosarcoma of the urinary bladder has been documented to occur equally in males as females as would be seen in the second section of the article
- It has been stated that the mean age of patients who have been reported to have leiomyosarcoma of the urinary bladder has ranged between 49 years and 64 years [3]. However, leiomyosarcoma of the urinary bladder has been reported in the younger age group as well as in very old individuals as would be seen in the article
- It has been stipulated that there is an increased risk for the development of primary leiomyosarcoma of the urinary bladder pursuant to:
  - cyclophosphamide treatment [4]
  - or radiotherapy
  - possibly after hereditary retinoblastoma [5]
  - Acrolein which is a metabolite of cyclophosphamide which is excreted in urine could cause haemorrhagic cystitis that does increase the risk for the development of carcinomas of the urinary bladder [3] and leiomyosarcoma of the urinary bladder would tend to be one of the carcinomas
  - As illustrated in the latter part of the article chronic ketamine use has been reported linked with the subsequent development of a case of primary leiomyosarcoma of the urinary bladder but the cause effect could not be explained

### Sites

- It has been iterated that primary leiomyosarcoma of the urinary bladder does occur at any site within the urinary bladder and it can on rare occasions involve the ureter or renal pelvis [3]
- Leiomyosarcoma of the urinary bladder quite often does involve the mucosa and submucosa and muscle layer of the urinary bladder
- Leiomyosarcoma of the urinary bladder could also occur as an extramural leiomyosarcoma that spares the mucosa of the urinary bladder as illustrated under miscellaneous narrations in the second part of the article
- Leiomyosarcoma of the urinary bladder may at the time of initial diagnosis be found to have involved the prostate gland in sporadic cases of advanced and aggressive tumours

### Aetiology

- Leiomyosarcoma of the urinary bladder is a rare tumour which accounts for 0.1% of malignancies of the urinary and it is said to be the commonest non-epithelial malignancy of the urinary bladder [3]; nevertheless, the exact cause or aetiology of majority of cases of leiomyosarcoma of the urinary bladder has not been clearly explained
- Leiomyosarcoma of the urinary bladder does originate or arise from the smooth muscle of the urinary bladder [3]
- Development of some cases of primary leiomyosarcoma of the urinary bladder has been linked with the use of cyclophosphamide, previous radiotherapy, and one case of leiomyosarcoma of the urinary bladder has been linked with chronic use of Ketamine
- Retinoblastoma has also been linked with the development of leiomyosarcoma of the urinary bladder as will be seen in the second part of the article

### Presentation

Leiomyosarcomas of the urinary bladder (LUBs) may present with any or some of the following:

- Visible haematuria
- Lower urinary tract symptoms of frequency, urgency, urge incontinence, poor urinary flow, interrupted flow, and incomplete emptying of the bladder
- Dysuria
- Low pain
- Lower abdominal pain.
- There may be a previous history of treatment for retinoblastoma in the past
- There may be a history of previous treatment use of cyclophosphamide
- There may be a history of previous radiotherapy
- There may be a history of recurrent urinary tract infections

#### Clinical examination findings

- The general and systematic examination would tend to be normal
- With visible haematuria, some patients may be clinically anaemic
- There may be tenderness in the lower abdomen, supra-pubic region, or the loin region
- There could be a palpable mass in the suprapubic region, or in one lower quadrant of the abdomen
- There may be tenderness in the loin in some cases of hydronephrosis due to ureteric obstruction

- If a patient has retention of urine this would be obvious and the patient would be catheterized

## Investigations

**Urine:** Urinalysis, urine microscopy and urine culture and sensitivity and general assessments that tend to be undertaken in the initial assessment of patients. In some situations the examinations would be normal and there may be visible or non-visible haematuria in other cases. If there is evidence of urinary tract infection, this will be treated according to the antibiotic sensitivity pattern of the disease to improve upon the general condition of the patient.

**Laboratory blood tests:** Haematology blood tests – Full blood count and coagulation screen are routine tests that are undertaken in the general initial assessment of patients and the results would tend to be normal but if there is any abnormality it would be further investigated and treated accordingly including blood transfusion of those who may be anaemic from gross haematuria.

**Biochemistry blood tests:** Serum urea, creatine, electrolytes, blood glucose and liver function tests are general routine tests that are undertaken as part of the general assessment of patients who have Leiomyosarcoma of the Urinary Bladder (LUB). The results of the routine biochemistry blood tests would tend to be normal but if there is any abnormality detected, it would be investigated and treated accordingly to improve the general condition of the patient. If there is impaired renal function, radiology imaging would indicate if there is hydronephrosis due to ureteric obstruction. In situations where there is hydronephrosis due to ureteric obstruction, insertion of per-cutaneous nephrostomy or antegrade or retrograde ureteric stenting procedure may be undertaken to preserve or improve the renal function of the patient prior to providing definitive surgical treatment for the malignancy.

## Radiology investigations

**Chest x-ray:** Chest radiograph is a routine investigation which tends to be undertaken in the initial assessment of patients and chest x-ray can also be undertaken as part of follow-up assessment of patients who have had treatment for leiomyosarcoma of the urinary bladder to ascertain if pulmonary metastases have developed but this has been superseded by CT and MRI scan of thorax, abdomen and pelvis but in certain parts of the world where CT and MRI scan facilities are not available, chest x-ray and ultrasound scan of abdomen and pelvis / renal tract continues to be undertaken.

### Ultrasound scan

- Ultrasound scan of abdomen, renal tract and pelvis tend to be an initial radiology imaging investigation of many patients who have Leiomyosarcoma of the Urinary Bladder (LUB). The scan would demonstrate the lesion in the urinary bladder, its position in the bladder, its size and relation to other structures as well as if there is any hydronephrosis or extension beyond the urinary bladder. The scan would also indicate if there are enlarged lymph nodes or metastatic lesions within the abdomen and pelvis
- Ultrasound scan guided percutaneous nephrostomy insertion can be undertaken as initial temporary treatment of obstructed hydronephrotic kidney to ensure improvement in and maintenance of good renal function preceding surgical treatment of the tumour. Antegrade ureteric stent can also be inserted under ultrasound scan guidance
- Ultrasound scan of abdomen and pelvis can be undertaken in addition to chest x-ray in the follow-up assessment of patients who have undergone surgical treatment for leiomyosarcoma of the bladder (LUB) but this has been superseded by CT scan of thorax, abdomen and pelvis in the developed countries but in developing countries where there are not sufficient CT scans and MRI scans are not available ultrasound scan of abdomen and pelvis are undertaken as routine follow-up assessment of the patients together with chest-x-ray
- At times though rare, cases of leiomyosarcoma of the bladder would be extra-mural in that case the lesions cannot be seen at cystoscopy but in order to ascertain what type of tumour or lesion, the mass seen on imaging is one can under-go an evaluating radiology image-guidance per-cutaneous biopsy of the lesion to establish the true nature of the lesion after histopathology examination of the biopsy which has been obtained pre-operatively under ultrasound scan guidance

## Computed tomography scan

- CT scan of abdomen, renal tract and pelvis tend to be an initial radiology imaging investigation of many patients who have Leiomyosarcoma of the Urinary Bladder (LUB). The scan would demonstrate the lesion in the urinary bladder, its position in the bladder, its size and relation to other structures as well as if there is any hydronephrosis or extension beyond the urinary bladder. The scan would also indicate if there are enlarged lymph nodes or metastatic lesions within the abdomen and pelvis
- CT scan guided percutaneous nephrostomy insertion can be undertaken as initial temporary treatment of obstructed hydronephrotic kidney to ensure improvement in and maintenance of good renal function preceding surgical treatment of the tumour. Antegrade ureteric stent can also be inserted under CT scan guidance
- CT scan of thorax, abdomen and pelvis tends to be used as part of the initial full staging of leiomyosarcoma of the urinary bladder in order to plan the management of each patient.
- CT scan of thorax, abdomen and pelvis tend to be undertaken as part of the follow-up assessment of patients who have undergone treatment for Leiomyosarcoma of the Urinary Bladder (LUB)
- At times though rare, cases of leiomyosarcoma of the bladder would be extra-mural in that case the lesions cannot be seen at cystoscopy but in order to ascertain what type of tumour or lesion, the mass seen on imaging is one can under-go an evaluating radiology image-guidance per-cutaneous biopsy of the lesion to establish the true nature of the lesion after histopathology examination of the biopsy which has been obtained pre-operatively under CT scan guidance

## Magnetic Resonance Imaging Scan

- MRI scan of abdomen, renal tract and pelvis tend to be an initial radiology imaging investigation of many patients who have Leiomyosarcoma of the Urinary Bladder (LUB). The scan would demonstrate the lesion in the urinary bladder, its position in the bladder, its size and relation to other structures as well as if there is any hydronephrosis or extension beyond the urinary bladder. The scan would also indicate if there are enlarged lymph nodes or metastatic lesions within the abdomen and pelvis
- MRI scan guided percutaneous nephrostomy insertion can be undertaken as initial temporary treatment of obstructed hydronephrotic kidney to ensure improvement in and maintenance of good renal function preceding surgical treatment of the tumour. Antegrade ureteric stent can also be inserted under ultrasound scan guidance
- MRI scan of thorax, abdomen and pelvis tends sometimes to be used as part of the initial full staging of leiomyosarcoma of the urinary bladder in order to plan the management of each patient
- MRI scan of thorax, abdomen and pelvis at times tend to be undertaken as part of the follow-up assessment of patients who have undergone treatment for Leiomyosarcoma of the Urinary Bladder (LUB)

- At times though rare, cases of leiomyosarcoma of the bladder would be extra-mural in that case the lesions cannot be seen at cystoscopy but in order to ascertain what type of tumour or lesion, the mass seen on imaging is one can under-go an evaluating radiology image-guidance per-cutaneous biopsy of the lesion to establish the true nature of the lesion after histopathology examination of the biopsy which has been obtained pre-operatively under MRI scan guidance

### Positron Emission Tomography / Computed Tomography scan

- PET/CT scan tends to be undertaken at times in the follow-up assessment of patients who have undergone treatment for leiomyosarcoma of the urinary bladder to ascertain if any metastatic lesions have developed
- Isotope bone
- Isotope bone scan can be undertaken to establish whether or not a patient who has been treated surgically has developed bone metastasiS

**Cystoscopy:** Cystoscopy is a routine examination that is undertaken in the initial assessment of many patients who present with haematuria or who are investigated for lower urinary tract symptoms. This procedure could initially be flexible cystoscopy that most often is undertaken under local anaesthesia and if the lesion is found the patient could be listed to undergo cystoscopy under general anaesthesia plus biopsy / trans-urethral resection of the tumour as well as examination of the mass bimanually under general anaesthesia. In situations when there is evidence of obstruction of the ureter based upon radiology imaging then insertion of a ureteric stent is undertaken during cystoscopy under general anaesthesia. Cystoscopy and trans-urethral resection of small urinary bladder tumours with complete resection of the tumour has been undertaken in some situations.

**Cytology features:** It has been stated that cytology examination in cases of leiomyosarcoma of the urinary bladder tends to show spindled cells that are associated with mild to moderate nuclear hyperchromasia [3].

### Macroscopy features

- The size of leiomyosarcoma of the urinary bladder has been stated to range between 3 cm and 15 cm and the mean size of the tumour has been 7 cm [3]
- The tumour quite often has been stated to be within the dome of the urinary bladder and the tumour also has tended to be poorly circumscribed, invasive and with ulcerating surfaces [3]
- With regard to high-grade tumours, necrosis tends to be found
- Some cases of leiomyosarcoma could be extramural tumours which do not involve the mucosa of the urinary bladder and such type of a case the mucosa of the urinary bladder would be seen as normal as illustrated in the second section of the article

**Microscopy examination features:** It has been iterated that in cases of primary leiomyosarcoma of the urinary bladder the microscopic examination features of the urinary bladder tumour would tend to reveal the ensuing features: [3]

- Cellular, interlacing fascicles of spindle-cells that have eosinophilic cytoplasm, para-neoplastic vacuoles as well as blunt ended nuclei.
- Infiltrative margins of the tumour tend to be seen which tend to invade the muscularis propria. [6]
- Variable amounts of nuclear atypia tend to be seen/
- Coagulative necrosis of the tumour tends to be commonly seen
- The leiomyosarcoma of the urinary bladder could be a myxoid tumour which would mimic inflammatory pseudo-tumour

### The tumour generally tends to be high grade and this would be typified by:

- Evidence of atypia
- 5+ r mitotic figures per 10 high-power fields
- Or evidence of abundant necrosis

The myxoid sub-type of leiomyosarcoma of the urinary bladder may mimic inflammatory myofibroblastic tumour; nevertheless, with regard to the myxoid sub-type of leiomyosarcoma of the urinary bladder, microscopy examination would show destruction of muscle fascicles at the tumour-muscle interface; the examination would also show nuclear pleomorphism and tumour necrosis. These features would not be present in inflammatory myofibroblastic tumour of the urinary bladder.

Rare cases of low-grade, well differentiated leiomyosarcomas of the urinary bladder do exist and in such tumours, there would tend to be less than 5 mitotic figures per 10 high-power fields upon microscopy examination of the tumour.

## Immunohistochemistry Staining Features

### Positive staining

In primary leiomyosarcoma of the urinary bladder immunohistochemistry staining of the tumour would exhibit positive staining as follows: [3]

- Smooth muscle actin – There tends to be positive staining in 80% of cases.
- H-caldesmon – There tends to be H-caldesmon positive staining [7]
- Muscle specific actin (HHF35)
- Desmin – there tends to be positive staining in less than 50% of cases
- Calponin
- Vimentin
- Often positive for cytokeratin Oscar or AE1/AE3 [8]

### Negative staining

It has been stated that leiomyosarcomas of the urinary bladder do exhibit negative staining for the following tumour markers:

- EMA, [9]
- S-100, [9]
- ALK-1 [9]
- 34betaE12, [3]
- CK5/6 [3]

Molecular / cytogenetics description

It has been stated that Leiomyosarcomas of the urinary bladder upon molecular and cytogenetic studies usually tends not to be diploid [3].

### Clinical Features and Outcome

- With regard to the clinical features of leiomyosarcoma of the urinary bladder, it has been stated that on the whole the tumour tends to be aggressive and that greater 60% of the patients develop metastatic disease or they die of their disease [3]

- It has also been iterated that even low-grade leiomyosarcomas of the urinary bladder may metastasize [10]
- The 5-year-survival rate for high-grade leiomyosarcoma has been stated to be 62% [3]
- Nevertheless, some cases of low-grade, superficial leiomyosarcomas of the bladder have been associated with good prognosis after TURBT alone or partial cystectomy alone even though these cases are sporadic cases as would be illustrated subsequently in the article
- Some leiomyosarcomas of the urinary bladder may recur after a long-period of no local recurrence or distant metastasis as has been illustrated in the latter part of the article

## Prognostic factors

- It has been stated that generally the prognosis of primary leiomyosarcoma has been poor with the subsequent development of local recurrence or metastases [3]
- The poor prognosis of leiomyosarcoma of the bladder has been associated with large muscle invasive and poorly differentiated of high grade tumours, but at times the short-term and medium-term outcome has been good
- Recently case of low grade, and low-staged tumours have been found to be associated with good short-term and medium-term outcome as illustrated in the second part of the article

## Treatment

With the general consideration that primary leiomyosarcomas have been noted to be aggressive tumours associated with poor prognosis the general management of the disease has been by radical cystectomy with the aim of complete excision of the tumour with tumour-free resection margins; however, other treatment options have been used for different cases of leiomyosarcoma of the urinary bladder depending upon the characteristics of the tumour and the co-morbidities of the patient. Some of the management options include:

- Radical cystectomy / cystoprostatectomy alone plus urinary diversion
- Radical cystectomy / cystoprostatectomy plus adjuvant / neo-adjuvant radiotherapy
- Radical cystectomy / cystoprostatectomy plus adjuvant / neo-adjuvant chemotherapy
- Radical prostatectomy / cystoprostatectomy plus adjuvant / neoadjuvant radiotherapy plus chemotherapy
- Partial cystectomy alone plus meticulous and careful follow-up with the plan to adopt further treatment as may be required
- Trans-Urethral Resection of the Urinary Bladder Tumour (TURBT) ensuring complete resection of the tumour and a careful follow-up with the plan to provide additional treatment as may be required

## Differential diagnosis

Some of the differential diagnosis of primary leiomyosarcoma of the urinary bladder includes:

- Inflammatory Myofibroblastic Tumour (IMT)
- In cases of IMT microscopy examination of the urinary bladder tumour does reveal a vascular and inflamed myofibloblastic proliferation with the absence of cytological atypia, and the tumour tends not to be as cellular as leiomyosarcoma, no evidence of necrosis, and no evidence of abnormal mitotic figures [3]

## Immunohistochemistry staining studies in IMT does show: [11]

Positive staining for ALK.

Negative staining for H-caldesmon

Post-operative spindle cell nodule

- In cases of post-operative spindle cell nodule microscopy examination of the urinary bladder lesion would show no evidence of atypia [3]
- In cases of post-operative spindle cell nodule there tends to a history of recent surgery or trauma [3]
- Sarcomatoid carcinoma of the urinary bladder
- In Sarcomatoid carcinoma of the urinary bladder, microscopy examination of the bladder tumour would tend to show epithelioid differentiation and immunohistochemistry studies would show strongly positive staining for keratin [3]

## Outcome

- Generally large poorly differentiated invasive leiomyosarcomas of the urinary bladder have been associated with inferior outcome in that many of the cases had ended associated with the development of metastases and death despite utilization of a combination of radical surgery and adjuvant therapy; nevertheless some patients have had reasonable long term outcome. Patients whose tumours have been associated with high mitotic figures per / 10 high-power fields have had worse prognosis and patients who have had low numbers of mitotic figures per 10 high power fields have had better outcome
- When there is complete excision of the tumour this would appear to be associated with better prognosis in comparison with presence of disease at the resection margin as well as cases of large advanced staged tumours
- Recent anecdotal evidence exists which has indicated that partial cystectomy alone with complete excision of small tumours that are confined to the urinary bladder without adjuvant therapy may be associated with good medium-term to long-term survival
- Recent evidence also exists that have shown that small superficial tumours that are completed resected by means of trans-urethral resection of bladder tumour alone could be associated with good short-term to medium-term outcome but careful follow-up would be required but this may only be related to tumours that are associated with low mitotic figures (less than 5) / 10 high-power fields
- A patient who had been disease free after 12 years follow-up pursuant to initial surgical treatment has been reported to have developed a recurrence therefore a long-term follow-up schedule is required for all patients

# Miscellaneous Narrations and Discussions from Some Case Reports, Case Series and Studies Related to Primary Leiomyosarcoma of the Urinary Bladder

Hamadalla et al. [2] reported 2 cases of primary leiomyosarcoma of the urinary bladder as follows:

## Case 1

A 71-year-old man manifested with haematuria and burning sensation on voiding of a few months duration. He was taking an alpha adrenergic blocker and five alpha reductase for lower urinary

tract symptoms related to benign prostatic hyperplasia. He had urine cytology examination which was normal and did not show anything to suggest malignancy. He had Computed Tomography (CT) scan which revealed a large mass within the right lower wall of the urinary bladder that had encroached upon the neck of the urinary bladder (Figure 1).

No enlarged lymph nodes were identified on CT scan of the pelvis and abdomen. He had isotope bone scan and chest radiograph which were normal. He underwent urethro-cystoscopy and biopsy of a fungating mass that was in the right side of the neck his urinary bladder. Some of the histopathological sections of the biopsy specimen did show a spindled-cell tumour that had exhibited marked atypia (Figure 2) as well as pleomorphic cells, that was associated with a high mitotic count of 20 per 10 high power fields (HPF) (Figure 3). There was necrosis which had involved 20% of the tumour. The tumour did reach the surface, with ulceration, as well as there was calcification on the surface of the tumour. Immunohistochemistry staining studies of the tumour exhibited the following features:

- Positive staining for actin (Figure 4)
- Few cells stained positively for desmin
- Negative staining for Uroplakin and Uroplakin III (Figure 4 C, and 4 d)

Based upon the histopathology and immunohistochemistry staining examination features of the tumour a diagnosis of high-grade leiomyosarcoma of the urinary bladder was made.

He underwent cystoprostatectomy and ileal conduit urinary diversion. Microscopic examination of the tumour did not reveal any glandular component. The tumour cells had invaded the anterior wall of the urinary bladder with extra-vesical extension into the soft tissue. There was tumour at the resection margin. Histopathology examination of the specimen showed a spindled-cell tumour which had involved the urinary bladder wall, the bladder neck and the prostate gland that had consisted of interlacing bundles of spindled-cells associated with pleomorphic nuclei, prominent nucleoli and a very high mitotic rate of greater than 20 per 10 high power fields. Bizarre giant tumour cells were also found. Multiple foci of tumour necrosis and calcification were observed in less than 50% of the surface area. There were no malignant cells within the trigone

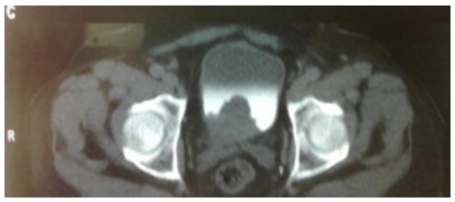

**Figure 1:** CT showing a large mass at the right lower wall of the bladder, encroaching upon the bladder neck [2]

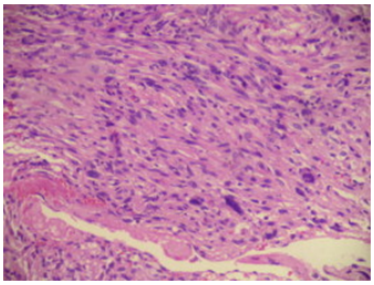

**Figure 2:** Microscopic findings of the leiomyosarcoma, showing spindle-shaped cells with marked atypia, (Haematoxylin and eosin, x 400) [2]

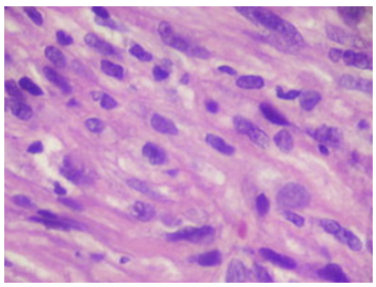

**Figure 3:** Microscopic findings of the leiomyosarcoma showing pleomorphic cells with a high mitotic count of 20/10 HPF (Haematoxylin and eosin, x 400) [2]

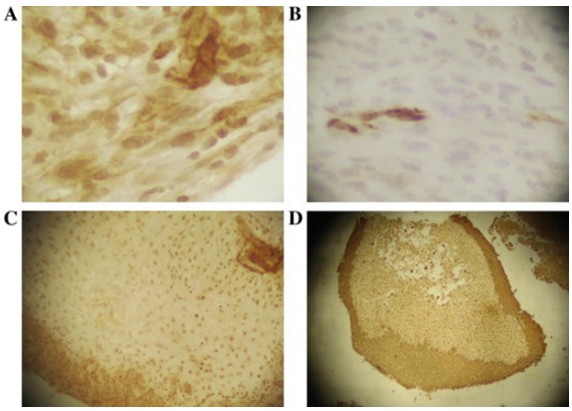


**Figure 4:** Immunostaining for: (A) Actin (positive); (B) Desmin (a few positive cells); (C) Uroplakin (negative); (D) Uroplakin III (negative) [2]

of the bladder. There was oedema, congestion as well as chronic inflammation within the rest of the bladder mucosa. Both seminal vesicles, the urethral resection margin, the right and left ureters were free of tumour. Immunohistochemistry staining showed that the tumour had exhibited focal positive staining for S-100 protein, and negative staining for cytokeratin and desmin. The features of the tumour were consistent with high grade tumour. He received adjuvant radiotherapy and chemotherapy. He presented with cough one year later and he had CT scan of thorax which showed bilateral pulmonary deposits, deposits in the pleura, and left superior pulmonary vein which had extended the left atrium. He received three treatment cycles of chemotherapy which included ifosfamide, and Adriamycin, with Mesna. He died 2 years pursuant to his surgery due to pulmonary involvement with no evidence of local recurrence. A lesson that would be learnt from this case report is that primary leiomyosarcoma of the urinary bladder is a very aggressive tumour and despite radical surgery, radiotherapy, and systemic chemotherapy the patient subsequently died after 2 years which would indicate that urologists, oncologists, and pharmacotherapy research workers would need to identify through research new chemotherapy options that would effectively destroy leiomyosarcoma tumour cells.

## Case 2

A 31-year-old man who had presented with a 3-months history of dysuria. He had ultrasound scan abdomen and pelvis as well as computed tomography scan of thorax, abdomen, and pelvis which showed a well-demarcated, contrast-enhancing mass on the right posterior-lateral aspect of his urinary bladder and right hydronephrosis. He had cystoscopy which showed a normal urothelial lining of the urinary bladder. He underwent laparotomy and excision of a mobile, extra-mural urinary bladder mass that had involved the distal ureter. The surgical excision of the mass entailed distal right ureterectomy, partial cystectomy, and re-implantation of

the right ureter over a double J ureteric stent. The stent was removed after 4 weeks. Pathology examination of the tumour showed grade II, 4.5 cm leiomyosarcoma of the wall of the urinary bladder with an intact urinary bladder mucosa and all the tumour resection margins were free of tumour by 0.25 mm. Immunohistochemistry staining studies of the tumour showed positive staining for caldesmon and desmin, and negative staining for myogenin. There were about 22 mitotic figures per 10 high power fields which had indicated that the tumour was a high-grade tumour. No lymph nodes were found. He had isotope bone scan which was normal. The tumour was staged as T1bNXM0. He received adjuvant external beam radiotherapy and combination chemotherapy with four cycles of ifosfamide/Mesna and doxorubicin monthly. He had follow-up CT scan at 4 months as well as cystoscopy which were normal but pursuant to that he was lost to follow-up and therefore the long-term follow-up outcome was not known.

Lindberg et al. [12] undertook a clinicopathology study of 34 cases of leiomyosarcoma of the urinary bladder. Lindberg et al. [12] summarized the results as follows:

- The tumours had occurred in 17 females and 17 males whose ages had ranged between 31 years and 91 years and the mean age of the patients was 65 years. The tumours had measured between 2 cm and 12 cm
- One of the tumours was well-differentiated, 17 tumours were moderately differentiated, and 17 tumours were poorly differentiated
- The mitotic rates had ranged between 1 and 30 mitoses per 10 high-power fields with a median of 12 mitoses per 10 high-power fields
- The tumours did show 0 to 60% necrosis with a median of 25% necrosis
- Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grades were 1 with regard to 3 cases; 2 with regard to 12 cases; 3 with regard to 19 cases
- National Cancer Institute (NCI) grades were 1 with regard to 2 cases; 2 with regard to 11 cases; 3 with regard to 21 cases
- Mayo grades were low with regard to 7 cases; and high with regard to 27 cases
- FNCLCC and NCI grades were noted to be identical with regard to 23 out of 34 cases that amounted to 68% of cases. Four of the cases were FNCLCC / NCI grade 2 or 3 and Mayo low-grade
- Clinical follow-up data was available for 25 out of the 34 patients that amounted to 74%
- Clinical follow-up of equal to or longer than 12 months was available for 17 of the 25 patients which had amounted to 68% with a median follow-up time of 52 months and the follow-up had ranged between 12 months and 120 months
- Adverse outcome was observed with regard to 9 of the 17 patients which amounted to 53% of the patients. Seven out of eight patients which amounted to 88% of patients who had had a clinical follow-up of less than 12 months died of their disease. Overall adverse effects developed with regard to 16 out of 25 patients which amounted to 64% of the cases. Metastatic disease was observed in 13 out of 25 cases that amounted to 52% of cases, with the lungs being the commonest site of metastasis which amounted to 62% of cases. Adverse outcome developed in 15 out of 23 cases which amounted to 65% of FNCLCC grade 2 or 3 leiomyosarcoma of the urinary bladder in comparison with zero out of two (0%) FNCLCC grade 1 tumours (p=0.15). Adverse effect developed in 15 of 23 (25%) NCI grade 2 or 3 leiomyosarcoma of the urinary bladder in comparison with zero out of two (0%) NCI grade 1 sarcomas (p=0.17) and in 13 out of 20 (65%) Mayo high-grade leiomyosarcomas of the urinary bladder in comparison with two out of five which amounted to 40% of low-grade lesions. All the results were found not to be statistically significant

## Lindberg et al. [12] made the ensuing conclusions

- Leiomyosarcoma of the urinary bladder does tend to occur in older adults of either sex and it is typified by aggressive biological behaviour and tends to be associated adverse outcome in more than 60% of cases
- Certain advantages of the FNCLCC system of grading of tumours could support its more widespread adoption for future studies

Yamada et al. [13] reported an 83-year-old man who had presented with visible haematuria. He had computed tomography (CT) scan of abdomen and pelvis which showed a large tumour within his urinary bladder that measured 4 cm x 3 cm (figure 5 a) as well as he had magnetic resonance imaging (MRI) scan which showed extra-vesical invasion and pelvic wall invasion by the tumours with right hydronephrosis (figure 5 b). He had CT scan of thorax and isotope bone scan which did not show any evidence of distant visceral metastases and based upon the radiology imaging features of the tumour the tumour was staged as T4N0M0. He underwent Trans-Urethral Resection of Bladder Tumour (TURBT) for histopathology diagnosis 18 days after his admission. He did not receive any adjuvant treatment. At 15 days pursuant to his undergoing TURBT, his clinical status had worsened with symptoms of dyspnoea. He had CT scan which showed multiple metastatic lesions within the lung, liver and retroperitoneal lymph node enlargement. He died 2 days later and an autopsy was undertaken. The autopsy showed gross multiple metastatic lesions within lungs, pleura, diaphragm, liver, and retroperitoneal lymph node enlargement. A final histopathology diagnosis of leiomyosarcoma was established based upon the immunohistochemistry staining features of the tumour which showed that the tumour had exhibited positive staining for

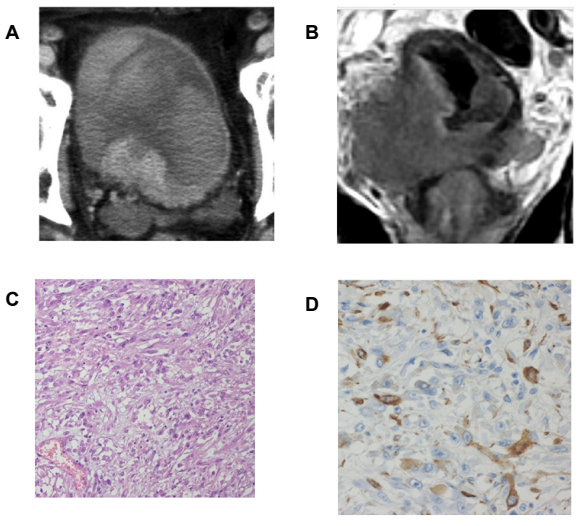


**Figure 5:**

a) Computed tomography shows a large bladder tumour measuring 4 cm x 3 cm and right hydronephrosis [13]

b) Magnetic resonance imaging shows extravesical invasion of the tumours [13]

c) Haematoxylin-eosin stain shows leiomyosarcoma of the bladder tumour [13]

d) : Immunohistochemical staining of the bladder tumour is positive for alpha-smooth muscle actin [13]

alpha smooth muscle actin, and vimentin, and negative staining for cytokeratin (Figure 5 c,d).

### Yamada et al. [13] stated the following:

- Primary leiomyosarcoma of the urinary bladder is relatively rare and few large case series of leiomyosarcoma of the urinary bladder reported in the literature
- Non-epithelial urinary bladder tumours do account for less than 5% of carcinomas of the urinary bladder overall and leiomyosarcomas of the urinary bladder do comprise 0.1% of all urinary bladder cancers [14]
- Rosser et al. [15] reported 36 cases of leiomyosarcoma of the urinary bladder and Lee et al. [16] reported 20 cases of leiomyosarcoma of the urinary bladder
- Rosser et al. [15] had iterated that the commonest presentation of leiomyosarcoma of the urinary bladder is haematuria which does account for 81% of presentations followed by pollakiuria which occurs in 28% of cases and dysuria which does occur in 19% of cases
- Their patient was referred to them because of visible haematuria but he was asymptomatic until his tumour had reached an advanced stage and had become locally invasive
- It has been stated that primary leiomyosarcoma of the urinary bladder had always been regarded as very aggressive tumours which would require aggressive surgical excision, and that radical cystectomy with wide resection margins should be undertaken whenever possible [1,17]
- Neo-adjuvant and adjuvant therapies had been utilized in 21% and 16% of patients at the MD Anderson centre respectively, and both treatment options did result in a doubling of disease-specific survival. Nevertheless, the result was not statistically significant which had reflected the small number in each group. Likewise, it was difficult to compute the impact of neo-adjuvant and adjuvant therapy upon the quality of life [16,17]
- Patients who have tumour positive surgical margins should be considered as candidates to undergo radiotherapy
- Patients who develop local recurrence or metastatic urinary bladder should undergo treatment by means of systemic chemotherapy (for example by utilization of the sarcoma chemotherapy protocol with the use of doxorubicin, ifosfamide, cisplatin, and docetaxel, and / or radiotherapy [16,17]
- Contemporary studies had indicated that these types of tumours could have a better outcome than was previously believed and that they do show remarkable 5-year-disease-specific survival rates of 59% to 62% [15,17]
- Some studies had indicated that patients who have leiomyosarcoma of the urinary bladder with low mitotic activity of less than 5 mitoses per 10 high-power fields and mild-to-moderate nuclear atypia have a good outcome, on the other hand, those patients who have leiomyosarcomas of the bladder with high mitotic activity of equal to or greater than 5 mitoses per 10 high-power field have a worse outcome [16]
- No statistically significantly relevant evidence regarding therapeutic outcome of leiomyosarcomas of the urinary bladder could be found in the literature. Treatment of patients who have leiomyosarcoma of the urinary bladder should be tailored upon case by case basis
- With regard to cases of leiomyosarcoma of the urinary bladder if feasible, aggressive surgical excision of the tumour and adjuvant therapy should be undertaken as early as possible

Gupta et al. [18] reported a 22-year-old lady who had presented with a 6-month history of dysuria and lower urinary tract symptoms. Her general and systematic examinations were normal. The results of her routine haematology and biochemistry blood tests were within normal range. She had ultrasound scan of her abdomen, renal tract and pelvis which showed a single urinary bladder mass that measured 2.9 cm x 2.7 cm x 3 cm near the neck of her urinary bladder. Her urine cytology examination was negative for malignant cells. She had contrast-enhanced CT scan which revealed a well-defined, homogeneous, contrast-enhancing endophytic soft tissue mass lesion near the neck of the urinary bladder (figure 6). She underwent Trans-Urethral Resection of the Bladder Tumour (TURBT). Histopathology examination of the specimen showed a tumour which had consisted proliferated elongated or spindled-shaped cells that had been arranged in bundles or fascicles or interlacing pattern (Figure 7). The cells had ovoid nuclei and fair amounts of lightly cytoplasm. There were 3 to 4 mitoses per 10 high-power fields. Immunohistochemistry staining studies of the tumour did illustrate that the entire tumour specimen had exhibited strongly positive staining for muscle actin, and strongly positive staining for desmin, as well as negative staining for pancytokeratin (Figure 8). Based upon the histopathology and immunohistochemistry staining features of the tumour a diagnosis low-grade leiomyosarcoma was made. She underwent adjuvant chemotherapy and radiotherapy. She received 6 cycles of ifosfamide and doxorubicin and she also had external beam fractionated radiotherapy. At her 12-month follow-up she was well with no evidence of local recurrence or distant metastasis based upon her clinical assessment and radiology imaging assessment.

Ribeiro et al. [19] reported a 31-year-old lady who had presented with progressive symptoms of urinary irritability which was associated with visible haematuria and a history of recurrent urinary tract infections. She had ultrasound scan and CT scan of abdomen and pelvis which showed a large sized mass which had occupied a large

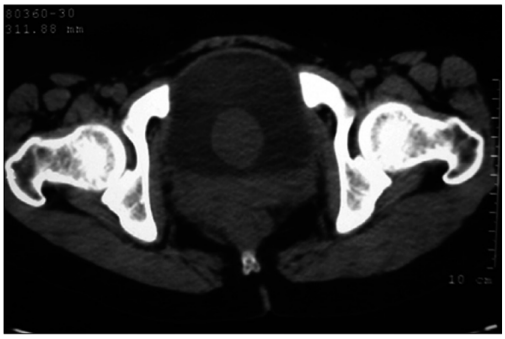

**Figure 6:** Contrast computed tomography scan of the pelvis showing the bladder mass near the bladder neck [18]

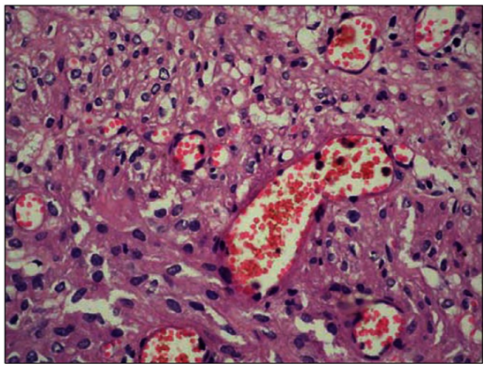

**Figure 7:** Microphotograph showing elongated or spindle-shaped cells disposed in bundles or fascicles or interlacing pattern (H&E, x 200) [18]

portion of her urinary bladder. She had cystoscopy and biopsy of the urinary bladder tumour and pathology examination of the specimen showed features consistent with a low-grade leiomyosarcoma. She underwent pelvic exenteration and urinary diversion by means of Bricker ileal conduit construction. There was complete excision of the tumour. Microscopic examination of the specimen showed features consistent with a stage II leiomyosarcoma which had comprised of muscle bundles, the lamina propria, and the mucosae. There was absence of vascular invasion by the tumour. She did not receive any adjuvant therapy. At her 12-month post-operative follow-up she was well with no evidence of recurrence.

Sato et al. [20] reported a 49-year-old lady who presented with a 12-month history of recurrent urinary tract infections and dysuria. She had CT scan which showed a heterogeneously-enhanced 4-cm mass which had involved her urinary bladder neck and anterior wall of her urinary bladder but no evidence of metastasis (Figure 9). She underwent Trans-Urethral Resection of the Urinary Bladder Tumour (TURBT) and pathology examination of the specimen confirmed leiomyosarcoma of the urinary bladder. There were 3 mitotic figures per high-power field. Immunohistochemistry staining studies showed that the tumour had exhibited positive staining for: alpha smooth muscle actin, and desmin, and focally positive staining for h-caldesmon, and calponin but the tumour was negatively stained for myogenin, S-100 protein, p40, and CK903, CDK4, and MDM2. Her symptoms resolved post-operatively. She underwent repeat TURBT 70 days after her first TURBT. At her 18-month follow-up she had remained free of local recurrence and metastasis. Her follow-up CT scan and cystoscopy were normal but she refused further follow-up so her long-term outcome could not be known.

Anastasiou et al. [21] reported a 43-year-old man who had presented with painless visible haematuria. He underwent cystoscopy and trans-urethral resection of a tumour which was seen at cystoscopy that resulted in complete resection of a single tumour. Pathology examination of the tumour showed features consistent with the diagnosis of leiomyosarcoma of the urinary bladder. The rest of the bladder was normal. Based upon his age and aggressiveness of the tumour a discussion was held with the patient regarding the various treatment options. It was decided that he should be managed conservatively / expectantly with aggressive follow-up. At his 1 year follow-up he was well with evidence of local recurrence or metastasis. Anastasiou et al. [21] made the ensuing statements:

- Leiomyosarcoma of the urinary bladder tends to be an aggressive tumour and less than 200 cases of leiomyosarcoma of the urinary bladder have been reported
- The treatment of primary leiomyosarcoma of the urinary bladder has been controversial even though in majority of cases an aggressive surgical treatment has been preferred and usually radical cystectomy has been performed in view of the fact that radical cystectomy had been considered to be associated with a superior disease-specific survival

A lesson learnt from this case report is that perhaps the short-term and intermediate-term outcome of some superficial leiomyosarcomas of the urinary bladder that have been treated by trans-urethral resection of bladder tumour alone may be good but the long-term outcome would not be known until cases that have been treated by trans-urethral resection of bladder tumour alone should be reported with long-term follow-up data and that it would be argued that there is need for all cases of leiomyosarcoma of the bladder that are treated by trans-urethral resection of bladder tumour alone should be entered into a global multi-centre trial so that biological behaviour of the tumour would be studied further

Bakaris et al. [22] reported a 44-year-old woman who had presented with visible haematuria. She had a CT scan of the pelvis which showed a urinary bladder mass along the left anterior-lateral wall. She underwent trans-urethral resection of the bladder tumour and pathology examination of the tumour showed features consistent with leiomyosarcoma. She underwent radical cystectomy and ileal

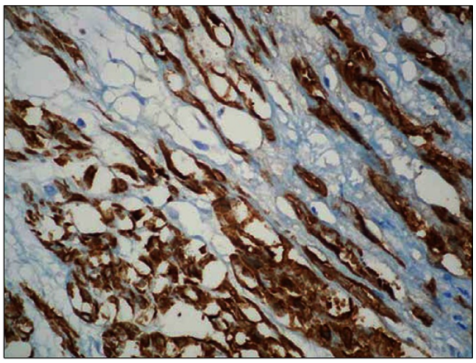

**Figure 8:** Immunohistochemical staining revealed the whole specimen to be strongly positive for smooth muscle actin and desmin (x400) [18]

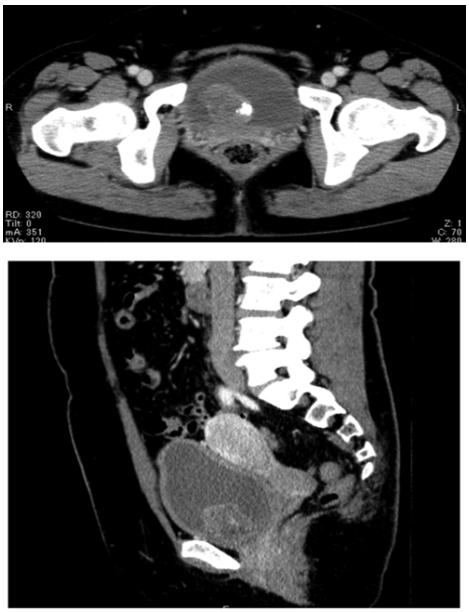

**Figure 9:** CT scan showing heterogeneously enhanced 4 cm mass involving the bladder neck and anterior wall. No enlarged lymph node was detected [20]

conduit construction. Macroscopic examination of the specimen showed an 11 cm x 6 cm x 5 cm solid mass on the left anterior-lateral wall and two 1 cm papillary tumours with different localization on the right and left lateral walls of the bladder. Pathology examination of the tumour showed that the masses were high-grade leiomyosarcoma and urothelial carcinoma. Bakaris et al. [22] stated the following:

- Due to the differences in the histogenesis and outcome, such cases should be differentiated from cases of carcinosarcoma of the urinary bladder
- The contemporaneous synchronous occurrence of urothelial carcinoma and sarcoma of the urinary bladder as two separate primary tumours is extremely rare
- To their knowledge seven cases of co-existing sarcoma and transitional cell carcinoma of the urinary bladder had been reported in the literature

Zhong et al. [23] reported a 31-year-old man who had developed leiomyosarcoma of the urinary bladder. He did not have any history of radiotherapy, systemic chemotherapy, or other significant event with the exception of a 5-year history of Ketamine abuse. The tumour was found on the left wall of the urinary bladder and pathology examination of the tumour which was resected by means of trans-

urethral resection of bladder tumour showed features consistent with the diagnosis of leiomyosarcoma of the bladder. A partial cystectomy was undertaken. Zhong et al. [23] iterated that in view of the fact that there had not been any reports of an association between leiomyosarcoma of the urinary bladder and chronic ketamine abuse, they would only speculate that chronic ketamine abuse could be a factor in the development of leiomyosarcoma of the bladder which is a rare malignancy.

## Tanquay et al. [24] Reported Two Cases of Leiomyosarcoma of the Urinary Bladder as Follows

### Case 1

A 53-year-old man with Wegener's granulomatosis who was treated for 6 years with cyclophosphamide did present with painless haematuria. He underwent initial cystoscopy and biopsy of a bladder tumour and pathology examination of the specimen showed a malignant spindle cell tumour. He underwent radical cystoprostatectomy and pathology examination of the specimen showed leiomyosarcoma of the urinary bladder.

### Case 2

A 21-year-old man who had received cyclophosphamide in early infancy for bilateral retinoblastoma had presented with haematuria. He underwent cystoscopy and trans-urethral resection of bladder tumour and pathology examination of the tumour confirmed leiomyosarcoma of the bladder. He underwent partial cystectomy two months subsequently.

The two cases have associated the use of cyclophosphamide with the subsequent development of leiomyosarcoma which clinicians and Urologists should have a high index of suspicion for.

Al Zahrani et al. [25] reported a 16-year-old female who had been diagnosed at the age of 6 months as having bilateral retinoblastoma who had received cyclophosphamide after surgical enucleation of the tumours. Pathology examination of a urinary bladder tumour which she developed was found to be that of leiomyosarcoma of the urinary bladder.

Xu et al. [26] reported a 31-year-old female who was treated by means of partial cystectomy for leiomyosarcoma of the urinary bladder. They reported that fortunately at her 7-year follow-up she was found to have good quality of life and no evidence of local recurrence or distant metastasis. Xu et al. [26] stated that they had found that partial cystectomy could be an acceptable option for the treatment of leiomyosarcoma in the low MSKCC (Memorial Sloan-Kettering Cancer Center) Stage.

Brucker et al. [27] reported the case of a twin who had bilateral retinoblastoma who developed leiomyosarcoma of the urinary bladder at the age of 17 years and again at the age of 39 years. Brucker et al. [27] reported that that at the age of 17 years, she was diagnosed with leiomyosarcoma of the urinary bladder after she had presented with recurrent urinary tract infections, haematuria and dysuria. She was treated by partial cystectomy. After a 12-years disease free interval, she was diagnosed as having a second leiomyosarcoma of the bladder. Brucker et al. [27] stated that their reported case does support the relationship between the genetic form of retinoblastoma and leiomyosarcoma and does illustrate the necessity for extensive follow-up and well-defined treatment of secondary neoplasms.

Nelius et al. [28] reported a case of leiomyosarcoma of the bladder that initially presented with urinary tract infection and lower abdominal pain. A life threatening episode of visible haematuria led the clinicians to finally diagnose leiomyosarcoma of the urinary bladder (Figure 10,11).

Doddamani et al. [29] reported a 30-year-old man who had presented with painless visible haematuria with clots of 2-months duration. When he was 3 years old he was diagnosed as having bilateral retinoblastoma in his eyes. His parents refused the request that he should undergo surgical enucleation of the tumours so he only underwent 18 cycles of radiotherapy his bilateral orbits. He was found on examination to have enlarged inguinal lymph nodes which were biopsied but pathology examination of the specimen showed inflammation only. He had ultrasound scan and CT urogram which showed a large mass that measured 6 cm x 6 cm on the right anterior-lateral wall of his urinary bladder. The upper renal tract was normal. He had cystoscopy which showed a large nodular lesion on the right anterior-lateral wall which was biopsied by trans-urethral resection. Pathology examination showed a high-grade sarcoma with only spindled-cells and no evidence of epithelial cells was seen; hence the possible differential diagnoses that were raised included: (a) leiomyosarcoma, (b) malignant peripheral nerve sheath tumour, and (c) sarcomatoid variant of urothelial carcinoma (carcinosarcoma) (Figure 12). Upon immunohistochemistry staining studies, the tumour exhibited strongly positive staining for cytoplasmic smooth muscle actin (Figure 13) and cytoplasmic vimentin, and focally positive staining for cytoplasmic desmin as well as cytokeratin which had been indicative of leiomyosarcoma. Immunohistochemistry staining of the tumour exhibited negative staining for epithelial membrane antigen (EMA) and S-100 which had excluded carcinosarcoma and peripheral nerve sheath tumour respectively and based upon the features of the tumour a diagnosis of leiomyosarcoma of the urinary bladder was confirmed. He refused to undergo genetic testing as well as to undergo radical surgery and he was referred to the oncologist for further management. He was lost to follow-up; therefore his long-term follow-up outcome was not available. Doddamani et al. [29] stated the ensuing:

- Retinoblastoma patients tend to have excellent survival pursuant primary treatment by means of enucleation, radiotherapy, or chemotherapy
- Patients who undergo chemotherapy or radiotherapy could develop second malignancies many years subsequently in view of DNA damage or genetic mutations
- The development of leiomyosarcoma of the urinary bladder is one of the subsequent possible malignancies that can ensue radiotherapy or chemotherapy but majority of cases reported had ensued chemotherapy
- Their reported case of leiomyosarcoma of the urinary bladder was the third to be reported following utilization of isolated radiotherapy

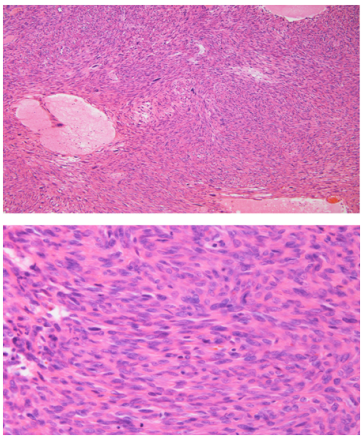

**Figure 10:** The tumour was composed of a proliferation of interlacing fascicles of atypical spindle shaped cells, accompanied by bizarre nuclei (1-12/HPF). Mitotic figures were frequently observed (3 / HPF in hot spot) [20]

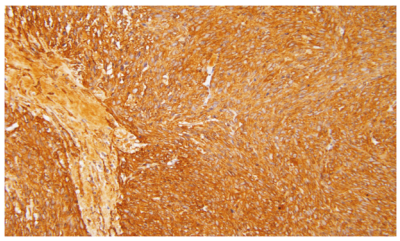

**Figure 11:** Tumor cells were positive for alpha-SMA [20]

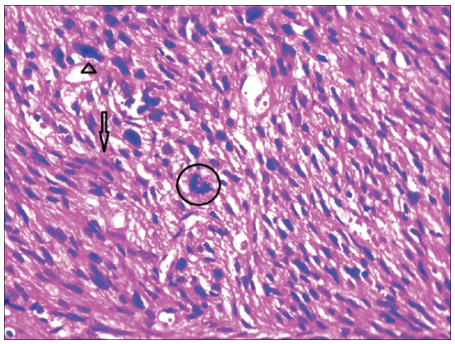

**Figure 12:** Haematoxylin and eosin staining x 100: Showing bundles and fascicles of markedly pleomorphic spindly cells (marked by an arrow), bizarre cells (marked by an arrow head), and atypical mitosis (marked by a circle) [29]

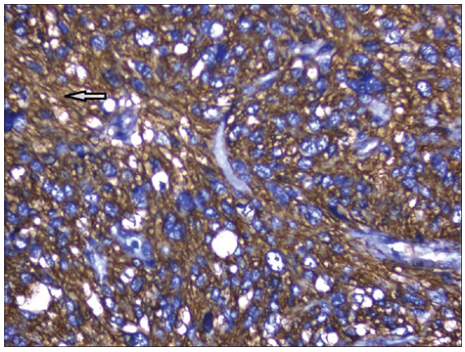

**Figure 13:** Immunohistochemistry (magnification x 100) showing strong smooth muscle actin cytoplasmic positivity [29]

## Conclusions

Less than 200 cases of LUB have been reported and hence a high index of suspicion would be required to diagnose the disease.

LUB may manifest de novo, or it may ensued treatment for retinoblastoma, radiotherapy treatment or chemotherapy many years later and an association with chronic ketamine use has been reported.

LUB has been regarded as an aggressive tumour and hence radical surgery plus adjuvant chemotherapy has been generally used previously and is most commonly used these days.

Recently partial cystectomy alone or trans-urethral resection of bladder tumour alone has been reported to be associated with good short-term and medium term follow-up case reports.

A global multi-centre trial would be required to streamline the treatment options and the indications for utilization of specific treatment options for LUB.

New chemotherapy medicaments should be developed that would more effectively destroy high-grade and high-staged LUBs.

## Acknowledgements

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