

LEIOMYOSARCOMA OF THE URINARY BLADDER: A CASE REPORT

Leiomiossarcoma de bexiga: um relato de caso

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ABSTRACT

Objectives: To describe a case of urinary bladder leiomyosarcoma (LMS), a rare malignant mesenchymal tumor. Less than 1% of primary bladder tumors are LMS, and only 200 cases have been reported in the literature, since the first description by Gusshaver, a century ago. **Methods:** A radical cystoprostatectomy, using Bricker reconstruction and rectosigmoidectomy was performed. In the intraoperative period, an extensive and hypervascularized mass was found, involving the abdominal wall and compressing the ureters and iliac arteries bilaterally. Resection of the extensive bladder and prostate lesion was performed in monobloc. The resected material was sent to anatomopathological analysis, which characterized a pleomorphic sarcoma fusiform cell type with necrosis, measuring 30x25x13 cm. After immunohistochemistry, a grade I (stage II in the TNM classification) leiomyosarcoma was evidenced. **Results:** The patient remained hospitalized for 15 days in the Intensive Care Unit (ICU) after acute renal failure after surgery, requiring dialysis. He had a good evolution in the postoperative period, despite maintaining dialysis for chronic renal failure. On the 22nd postoperative day, he was constipated, but with a functioning Bricker and with no particularities in the surgical wound. **Conclusion:** Although the therapeutic approach to bladder LMS is not a consensus in the literature, a more radical treatment can be justified in the situation of an aggressive tumor, which often has a poor prognosis.

Keywords: bladder neoplasm, cystectomy, neobladder, leiomyosarcoma

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INTRODUCTION

Leiomyosarcoma (LMS) of the urinary bladder is a malignant mesenchymal tumor that originates from smooth muscle cells of the bladder. LMS of the urinary bladder is rare – less than 1% of all primary bladder tumors¹. They are highly aggressive tumors that have been associated with substantial morbidity and mortality, which confers poor prognosis to these tumors if they are not treated early. There have been about 200 cases reported in the literature since Gushaver first described it a century ago².

The following case report was performed due to the small incidence of LMS in the urinary bladder and by the surgical approach used in the treatment, considering there is no consensus in the literature about the therapeutic management of this kind of tumor.

CASE REPORT

N.C., 43 years-old, male, white, Brazilian, referred to the Oncology Service of Hospital do Rocio due to the presence of a pelvic mass associated with abdominal pain, weak urine stream, chronic kidney failure, and hematochezia. The patient had undergone transurethral resection (TUR) six years before due to vesical leiomyosarcoma, in another service and had not continued his follow-up. He had not performed adjuvant radiation therapy back then. He had undergone a new TUR in another service about two months before the appointment in our service. The histopathological examination of the resected lesion in the bladder neck showed no histological abnormalities that could suggest malignancy.

The patient had no family history of cancer. He used to work as a metallurgist and reported exposure to heavy metals, with a history of alcoholism, smoking and high blood pressure. Previous colonoscopies showed voluminous hemorrhoids.

During the appointment, the patient was alert and oriented, appeared moderately ill, presented a mild conjunctival pallor, but no scleral icterus. Physical examination showed a globose and soft abdomen, presenting a pelvic mass of around 20 cm, which was palpable at the umbilical scar. Lab exams evidenced creatinine of 4.31 mg/dL (reference value: 1.5 mg/L).

The pelvic and upper abdominal magnetic resonance imaging (MRI)

previously performed in another service showed an expansive and lobulated lesion, with partially defined limits, located in the pelvic cavity with its center in the anterior extraperitoneal space, without a cleavage plane with the prostate and compressing the bladder, reducing its capacity. It extended upwards to the upper abdomen by bulging out anteriorly and arching the rectus abdominis muscles, but without signs of infiltration. Posteriorly, it extended to the rectum bilaterally, compressing the mesorectal fascia. Laterally, it occupied the obturator region and surrounded the peripheral region of the prostate and seminal vesicles. Was asymmetric and presented a larger volume to the left of the midline, compressing the left external iliac vein. The lesion was hypointense in T1 and showed heterogeneous signal characteristics and contrast enhancement in T2, presenting multiple nonenhancing hypointense areas in its interior, which are compatible with necrosis. The lesion measured around 23.3 x 17.8 x 13.2 mm. There was no compression of the pyelocalyceal system.

Contrast-enhanced computed tomography (CT) of the abdomen was performed around one month and a half after the abdomen and pelvis MRI, showing a large pelvic lesion invading the bladder, prostate and rectum with compression of the pyelocalyceal system that measured 14x20 cm. Contrast-enhanced CT of the chest was within the normality parameters.

The proposed surgical treatment comprised a radical cystoprostatectomy and reconstruction with the creation of an ileal conduit. In the intraoperative period, we found an extensive hypervascularized mass in the bladder, involving the abdominal wall and compressing the ureters and iliac arteries bilaterally. Monobloc resection of the lesion was performed together with segmental resection of the rectus abdominis muscle and primary closure without the need of reconstruction using meshes and/or patches. The compression of ureters was extrinsic, i.e. they were not invaded as the iliac arteries, therefore it was not necessary to use grafts for reconstruction. Lymphadenectomy was not performed. The ureters presented proper length for the ileal conduit construction, and segment of around 20 cm of

terminal ileum was used for this purpose. The ureters were catheterized with a 16 FR nasogastric tube, which was exteriorized through the stoma and removed after 21 days.

The surgical procedure lasted around two hours with an estimated bleeding volume of 1 L, needing transfusion of one concentrate of red blood cells. The use of vasoactive drugs was not necessary.

The histopathological analysis revealed a pleomorphic sarcoma fusiform cell type with necrosis, measuring 30x25x13 cm and weighing 4.4 kg that was infiltrating the vesical wall externally. The mitotic index was seven mitoses per 20 high power fields. The prostate, the seminal vesicles and the vas deferens were free of tumor cells. The material was sent for immunohistochemical analysis that showed grade 1 LMS, stage II, in the TNM staging classification.

The patient remained hospitalized for 15 days in the Intensive Care Unit due to the development of acute-on-chronic kidney disease after surgery, which required dialysis (Clavien-Dindo IVa complication, according to the classification of surgical complications by Dindo *et al.*)³. Improved in the postoperative period, despite maintaining the chronic kidney disease requiring dialysis. By the 22nd postoperative day, the patient was still constipated, but presented functioning Bricker and no particularities in the operatory wound.

Was then referred to chemotherapy and adjuvant radiation therapy, which began three months after surgery. The chemotherapy plan was three cycles of 75 mg/m² cisplatin and 175 mg/m² paclitaxel.

Around seven months and a half after surgery, a large incisional hernia was found (Clavien-Dindo IIIa complication, according to the classification of surgical complications by Dindo *et al.*)³ and, therefore, expectant therapeutic management was chosen.

DISCUSSION

LMS is a malignant mesenchymal tumor that presents controversies regarding the epidemiological profile of its patients. In a study carried out by Yamada *et al.*, this tumor is more prevalent in the male gender (56% vs 44%), in middle-aged patients or in the elderly, with a mean age at diagnosis of 65^{1,4,5}. However,

in a review carried out by Ribeiro *et al.*, similar to the study by Yun Fei Xu *et al.*, LMS of the urinary bladder presents a higher incidence in women of reproductive age, which may suggest the hypothesis that hormones can have a role in the tumor pathophysiology^{6,7}. A series of cases by Rodriguez *et al.* describes that the incidence of LMS in the urinary bladder is around 0.23 cases to every 1 million residents, thus reinforcing its rarity⁸.

Several risk factors have been suggested for the development of LMS, the main ones include mutation of the retinoblastoma gene, systemic chemotherapy with cyclophosphamide and pelvic radiation therapy^{2,9}.

Common clinical manifestations of LMS include dysuria, massive hematuria and/or abdominal pain. Hematuria is usually painless and is the most common symptom (affects around 80% of patients)², followed by urinary frequency and dysuria, abdominal mass, and suprapubic discomfort⁶. There may be obstructive symptoms, depending on the size of the tumor^{5,10,11}. The most common locations of the LMS of the urinary bladder are the dome (50%) and the lateral walls (25%), and it is relatively rare in the vesical trigone. Most of these tumors are restricted to the submucosa, and a few of them affect the muscularis propria, extend beyond the vesical wall or are multifocal⁷.

Less than 15% of LMS are identified in the early stages (T1)¹¹. The diagnosis usually occurs in the advanced stage: 50% of the patients already present a locally advanced disease or distant metastases. This happens because more than 60% of the tumors show aggressive characteristics and usually metastasize early⁶. The most common distant metastases sites are lung, liver, bones and brain⁷. Prognosis in these cases is very poor, especially in areas with poorly differentiated histology and previous non-surgical treatment⁸. In an analysis of 35 patients with LMS of the urinary bladder by Rosser *et al.*, the overall survival rate in five years was 62%¹⁰. Another study carried out by Rodríguez *et al.* showed a mean overall survival rate of 46 months, with a 47% survival rate in five years, which dropped to 35% in ten years⁸.

TUR is essential for the diagnosis and staging of bladder tumors, considering

it allows the determination of the histological type, lesion depth, and histological grade. In addition, it is curative for tumors invading the lamina propria (sub-epithelial connective tissue), which correspond to T1a stage tumors¹².

There is no consensus about the treatment for LMS, but aggressive surgery has been the most commonly employed treatment. The gold-standard surgical technique involves en bloc resection of the bladder together with the prostate and seminal vesicles in men. In women, bloc resection of the bladder with the uterus, uterine cervix, and vaginal vault in women, associated with bilateral pelvic lymphadenectomy. The removal of the urachus and peri-vesical fat that involves the upper vesical dome is also recommended. Patients with locally advanced disease may benefit from neoadjuvant chemotherapy^{2,7}. The counterpoint of the aggressive surgical approach resides in the probable loss of vesical function and subsequent loss of quality of life⁶.

Radical cystectomy is the surgical procedure of choice for treating invasive tumors of the bladder. The most common indication for this procedure is a muscle-invasive bladder tumor (T2 or more) without evidence of distant metastases¹³. In general, this includes resection of margins free of tumor invasion measuring around two to three cm and is followed by adjuvant radiation therapy and chemotherapy¹⁴.

It is also necessary to reconstruct the bladder for maintenance of urinary function. Reconstructions can be classified in internal or external and continent or incontinent. The two main techniques

include the Bricker ileal conduit and Studer neobladder. Studer neobladder technique involves the creation of a continent orthotopic bladder using a portion of the ileum and provides more quality of life for the patient, considering it is more similar to the regular micturition physiology¹⁵. Bricker ileal conduit technique, on the other hand, uses a segment of the ileum, to which ureters are anastomosed to create a urinary diversion to an incontinent stoma¹⁶. During preoperative planning, the reconstruction technique (Bricker or Studer) to be performed is chosen, which depends on factors such as patient's age, clinical condition, oncological condition, preoperative continence, adjuvant treatment need, patient and surgeon's preference¹³. However, the choice may change according to the intraoperative conditions.

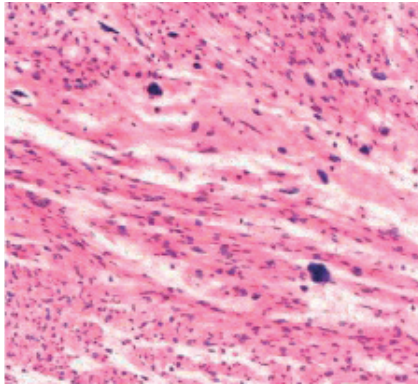
Partial cystectomy is considered an alternative procedure to radical cystectomy, given it presents benefits such as the preservation of the bladder's function and lower morbidity to the patient¹⁴. It is generally indicated for young patients with small-sized tumors. To be eligible for partial cystectomy, the patient must have a T1 (tumor involving the lamina propria) or T2 (tumor invading the muscularis propria) tumor, comprised of small masses (smaller than four centimeters) at stages one or two in the Memorial Sloan-Kettering Staging System for Soft Tissue Sarcomas (reproduced in Table 1)¹⁷. Moreover, these tumors shall not be located on the neck or trigone of the bladder⁷.

Partial cystectomy has been associated with higher rates of tumoral recur-

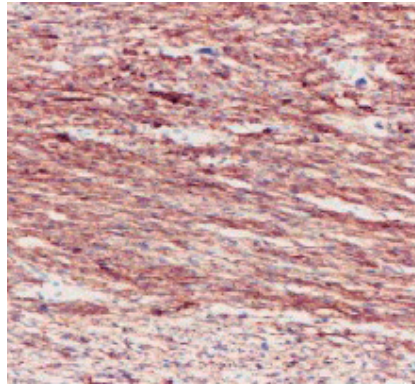
TABLE 1 - Memorial Sloan-Kettering Staging System for Soft Tissue Sarcomas.

PROGNOSIS	FAVORABLE	UNFAVORABLE
Size (cm)	Smaller than five centimeters	Bigger than five centimeters
Invasion depth	Superficial	Profound
Histological grade	Low	High

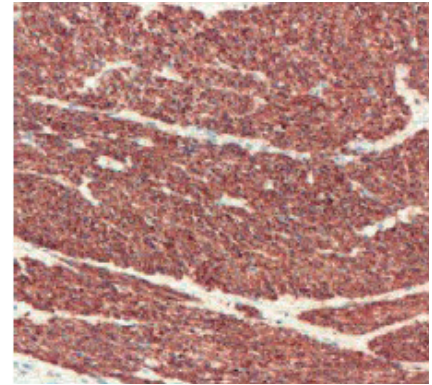
Stage 0: tumors that present three favorable signs; stage 1: two favorable signs; stage 2: one unfavorable sign or one favorable sign and two unfavorable signs; stage 3: three unfavorable signs; stage 4: presence of distant metastases. Source: modified from Aljabab, A, S. *et al.*¹⁷



CELLS DISPOSED IN FASCICLES (A)



DESMIN (B)



CALDESMON EXPRESSION (C)

The images above are part of the medical record of the case report. Pleomorphic sarcoma fusiform cell type constituted by cells disposed in fascicles and showing moderate nuclear pleomorphism (A). The mitotic index is 6 per 10 high-power fields. Immunohistochemistry was positive for desmin (B), Caldesmon (C) and 1A4 expression.

TABLE 2 - Transcription of the conclusion of anatomopathological report

ANTIBODIES	RESULTS
Desmin (intermediate muscle cell filament)	Positive
Caldesmon	Positive
Smooth muscle actin	Positive
Protein s-100	Negative
cd117 - gene kit product	Negative
mdm2	Negative

rence that varies between 40 and 80%, based on a series of case reports. However, overall survival is equivalent when compared to radical cystectomy¹². Strander *et al.*¹⁸ and Cumplido *et al.*¹⁹ reported that adjuvant radiation therapy with or without associated adjuvant chemotherapy after partial cystectomy is capable of improving the LMS of the urinary bladder prognosis.

The overall local recurrence rates vary between 16 and 34% in 38 months, and most of them occur in the pelvis^{2,6}. In this scenario, the treatment is based on systemic chemotherapy, associated or not with external pelvic radiation therapy².

Patients with a locally advanced disease may benefit from neoadjuvant

chemotherapy, and the main drugs employed include doxorubicin, ifosfamide, cisplatin, adriamycin, and vincristine¹².

The best prognostic factor is the presence of free surgical margins. Other favorable prognostic factors, based on the study carried out at the Memorial Sloan-Kettering Cancer Center, include tumor size < five centimeters, low histological grade, and bladder or para-testicular tumor location^{2,17,20}.

Strict follow-up with CT of the abdomen and pelvis, chest X-rays and cystoscopy (in cases where the patient underwent partial cystectomy) are very important, especially in the first postoperative year, in order to early diagnose tumoral recurrences and distant metastases

early^{7,14}. However, one of the limitations of this study was the impossibility of including the patient's preoperative abdominal CT due to internal problems of the service where the patient was operated.

CONCLUSION

Although the LMS of the urinary bladder therapeutic approach is not a consensus in the literature, choosing an aggressive treatment modality may be justifiable, because this tumor is aggressive and has a poor prognosis. Nonetheless, less aggressive modalities are becoming more viable, considering they can improve patients' quality of life with the same survival rate in comparison with a more aggressive treatment. Therefore, LMS of the urinary bladder is a rare tumor, and long-term studies are required in order to compare the efficacy of the surgical resection modalities and the benefit of adjuvant therapies in its treatment.

DISCLOSURES

There is no conflict of interests to declare.

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