Primary leiomyosarcoma of the ureter: A case report

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Abstract. Malignant tumors of the smooth muscle of the ureter are extremely rare, with ~13 cases of leiomyosarcoma of the ureter being reported to date. A 59-year-old Caucasian woman presented to 'Umberto I' Hospital (Nocera Inferiore, Italy) with acute abdominal pain, predominantly in the right lumbar fossa. The patient exhibited a functional single kidney, due to left renal atrophy for a long-standing stenosis of the pyelo-ureteric joint. With the exception of this condition and hypertension (under medical therapy), the patient was in excellent clinical condition. Furthermore, the patient was not a smoker. Computed tomography indicated a stricture with a peri-ureteral soft tissue mass of 45x52 mm at the middle third of the ureter at the level of common iliac vessels. Laparoscopic excision with safety margin and a right tension free end-to-end anastomosis between the two stumps of the ureter was performed. The diagnosis of leiomyosarcoma of the right ureter was made by pathological examination. Although leiomyosarcoma is rarely noted in the urinary tract, it should be considered in the differential diagnosis of ureteral stricture disease and retroperitoneal tumors.

Introduction

Malignant tumors of the smooth muscle can occur anywhere in the body, particularly with higher frequency in the gastrointestinal tract and in the uterus. In the genitourinary tract, this type of tumor affects the kidney more commonly than the ureter. Leiomyosarcoma of the ureter is an extremely rare neoplasm; in fact, ~95% of ureteral tumors are primitive epithelial tumors, which are generally transitional cell carcinomas. In non-transitional cell carcinoma, the most common type is squamous cell carcinoma (0.7-7%) and adenocarcinoma (1%). Sarcomas are rapidly growing tumors, with the ability to invade the adjacent structures. In the case of leiomyosarcomas, early metastasis to the mesentery, lungs, liver and regional lymph nodes are common (1-4). Generally, these tumors don't cause hematuria due to the lack of involvement of the ureteral mucosa (5,6) while, in 2/3 of cases, the typical sign is the ureteric obstruction. With regard to leiomyosarcoma of the ureter, a limited number of reports have been reported in the literature. The first case of a leiomyosarcoma arising in the genitourinary tract (exactly in the renal pelvis) was reported by Ribbert in 1886 in a 4-year-old girl (7). To the best of our knowledge, from 1886 until 2022, only 13 cases of primary leiomyosarcoma have been described as reported in Table I (8-19). In particular, in the case reported by John E. Kraus, metastasis to the pituitary gland from leiomyosarcoma of the ureter is shown (9). In the present study, the clinical features, histological details, imaging and treatment of ureteral leiomyosarcoma were reported in a 59-year-old female patient; moreover, a systematic review of the literature was performed.

Case report

A 59-year-old Caucasian woman presented to our hospital (Umberto I Hospital in Nocera Inferiore) with an acute pain in the right lumbar fossa. The patient exhibited a functional single kidney, due to left renal atrophy for a long-standing stenosis of the pyeloureteric joint. With the exception of this condition and hypertension (under medical therapy), the patient was in excellent clinical condition (with a history of previous surgery of cholecystectomy); furthermore, she was not a smoker. In the emergency room the functional tests indicated acute renal failure, with an important increase in the creatinine and urea blood levels (creatinine: 3,9 mg/dl; urea: 95 mg/dl). Ultrasound examination indicated moderate right hydronephrosis [transverse diameter (DT) of renal pelvis: 30 mm]. Due to this reason, the patient underwent right

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Table I. PubMed search for previous publications of primary leiomyosarcoma of the ureter in humans from 1886.

First author/s, year	Number of cases	Sex of patient	Ethnicity of patient	Patient age, years	Site of malignancy	(Refs.)
Ribbert, 1886	1	Female	Caucasian	4	Renal pelvis	(7)
Rademaker, 1943	1	Female	Caucasian	59	Ureter	(8)
Rossien and Russel, 1946	1	Female	Caucasian	55	Ureter	(10)
Alznauer, 1955	1	Female	Caucasian	60	Ureter	(11)
Werner *et al*, 1959	1	Female	Caucasian	60	Ureter	(12)
Rushton *et al*, 1983	1	Female	African-American	53	Ureter	(13)
Márquez-Moreno *et al*, 2003	1	Female	Caucasian (Spanish)	38	Ureter (pelvic tract)	(14)
Shirotake *et al*, 2006	1	Female	Caucasian (Japanese)	60	Ureter	(15)
Lv *et al*, 2008	1	Female	Caucasian (Japanese)	Middle aged	Ureter	(16)
Aubert *et al*, 2012	1	Female	Caucasian	57	Ureter	(17)
Aboutaleb *et al*, 2022	1	Male	Pakistani	57	Ureter	(18)
Gan *et al*, 2022	1	Male	Caucasian	59	Ureter	(19)

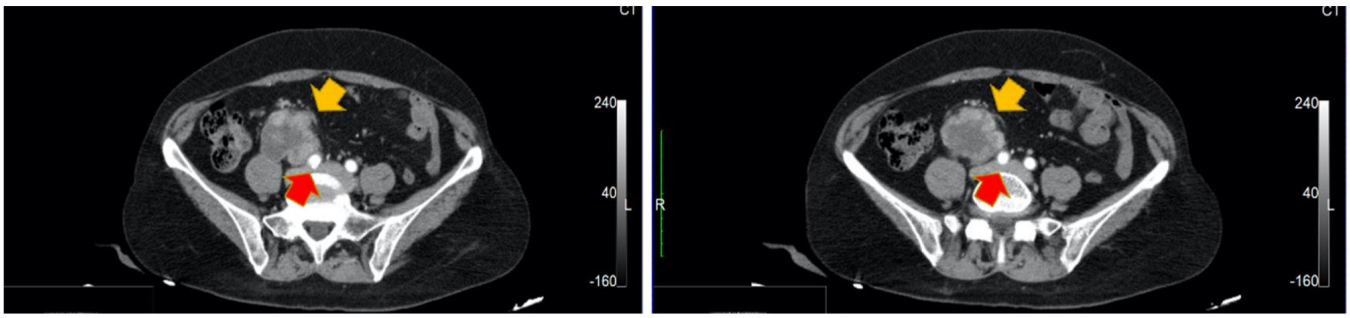

Figure 1. Computed tomography of the abdomen and pelvis. The yellow arrow indicates the leiomyosarcoma of the ureter, while the red arrow indicates the right common iliac artery.

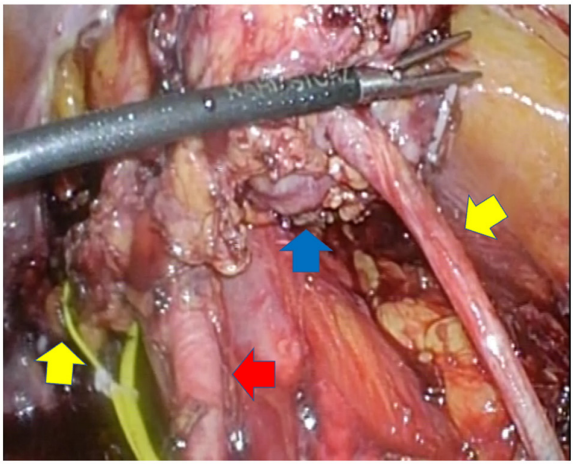

Figure 2. Laparoscopic view of the ureteral mass, compressing the ureter 'ab estrinseco', which was isolated on a yellow vessel loop. Both yellow arrows indicate the ureter (the distal and proximal portions of the ureter, separated by the leiomyosarcoma), while the blue arrow indicates the leiomyosarcoma of the ureter. The red arrow indicates the right common iliac artery.

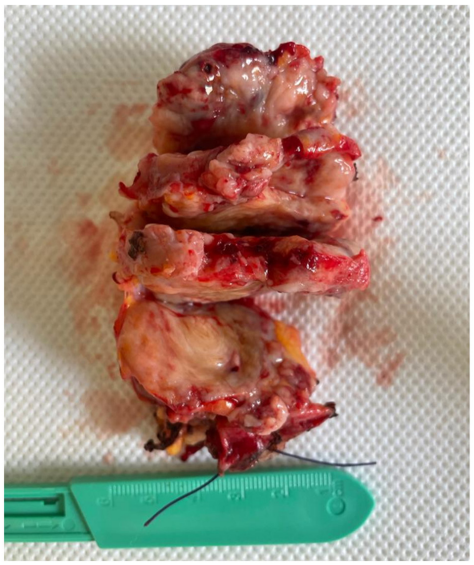

Figure 3. Leiomyosarcoma of the ureter.

percutaneous nephrostomy placement under local anesthesia, in order to improve the kidney function. Computed tomography (CT) of the abdomen and pelvis (Fig. 1) indicated the presence of a voluminous formation, with polylobed margins, with maximum axial dimensions of 45x52 mm (dAP x dT), with a cranio-caudal extension of 46 mm, with a peripheral

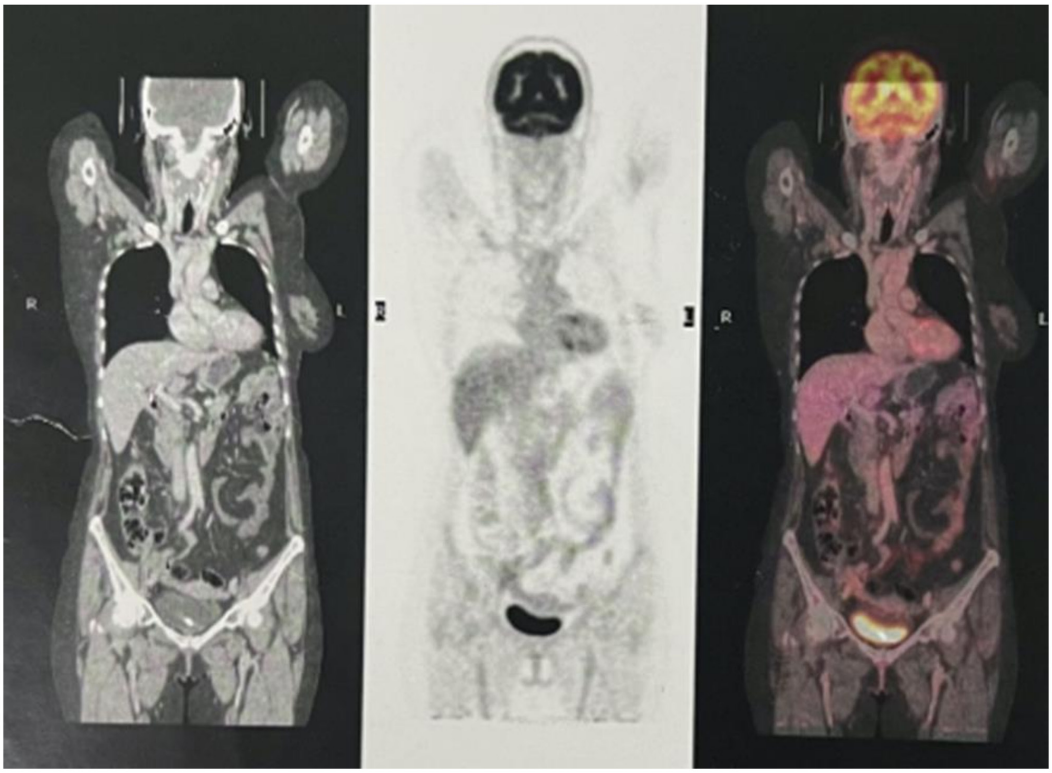

Figure 4. Positron emission tomography-computed tomography scan following diagnosis of leiomyosarcoma, which indicated no evidence of metastasis.

rim featuring intense post-contrastographic impregnation and a hypodense central core, as per necrotic-colliquative phenomena; this formation appeared inseparable from the right ureter in its mid-distal section and indicated a cleavage plane posteriorly with the anterior margin of the psoas muscle and with the right common iliac artery. The appearance of the bladder was normal. Therefore, the diagnosis was performed between the following two pathological entities: retroperitoneal adenomegaly extrinsically compressing the ureter or an urothelial tumor developing extrinsically. Cystoscopy indicated lack of abnormality; diagnostic ureteroscopy revealed a narrowing of the lumen of the ureter, without any mass noted in the ureteric lumen. Ureteric washings were inconclusive due to insufficient number of cells. Therefore, under general anesthesia in the lithotomy position, an arrangement of trocars similar to that used during radical prostatectomy was achieved with transperitoneal access; based on this arrangement, a mass was identified which incorporated the portion of the ureter at the junction with the iliac vessels resembling a 'sleeve'. A blunt dissection released the tumor from the right common iliac vessel (Fig. 2), due to the presence of a definite line of cleavage between the mass and the common right iliac vessel. Therefore, this tumor was resected with a safety margin of 1 cm. Subsequently, an optimal ureteric length was mobilized and a tension free end-to-end anastomosis between the two stumps of the ureter was performed without complication. In the same session of the surgery, a double J stent 7 Fr/24 cm was placed retrogradely. The patient was discharged following 5 days post-surgery and during the recovery she underwent medical therapy with ceftriaxone. At pathologic examination a diagnosis of a high-grade leiomyosarcoma of the right ureteral wall, extensively infiltrating the peri-ureteral tissues and the ureter itself (2017 UICC classification: pT2a) was made (Fig. 3), with a strong staining for smooth muscle actin (SMA) at immunohistochemistry (Actin+, S100-, CK-, CD117-, HMB45-). The cutting margins of the ureter were negative. Following surgery, adjuvant chemotherapy was performed although the positron emission tomography CT scan did not demonstrate distant metastasis (Fig. 4). The patient did not exhibit recurrence at 3, 6 and 9 months following the CT scan examination. After the operation, the renal function was normal and, at the removal of DJ PV stent, the patient didn't suffer from stenosis of uretero-ureteral anastomosis which is a complication of this type of surgery. Almost 2 years have passed since the operation and the follow-up program shows no signs of recovery of the disease.

Discussion

Leiomyosarcoma is a rare and highly malignant tumor, accounting for 10-20% of soft-tissue sarcomas; its incidence is generally noted in middle-age subjects; women are affected by this neoplasm more commonly than men (16). The prognosis is extremely poor (2,15-17,20,21) due to the frequent tendency to develop secondary localizations, which may already be present at diagnosis or appear at a subsequent time. The mesentery, lung, liver and lymphatic vessels are generally affected as the main areas of metastasis (2). To the best of our knowledge, a literature review (performed with a PubMed search) has revealed only 13 cases of primary leiomyosarcoma of the ureter from 1886 to 2022. Generally, the majority of the tumors arising from the ureter are transitional cell carcinomas (17), with smooth muscle tumors being more common in tumors

of the bladder and kidney. No clinical pattern has been associated with ureter leiomyosarcoma; however, patients generally complain of flank or abdominal pain, urinary tract infection and obstructive uropathy (22). As with the present case report, diagnosis is based on the anatomopathological analysis with immunohistochemical markers. The mass may be visualized on ultrasound and has been described as cystic (3). Ureter leiomyosarcoma lacks a characteristic enhancement pattern on the CT scan adequate to derive a diagnosis (17), probably due to the low number of cases studied. In general, this type of tumor is derived from the wall of the ureter, which develops as eccentric or circumferential parietal thickening (23). In the present case, a nodular mass of the wall of the ureter was developing exophytically with 'crown' enhancement (a hypodense centre and highly enhanced periphery); the hypodensity of the centre of the lesion is caused by necrosis phenomena which are more visible depending on the voluminous nature of the neoplastic mass and/or the higher degree of malignancy (24). However, when a retroperitoneal nodular mass is discovered, which is in contact with the ureter, several diagnostic hypotheses must be investigated. First of all, due to its frequency, a diagnosis of urothelial carcinoma must be excluded, especially in case of haematuria (25); however, the patient did not exhibit this sign, directing clinical suspicion towards other pathologies. Furthermore, in the case of urothelial carcinoma, the lesions are readily multifocal and with synchronous involvement of the bladder in ~40% of cases (23,25,26). In the present case report, the lesion was single and the bladder was free from any alteration. Furthermore, in lymphoproliferative disease, secondary localization of a urogenital cancer or an infection (tuberculosis) must also be excluded when the diagnosis of leiomyosarcoma is suspected. In patients suffering from lymphoproliferative disease, adenomegalies indicate the following characteristic aspect: they are generally multiple, perivascular and confluent (in the absence of contrastographic impregnation); in the present case report, the clinical context will suggest the diagnosis. In a patient suffering from tuberculosis the adenopathies could mime the aspect discussed in the lesion noted in the present study since they are much smaller than lymphomas and poorly confluent; furthermore, following injection of the contrast medium, the centre of these adenopathies is hypodense while the peripheral contours indicate contrastographic enhancement (24). The analysis of the contact angles may aid the differential diagnosis; in effect, the contact angles are obtuse in the case of leiomyosarcoma, while they are acute when an extrinsic site of the adenomegaly type compresses the ureter. However, this is theoretical and in practice it is often difficult to differentiate these two pathologies. However, patients of this type may less commonly exhibit melanoma and lung cancer, which can cause retroperitoneal metastases (24); therefore, their diagnosis must also be excluded. A final pathology to consider is retroperitoneal fibrosis which presents as an infiltration 'sheathing' the ureter, usually medially, causing proximal (unilateral or bilateral) hydronephrosis (24). In this case, the clinical context is again a key element for the diagnosis. Therefore, considering this abundance of pathologies, the anatomopathological analysis of the mass following surgical treatment (more specifically on the evaluation of the immunohistochemical markers in the case of leiomyosarcoma of the ureter) is mandatory for definitive diagnosis. Following immunohistochemical analysis, leiomyosarcoma is negative with regard to the expression levels of epithelial markers (cytokeratins and epithelial membrane antigens) and positive for desmin and SMA (indicating the smooth muscle origin of the tumor). Negative expressions of myoglobin, cytokeratin and S-100 aid to rule out rhabdomyosarcoma, sarcomatoid carcinoma and melanoma, respectively (27,28). By noting the aggressive nature of the condition, the choice of treatment has been reported as total nephroureterectomy with *en bloc* resection of the tumor (22,29). By contrast, certain cases have been managed with tumor excision and ureteroureterostomy without signs of recurrence, similar to those noted in the patient of the present study. As noted in the present case, in the case by Kolhartkar *et al* (29), the nephroureterectomy was not performed because the tumor was derived from the patient's only functioning kidney. Radiotherapy can be considered for larger tumors and/or if the margins of the resection are affected (16,21). Adjuvant chemotherapy (based on doxorubicin, ifosfamide, gemcitabine and docetaxel) has not been proven to be effective, having a role in the metastatic disease (18). It is recommended that adjuvant chemotherapy (based on Ifosfamide plus Epirubicin) should be used in the patient of the present study hoping for an adequate prognosis. Due to the rarity of the condition, the management is not standardized and it is mainly based on modes of treatment of epithelial tumors of the ureter. In the present case report, surgical excision of the ureteric mass with safety margin was performed.

Although leiomyosarcoma is rarely noted in the urinary tract, it should be considered in the differential diagnosis of ureteral stricture disease and tumors. For this reason, it is important to report primary ureter leiomyosarcoma cases to assist further studies investigating the condition and the optimal approach to its treatment; in the present case report, no malignant recurrence was observed 12 months following tumor resection and uretero-ureterostomy.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

RB was the major contributor in writing the manuscript. RB and GM made substantial contributions to the conception and design of the study. DF and RC assisted with imaging

acquisition. RB and GM confirm the authenticity of all the raw data. RS, UDM, OI, TP, CB and GDL interpreted the patient data regarding urological disease. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was conducted according to the guidelines of the Declaration of Helsinki. However, ethics approval was not required because this was a case report that did not include procedures outside of common and correct clinical practice. Furthermore, the patient included in the study provided their written informed consent for the processing of their medical data.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the present study and for processing their medical data.

Competing interests

The authors declare that they have no competing interests.

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