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Case Report

Synchronous primary tumors of the bladder: Successfully managed case ☆☆☆

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ABSTRACT

The coexistence of 2 primary bladder tumors of different histogenesis is very rare. Synchronous leiomyosarcoma LMS of the bladder and urothelial carcinoma are even rarer. We report here the case of a 48-year-old patient who presented with hematuria and symptoms of bladder irritation. Cystoscopy showed a superficial bladder tumor which occupies the entire bladder lumen. Transurethral resection of bladder tumor (TURBT) was performed and revealed a noninvasive low-grade papillary urothelial carcinoma pTa with nonvisualized muscularis. A second TURBT could not remove any muscle. The decision for a radical cystectomy was performed with Bricker derivation and pelvic lymph node dissection to control bleeding. The final pathology demonstrated concurrent urothelial carcinoma and leiomyosarcoma LMS. In this report, we presented a unique case of urinary bladder leiomyosarcoma with noninvasive urothelial carcinoma. The rarity of this association and its clinical similarity to other common tumors, including infiltrative urothelial tumors, leading to misdiagnosis, are also described.

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Introduction

Bladder cancer is the 10th most common cancer worldwide [1]. Urothelial cell bladder cancer represents 90% of bladder cancer while mesenchymal tumors account for fewer than 5% [2]. Leiomyosarcoma LMS of the bladder is a malignant mesenchymal tumor with muscle differentiation. It is a rare tu-

mor that accounts for approximately 1% of malignant bladder tumors [3]. The coexistence of 2 different histogenesis tumor of bladder is very rare. We hereby present a rare case of synchronous LMS and urothelial carcinoma of the bladder and describe clinical, radiological, and therapeutic features. A particular therapeutic approach is presented here, with relevant literature review.

Abbreviations: LMS, leiomyosarcoma; TURBT, Transurethral resection of bladder tumor; CT, computed tomography; IHC, Immunohistochemistry; FNCLCC, The Federation Nationale des Centres de Lutte Contre le Cancer.

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Case report

A 48-year-old male without previous pathological history or toxic behavior was admitted with complaints of macroscopic hematuria and symptoms of bladder irritation with severe anemia (hemoglobin of 4 g/dL). After transfusion with 6 blood units, cystoscopy was performed and revealed a superficial bladder tumor with a mass occupying 80% of bladder lumen. The patient underwent transurethral resection of bladder tumor (TURBT). Pathological examination showed of a noninvasive low-grade papillary urothelial carcinoma pTa. However, the muscularis was not visualized. A second TURBT could not remove any muscle. An abdominal and pelvic computed tomography scan (CT) showed a highly vascularized left posterolateral bladder tumor mass occupying the entire bladder wall and the entire bladder lumen (Fig. 1). Given this radiological appearance, the diagnosis of a tumor infiltrating the bladder muscle was strongly suspected; nevertheless, a tumor with a muscular origin could not be excluded. The tumor could not be completely resected, and a radical cystectomy was performed with pelvic nodes dissection and Briker type derivation ensuring R0 surgery. Macroscopical examination showed a voluminous bladder neoplasm with sub-mucosal development and fasciculated appearance measuring 8 × 7.5 × 7 cm and weighing 360 g (Fig. 2). The mucosa is largely ulcer-

ated with the presence of areas of papillary vegetation. Microscopic analysis revealed the co-existence of a superficial tumor of low-grade papillary carcinoma classified pTa, with neoplastic spindle cell proliferation arranged in interlacing bundles with hyperchromatic nuclei and frequent mitoses (greater than 8 mitoses per 10 high-power fields) (Fig. 3). The presence of necrosis areas estimated at 20% of the tumor surface. Immunohistochemistry (IHC) staining was performed. The panel of monoclonal antibodies consisted of cytokeratin AE1 / AE3, smooth muscle actin, h-Caldesmon, desmine, and myogenin. Tumor cells were strongly and uniformly positive for smooth muscle actin (Fig. 4), positive for h-Caldesmon and negative for myogenin and other markers. This morphological and immunohistochemical aspect was compatible with LMS. The final pathological analysis concluded to a completely resected bladder leiomyosarcoma LMS infiltrating deep muscle and ranked FNCLCC Grade II with negative margins, associated with a noninvasive low grade urothelial carcinoma. The postoperative course was uneventful, and the patient was discharged on the sixth postoperative day. A multidisciplinary team meeting did not qualify the patient for adjuvant chemotherapy or radiotherapy due to the absence of poor prognostic factors (grade 2 and negative margin). The patient remained free of recurrence 11 months after his treatment.

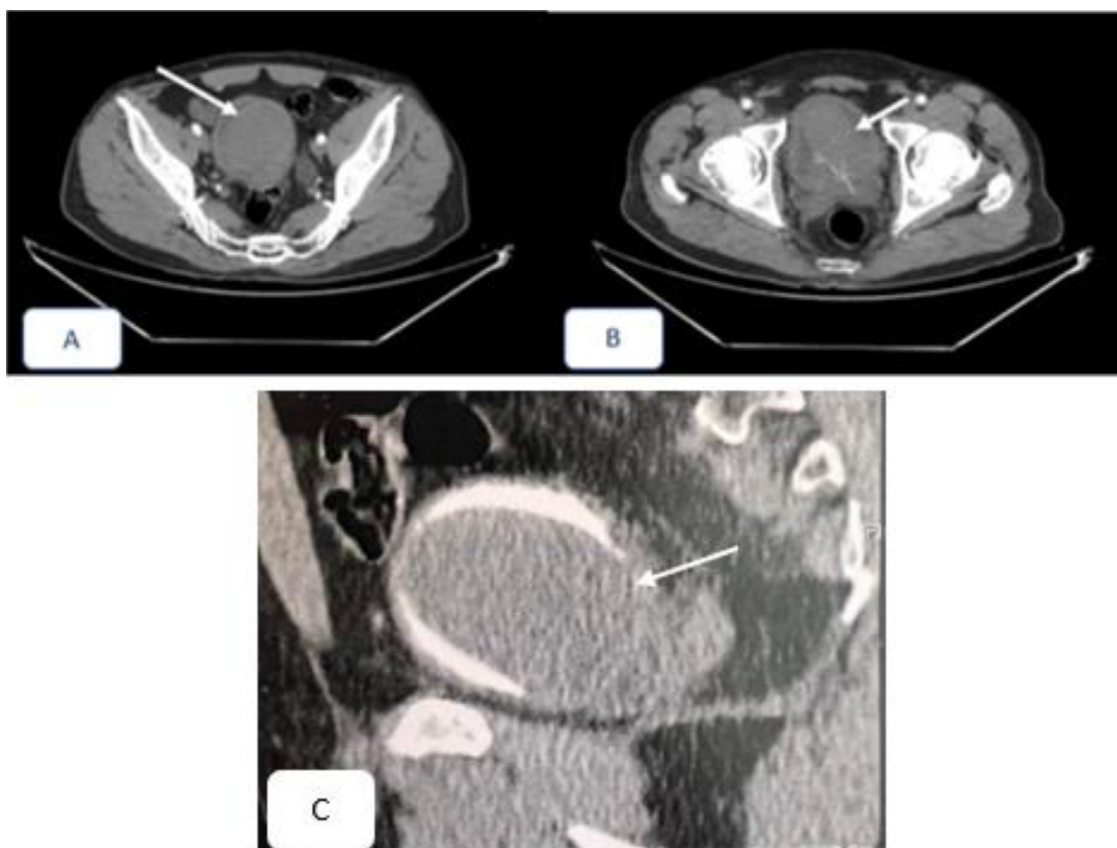


Fig. 1 – (A and B) Contrast-enhanced CT scan axial section showing a heterogeneous mass with contrast enhancement and highly vascularized of the left posterolateral bladder, enclosing the 2 ureteral meatus. (C) Contrast-enhanced CT scan sagittal section excretory phase showing budding mass occupying almost the entire bladder lumen.

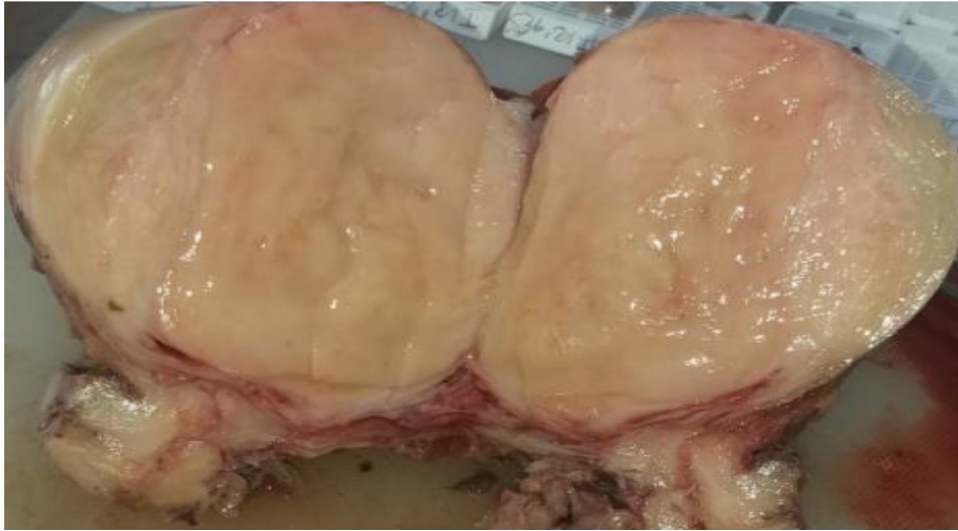


Fig. 2 – Voluminous bladder neoplasm with sub-mucosal development and fasciculated appearance measuring 12 x 9 x 6 cm and weighing 360 g.

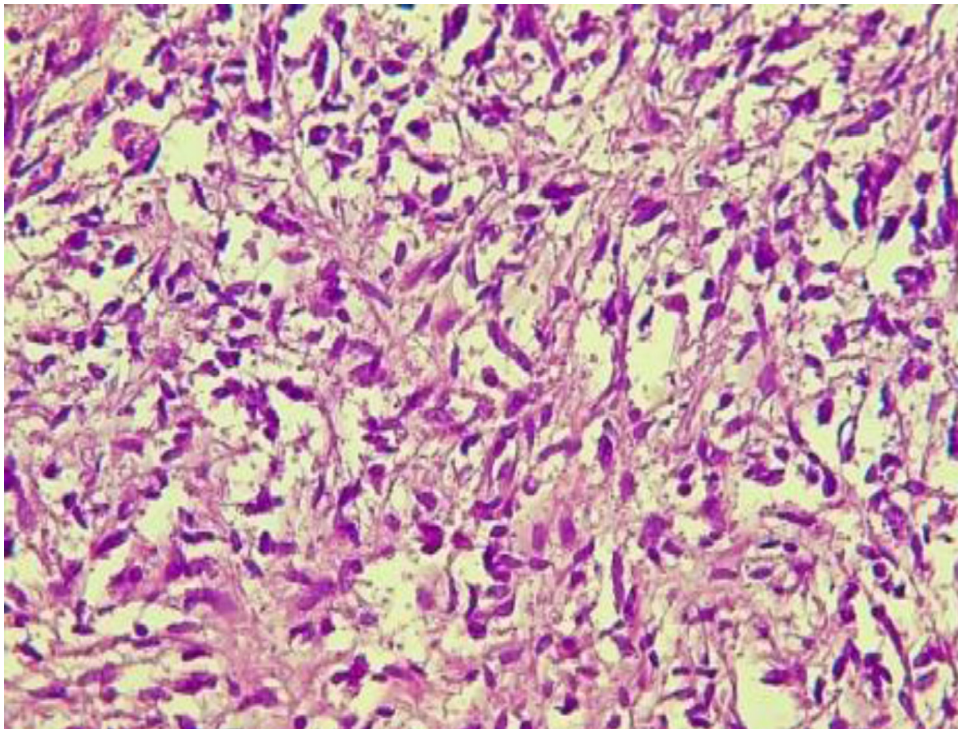


Fig. 3 – Biopsy shows neoplastic spindle cell proliferation arranged in interlacing bundles and fascicles. Stain: hematoxylin and eosin; magnification: 40 x.

Discussion

Here we illustrate an unusual case of leiomyosarcoma with noninvasive low-grade urothelial carcinoma arisen in the urinary bladder. The concurrent occurrence of neoplasms involving different tissues in the same organ is a phenomenon that has long been observed but continues to be little understood and exceedingly rare. According to the International

Agency for Research on Cancer (IARC), the diagnosis of synchronous primaries is made within an interval of less than 6 months [4]. To the best of our knowledge, fewer than 10 cases of synchronous urothelial carcinoma and leiomyosarcoma (LMS) have been reported in the English literature [5].

In fact, nonurothelial neoplasms rarely occur in the urinary bladder. Leiomyosarcoma represents the most common subtype of malignant mesenchymal tumors in this organ, but still accounts for less than 1% of all primary bladder tumors



Fig. 4 – Image showing strongly and uniformly positive smooth muscle actin staining. : 20x.

[6,7]. In a systematic review reported by Ziechang et al., 210 cases of urinary bladder leiomyosarcoma have been reported between 1970 and 2018. Moreover, several risk factors were revealed by this review including long-term chemotherapy with cyclophosphamide, chronic bladder irritation, radiation, and retinoblastoma gene mutation [7]. None of these risk factors were identified in our patient.

Clinical symptoms of bladder LMS are identical to those of urothelial carcinoma. The main symptom is hematuria present in 81% of cases [2,5,6]. It may be isolated or associated with pelvic and abdominal pain and symptoms of bladder irritation like dysuria and pollakiuria. Patients may present with either severe obstructive urinary symptoms (acute urine retention) or obstructive uropathy, if the tumor is very huge and infiltrating. Our patient was referred to us with macroscopic hematuria, but he had no symptoms until the tumor reached an advanced stage and became locally invasive.

Bladder LMS does not present characteristic images. Histological examination with IHC staining studies is the most credible conclusive method of diagnosing leiomyosarcoma and differentiating it from other more frequent primary bladder neoplasia.

Macroscopically, leiomyosarcomas are large, solid, white, soft with focally necrotic tumors.

Histologically, LMS consists of a malignant proliferation of spindle cells with variable mitotic index. Also, the microscopic exam provides information on the percentage of necrosis and the degree of differentiation. It is important to note that there is no standardized histologic grading system for LMS of the urinary bladder. The Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system, which is used for sarcomas of the soft tissues, has not been verified for visceral LMS due to the rarity of tumors at these unusual

anatomic sites [11]. It can be associated with other bladder tumor such as urothelial carcinoma or papillomatosis [5,6], as in our patient's case.

However, Immunohistochemistry is necessary; the monoclonal antibody panel is composed of cytokeratin 5/6, 7, and 20, vimentin, smooth muscle actin, calretinin, CD-117, TTF1, EMA, CD-34, and S-100 protein. In our case, the tumor cells were positive for anti-smooth muscle actin antibodies.

Prognostic factors are tumor size, grade 3, lymph node involvement and tumor resection margins [10]. Prognosis is usually poor, especially in large invasive tumors, and those with high-grade histologic features.

Given the rarity of LMS of the bladder, the management is not standardized; hence, the interest of a multidisciplinary therapeutic approach. Surgery remains the only curative treatment. The aim of surgery should be to achieve R0 resection with negative margins of more than 2 cm [8]. Radiation therapy is indicated if tumor resection margins are reached and may also be indicated after multidisciplinary discussion, taking into account risk factors for local recurrence including tumor size and grade [9]. Adjuvant chemotherapy does not have a standard consensus, but can be proposed if poor prognostic factors described in the literature [10]. The median survival was 46 months for patients diagnosed with bladder LMS. The 5-year and 10-year survival was 47% and 35%, respectively [8].

There are 2 main reasons to present this interesting case report. First is the unusual coexistence of 2 different histogenesis tumor of bladder and to make clinicians aware of this clinical entity as a differential diagnosis when a bladder mass is identified in the presence of a noninfiltrative urothelial tumor. Second one is the management which requires multidisciplinary approach that takes into consideration prognostic factors.

Conclusion

The association of leiomyosarcoma LMS with a superficial urothelial tumor remains an exceptional entity. Complete resection allows long term control of the disease. The purpose of this case report is to think of the differential diagnosis in particular leiomyosarcoma in face of large tumors of bladder with noninfiltrative urothelial tumor. In this rare scenario, a multidisciplinary approach is extremely helpful as discussion with clinicians with various expertise can formulate the best treatment options for this patient.

Patient consent

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contributions

FR and GR were involved in the analysis of the data and the literature search and wrote the manuscript. MM helped with the patient management and revision the manuscript. RM contributed to the preparation of this manuscript, and interpretation of the case. All the authors have read and approve the final version of the manuscript.

Declaration of figures' authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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