Case Report

Successful treatment of a 4-year-old girl with pure malignant rhabdoid tumor of the bladder: a case report

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Background: Extracranial malignant rhabdoid tumors (eMRTs) are rare, highly aggressive neoplasms, predominantly arising in the kidneys, with bladder involvement being extremely uncommon. Optimal management strategies, particularly bladder-preserving approaches, are not well-established due to the rarity of these cases.

Case Description: We report the case of a 4-year-old girl who presented with persistent gross hematuria. Imaging revealed a large bladder mass and histopathological examination confirmed the diagnosis of an extrarenal rhabdoid tumor with loss of *SMARCB1* expression. The patient underwent a multimodal treatment approach, including bladder-preserving surgery, 12 cycles of high-dose MRTK-2020 neoadjuvant chemotherapy [comprising actinomycin D, vincristine, doxorubicin, cyclophosphamide (AVDC), ifosfamide, carboplatin, and etoposide (ICE)], followed by adjuvant radiotherapy. Remarkably, the patient achieved complete remission after two cycles of chemotherapy and remained in continuous remission with no evidence of disease at the 15-month follow-up.

Conclusions: This case underscores the diagnostic challenges of malignant rhabdoid tumors (MRTs) in bladder pathologies and highlights the significance of considering such tumors in differential diagnoses. Despite the limited evidence base, bladder-preserving surgeries, when feasible, should be considered and accompanied by adjuvant therapies for optimal outcomes. This case illustrates the potential for successful treatment of pure MRTs of the bladder using a combination of surgery, chemotherapy, and radiotherapy.

Keywords: Bladder; rhabdoid tumor; *SMARCB1*; treatment; case report

Submitted Jul 02, 2024. Accepted for publication Sep 29, 2024. Published online Oct 23, 2024.
doi: 10.21037/tp-24-255
View this article at: https://dx.doi.org/10.21037/tp-24-255

Introduction

Extracranial malignant rhabdoid tumors (eMRTs) are highly aggressive neoplasms that primarily originate in the kidneys, often characterized by a poor prognosis (1). These tumors are known for their rapid progression and resistance to conventional treatments, making early diagnosis and comprehensive management crucial. Although eMRTs typically arise in the kidneys, they can also occur in other soft tissues, including the liver, chest wall, and retroperitoneum. However, involvement of the bladder is a relatively infrequent occurrence and presents unique diagnostic and therapeutic challenges. There have been a limited number of published case reports documenting isolated pure MRT of the bladder, with a total of nine cases identified thus far. Among these cases, five of them

reported a survival rate exceeding one year. It is noteworthy to mention that all of these individuals underwent complete tumor resection and received chemotherapy.

Here, we report a rare case of a 4-year-old female diagnosed with a pure malignant rhabdoid tumor (MRT) of the bladder. This case is notable not only for the unusual location of the tumor but also for the successful use of a bladder-sparing approach combined with radiotherapy and neoadjuvant chemotherapy. This report aims to highlight the importance of considering MRTs in the differential diagnosis of bladder masses in pediatric patients. Moreover, with the successful treatment of this rare case, we propose a hypothesis that children with MRT originating solely in the bladder can benefit from a combination of partial cystectomy and adjuvant chemotherapy and radiation therapy as the optimal treatment approach. We present this case in accordance with the CARE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-255/rc).

Case presentation

A 4-year-old Chinese girl was referred to our clinic due to the presence of persistent gross hematuria for a duration of 1 month. She had no familial history, past medical, and past surgical history. Physical examination revealed no obvious positive signs. A renal and bladder ultrasound (US) revealed the presence of a substantial, solid, and varied mass originating from the bladder wall, measuring 36×22 mm^2 in size (*Figure 1A*). Abdomino-pelvic computed tomography (CT) scan revealed an irregular neoformative mass measuring 2.8 cm × 2.5 cm × 2.0 cm in the bladder (*Figure 1B*).

The patient subsequently underwent a cystoscopy and transurethral resection of a bladder tumor (TURBT) at an outside hospital. Histopathologically, the tumor cells demonstrated a small and round morphology, while immunohistochemical analysis revealed a negative *INI1* tumor expression. Specifically, the tumor was subjected to deletion testing using multiplex ligation probe amplification. This analysis revealed the presence of a single deletion in chromosome 22, which encompassed the *SMARCB1/INI1* gene locus (*Figure 1C*). These findings were consistent with the diagnosis of an extrarenal rhabdoid tumor.

After the surgery, both positron emission tomography and repeat CT scan were performed, and they confirmed the absence of distant metastases. She underwent treatment with the MRTK-2020 regimen, which consisted of a total of 12 cycles of high-dose alkylating chemotherapy. The chemotherapy agents included actinomycin D, vincristine, doxorubicin, cyclophosphamide (AVDC), ifosfamide, carboplatin, and etoposide (ICE). The patient achieved remission after two cycles of induction chemotherapy and maintained a continuous complete remission status after receiving maintenance chemotherapy. Due to the aggressive nature of the disease, consolidation therapy with adjuvant radiotherapy was administered following chemotherapy. She successfully completed her treatment without encountering any noteworthy adverse events. Magnetic resonance imaging (MRI) scans of the pelvis were conducted every 3 months following the treatment (*Figure 1D*), revealing no signs of recurrence 15 months post-surgery.

All procedures performed in this study were approved by the ethics and plan review committee of Nanjing Medical University and in accordance with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the parents of the child for publication of this case report and accompanying image. A copy of the written consent is available for review by the editorial office of this journal.

Highlight box

Key findings

- This case report highlights the successful treatment of a 4-year-old girl with a rare pure malignant rhabdoid tumor (MRT) of the bladder, emphasizing the potential for positive outcomes through a combination of bladder-preserving surgery, chemotherapy, and radiotherapy.

What is known and what is new?

- MRTs are rare and aggressive neoplasms, commonly originating in the kidneys, with a poor prognosis, especially when occurring outside the renal region.
- This case demonstrates that even with a rare presentation of a pure MRT of the bladder, successful treatment can be achieved through a multimodal approach combining bladder-preserving surgery, chemotherapy, and radiotherapy.

What is the implication, and what should change now?

- This case suggests that early diagnosis and a multimodal treatment approach, including bladder-preserving surgery, chemotherapy, and radiotherapy, can lead to successful outcomes in patients with pure MRTs of the bladder.
- Clinicians should consider bladder-preserving surgical options and the integration of adjuvant therapies as a viable treatment strategy for similar rare cases to improve patient outcomes.

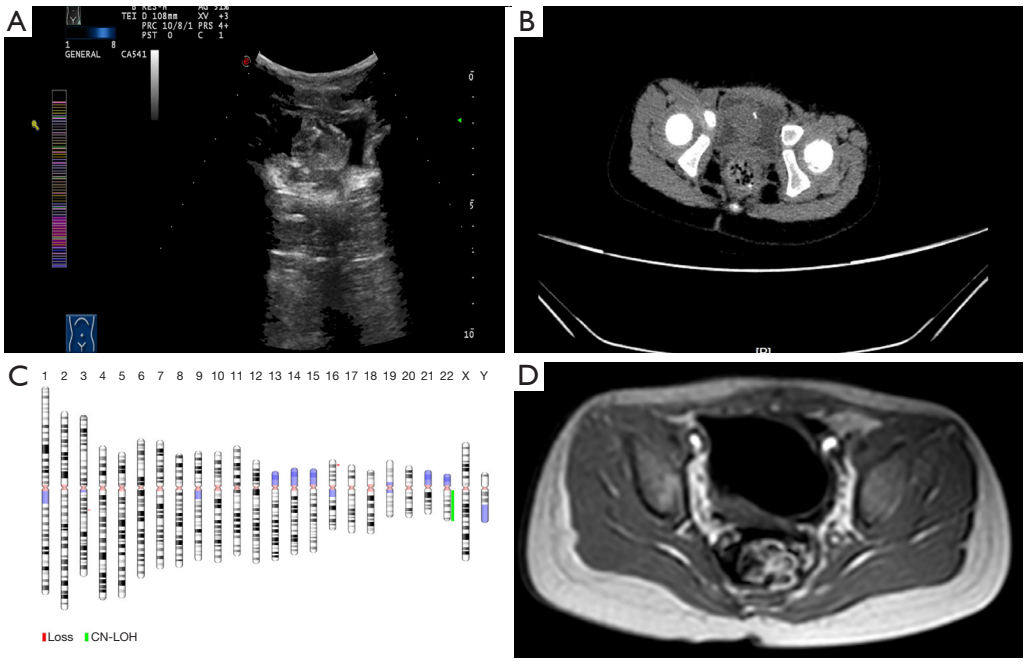

Figure 1 Imaging and genetic analysis of the bladder tumor in a 4-year-old patient. (A) Bladder US reveals the presence of an intravesical mass. (B) CT imaging shows an irregular mass within the bladder, with relatively well-defined margins and a size of approximately 28 mm × 25 mm × 20 mm. (C) The gene chip testing results revealed the presence of a heterozygous deletion in the *SMARCB1* gene. (D) Post-treatment MRI reveals no signs of recurrence 15 months after the initial surgery and chemotherapy. CN-LOH, copy neutral loss of heterozygosity; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging.

Discussion

eMRTs were identified as a separate condition in the 1980s, and the kidney is the most frequently affected area (2). However, there have also been cases of MRTs occurring in extra-renal sites, including the soft tissues of the trunk, head and neck, abdomen, pelvis, and retroperitoneum. Pure rhabdoid tumors of the bladder are exceptionally uncommon among pediatric patients, with only nine case reports documented in the literature. These cases encompass a wide range of ages, spanning from antenatal up to 17 years old, and a summary of these reports is presented in *Table 1* (3-11). Among the patients mentioned above, seven underwent bladder-preserving tumor resection, one underwent radical cystectomy, and one underwent transurethral resection of the tumor. In addition, all patients received adjuvant chemotherapy following the surgery, with four of them also receiving concurrent radiotherapy. Five patients were followed up for over 1 year, of whom only one succumbed to distant metastasis, while the remaining four achieved disease-free survival.

Extrarenal MRTs are highly aggressive tumors that have a high propensity for early metastasis. The 5-year overall survival (OS) rate for these tumors is only 17–36% (1,12,13). Bourdeaut *et al.* reported a solitary survival case among a cohort of 26 patients with eMRTs (14). This study confirmed the bleak prognosis associated with Extrarenal MRTs despite treatment interventions. A study was conducted utilizing data from the Surveillance, Epidemiology, and End Results (SEER) database, in which a total of 229 patients diagnosed with MRTs were enrolled (15). The distribution of MRT subtypes included 81 cases of atypical teratoid/rhabdoid tumor (ATRT), 103 cases of eMRT, and 45 cases of renal MRT (MRTK). The study findings revealed a 5-year OS rate of 33%±3.4%. In a systematic review conducted by Xie *et al.*, it was observed that MRTK is a common finding in infants, typically occurring around the age of 10 months. On the other hand, extrarenal MRTs tend to manifest in older children, with a median age of 25.9 months (1).

Assadi *et al.* presented a rare case of bladder MRT and highlighted its comparatively less aggressive behavior relative to other eMRTs (11). The case was successfully managed with bladder-preserving surgery, adjuvant

Table 1 Reported cases of extrarenal MRTs with a primary tumor in the bladder in pediatric patients have been histologically confirmed

Time	Age (years), sex	Chemotherapy	Surgical	Radiation	Outcome	Ref. number
1989	6, female	Adjuvant: 6 cycles vincristine, adriamycin, and cyclophosphamide	Transurethral resection of tumor	No	NA	(3)
2001	4, female	Adjuvant: 8 cycles vincristine, ifosfamide, and etoposide followed by 4 cycles of vincristine, actinomycin D, and cyclophosphamide and 4 cycles of vincristine, cyclophosphamide, and doxorubicin	Partial cystectomy	No	Alive 2 years after diagnosis	(4)
2004	4, female	Neoadjuvant: 4 cycles ifosfamide, vincristine, and actinomycin D Adjuvant: 13 cycles vincristine, cyclophosphamide, doxorubicin, and etoposide alternating with ifosfamide	Partial cystectomy	No	Alive 9 years after diagnosis	(5)
2012	3, male	Adjuvant: vincristine, doxorubicin, cyclophosphamide, carboplatin, and etoposide	Partial cystectomy	Yes	Alive 6 months after diagnosis	(6)
2014	17, female	Neoadjuvant: 2 cycles of doxorubicin, ICE; 9 cycles of high-dose alkylating chemotherapy: vincristine, cyclophosphamide, actinomycin D, ICE	Robotic uterine, cervical and vaginal sparing cystectomy and intracorporeal formation of an ileal conduit	Yes	Alive 1 year after diagnosis	(7)
2015	14, male	Neoadjuvant: vincristine, cisplatin, doxorubicin, cyclophosphamide, etoposide, and actinomycin D Adjuvant: vincristine, doxorubicin, cyclophosphamide, temozolamide, and actinomycin D	Partial cystectomy	No	DOD	(8)
2019	Antenatal, unknown	Alternating courses of VDC and ICE chemotherapy as per the EPSSG NRSTS 2005 protocol	Partial cystectomy	No	Alive 18 months after diagnosis	(9)
2020	1, female	Adjuvant: 4 cycles of VDC, 4 cycles of ICE	Partial cystectomy	Yes	NA	(10)
2021	2, male	AREN0321, revised regimen UH-1 (30 weeks of 5 agent chemotherapy: vincristine, doxorubicin, cyclophosphamide, carboplatin, and etoposide)	Partial cystectomy	Yes	Alive 18 months after diagnosis	(11)
2024	4, female	Adjuvant: 6 cycles of AVDC, 6 cycles of ICE	Partial cystectomy	Yes	Alive 15 months after diagnosis	Current case

MRT, malignant rhabdoid tumor; NA, not available; ICE, ifosfamide, carboplatin, and etoposide; DOD, died of disease; VDC, vincristine, dactinomycin, cyclophosphamide; AVDC, actinomycin D, vincristine, doxorubicin, cyclophosphamide.

radiotherapy, and chemotherapy, emphasizing that bladder-preserving surgery should be prioritized when complete resection with negative margins is feasible. The authors also noted that the earlier detection of bladder MRTs, often due to gross hematuria, may contribute to a more favorable prognosis compared to other eMRTs, which are typically identified at more advanced stages. According to Shelmerdine *et al.*, US is considered the primary imaging modality for evaluating bladder lesions in children (16). It is crucial to ensure that the bladder is fully distended during the examination to prevent misinterpretation of bladder wall thickening as a mass or overlooking small soft-tissue

lesions. When additional imaging is necessary, MRI is preferred due to its superior ability to accurately depict soft-tissue and determine the extent of the disease. The article also highlights the challenges associated with distinguishing certain types of bladder tumors, such as papillary urothelial neoplasms of low malignant potential (PUNLMPs), from noninvasive urothelial carcinomas. In the patient reported in this study, bladder US, along with CT and MRI, was promptly performed following the initial presentation of gross hematuria. These imaging studies provided strong evidence to support the early decision-making process for treatment.

Currently, the treatment experience for eMRT is primarily based on small-sample retrospective studies. However, there is a shortage of large-sample randomized controlled and prospective studies that can provide optimal treatment protocols. The majority of patients undergo a multimodal combination therapy, which involves intensive chemotherapy, early surgical removal of the primary tumor (if feasible), local radiotherapy to all areas affected by the disease, or high-dose chemotherapy followed by autologous stem cell transplantation. Commonly utilized chemotherapeutic agents include anthracyclines, alkylating agents, platinizing agents, and periwinkle alkaloids.

After conducting a comprehensive review of the available literature, it has been ascertained that bladder MRTs are a rare form of malignancy that tend to display a comparatively less aggressive nature when contrasted with other eMRTs (1,3-11). Furthermore, for patients with primary rhabdoid tumors originating in the bladder, complete tumor resection with bladder preservation is a feasible option. This surgical approach not only achieves favorable therapeutic outcomes but also improves the long-term quality of life for the pediatric patient. Additionally, adjuvant chemotherapy and radiation therapy also play a crucial role in the multidisciplinary management. Based on the existing literature, adjuvant chemotherapy and radiotherapy were administered to the child following partial cystectomy as part of her treatment plan. As a result, the primary disease had remained in a state of continuous remission for a duration of 15 months.

Conclusions

In conclusion, we have identified a rare case of pure MRT of the bladder and thoroughly examined its diagnosis and treatment. Diagnosing this disease remains a substantial challenge. It also reminds clinicians to consider the possibility of MRTs when encountering the differential diagnosis of bladder occupancy.

Acknowledgments

We gratefully acknowledge the pathologists in the Children's Hospital of Nanjing Medical University for their expertise and generous provision of data.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-255/rc

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-255/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-255/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were approved by the ethics and plan review committee of Nanjing Medical University and in accordance with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the parents of the child for publication of this case report and accompanying image. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Li J, Bao J, Hu T, Zhao Q, Zhou J, Zhou L, Li T. Successful treatment of a 4-year-old girl with pure malignant rhabdoid tumor of the bladder: a case report. Transl Pediatr 2024;13(10):1879-1884. doi: 10.21037/tp-24-255