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A Rapid Progression of Disease After Surgical Excision of a Malignant Rhabdoid Tumor of the Bladder

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Abstract

Extrarenal malignant rhabdoid tumors (MRTs) are rare tumors with a poor prognosis. Five-year overall survival for patients with MRTs is poor at approximately 20%.¹ There are 5 case reports of histologically confirmed primary MRT of the bladder in pediatric patients. Herein, we report a case of an MRT of the bladder in a 14-year-old boy and discuss the preoperative evaluation, treatment options, and possible etiologies of metastasis after radical surgery.

Extrarenal malignant rhabdoid tumors (MRTs) are rare tumors with a poor prognosis. Five-year overall survival for patients with MRTs is poor at approximately 20%.¹ Although MRTs of the kidney are the most common genitourinary site, representing 2% of pediatric renal tumors,² extrarenal MRTs can exist in other parts of the genitourinary tract, including the bladder.³ There are 5 case reports of histologically confirmed primary MRT of the bladder in pediatric patients and are summarized in Table 1.^{4–8} Here we present a case of an MRT of the bladder in a 14-year-old boy.

CASE REPORT

A 14-year-old boy presented with intermittent gross hematuria. A renal and bladder ultrasound revealed a large, solid, heterogenous mass arising from the bladder wall measuring 5.1 × 4.1 × 5.5 cm (Fig. 1). Magnetic resonance imaging of the abdomen or pelvis suggested possible local extension into the adjacent abdominal wall and colon (Fig. 2).

He underwent a cystoscopy and transurethral resection of bladder tumor for diagnostic purposes. Approximately 30% of the tumor was resected, and pathology revealed an MRT with a mutation in exon 3 of the *SMARCB1/INI1* tumor suppressor gene on 22q11.2. A staging computed tomography of the thorax revealed multiple 1-to 2-mm lung nodules concerning for metastasis and a 7-mm ill-defined lucent lesion in the T12 vertebral body. A whole body positron emission tomography showed no evidence of metastasis. Given the

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local extent and aggressiveness of the tumor, upfront resection was not attempted and neoadjuvant chemotherapy was initiated based on a protocol for treating atypical teratoid rhabdoid tumors by Chi et al.⁹ Agents delivered included vincristine, cisplatin, doxorubicin, cyclophosphamide, etoposide, and actinomycin.

Repeat magnetic resonance cross-sectional imaging after 18 weeks of chemotherapy revealed stable disease with a slight interval decrease in the bladder mass, but continued presence of small lung nodules. Cystoscopy with repeat biopsies revealed necrotic tissue with no viable tumor. Additionally, he underwent multifocal lung biopsies that revealed no evidence of metastasis.

In the setting of a negative metastatic workup and measurable regression of the primary tumor, surgical intervention was undertaken. Pelvic exenteration, radical cystectomy with urinary diversion, and partial cystectomy were discussed with the family before the operating room. Partial cystectomy was performed after intraoperative assessment revealed no gross invasion into the colon or surrounding structures and results of multiple biopsies of the bladder were negative. Pathology of the bladder specimen again was consistent with an MRT with lymphovascular invasion. Tumor margins were negative, and there was no evidence of metastatic disease in the pelvic lymph nodes, implying good local control. The patient was discharged on postoperative day 3 without complication. He was given adjuvant chemotherapy; however, repeat imaging performed 2 months after surgery revealed widespread metastatic disease including multiple large lung nodules, numerous liver lesions, bulky pelvic adenopathy, and new bony lesions in the thoracic and lumbar spine. The patient was provided palliative care and died 3 months after the partial cystectomy.

COMMENT

Pure rhabdoid tumors of the bladder in pediatric patients are exceedingly rare with only 5 case reports in the literature.^{4–8} These reports are summarized in Table 1.

Extrarenal MRTs are aggressive tumors that show early metastatic potential with a 5-year overall survival rate of just 20%.² Whereas MRTs of the kidney tend to occur in infants,² extrarenal MRTs tend to present in older children at a median age of 7.3 years.¹ Initial workup should include cross-sectional imaging of the chest, abdomen, and pelvis.

Extrarenal MRTs are defined histologically by the presence of sheets of tumor cells with eccentric nuclei, prominent nucleoli, and eosinophilic cytoplasm with eosinophilic inclusions.¹⁰ The diagnosis is confirmed by lack of immunohistochemical staining for *SMARCB1/INI1*, showing loss of protein expression.^{10–12}

Treatment includes chemotherapy, wide surgical excision, with possible radiation therapy (although the efficacy of radiation is unknown). Chemotherapy regimens tend to be based on Wilms tumor protocols and often include vincristine, dactinomycin, doxorubicin, and cyclophosphamide, as well as cisplatin, etoposide, ifosfamide, and carboplatin.⁷ Others have been treated according to primitive neuroectodermal tumor/medulloblastoma protocols,¹⁰ or modification of a regimen initially developed for the third intergroup rhabdomyosarcoma study group trial.⁹

Wide surgical excision is vital for long-term survival in these patients. In a retrospective study of University of California, Los Angeles' 20-year history with pediatric extracranial MRTs, 5 of the 14 patients with extracranial MRTs were long-term survivors (range, 26–104 months).¹³ Complete surgical resection correlated positively with survival.¹³ All 5 long-term survivors underwent surgery for local control with 4 of the 5 survivors having complete resection. There were no survivors among those with unresectable disease. Therefore, Madigan et al¹³ concluded that complete surgical excision is mandatory for successful treatment. Additionally, salvage is not successful after disease progression or recurrence.

The patient described herein presented a management dilemma. MRT is an aggressive tumor with poor overall survival rates and requires multimodal therapy for hope of long-term survival. We initially deferred extirpative surgery until metastatic workup was negative and after what appeared to be a satisfactory response to chemotherapy. Although surgical resection improves overall survival, the possibility of rapid tumor growth postoperatively presents a challenge that must be considered as part of any management algorithm for this aggressive tumor.

There have been several reports linking surgical excision to both local and systemic cancer growth postoperatively, either by activation of micrometastasis or development of new metastasis. A report by van der Bij et al¹⁴ postulates that the stress response from surgery results in immunologic and hematologic effects promoting postoperative tumor development and spread. Several mechanisms for tumor growth have been proposed. First is suppression of anti-tumor immunity with studies showing transient suppression of immunologic function immediately after surgery.¹⁵ Another mechanism for increased postoperative tumor growth is from alterations in gene expression in tumor cells, with increased release of tumor growth factors and proangiogenic factors that promote wound healing and may also promote growth of previously dormant micrometastasis.¹⁴ Finally, chemotherapy regimens are halted for surgical resection, which may provide an opportunity for micrometastatic disease to progress. It is possible that these mechanisms contributed to our patient's progression 2 months after surgical resection; however, the mechanism of this patient's progression on systematic therapy remains unknown.

We suspect that the microscopic nodules identified in his lungs on initial workup were metastatic lesions in spite of the initially comforting negative results of biopsies. The break in chemotherapy regimen and immunologic or hematologic effects of surgery could have contributed to the rapidity of disease progression although we suspect that this would have occurred regardless of the intervention pursued because of the aggressive tumor. Reviewing our case with the case reports available in the literature, we feel that surgical resection should be reserved for patients with no suggestion of metastatic disease and therefore, patients who have the best chance of improving survival with local resection.

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Figure 1.
Renal-bladder ultrasound revealing large bladder mass.

Figure 2.
Magnetic resonance imaging of abdomen and pelvis confirming large bladder mass with possible extravesical extension.

Table 1

Reported pediatric cases of histologically confirmed extrarenal MRT with bladder primary

Age, y	Ref Number	Chemo Regimen	Surgical Treatment	Radiation Therapy
14, male	Current case	Neoadjuvant: vincristine, cisplatin, doxorubicin, cyclophosphamide, etoposide, and actinomycin D Adjuvant: vincristine, doxorubicin, cyclophosphamide, temozolamide, and actinomycin D	Partial cystectomy	No
3, male	7	Adjuvant: vincristine, doxorubicin, cyclophosphamide, carboplatin, and etoposide	Partial cystectomy	Yes, adjuvant 4500 cGy
4, female	5	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
4, female	6	Neoadjuvant: 4 cycles ifosfamide, vincristine, and actinomycin D Adjuvant: 13 cycles vincristine, cyclophosphamide, doxorubicin, and etoposide alternating with ifosfamide	Partial cystectomy	No
9, male	4	Neoadjuvant: vincristine, doxorubicin, and cyclophosphamide followed by carboplatin, cyclophosphamide, and etoposide Adjuvant: AREN032-UH-1 protocol	Cystoprostatectomy, Indiana pouch, left nephroureterectomy	Yes, adjuvant 36 Gy
6, female	8	Adjuvant: 6 cycles vincristine, adriamycin, and cyclophosphamide	Transurethral resection of tumor	No

MRT, malignant rhabdoid tumor; Ref, reference.