CASE REPORT
Turk J Surg

Evaluation of pediatric prostatic and retroperitoneal embryonal rhabdomyosarcoma with high Ki-67-case series study

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ABSTRACT

Embryonal rhabdomyosarcoma (ERMS) is a highly aggressive pediatric malignancy that can develop in various anatomical locations. This case series presents four pediatric patients diagnosed with ERMS, including one with the uncommon presentation of prostatic rhabdomyosarcoma. By analyzing clinical features, treatment strategies, and outcomes, this study aims to provide insights into the challenges of managing this malignancy in different anatomical sites.

Keywords: Embryonal rhabdomyosarcoma, Ki-67 proliferation index, children, rhabdomyosarcoma recurrence

INTRODUCTION

Embryonal rhabdomyosarcoma (ERMS) is a rare and aggressive pediatric malignancy which can manifest in various anatomical locations. This case series examines four pediatric patients diagnosed with ERMS, including one with the uncommon presentation of prostatic rhabdomyosarcoma. By analyzing their clinical features, treatment strategies, and outcomes, this series aims to shed light on the variability and challenges of managing this rare malignancy in different anatomical locations.

CASE REPORTS

Case 1

A 2-year-old male patient presented with a recurrent mass on the left side of his back, previously diagnosed as rhabdomyosarcoma. Physical examination revealed a firm, palpable mass extending from the 10th to 12th ribs, reaching the kidneys. An incision scar from a prior surgery at 10 months of age was noted. Computed tomography (CT) showed the tumor extending to the spleen and kidney, with no signs of metastasis (Figure 1A).

The previous incision site was reopened for surgical access. The tumor originated subcutaneously. Infiltrated the muscles, paravertebral fascia, and diaphragm It was invasive to the 10th, 11th, and 12th ribs, all excised along with the mass.

However, 11 weeks post-surgery, the patient returned with a recurrent mass. Another surgery was performed to remove the tumor in the left upper thoracic region. Pathology confirmed ERMS with clear surgical margins, with the Ki-67 proliferation index reported at 75%. Immunohistochemical staining also showed positive desmin, SMA, FLI-1, and myogenin results.

No fluorodeoxyglucose-18 (FDG) uptake on PET-CT after resection (Figure 1B). Despite complete excision, the patient developed a recurrent tumor protruding from the skin near the vertebral column at the L1-L2 levels, extending toward

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the aorta (Figure 1C, D). This tumor was excised after being dissected from the aorta and diaphragm. Additionally, those areas were marked for radiotherapy with titanium clips. The tumor was classified as stage III and high risk according to Children's Oncology Group (COG) risk stratification (Table 1). Subsequently, the patient underwent multiple surgeries in his home country due to recurrent disease and received chemotherapy and radiotherapy. The patient received a chemotherapy combination containing vincristine, irinotecan, and temozolomide. After chemotherapy, a total radiotherapy dose of 50.4 Gy was applied to the primary tumor site in 33 sessions. Three months after completing the treatment, recurrence developed in the primary site. Repeated operations and chemotherapy courses were unsuccessful, and the patient ultimately succumbed.

Case 2

A 1-year-old male patient presenting with an intra-abdominal mass was admitted to our hospital. Following chemotherapy, ultrasonography (USG), revealed grade 3 hydronephrosis in the left kidney and grade 1 hydronephrosis in the right kidney, with dilated ureters, more pronounced on the left side. Additionally, a mass measuring approximately 100x43 mm was detected, displacing the bladder superolateral to the left and positioned posterior to the bladder. A Doppler USG further characterized the mass as a hypervascular, mixed echogenic, well-circumscribed solid mass. Magnetic resonance imaging (MRI) confirmed the presence of an intrapelvic retroperitoneal malignant solid mass measuring 12.5×10 cm (Figure 2A).

A few days later, triphasic abdominal CT revealed a larger tumor, measuring 13x8x10.5 cm, located retroperitoneally and displacing the bladder anteriorly. The mass displayed extensive necrotic areas and non-homogeneous opacification of vascular structures but showed no signs of invasion. It was also compressing the left ureter, leading to a decision to proceed with surgical intervention.

During surgery, cystoscopy revealed significant hypertrophy of the bladder and urethra, necessitating a biopsy. A firm, encapsulated mass was found occupying the entire pelvis, extending above the umbilicus, and originating from the prostate, with attachments to the bladder and colon. The mass,

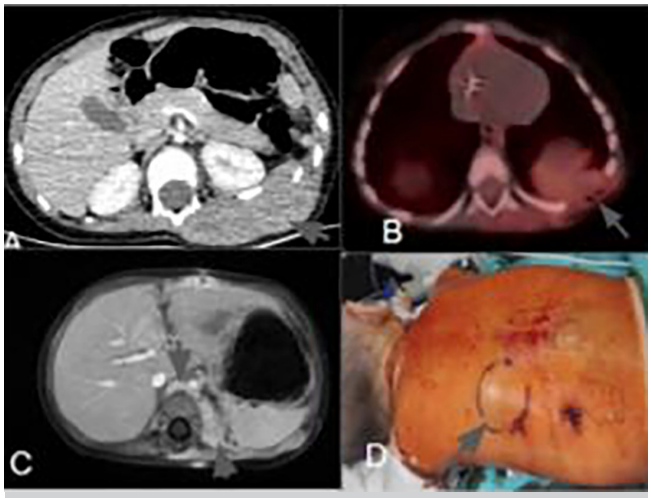

Figure 1. A. CT image of the retroperitoneal mass near the spleen and kidney. **B.** PET-CT image pre-resection metabolic activity. **C.** MRI of recurrent tumor at L1-L2 levels. **D.** Postoperative view; showing the recurrent tumor site.

PET-CT: Positron emission tomography-computed tomography, MRI: Magnetic resonance imaging

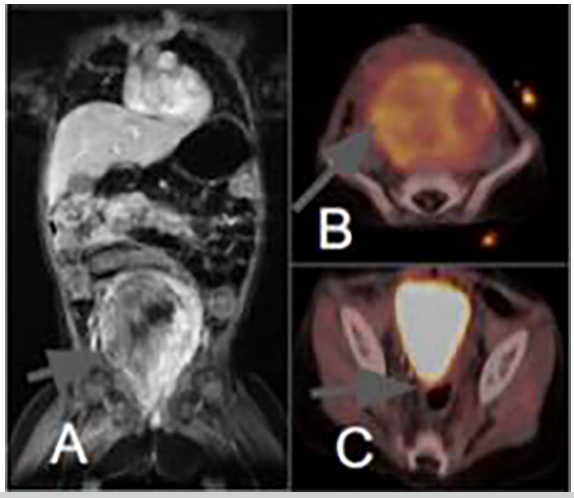

Figure 2. A. Preoperative MRI showing a large prostatic tumor displacing the iliac vessels laterally. **B.** PET-CT prior to surgery, confirming metabolic activity. **C.** Postoperative PET-CT: Indicating no metabolic activity.

PET-CT: Positron emission tomography-computed tomography, MRI: Magnetic resonance imaging

Table 1. Patient and clinical characteristics with risk group stratification according to the children's oncology group

Case	Age (years)	Tumor location	Tumor size (cm)	Lymph node involvement	Distant metastasis	Surgical resection	Ki-67 index (%)	Stage	Risk group
1	2	Paravertebral	Extensive	No	No	Multiple, incomplete	75	III	High
2	1	Prostate	12-13	Para-aortic, iliac	No	Complete	25	IIB	Intermediate
3	7	Retroperitoneum	4.5	No	No	Complete	2	III	Intermediate
4	4	Pelvic	5x3x5.5	Retroperitoneal	Iliac bone	Incomplete	75	IV	High

approximately 12-13 cm in size, caused right-sided ureteral dilation with minimal dilation on the left. It was fully resected.

Additionally, both para-aortic and iliac lymph node dissections were performed, and the prostate was excised along with the tumor. Titanium clips were placed to mark the dissection area.

Immunohistochemical staining of the surgical samples showed a Ki-67 proliferation index of 25%, along with positive CD34, p53, and S100 staining. A bladder biopsy revealed a Ki-67 index of 35-45%, with focal positive staining for myogenin, desmin, and MSA. WT1 displayed cytoplasmic staining, consistent with ERMS. The tumor was classified as stage IIB and intermediate risk (Table 1).

Following surgery, the patient was referred to the department of oncology for a comprehensive treatment plan that included chemotherapy. One-month post-surgery, an abdominal MRI showed no residual intra-abdominal mass. The patient underwent combination chemotherapy with vincristine, actinomycin, and cyclophosphamide, followed by a total of 41.4 Gy of radiotherapy to the primary tumor site in 23 sessions.

Nine months later, after completing chemotherapy, a PET/CT scan indicated an almost complete therapeutic response, with no pathological FDG uptake suggestive of residual tumor tissue (Figure 2B, C). The patient has remained in good health for the past three years.

Case 3

A 7-year-old female patient was admitted with an intra-abdominal mass previously diagnosed as rhabdomyosarcoma. She had undergone surgery five years earlier.

Physical examination revealed a Pfannenstiel incision scar, growth retardation, a skin rash, and thrombocytopenia on blood analysis. MRI identified a retroperitoneal mass, although no significant tumor focus was detected during cystoscopy (Figure 3A). Biopsies were obtained from suspected regions.

PET-CT imaging showed uptake on the left side of the bladder and lymphadenopathy (LAP) involvement (Figure 3B). During surgery, a 4.5 cm mass was found adhering to and surrounding the left ureter, left external and internal iliac vessels, the iliac vein, bladder, and uterus. The mass extended from the left lateral bladder to the vulva. Complete resection was achieved, and titanium clips were placed to mark the borders of the resection area.

The mass appeared firm and exhibited a dirty yellow coloration. A retroperitoneal lymph node dissection was performed, though no significant pathological lymph node involvement was identified. Biopsies were obtained from the omentum and lymph nodes in the iliac chain and para-aortic region. A tumor-free surgical margin was achieved, and no tumor cells were found in the bladder. The tumor was classified as stage III, intermediate risk (Table 1).

Immunohistochemical staining showed a Ki-67 proliferation index of 1-2%, indicating a low proliferation rate. The patient has remained disease-free for one year, with no recurrence observed. Post-surgery, the patient was referred to the department of oncology for a multi-modal treatment plan, which included chemotherapy and radiotherapy. Both chemotherapy and radiotherapy were subsequently administered. All treatment courses were unsuccessful, and the patient ultimately passed away.

Case 4

A 4-year-old male patient was referred to our hospital after undergoing surgery at another center earlier in the year, where complete removal of the mass could not be achieved. The patient was subsequently started on chemotherapy and referred for further treatment.

Physical examination revealed no remarkable findings. The midline incision was intact without dehiscence, and a nephrostomy catheter was present on the right side due to hydronephrosis. The USG indicated grade IV hydronephrosis in the right kidney, with marked dilation of the proximal ureter, while the distal ureter was not visualized. A small fusiform LAP was identified in the retrocaval region at the right renal level. Lower abdominal MRI revealed a 5x3x5.5 cm mass with dense components and septations, extending from the right iliac chain toward the bladder and rectum. The mass appeared cystic and necrotic, involving the right internal iliac vascular structures and displacing the external iliac vascular structures anteriorly. A focal lesion, measuring 15x6 mm and showing mild contrast enhancement, was also noted on the left iliac bone (Figure 4A).

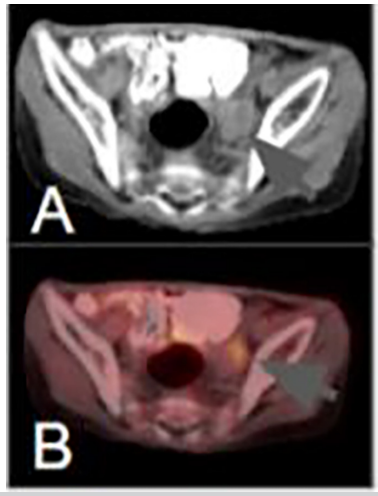

Figure 3. A. MRI image showing recurrent retroperitoneal tumor near iliac vessels and bladder. **B.** Preoperative PET-CT image demonstrating pathological FDG uptake near the left bladder and lymph nodes.

PET-CT: Positron emission tomography-computed tomography, MRI: Magnetic resonance imaging, FDG: Fluorodeoxyglucose

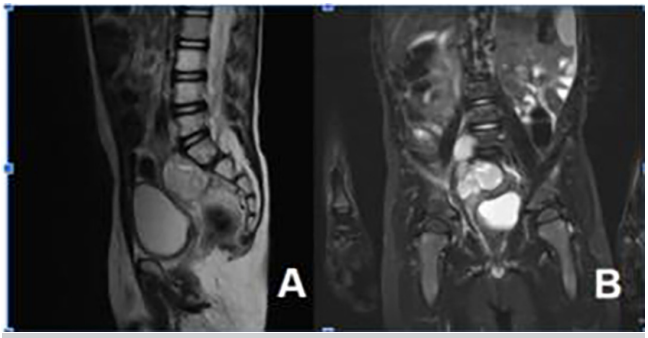

Figure 4. A. Preoperative MRI of the retroperitoneal mass near the iliac vessels and rectum. **B.** Postoperative MRI confirming residual tumor progression in the distal right psoas muscle and recurrence near iliac structures.

MRI: Magnetic resonance imaging

During the operation, the mass, measuring approximately 5x3x5.5 cm, was carefully dissected from critical anatomical structures, including the aorta, vena cava, right ureter, bladder, and rectum in the retroperitoneal area. Notably, a thrombus extending distally from the confluence of the vena cava and iliac veins was identified and addressed. Due to significant tumor invasion into the lower ureter and proximal rectum, en bloc resection of the affected ureteral segment, a 5 cm portion of the rectum, and the retroperitoneal mass, was performed. Adhesions from prior surgeries were meticulously removed to facilitate clear margins. Titanium clips were strategically placed to mark resection boundaries for subsequent radiotherapy, and a retroperitoneal lymph node dissection extended to the superior mesenteric artery.

Reconstruction involved a side-to-end anastomosis between the lower sigmoid colon and rectum to restore bowel continuity. Postoperative biopsies confirmed the presence of residual tumor cells at the margins, indicating the need for further oncological management.

Immunohistochemical staining of the surgical samples indicated a Ki-67 proliferation index at 75% with focal positive staining for myogenin, while desmin showed cytoplasmic staining, which is characteristic of ERMS. Two months post-surgery, the cystic necrotic mass in the distal portion of the right psoas muscle, measuring 7x2.6x1.7 cm and located near the right iliac vascular structures, was causing mild compression. Compared to a previous scan, the lower component of the mass had been resected, though progression was noted in the remaining upper portion revealed on MRI (Figure 4B). A hypointense fusiform lesion was also observed on the right iliac bone. The tumor was classified as stage IV and high risk (Table 1).

DISCUSSION

The Ki-67 proliferation index is a valuable marker in assessing tumor aggressiveness and prognosis in ERMS, particularly in recurrent cases. Studies indicate that higher Ki-67 expression is associated with increased tumor proliferation, poor differentiation, and a heightened risk of recurrence (1-3). In recurrent ERMS, Ki-67 may indicate the tumor's response to treatment and the likelihood of further progression.

While the role of Ki-67 in initial diagnosis and risk stratification is well-established, its utility in monitoring recurrent disease is gaining attention, offering the potential for tailoring aggressive treatment strategies.

Incorporating Ki-67 into the evaluation of recurrent ERMS could improve prognostication and guide decisions regarding the intensity of salvage therapy and multimodal approaches (4,5). Our study found a strong correlation between local recurrence and the Ki-67 proliferation index in pediatric patients with ERMS. Unfortunately, patients with high Ki-67 index and retroperitoneally located tumors demonstrate a higher likelihood of recurrence, even after complete resection. This is mainly attributed to the close anatomical relationship between these tumors and critical structures, including the iliac arteries, veins, ureters, and sacral plexus.

Additionally, the presence of microinvasions in this region further increases the risk of recurrence, making complete surgical clearance challenging. While tumor size is generally considered a prognostic factor, one of our cases showed no recurrence during follow-up despite a large mass originating from the prostate. This may be due to the prostate's encapsulated nature, which allowed for complete resection and thereby helped prevent recurrence, even with a high Ki-67 index.

The primary goal of surgical management in ERMS is achieving complete resection with clear margins, which is crucial for local control. However, complete resection is sometimes challenging due to the infiltrative nature and location. Achieving a clear margin for resection is challenging when the ER source originates from retroperitoneal muscle tissue. Adjuvant chemotherapy plays a crucial role in managing micrometastatic disease and improving overall survival rates. In some cases, radiotherapy significantly improves patient outcomes. In instances where complete surgical resection is not feasible due to proximity to critical structures and recurrences, a biopsy followed by neoadjuvant chemotherapy may be helpful to shrink the tumor and make a subsequent resection feasible (6-11).

In conclusion, our findings suggest that a low Ki-67 index and complete surgical removal significantly reduce the risk of tumor recurrence. However, even with full excision, recurrences were noted in retroperitoneal tumors with a high Ki-67 index. In contrast, for embryonal sarcomas originating from the prostate, recurrence rates were reduced despite the tumor's large size and high Ki67 index, likely due to complete removal. These findings highlight the crucial role of tumor location in prognosis,

particularly in achieving complete resection. Moreover, our cases illustrate a strong association between tumor recurrence and high Ki-67 index levels in rhabdomyosarcoma. The recurrence rate appears to be lower in prostatic tumors, which benefit from the encapsulation characteristic of the organ.

Ethics

Informed Consent: Informed consent forms were signed by parents of each patient.

Footnotes

Author Contributions

Surgical and Medical Practices - M.A., E.S., K.Y., S.G.; Concept - M.A.; Design - M.A., E.S., S.G.; Data Collection or Processing - M.A., K.Y., E.B.B.; Analysis or Interpretation - M.A.; Literature Search - M.A., E.B.B.; Writing - M.A., K.Y., S.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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