



Case report

Delayed diagnosis of pediatric bladder and prostate rhabdomyosarcoma – causes and consequences

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ABSTRACT

Introduction: Pediatric rhabdomyosarcoma (RMS) is a rare disease, affecting 4.5-6.0 per 1 000 000 children a year. Bladder and/or prostate (B&P) is the primary tumor site in approximately 10% of patients. Initial symptoms of B&P RMS in children may mimic more common, benign conditions such as urinary tract infections (UTIs), functional disorders, and congenital anomalies of the urinary tract.

Aim: The study aims to emphasize the role of careful clinical examination and strict following the diagnostic guidelines in early detection of pediatric B&P RMS in primary care and emergency department settings.

Case study: We present two male patients aged 2.5 and 3 years with embryonal B&P RMS initially manifesting as atypical and/or recurrent UTI. In both children, proper diagnoses were delayed due to careless physical examination and failure to adhere to the current guidelines for UTI management. Despite symptoms of an atypical and severe course of UTI, no imaging examinations had been performed for several weeks until dramatic deteriorations of patients' general conditions occurred.

Results and discussion: The prolonged diagnostic processes caused unnecessary suffering of both children and significant delay of oncological treatment in one. In the latter patient, bladder preservation was not possible, resulting in decreased quality of life.

Conclusions: Due to its rarity, B&P RMS is infrequently included in the differential diagnosis in children with recurrent or atypical UTI. However, thorough physical examination and adherence to the guidelines of UTI management enable timely diagnosis of underlying malignancy. Early diagnosis of B&P RMS leads to a better prognosis, less intensive treatment, and improved quality of life of B&P RMS survivors.

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1. INTRODUCTION

Pediatric rhabdomyosarcoma (RMS) is a rare disease, with estimated incidence of 4.5-6.0 per 1 000 000 children a year. Still, it is the most common soft tissue sarcoma in children, accounting for around 4.5% of all malignancies in this age group.^{1,2}

The recent WHO classification of tumors of soft tissue and bone (2020) distinguishes four major histological subtypes of RMS: embryonal, alveolar, spindle cell and pleomorphic RMS.³ Among them, embryonal RMS (RME) and alveolar RMS (RMA) are the most common in children, accounting for 57% and 23% of all cases, respectively.⁴ RME usually develops in children under 10 years of age and is associated with favorable prognosis.⁵ Conversely, RMA is characterized by more equal age distribution, aggressive biology, tendency to early dissemination and poor outcomes.⁶

As a primitive mesenchymal neoplasm, RMS may develop anywhere in the body.⁵ Genitourinary tract tumors constitute approximately 15%–20% of all RMS. They affect mainly children younger than 5 years old and are usually of embryonal histology.^{5,7,8} Bladder and prostate (B&P) are the most common genitourinary RMS locations in male patients. Due to frequent difficulties in defining the organ of origin, these tumors are usually classified together. Typical clinical manifestation of B&P RMS is pain, dysuria and hematuria. In advanced stages, the mass effect of growing tumor may result in abdominal distention, urine retention and constipation. In some children, passing small fragments of tumor tissue in urine may occur.⁷

Notably, initial symptoms of B&P RMS in children may mimic more common, benign conditions such as urinary tract infections (UTIs), functional disorders and congenital anomalies of kidney and urinary tract (CAKUT).

2. AIM

The aim of the study is to emphasize the role of careful clinical examination and strict following the basic guidelines of UTI management in early detection of pediatric B&P RMS in primary care and emergency department settings.

3. CASE STUDY

3.1. Case 1

A 3-year-old boy presented at the general practitioner (GP) office with increasing lower abdominal pain and dysuria. A UTI was diagnosed and treated with antibiotics. No urinalysis or urine culture were performed. Despite the treatment, the symptoms persisted and after 2 weeks complete urinary obstruction with severe abdominal pain occurred. Since the analgesic drugs caused only slight improvement, the child was brought to the emergency department, where bladder catheterization relieved his symptoms. Over 800 mL of urine was obtained. No diagnostic procedures were performed, symp-

toms were attributed to UTI and child's inability to control urination. During following days, the situation repeated 3 times. Eventually, the ill-appearing, suffering child was admitted to the pediatric ward. A huge prostate tumor compressing bladder was revealed by ultrasonography (USG), so the patient was immediately transferred to the pediatric oncology clinic.

At admission, the child needed constant catheterization of the bladder and pain-relieving drugs. In the computer tomography (CT) scan, an extensive pathological mass measuring 73 × 82 × 130 mm, filling all the minor pelvis was visible (Figure 1). Numerous enlarged lymph nodes suspicious for metastases were also present along the iliac vessels. A laparoscopic surgical diagnostic biopsy was performed, complicated with tumor rupture with massive peritoneal bleeding. Due to highly advanced disease, life-saving chemotherapy (CHT) was immediately introduced. Based on histopathological analysis, RME was diagnosed and the child continued treatment according to the Cooperative Weichteilsarkom Study Group (CWS) protocol for high-risk sarcomas. When tumor size decreased, a subtotal bladder-preserving resection involving prostate, vas deferens and seminal vesicles was performed. To avoid external beam radiotherapy of the minor pelvis, the child was referred to Gustave Roussy Institute, Paris, France, where further surgical resection of the small remaining tumor of the prostate was performed followed by brachytherapy initiation. Currently, the patient remains cancer-free 7 years after oncological treatment. However, he suffers from incontinence and urgency of urination. Also, fertility impairment will appear as a late treatment consequence.

3.2. Case 2

A 2.5-year-old boy presented to the GP with lower abdominal pain and dysuria. No urinalysis was performed. The urine culture revealed *Enterococcus faecalis* UTI. Antibiotic therapy with amoxicillin and clavulanic acid led to a temporary improvement. After 6 weeks, the symptoms of UTI returned.

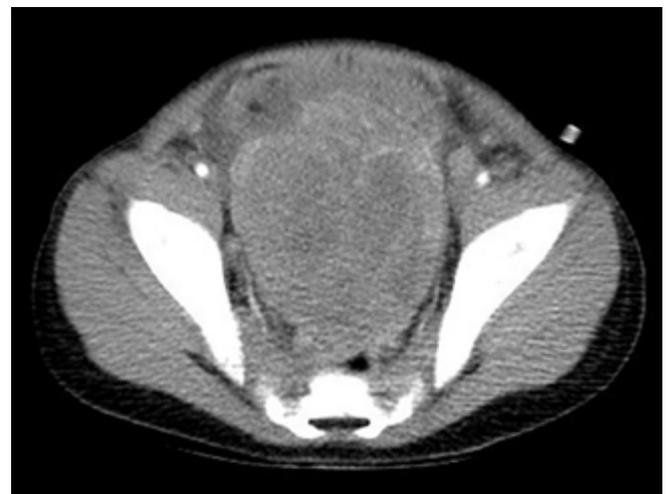


Figure 1. Patient 1: The CT examination of the pelvis at diagnosis. A solid-cystic pathological mass originating from prostate, measuring 73 × 82 × 130 mm, with heterogeneous contrast enhancement.

At that time, the mother noticed that the child occasionally excreted blood clots with urine. The re-infection was treated empirically with cefuroxime, with no response. During both infections, no thorough physical examination or USG of abdomen were performed. The GP suspected that recurrent UTIs were due to phimosis and referred the child for circumcision. No physical examination of abdomen or any imaging studies were performed before or after the surgery. The symptoms did not relieve after the circumcision. The child had another severe UTI episode with purulent discharge from the urethra, once again unsuccessfully treated with antibiotic therapy.

Ultimately, the parents brought their suffering child to the regional pediatric hospital, where he was diagnosed with UTI and simultaneous viral gastrointestinal tract infection. During the hospitalization the boy vomited several times and passed blood, mucous and purulent excretions with urine. The symptoms slightly improved after antibiotic treatment (ampicillin); however, proteinuria, erythrocyturia and leukocyturia persisted. Eventually, USG examination was performed, revealing a huge bladder mass filling 2/3 of the bladder lumen. The child was referred to the pediatric oncology clinic – over 2 months after the onset of symptoms.

At the admission to clinical hospital, the child was malnourished, ill-appearing and suffering from severe pain. A pathological mass was palpable in the suprapubic region. To provide the urine outflow, the patient needed insertion of the bladder catheter and, later, of the suprapubic cystostomy. The magnetic resonance (MR) examination of abdomen and pelvis revealed extensive, irregular bladder mass measuring $62 \times 45 \times 46$ mm, infiltrating the internal urethral meatus and ureteral orifices, leading to hydronephrosis (Figures 2 and 3). Four enlarged lymph nodes suspicious for metastases were also detected nearby the bladder and along the external iliac vessels.

The biopsy of the tumor displayed RME histology. Immediately after, the child started oncological treatment according to the high-risk group of CWS protocol for soft tissue sarcomas. After 8 courses of intense CHT, the tumor diminished significantly. However, due to persistent infiltration of the bladder walls, the bladder-preserving surgery was not feasible and the cystectomy had to be performed. An intestinal pouch and urostomy were done to ensure a urine outflow. The surgery was macroscopically complete; however, the resection margins were positive for tumor cells (microscopically incomplete resection, R1). Pathological examination revealed also one metastatic common iliac lymph node. Therefore, the second-line CHT according to CWS protocol was initiated. Currently, the patient has completed 2 cycles of the second-line CHT and is undergoing pelvis radiotherapy.

4. DISCUSSION

The symptoms of B&P RMS in children may occur relatively early in the course of disease. However, they are often non-specific and include pain, dysuria and/or hematuria – a constellation of symptoms suggestive for UTI.^{7,8} Moreover,



Figure 2. Patient 2: The MRI examination of the abdomen and pelvis at diagnosis. A T1-weighted coronal image showing bilateral hydronephrosis due to bladder tumor compressing ureteral orifices and internal urethral meatus.

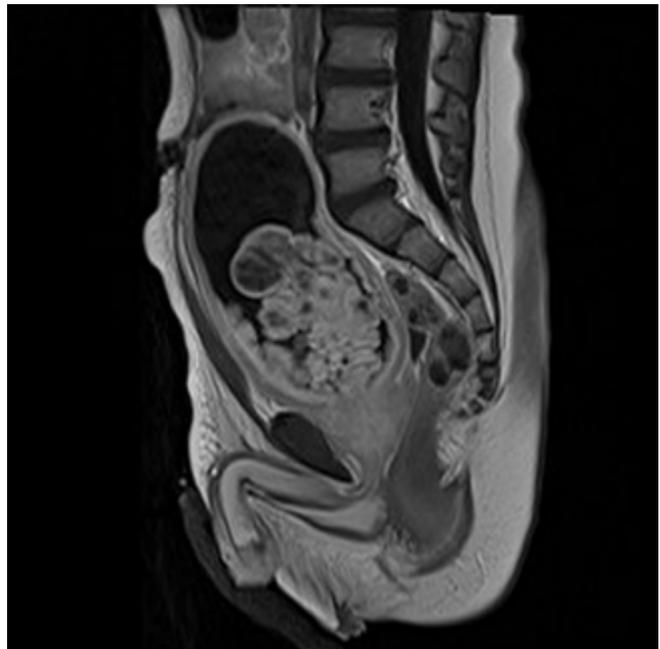


Figure 3. Patient 2: The MRI examination of the abdomen and pelvis at diagnosis. A T1-weighted sagittal image – huge pathological solid mass measuring $62 \times 45 \times 46$ mm, filling 2/3 of the bladder lumen.

the urinary tract obstruction caused by growing tumor predisposes to the development of concomitant UTI.

Indeed, both of the described patients initially presented at the GP offices with uncharacteristic abdominal pain and dysuria. The initial diagnoses of UTIs were made and, consequently, antibiotic treatments were administered. According to the current expert recommendations for management of UTI in children (including both Polish and European guidelines), every diagnosis of UTI should be confirmed by urinalysis and urine cultures.^{9,10} In the first patient, these tests were not performed initially, in the second patient only the urine culture was obtained.

Moreover, in both presented patients no abdominal USG or any other imaging studies were conducted despite atypical and severe course of disease. According to the above-mentioned recommendations, USG examination should be performed in every child with higher risk of CAKUT – in all children younger than 24 months of age and in older children with pyelonephritis, recurrent UTI or atypical course of UTI. Atypical course of UTI is defined as the presence of at least one of the following: failure to respond to antibiotic treatment within 48 h, severe clinical condition of the patient, urosepsis, urinary tract obstruction, palpable abdominal mass, elevated serum creatinine and non-*Escherichia coli* infections.^{9,10} These factors were present in both patients: no response to antibiotic therapy and, later, complete urinary tract obstruction in the first patient and multiple recurrent UTIs with persistent difficulties in urination in the second. In this child, at admission to pediatric oncology clinic, a significantly enlarged bladder with tumor mass was easily palpable in suprapubic area. However, it was not discovered before, because the patient's abdomen was not examined, even before the circumcision which was performed as phimosis was thought to be responsible for dysuria.

Furthermore, the second patient experienced episodes of excreting blood clots with urine. Hematuria in children (both macro- and microscopic) may occur in the course of UTI but may also be associated with wide spectrum of other, more serious diseases. They include also malignancies of the B&P and kidney, such as Wilms tumor, typical for the age of the patients presented. Therefore, in the second patient, presence of blood clots in the urine should be another strong indication to immediately perform the ultrasound of the pelvis and abdomen.

Proper diagnoses of malignancy were delayed in both patients and they were admitted to the pediatric oncology department in poor clinical condition, suffering from severe pain related to disease and previous medical interventions, requiring constant bladder catheterization. The children were diagnosed at advanced stage of disease, when the primary non-mutilating resection of the tumor was not feasible.

The prognosis in RMS has improved significantly during recent decades, reaching more than 75% probability of the 5-year overall survival in localized B&P tumors.^{5,11} This progress has been achieved thanks to intensive risk-adapted multimodal oncological treatment. However, B&P RMS survivors commonly experience treatment side-effects, such as:

urinary incontinence, recurrent UTIs, decreased renal function, infertility and secondary malignancies.^{12–14} Therefore, the modern therapy of B&P RMS is aimed at preserving the bladder and sexual function. In most cases the upfront biopsy followed by aggressive CHT, radiotherapy and, if necessary, delayed surgery of the residual tumor mass is preferred to avoid cysto-prostatectomy.⁸ In some centers, perioperative brachytherapy is successfully used to reduce the irradiation sequelae.^{15,16} The children treated with bladder-sparing strategies have comparable outcomes and better quality of life compared to patients treated with radical cystectomy.^{15–17}

In the first patient, intense CHT produced dramatic regression of the primary tumor and metastatic lymph nodes, which enabled bladder-sparing subtotal resection of the remaining tumor followed by adjuvant brachytherapy. Such a strategy was not possible in the second child, due to massive bladder wall infiltration by RME at diagnosis. In spite of very good response to CHT, bladder-sparing delayed resection was not feasible, resulting in severe mutilation and decreased quality of life.

5. CONCLUSIONS

B&P RMS is a rare disease which may not be initially considered in differential diagnosis in children with recurring or atypical UTI. However, careful physical examination and adherence to the guidelines of UTI management aimed at detecting more common CAKUT, may also allow for an early diagnosis of this malignancy. Early proper diagnosis of B&P RMS may lead to better prognosis and, diminishing the treatment burden, improve quality of life of B&P RMS survivors.

Conflict of interest

None declared.

Funding

None declared.

Ethics

Informed consents from the parents of presented children were obtained.

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