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CASE REPORT

Management of the local relapse of the bladder – prostate rhabdomyosarcoma

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ABSTRACT

Introduction: Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children. Genitourinary locations occur in approximately 20–30% of cases. Children with RMS localized in the bladder or/and prostate require multi-modal therapy with systemic chemotherapy in conjunction with surgery or radiation therapy to maximize local tumour control.

Material and methods: The report presents a case of a 3-year-old boy diagnosed in 2015 with embryonal RMS, who was treated due to relapse of RMS in the urinary bladder in 2016–2018. The patient was treated with chemotherapy, radiotherapy, and surgery (the urinary bladder was excised, and a neobladder was created according to Florida-pouch procedure). Currently, the patient is in the 3rd year of observation after the end of oncological treatment

Conclusions: The treatment for RMS localized in the bladder puts the priority on organ-sparing techniques. Radiotherapy or brachytherapy are standard supplementary treatments. However, in the case of relapse, mutilating rescue surgery still has value.

KEY WORDS:

surgical treatment, bladder tumour, rhabdomyosarcoma.

INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma as well as the third most common extracranial solid tumour in children [1–3]. Rhabdomyosarcoma is classified as a small, round, blue-cell tumour of childhood [1]. The International Classification of RMS outlines 6 major pathologic subtypes of RMS: embryonal (botryoid); embryonal (spindle cell); embryonal, not otherwise specified (NOS); alveolar, NOS or solid variant; anaplasia, diffuse; and undifferentiated sarcoma [1].

Age at presentation follows a bimodal distribution [3]. With the vast majority of cases occurring in children or adolescents, two-thirds of reported cases occur before the age of 10 years [1]. It is more likely to occur in boys than in girls [3]. In most cases, there are no clear predisposing factors for the development of RMS. However, it has been correlated with familial cancer syndromes and congenital abnormalities [3]. According to the literature, one-third of RMS cases occur in the head and neck (including parameningeal locations), while genitourinary locations are found in approximately 20–30% of cases [1, 2]. The next most common sites are the trunk and extremities [1].

The pretreatment staging system based on the tumour/node/metastasis system includes primary tumour location, lymph node involvement, distant metastatic disease, and size [1]. The urinary bladder and prostate are described as unfavourable primary sites [1].

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Rhabdomyosarcoma typically presents as an asymptomatic mass [3]. The specific symptoms vary based on the site of occurrence and extent of disease [3]. Tumours involving the bladder, urinary tract, or prostate can cause obstruction, constipation, haematuria, and changes in urinary frequency [1].

It is important to underline that the approach to RMS differs between the largest study groups [2]. However, children with RMS localized in the bladder or/and prostate require multi-modal therapy with systemic chemotherapy in conjunction with either surgery or radiation therapy, or even both modalities, to maximize local tumour control [2].

CASE REPORT

A 3-year-old boy who had previously been treated with chemotherapy due to embryonal RMS diagnosed in 2015 was admitted to the Department of Paediatric Surgery to remove the residual lesion in the urinary bladder.

The diagnosis of embryonal RMS was established in 2015. Then, magnetic resonance imaging (MRI) of the pelvis with contrast revealed a bladder tumour measuring 37 × 62 × 50 mm with strong post-contrast reinforcement, not exceeding the bladder wall. The additional imaging studies excluded the presence of metastases. Based on the size of the tumour, location, and absence of metastases, the child was qualified for treatment according to the Cooperative Weichteilsarkom Studiengruppe (CWS) Guidance protocol of therapeutic group E. After 3 cycles of chemotherapy, the MR study revealed a tumour size regression of about 50% of the initial mass. Treatment was continued according to the protocol. The boy was qualified for surgical treatment after 7 cycles of chemotherapy.

The surgical treatment was performed under general anaesthesia on 16 March 2016. A median upper and lower laparotomy was performed with excision of the lesion in the urinary bladder (invading the right ureter orifice) and replantation of the right ureter above the resection line. The histopathological examination revealed so-called curative resection (R0).

After the end of intensive oncological treatment, maintenance chemotherapy was implemented according to the CWS Guidance protocol (O-TI/TE), which was carried out in the period 29 June – 12 December 2016.

The imaging studies were performed after the end of oncological treatment. The magnetic resonance of the pelvis (17 January 2017) showed a stationary image of postoperative changes. The study revealed a banded thickening of the bladder wall on the right side at a length of approximately 21 mm, with a thickness of up to 3.5 mm. No diffusion limitations were visible. After administration of a contrast agent, homogeneous strengthening was visible (postoperative fibrous changes – the image as in the previous study). A computed tomography (CT) examination of the thorax and abdominal cavity did not show any pathology. After a detailed analysis of the course of the entire oncological treatment, the child was qualified for local radiation therapy in the primary tumour area.

Radiation therapy was performed under general anaesthesia in the period 27 February – 31 March 2017. Two full weeks of local radiation therapy were performed in the primary tumour area (27 February – 3 March 2017 and 6–10 March 2017) without complications. In the third week of radiation therapy, only one day was performed because the child presented symptoms of an upper respiratory tract infection and was not qualified for general anaesthesia. The boy was successfully treated with hypertonic solution inhalations and oral clarithromycin. Controlled chest radiographs did not reveal any pathologies. After improvement, radiation therapy was continued 20–24 March 2017. However, on 22 March 2017, no full exposition was performed due to technical reasons. The last week of radiotherapy was performed on 27–31 March 2017. Controlled MRI, chest CT, and ultrasound were performed. On pelvic examination (18 October 2017), a pathological tissue mass was observed with total dimensions of 15 × 11 × 17 mm from the level of the internal urethral orifice, protruding into the bladder and contrasting against its background. A local recurrence of RMS was suspected. Additionally, imaging diagnostics were expanded to determine the stage of the disease. In chest cavity and abdomen CT, PET CT no metastatic lesions were found.

The patient was again admitted to the Department of Paediatric Surgery to confirm the diagnosis. Firstly, a cystoscopy under general anaesthesia was performed on 25 October 2017. During cystoscopy, sore pressure on the glans of the penile has been noticed. The catheter was removed. While passing through the neck of the urinary bladder, a small, smooth-bordered tumour was observed growing from the frontal wall of the bladder. The mucosal membrane was slightly reddish. Samples were collected for histopathological examination. The patient was again catheterized. Secondly, a biopsy of the bone marrow of the ala of the pelvis was performed. Thirdly, a Broviac catheter was inserted into the left external jugular vein.

The results of the histopathological exams indicated the local recurrence of the disease, without metastatic lesions in the bone marrow examination.

After analysing previous treatments, it was decided to include CEVAIE chemotherapy. The CEV block was administered, followed by VCR on the 8th day of the chemotherapy cycle. The administration of VCR for the 15th day of the cycle was abandoned due to infectious complications related to febrile neutropaenia. Then the drugs due for the I3VE block were administered.

Six weeks later, an ultrasound examination and MRI were performed. A massive circular thickening of the bladder wall was seen (diameter 18 mm) (Figure 1). The lesion was affecting the right ureter. Adipose tissue surrounding the bladder was oedematous. A small amount

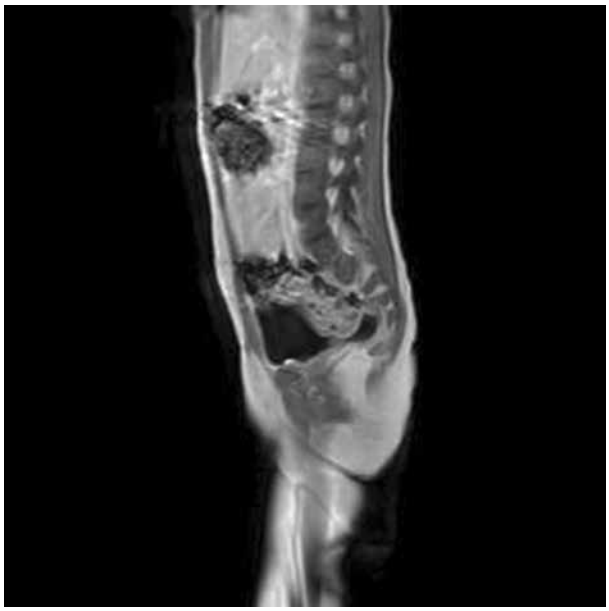

FIGURE 1. Massive circular thickening of the bladder wall (diameter 18 mm)

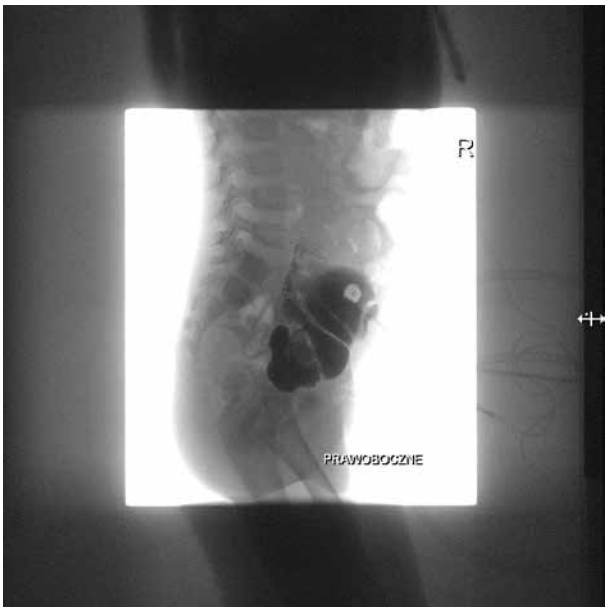

FIGURE 2. Lesion (diameter 0.5 cm)

of free fluid inside the pelvis was seen. A progression of relapse of RMS during CEVAIE therapy was diagnosed.

In the right ala of the pelvis, a lesion (diameter 0.5 cm) was seen (Figure 2). The intensity of the lesion on images increased with contrast injection.

On 11 December 2017, median laparotomy with a section of pubic symphysis was performed. The urinary bladder was removed and sent for histopathological examination, and regional lymph nodes were sampled.

During the procedure, the tumour inside the urinary bladder was separated from the surrounding tissues. The ureters were cut off from the bladder. The obtained samples were sent for histopathological examination. A Redon catheter was inserted via the urethra and left in the retroperitoneal space. In the next step, the ileocaecal complex, including the valve, was opened, isolated, and washed. Then, an appendectomy was performed. The continuity of the gastrointestinal tract was restored. Both ureters were inserted into the caecum and catheters were inserted.

A neobladder was created according to Florida-pouch procedure:

- isolation of the ascending colon and caecum,
- implantation of ureters,
- closure to form a pouch,
- installation of the ileal continent conduit,
- drainage and closure of the abdomen.

On the ileum, a valve was created and implanted in the abdominal cavity layers. The sac was closed and the Cystofix was left. In the postoperative period, the urinary tract infection was diagnosed. The microbiological examination of urine revealed *Escherichia coli* resistant to penicillin. Effective treatment according to the antibiogram was implemented.

X-ray and ultrasonography examinations were performed. In the X-ray performed 2 weeks after the surgery, small amounts of fluid in the upper part of the abdomen, along with slightly thickened small intestine in this area, were seen. In the ultrasonography examination, the pelvises of the kidneys were enlarged (left – up to 1.5 cm, right – up to 2 cm), and the proximal parts of the ureters were enlarged up to 1.1 cm.

The urethral catheters were removed on the 14th day after surgery, and the urinary catheter from the neobladder was removed on the 22nd day after surgery.

The patient's mother was given instructions on how to catheterize the bladder and how to rinse the bladder with saline.

On 29 December 2017, retrograde micturition cystourethrography was performed. Via the catheter inserted into the bladder, 20 ml of staining fluid was injected. No urine leakage was noticed during the examination (Figures 3, 4).

In the ultrasonographic examination (4 January 2018), a slight improvement was noted. The "neobladder" with intestines was localized in the pelvis minor; no urine was seen nearby. The right ureter was 1.2 cm in diameter. The kidney structure was less hyperechoic and with better corticomedullary differentiation when compared to the previous postoperative ultrasonographic examinations.

After analysing the previous treatment, it was decided to include treatment according to the ACCTTIVE scheme (6 blocks of chemotherapy according to the ACCTTIVE scheme were given). A cardiological consultation revealed no pathologies in the circulatory system. In total, for the treatment of recurrence, the patient received 8 blocks of chemotherapy – 2 cycles of chemotherapy according to the CEVAIE scheme and 6 blocks of chemotherapy according to the ACCTTIVE scheme.

In the control ultrasound examination of the abdominal cavity and pelvis minor (2 May 2018), a slightly

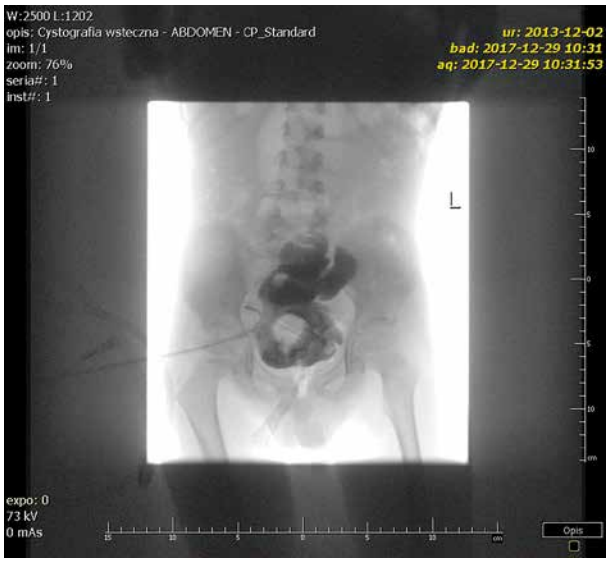

FIGURE 3. Pelvises of the kidneys – up to 1.5 cm

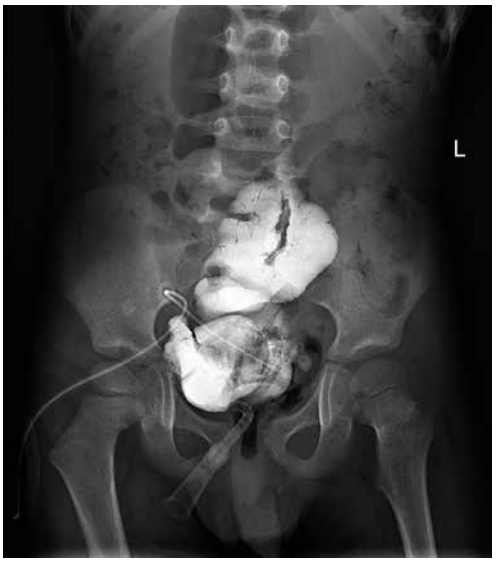

FIGURE 4. Pelvises of the kidneys – up to 2 cm

widened calyx-pelvic system of the right kidney (pelvis in AP 0.5 cm) was seen, calyces of all groups were widened to 0.7 cm. Moreover, the dilated calyx-pelvic system of the left kidney, the left renal pelvis widened to approximately 0.7 cm (in the AP dimension), and the calyces of all groups widened to 1 cm were visible. No pathologies of the spleen were seen. The intraperitoneal space was obscured by intestinal gases. A neobladder formed from the large intestine was seen. When filled with urine, it had irregular and non-thickened walls, without pathological reflections in the lumen. There was no free fluid in the abdomen, and no pathological fluid reservoirs or pathological vascularization in the fistula area.

Control CT of the chest cavity performed in January and May 2018 showed no pathology.

Then the boy received 7 blocks of maintenance chemotherapy treatment according to the vinblastine-cyclophosphamide CWS 2002 scheme (cyclophosphamide at a dose of 50 mg for 21 days, VBL once a week at the beginning of each week of treatment, and after 3 weeks, a 1-week break in treatment was planned).

In the CT of the chest cavity performed in January 2019, the lungs had no visible focal lesions, and there were no evidently enlarged pathological lymph nodes in the mediastinum and the lung cavities. The end of the vascular catheter was seen in the lumen of the superior vena cava. The bone structures visualized in the examination did not show any lesions suspected of being of metastatic nature.

In another control abdominal ultrasound, retention of urine in the collection system of the left kidney was seen. The pelvis of the left kidney in the AP dimension was widened to 1.4 cm. The calyces of all groups widened to 1.5 cm (upper calyx). Sub-pelvic segment of the ureter up to 1 cm was visible in a short section. A newly formed bladder was filled with urine up to a volume of 70 cm^3 with irregular, non-thickened walls and with moving multi-shaped reflections in the lumen, which were located adjacently and had dimensions of up to 20 mm.

Cardiac consultation performed after treatment revealed a morphologically and functionally normal circulatory system.

Pelvic MR examination performed after the completion of planned oncological treatment did not show any features of recurrence of the disease.

Currently, the patient is in the 3rd year of observation after the end of oncological treatment and remains under the care of the Department of Bone Marrow Transplantation, Oncology, and Paediatric Haematology. Moreover, he is regularly admitted to the Department of Paediatric Surgery to perform control MR examinations. He also remains under the care of paediatric nephrologists. Imaging examinations performed in 2021 (CT, MR) do not show signs of relapse. In the urinary system, there are no features of urine retention in the right kidney. However, there are features of urine retention in the left kidney (pelvis dilated to 2 cm in the AP dimension, calyces of the upper group widened to 2 cm, calyces of other groups up to 1.6 cm), and the left ureter is dilated in the sub-pelvic segment to 0.8 cm, in the middle part up to 1.3 cm, and in the segment before the reconstructed bladder to 1 cm. Laboratory test results, apart from mild hypokalaemia, are without abnormalities. The patient receives vitamin D_3 and kalium (potassium). As well as catheterization and rinsing of the bladder, the patient has to perform a general urine test/microbiological examination every week and in the case of increased body temperature.

CONCLUSIONS

Embryonal RMS is the most common paediatric soft-tissue sarcoma [4]. Typically, it presents as an asymptomatic mass. However, tumours involving the bladder, urinary tract, or prostate often cause obstruction, consti-

pation, haematuria, and changes in urinary frequency [1]. The diagnosis of RMS may be suspected clinically but needs to be confirmed by biopsy [1]. A full evaluation should be performed [1]. Preoperative treatment/evaluation of paediatric RMS involves history and physical examination, measurement of the lesion, complete blood cell count with differential and platelets, urinalysis, electrolytes, creatinine, calcium and phosphorus, liver function tests (alkaline phosphatase, lactate dehydrogenase, bilirubin, transaminases), bone marrow biopsy, chest radiograph, MRI/CT of the primary lesion, CT of the chest, MRI/CT of the head (for head tumors), bone scintigraphy, cerebrospinal fluid cytology for parameningeal tumours, and electrocardiography or echocardiography [1]. Primary resection of the tumour is a very important step of the treatment because the prognosis in RMS patients is linked to the amount of residual disease present after resection [1]. The best outcomes of treatment are seen among patients with completely resected tumours [1]. No microscopic residual disease offers the best chance for cure [1]. However, complete tumour resection in sites such as the bladder or prostate is not always feasible [1].

The operative approach depends on the primary tumour site, size, presence or absence of lymph node involvement, and distant metastases [1]. Decisions on treatment in such challenging cases must be made in the context of the multidisciplinary team, including the surgeon, oncologist, paediatric radiologist, and radiotherapist [1]. Such an approach allows for optimal patient care. Modern treatment concepts for bladder/prostate rhabdomyosarcoma (BPRMS) are designed to improve survival, reduce therapy intensity, and increase bladder preservation rates [5].

The increase in the bladder preservation rate was possible thanks to the development of conservative strategies including pulsed dose rate brachytherapy, which is feasible in very young patients and is associated with acceptable acute toxicity rates or partial surgery combined with brachytherapy [6–8].

To conclude, the philosophy of the treatment for bladder RMS offers a priority for organ-sparing techniques. Radiotherapy or brachytherapy are standard supplementary treatments. However, in the case of relapse mutilating rescue surgery still has value. Immediate reconstruction of the bladder is technically easier and lessens the extent of mutilation. It should be underlined that approximately 30% of RMS patients experience relapse, which puts them at risk of death from the progressive disease [1]. Among the factors associated with a better prognosis for recurrent disease are embryonal/botryoid histology, stage or group I of the disease, and relapse more than one year after completing primary therapy [1].

Patients with local relapse compose a very challenging patient population. Those with primary tumours localized in the bladder require repeated operations that are difficult and often mutilating [1]. According to the literature, in the long-term continent colonic urinary reservoirs (Florida-pouch) have an acceptable complication rate [9–11]. The most common problem is ureteral obstruction, especially in patients who have previously undergone it [9]. Moreover, the patients in whom longer bowel segments were resected, such as those with the conversion from another type of diversions, experienced a greater number of complications, especially ureteral obstruction associated with repeated reimplantation and metabolic derangement [9].

It should be underlined that radiotherapy puts the paediatric patient at risk of complications [12–14]. The extent of irradiation and the dose of radiation therapy (usually 40–50 Gy) in the treatment of RMS depend on the stage of the disease and the chemical treatment program adopted [13]. The optimal timing of radiotherapy treatment in RMS is still debated [14]. The appropriate choice of technique must take into account many factors; for example, determining the optimal solution for the specific tumour site, the extent of the disease, and the age of the patient, to maximize local control and the chance of cure [14].

Children successfully cured of RMS can live for many years [13]. The potential late toxicity of treatment can affect the quality of life of survivors [14]. Furthermore, children are treated with radiation therapy and chemotherapy [13]. The combined action of both methods can lead to serious side effects, for example, myocardial damage, pulmonary fibrosis, cirrhosis, kidney damage, and small intestine fibrosis [13]. In young children, growth disorders can occur, especially affecting the long bones [13, 14]. Furthermore, children treated for cancer have an increased risk of developing another cancer [13].

The treatment of RMS is constantly evolving. In 2021 Yechieli *et al*. published a paper that reviewed and contrasted the North American and European practice patterns, though ultimately the principles of staging, surgery, radiation therapy, and chemotherapy are similar in both the Children's Oncology Group (COG) and International Society of Paediatric Oncology (SIOP) treatment approaches [15]. Their efforts were underway to investigate improved local control rates in higher-risk patients using radiation dose escalation strategies and delayed primary excision in select cases [15]. They suggest that utilization of radiotherapy is more standardized within the COG framework, while International SIOP favours surgical resection in some scenarios [15]. According to the review, in the European approach surgical resection is a key pillar of local therapy for RMS [15]. Following induction chemotherapy, surgical resection is performed when any residual mass can be completely excised without causing a significant organ or functional impairment [15]. This means that selected patients with standard risk tumours and R0 resection can avoid radiotherapy. For other children it can enable use of a lower dose of radiotherapy [15].

Treating patients with the local relapse of bladder-prostate RMS remains a challenge for paediatric surgeons, paediatric oncologists, and radiation therapists.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Levy SM, Hetz RA, Letourneau PA, et al. Rhabdomyosarcoma. In: Holcomb GW, et al, eds. Ashcraft's pediatric surgery (sixth edition). W.B. Saunders 2014, 979-988.
2. Komasara L, Gołębiewski A, Anzelewicz S, et al. A review on surgical techniques and organ sparing procedures in bladder/prostate rhabdomyosarcoma. Eur J Pediatr Surg 2014; 24: 467-473.
3. Mollen KP, Rodeberg DA. Diagnosis and Treatment of Rhabdomyosarcoma. In: Coran AG, Caldamone A, eds. Pediatric Surgery, 7th ed. Mosby 2012, 491-499.
4. Dantonello TM, Lochbühler H, Schuck A, et al. Challenges in the local treatment of large abdominal embryonal rhabdomyosarcoma. Ann Surg Oncol 2014; 21: 3579-86.
5. Seitz G, Fuchs J, Sparber-Sauer M, et al. Improvements in the treatment of patients suffering from bladder-prostate rhabdomyosarcoma: a report from the CWS-2002P trial. Ann Surg Oncol 2016; 23: 4067-4072.
6. Chargari C, Haie-Meder C, Guérin F, et al. Brachytherapy combined with surgery for conservative treatment of children with bladder neck and/or prostate rhabdomyosarcoma. Int J Radiat Oncol Biol Phys 2017; 98: 352-359.
7. Chargari C, Martelli H, Guérin F, et al. Pulsed-dose rate brachytherapy for pediatric bladder prostate rhabdomyosarcoma: compliance and early clinical results. Radiother Oncol 2017; 124: 285-290.
8. Jenney M, Oberlin O, Audry G, et al. Conservative approach in localised rhabdomyosarcoma of the bladder and prostate: results from International Society of Paediatric Oncology (SIOP) studies: malignant mesenchymal tumour (MMT) 84, 89 and 95. Pediatr Blood Cancer 2014; 61: 217-222.
9. Webster C, Bukkapatnam R, Seigne JD, et al. Continent colonic urinary reservoir (Florida-pouch): long-term surgical complications (greater than 11 years). J Urol 2003; 169: 174-176.
10. Lockhart JL, Pow-Sang JM, Persky L, et al. A continent colonic urinary reservoir: the Florida-pouch. J Urol 1990; 144: 864-867.
11. Sanford EJ, Pow-Sang JM, Helal MA, et al. [Continent urinary diversion with the Florida-pouch]. Prog Urol 1992; 2: 616-622.
12. Krawczuk-Rybak M. Powikłania narządowe leczenia skojarzonego wczesne i odległe. In: Chybicka A, Sawicz-Birkowska K, eds. Onkologia i hematologia dziecięca. PZWL 2008, 1042-1063.
13. Skowrońska-Gardas A. Radioterapia w leczeniu nowotworów u dzieci. In: Chybicka A, Sawicz-Birkowska K, eds. Onkologia i hematologia dziecięca. PZWL 2008, 161-167.
14. Mandeville HC. Radiotherapy in the management of childhood rhabdomyosarcoma. Clin Oncol 2019; 31: 462-470.
15. Yechieli RL, Mandeville HC, Hiniker SM, et al. Rhabdomyosarcoma. Pediatr Blood Cancer 2021; 68: e28254.