

Review Article

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Intensity Modulated Radiotherapy in the Complex Treatment of High-Risk Wilms' Blastemal Tumor with Thrombosis in the Inferior Vena Cava - A Clinical Case from Our Practice

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ABSTRACT

Nephroblastoma is a malignant tumor that is diagnosed in children under 5 years of age. Complex treatment is required, including chemotherapy, surgery and, if necessary, local abdominal radiotherapy. The high-risk group with diffuse anaplastic or blastemal nephroblastoma after completion of chemotherapy (Ch) requires careful consideration of the timing of surgical intervention and the necessary postoperative radiotherapy.

We present this a child with high-risk blastemal type nephroblastoma with thrombosis in the inferior vena cava to emphasize how important and significant it is to carry out all components in the complex treatment, namely preoperative chemotherapy, surgical treatment, postoperative local radiotherapy, postoperative chemotherapy, and in the case of pulmonary metastases, if possible, their surgical removal and the conduct of radiotherapy to both lungs.

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Introduction

Wilms' tumor (WT) accounts for approximately 95% of childhood renal tumors, predominantly of renal origin [1]. Nephroblastoma (NB) presents in children under 5 years of age as an abdominal mass, often discovered by parents during bathing or by a pediatrician during a routine physical examination. Although often asymptomatic, the following symptoms may occur: abdominal pain, hematuria, and in some cases hypertension [2]. Patients are divided into low-, intermediate-, and high-risk groups according to the degree of tumor necrosis and the relative proportion of each of the three cellular components (epithelial, stromal, or blastemal). Patients with diffuse anaplastic or blastemal NB after completion of chemotherapy (Ch) are classified as high-risk histological type [3]. New treatment strategies are needed in patients with anaplastic Wilms tumors (AWTs) to improve disease-free survival (EFS) and overall survival (OS) [4]. In this article, we present a child with high-risk NB with inferior vena cava thrombosis who underwent a complex treatment including preoperative chemotherapy (Ch), surgery, and postoperative local radiotherapy (RT).

Clinical Case

We present a 4-year-old child with a complaint of hematuria in November 2024. Computed tomography (CT) of the abdomen showed a large tumor mass originating from the upper pole of the left kidney. The tumor had axial dimensions of 86/102 mm with infiltration into the left renal vein, inferior vena cava and

partially the right renal vein. No evidence of distant hematogenous metastases (Figure 1).

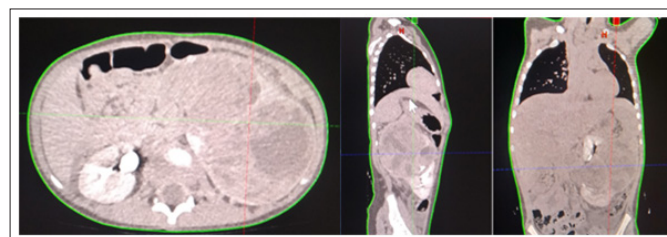


Figure 1: Abdominal Computed Tomography Scan Shows a Large Tumor Mass Originating from the Upper Pole of the Left Kidney.

Diagnosis

Most likely it is Wilms' tumor. The oncology committee decided to conduct neoadjuvant chemotherapy for localized Wilms' tumor according to the SIOP 2001 protocol with Vincristine and Liovac. After two courses of chemotherapy, the child was referred to the Pediatric Urology Clinic, where the control computed tomography (CT) reported a reduction of the tumor, including its intravascular infiltration. The planned surgery was postponed due to logistical difficulties in providing a vascular surgeon. In February 2025, another course of chemotherapy (Ch) with vincristine and pharmarubicin (epirubicin) was performed. The child was again referred for surgery, but this time the possibility of surgical intervention was again rejected due to the categorical refusal of the vascular surgeon in view of the high surgical risk. In March 2025, the repeat CT scan reported shows an enlarged tumor size of the left kidney 85/83/99 mm compared to 56/48/61 mm

on previous examination (Figure 2). From March to May 2025, 4 courses of Ch with vincristine and pharmarubicin were performed. After 6 courses of neoadjuvant Ch, MRI reported a large (450 ml) locally advanced Wilms tumor of the left kidney with an increasing cystic necrotic component and limited diffusion of solid tumor foci. A thrombus associated with the tumor was observed in the inferior vena cava at the level of its venous confluence with the liver with a clearly visible lumen in the lower part of the hepatic segment and suspected complete occlusion in the upper part of the hepatic segment. There was no evidence of distant hematogenous metastases.

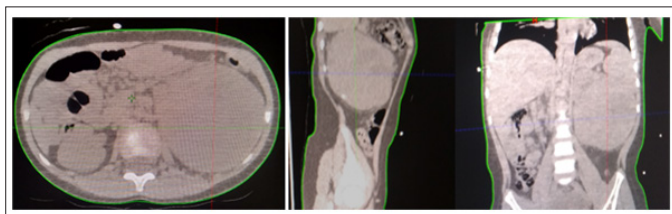


Figure 2: Computed Tomography Scan Shows an Enlarged Tumor Size of the Left Kidney 85/83/99 mm Compared to 56/48/61 mm on Previous Examination.

On 28.05.2025 the child was operated in Germany /University Clinic in Heidelberg/, where radical surgery of the primary tumor, lymphatic dissection and simultaneous removal of the thrombus in the inferior vena cava were performed.

Intraoperatively

The renal tumor was radically removed. The inferior vena cava contains a minimal amount of thrombotic material and shows signs of chronic inflammatory thickening of the wall.

Macroscopically

506 g preparation of a renal tumor measuring 15.5 cm / 11 cm / 6 cm with a ureter length of 11 cm. The fat capsule is 3 cm wide. A predominantly cystic tumor measuring 9.5 / 8.5 / 7 cm with a white viscous surface, limited by a 2 mm capsule, is found. No large-area necrosis is visible on the tumor surface. Macroscopically, the tumor infiltrates the renal parenchyma.

Histological Result

In the renal parenchyma, an expansively growing capsule-limited malignant neoplasm with regressive changes is observed /fibrosis and signs of myxoid loosening in 35% of the tumor surface/. The vital tumor occupies over 95% of the tumor surface. It consists of blastoma components consisting of small to medium-sized oval cells with hyperchromic oval nuclei, eosinophilic cytoplasm with moderate polymorphism, medium-dense nuclear chromatin and prominent nucleoli. There is no evidence of local or diffuse neoplasia. Single tubular structures under 5% of the vital tumor in the form of primitive cuboidal cells with scarce eosinophilic cytoplasm. The vital tumor is 95% with the content of an undifferentiated blastoma component. 6 are the dissected lymph nodes without the presence of metastases.

Conclusion

Nephroblastoma with undifferentiated blastoma component. - high risk, given the preoperative chemotherapy with a reported vital tumor. In June-July 2025, the child underwent postoperative intensity-modulated radiotherapy (IMRT) in the left abdominal

region with CTVp (preoperative tumor volume + 1 cm distance in all directions) and CTVn (para-aortic lymph nodes) with a daily dose (DD) of 1.6 Gy up to a total dose (TD) of 14.4 Gy, using 9 fractions. (Figure 3A, Figure 3B). Immediately after this, we performed surdosage/ boost in the tumor bed with a reduced CTVp distance, considering the preservation of the surrounding normal critical organs at DD 1.8 Gy up to TD 10.8 Gy (in the tumor bed up to TD 25.2 Gy) (Figure 4A, Figure 4B). The child was referred to pediatric oncohematology for adjuvant Ch. Given the data on the significantly delayed operation and the intraoperative finding of a vital tumor containing an undifferentiated blastoma component, despite the preoperative Ch, a decision was made to continue the child's treatment with intensive adjuvant Ch - 4 courses according to the ICE regimen /Ifosfamide, Carboplatin and Etoposide/.

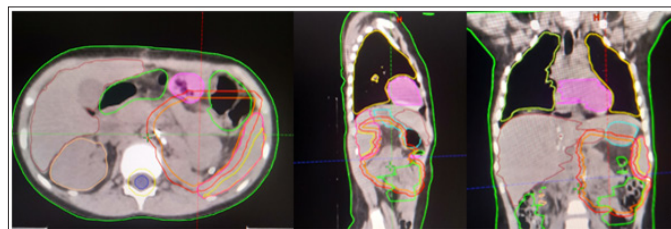


Figure 3A: Contouring of the Target Volumes CTVp and CTVn, in which a Total dose (TD) of 14.4 Gy should be Delivered, using 9 Fractions.

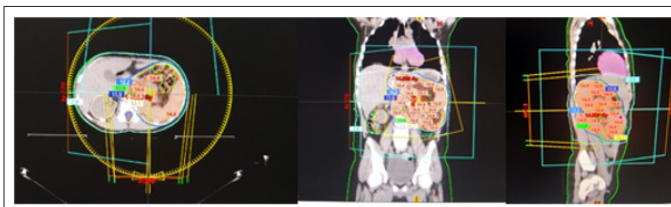


Figure 3B: Postoperative Intensity-Modulated Radiotherapy (IMRT) using the VMAT Method to the Left Abdominal Region with CTVp (Preoperative Tumor Volume + 1 cm Distance in all Directions) and CTVn (Para-Aortic Lymph Nodes) with a Daily Dose (DD) 1.6 Gy up to a Total Dose (TD) 14.4 Gy, via 9 Fractions.

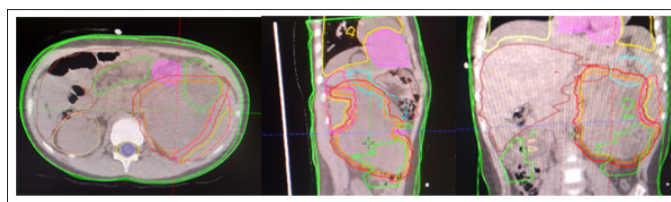


Figure 4A: Contouring of the CTVp/Boost Target Volume (Tumor Bed) in which a Total Dose (TD) 10.8 Gy must be Delivered. The TD from the Two Irradiations up to 25.2 Gy.

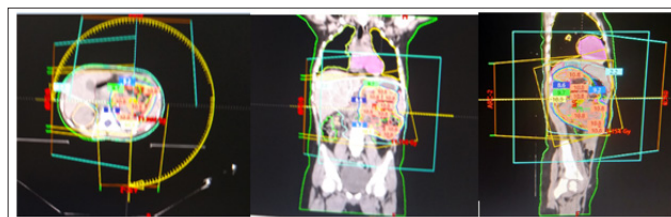


Figure 4B: IMRT using the VMAT Method for Overdosage/ Boost in the Tumor Bed with Reduced CTVp Distance, Considering the Preservation of Surrounding Normal Critical Organs at DD 1.8 Gy up to TD 10.8 Gy (in the Tumor Bed up to a TD 25.2 Gy).

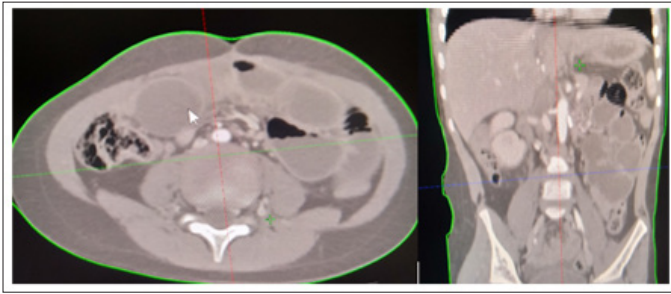


Figure 5: Abdominal CT with Contrast/ September 2025- Intestinal Ileus, most Likely Brid-Ileus.

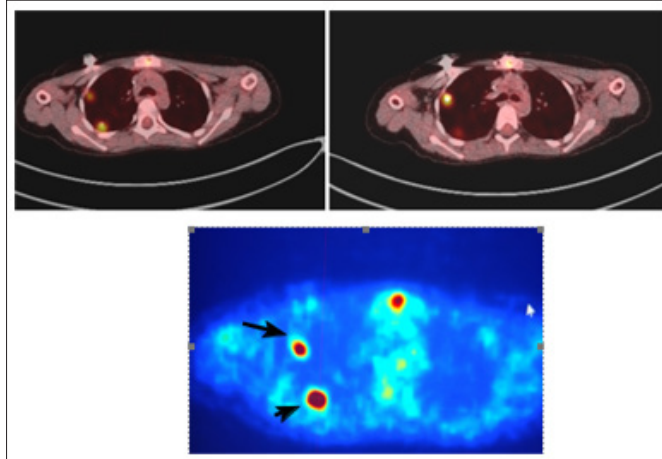


Figure 6: PET/CT from January 2026, which Demonstrates the Two Hypermetabolic Pulmonary Nodules in the Upper Lobe /2nd and 3rd Segments/ of the Right Lung.

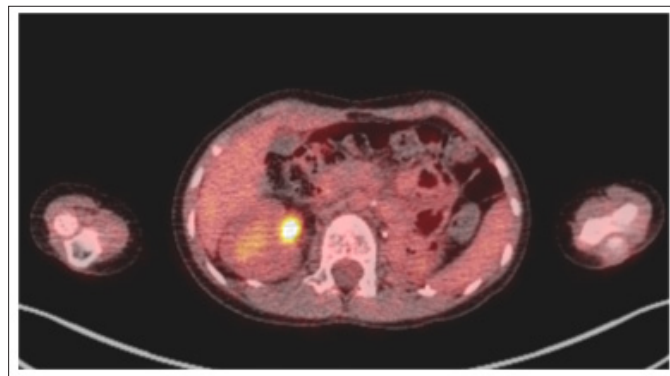


Figure 7: PET/CT from January 2026 without Local Recurrence.

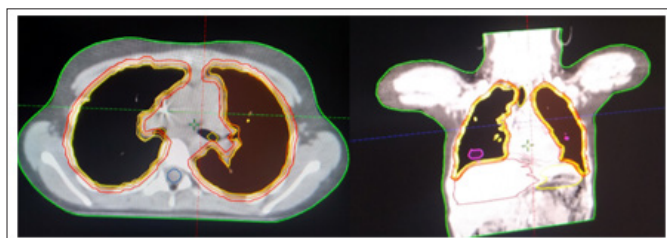


Figure 8A: Contouring of Both Lungs for the Purpose of Irradiation.

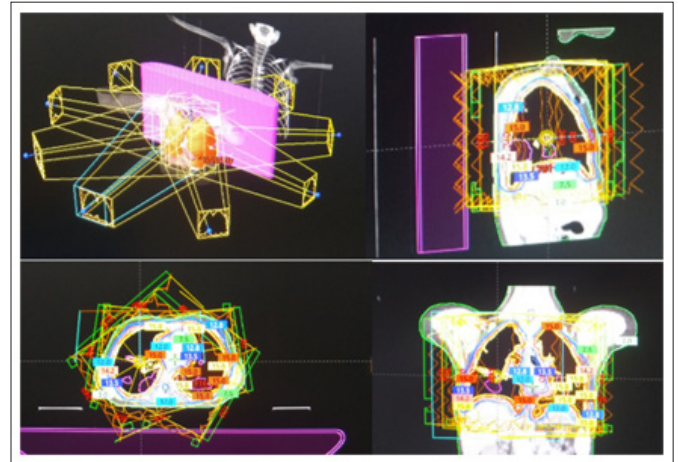


Figure 8B: IMRT to the Lung Area/Bilateral with DD 1.5 Gy up to TD 15 Gy.

Two courses of Ch were administered, after each of which the child had drug-induced bone marrow anaplasia. Due to abdominal pain accompanied by profuse vomiting, a contrast-enhanced computed tomography of the abdomen was performed in September 2025. Significantly dilated intestinal loops of the duodenum and jejunum were noted with a transition zone between the dilated loops and the normal lumen of the small intestine at the level of the ileal junction. The ileal loops are collapsed and appear free of a small amount of fluid in the pelvis and lower abdominal area. Right kidney – compensatory enlarged with preserved shape, parenchymal zone and drainage. Left kidney – not scanned. No contrast-enhancing formations are visible in its bed. No evidence of secondarily enlarged intra-abdominal lymph nodes. Surgical clips in the area of the transition part of the inferior vena cava and in the bed of the left kidney. Evidence of a small amount of free fluid in the pelvis.

Conclusion: Intestinal ileus, most likely brid-ileus. (Figure 5) The child was urgently referred to a pediatric abdominal surgeon. On 23.01.2026, the control computed tomography of the whole body revealed data on two pulmonary metastases in the right lung. The lungs have preserved density characteristics and vascular architectonics of the pulmonary parenchyma bilaterally. The metastasis in the second pulmonary segment on the right measures 13.5 mm x 11 mm, and that in the third segment on the right measures 9.7 mm x 10.5 mm. Before undertaking surgical removal of the pulmonary metastases, the pediatric pulmonary surgeon requires a mandatory PET/CT, which proves the two hypermetabolic pulmonary nodules in the upper lobe /2nd and 3rd segments/ of the right lung (Figure 6) without evidence of locoregional recurrence of the primary tumor (Figure 7), as well as without other foci of distant hematogenous dissemination. On 06.02.2026. surgical resection of the two metastatic pulmonary nodules was performed with histological confirmation that they were metastases from NB. Given the high-risk NB, despite radical surgery of both lung metastases, after a one-month interval, the child was assessed for additive postoperative irradiation of both lungs. In March 2026, IMRT was performed in the lung area/ bilaterally with DD 1.5 Gy up to TD 15 Gy (Figure 8A, Figure 8B). The child was referred to Pediatric Oncohematology to assess the need for subsequent maintenance Ch.

Discussion

Tumor staging and histological classification are readily achievable in resource-limited settings and remain valid prognostic classifiers

in middle-income countries such as ours [5]. Based on the impact of preoperative chemotherapy, the SIOP classifies NB subgroups by risk level, which is determined by the histological changes in the tumor after chemotherapy [6]. Approximately 6% of Wilms tumors have cells with nuclear enlargement, nuclear atypia, and irregular mitotic figures and are considered to have anaplastic histology (AH). Patients with anaplastic Wilms tumors of stages II to IV are treated with vincristine, doxorubicin, cyclophosphamide, and etoposide for 24 weeks, surgery, and postoperative radiotherapy to the area of the resected kidney bed, along with the tumor [4]. Surgery is the mainstay of treatment for almost all children with Wilms tumor. The primary goal of surgery is complete radical tumor removal to prevent its spread into the abdominal cavity. The standard surgical procedure for unilateral nephroblastoma is transperitoneal radical nephroureterectomy with unilateral lymphadenectomy. Extended lymphadenectomy is not required, but the perihilar, paraaortic, and paracaval lymph nodes should be removed in all cases. In the presented child, surgery was postponed because a tumor thrombosis of the inferior vena cava was diagnosed, requiring a combined surgical team consisting of a pediatric abdominal and vascular surgeon. The neoplastic thrombus is usually diagnosed at the same time as the tumor, although in some cases, the diagnosis of the thrombus may precede the diagnosis of nephroblastoma [7]. Tumor histology and its stage after surgery are important factors in classifying the respective disease risk. In the SIOP 6 study, response to preoperative Ch was identified as an important parameter for stratification, and the SIOP 93–01 study showed worse outcomes in patients with blastoma-type tumors (5-year disease-free survival/EFS 67%) [8]. Despite six preoperative courses of chemotherapy, the vital tumor occupied over 95% of the tumor surface and contained blastoma components composed of small to medium-sized oval cells with hyperchromic oval nuclei, eosinophilic cytoplasm with moderate polymorphism, moderately dense nuclear chromatin, and prominent nucleoli. The time between nephrectomy and RT has a significant impact on therapeutic outcomes [9]. The UMBRELLA-SIOP 2016 protocol recommends an interval of 2 to 4 weeks [10]. The criteria for classifying children into stage III are somewhat heterogeneous, including variables that may relate to tumor biology (lymphatic invasion, tumor thrombosis), surgeon skill (intraoperative rupture, incomplete resection), or other factors that may be independent of the inherent aggressiveness of the tumor (e.g., spontaneous preoperative tumor rupture) [11]. According to the COG protocol, postoperative local radiotherapy (RT) is required for all anaplastic tumors (AT) [12,13]. RT is particularly useful for preventing local recurrence and treating lung, liver, brain, and bone metastases [14]. Limited access to supportive care, RT, and some chemotherapeutic agents (i.e., carboplatin, alkylating agents) limits the ability to intensify therapy in high-risk tumors [15]. After a four-week interval, we performed postoperative intensity-modulated radiotherapy (IMRT) to the left abdominal region with CTVp (preoperative tumor volume + 1 cm distance in all directions) and CTVn (para-aortic lymph nodes) with a daily dose (DD) of 1.6 Gy up to a total dose (TD) of 14.4 Gy using 9 fractions (Figure 3B). We then performed an overdose (boost radiotherapy) in the tumor bed with a reduced distance from the CTVp, considering the preservation of surrounding normal critical organs with a DD of 1.8 Gy to a TD of 10.8 Gy (total in the tumor bed to a TD of 25.2 Gy) (Figure 4B). The blastoma type WT, defined as a tumor consisting of at least $\geq 66\%$ viable blastema after preoperative Ch [16], can by definition only be classified in tumors treated with chemotherapy before surgery [8,17]. Given the data on compromising preoperative therapy with delay of surgery and high-risk NB, it was decided to conduct intensive adjuvant Ch (4

courses of ICE regimen /Ifosfamide, Carboplatin and Etoposide/). Two courses of adjuvant Ch were performed, after each of which the child had drug-induced bone marrow aplasia. In addition to the bone marrow aplasia, a complication of subileus occurred, which delayed the application of adjuvant Ch. This is the prerequisite for the development of two pulmonary metastases in the right lung (Figure 6). According to Berger et al., pulmonary metastases account for 93.5% (29/31) of distant metastases in WT [18]. In order to perform surgery, the pediatric thoracic surgeon requested a PET/CT scan to verify the pulmonary metastases by their increased metabolic activity. Due to the high-risk histology, despite their surgical removal with tumor-clear resection lines, the child required IMRT to both lungs to a total dose of 15 Gy due to the high-risk histology. We performed postoperative RT to both lungs up to a TD 15 Gy (Figure 8B). We present this clinical case to emphasize how important and significant it is to carry out all components in the complex treatment of high-risk NB, namely preoperative chemotherapy, surgical treatment, postoperative local radiotherapy, postoperative chemotherapy, and in the case of pulmonary metastases, if possible, their surgical removal and the conduct of radiotherapy to both lungs [17,18].

Conclusion

Blastemal type WT is a high-risk neoplasm requiring aggressive chemotherapy, possibly radical surgery, and a short time interval (probably about two weeks) after surgery for postoperative local radiotherapy. Adjuvant chemotherapy is necessary after radiotherapy to reduce the risk of distant hematogenous metastases. In the case of pulmonary metastases, despite their radical extirpation, radiotherapy up to 15 Gy in the area of both lungs is required, followed by chemotherapy.

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