Nonresponsiveness to Chemotherapy: A Formidable Surgical Challenge in Wilms' Tumor with Intracardiac Extension

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Introduction

Intracaval tumor extension is reported in 4 % to 10 % of cases, mostly into the infrahepatic portion. However it may rarely extend into the right atrium (1.4 %) [1]. The management of tumors that extend into the inferior vena cava is determined by extent of tumor thrombus, possibility of tumor embolus, histology type, responsiveness of the tumor to chemotherapy, and tumor stage at presentation [1, 2]. However, neoadjuvant chemotherapy followed by surgery is advocated in tumor with intravascular extension [1, 3].

Case

A 7-year-old previously healthy girl was admitted to pediatric medicine unit in our hospital with chronic abdominal pain, weakness and loss of weight. Clinical examination was normal. On imaging, it showed right renal pelvic mass measuring 3.4×3.1 cm with extension into the right renal vein and there was large tumor with calcification occupying entire inferior vena cava which was 3 cm wide with right atrial extension with bilateral pleural effusion. (Figs. 1a and 2a)

Per-cutaneous computed tomography (CT) guided tumor biopsy revealed favorable Wilms' tumor. With stage III disease, the patient underwent 8 weeks of neoadjuvant chemotherapy with Vincristine, adriamycin, actinomycin. A repeat CT scan showed no response to chemotherapy and there was persistent tumor extension into the retrohepatic inferior vena cava and right atrium. (Figs. 1b and 2b)

The child was operated with facility for Cardio-Pulmonary Bypass and Transesophageal Echocardiogram (TEE) available. After induction, TEE confirmed the tumor thrombus extending above the diaphragm into the right atrium. The patient underwent right radical nephrectomy through right upper abdominal transverse incision. After obtaining control and temporary occlusion of the suprarenal and infrarenal inferior vena cava, cavotomy were performed to remove the tumor thrombus. Thrombus was densely adherent to inferior vena cava, thus it was possible to remove only infrahepatic thrombus from this cavotomy. (Fig. 3)

The inferior vena cava was repaired. Repeated TEE confirmed residual supradiaphragmatic inferior vena caval and right atrial tumor. After cardiopulmonary bypass was established, right atrium was opened. There was hard thrombus which was densely adhered to the right atrium as well as to wall of suprahepatic part of inferior vena cava. It was difficult and challenging to remove the thrombus as it was densely adhered. But with persistent effort and perseverance; it was possible to remove the thrombus completely (Fig. 4a and b) and there was free backflow of blood from inferior vena cava. Repeat TEE confirmed thrombus free right atrium and IVC.

Histological examination of the inferior vena cava thrombus identified viable tumor with cartilaginous degeneration. The patient completed 24 weeks of adjuvant chemotherapy, whole lung radiation, and right flank radiation with a boost to the inferior vena cava. Postoperative imaging after 3 months

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Fig. 1 **a** CT picture showing right renal and IVC mass pre chemotherapy. **b** CT picture showing right renal and IVC mass post chemotherapy

revealed no residual tumor. Child is asymptomatic at 1 year follow up.

Discussion

Wilms' tumor with intravascular extension occurs in 4–10 % of patient and 1.4 % has intraarterial extension. The focus of current research is improved patient selection for risk-adapted stratification of treatment to minimize surgical morbidity and mortality [1, 4, 5].

Intracaval tumor extension is mostly into the infrahepatic portion but it may extend into the right atrium. Most patients with tumor thrombus in the inferior vena cava are asymptomatic, and diagnosis is only made on imaging investigations. Symptoms suggestive of intracaval extension were rare and include varicocele, pulmonary distress, and lower limb edema. In 53 (89 %) of 59 patients (UKW-3 TRIAL), the diagnosis of inferior vena cava involvement was made before surgery by radiological investigations. However, in 6 the diagnosis was only found at surgery [1, 6].

The traditional approach to extension of Wilms' tumor into inferior vena cava used to be primary surgical resection, which

Fig. 2 **a** CT picture showing right atrial mass pre chemotherapy. **b** CT picture showing right atrial mass post chemotherapy

was associated with significant morbidity and mortality [7]. The SIOP group recommends neoadjuvant chemotherapy for most patients with a presumed diagnosis of Wilms' tumor. The Children's Oncology Group/NWTS studies indicate that in a child with Wilms' tumor and an intracaval thrombus above the level of the hepatic veins, preoperative chemotherapy should be given. This recommendation was based on the observation that most patients experience shrinkage of the tumor thrombus in response to chemotherapy. In some cases, shrinkage can avoid cardiopulmonary bypass (CPB) [2, 8].

Surgical complications in patients with intravascular tumor extension treated with initial surgery were as high as 43 % in NWTS-3, which decreased to 26 % in NWTS-4 [2, 8]. These include massive hemorrhage which was the most common followed by tumor embolisation with acute cardiac decompensation or arrest. Neoadjuvant chemotherapy lowered the complication rate to 13.2 %. ($P=0.053$) [2, 5, 8]. In the UKW3 trial,

Fig. 3 Intra-operative photograph showing cavotomy with removal of tumor Thrombus

preoperative chemotherapy was used in 52 of 59 patients with intracaval extension. Significant shrinkage of the thrombus and tumor was demonstrated in the majority and avoided the need for cavotomy at the time of delayed nephrectomy in nearly 50 % of patients. However, this approach also has risks which include complications before surgery including pulmonary embolism, tumor progression, febrile neutropenia, acute respiratory distress syndrome, which may be fatal [2, 5, 8].

Concern regarding endothelial adherence of tumor thrombus from preoperative therapy was expressed by deLorimier, who found an increased rate of thrombus fibrosis in patients so treated [9]. In the NWTS-4 series, tumor was adherent to the blood vessel in 43.7 % of initial surgery cases versus 61.7 % of neoadjuvant chemotherapy cases ($P=0.04$) [2]. But in our case, this post-chemotherapy changes made resection formidably difficult.

According to Shamberger et al., in patients with Wilms' tumor and inferior vena cava thrombus, there was no difference in complication rate between the initial surgery group and the neoadjuvant chemotherapy group, when all types of complications were taken into account. Thus, which approach is best should be determined on an individual basis [2, 8]. According to Nini Khozeimeh et al., in these patient with risk for pulmonary embolus, initial surgical therapy is recommended [2]. In UKW3 trial, they proposed that routine use of preoperative chemotherapy is the mainstay in the management of such patients and primary surgery is indicated in a patient with thrombus that might dislodge and cause acute symptoms [1].

But in index case though histology was suggestive of favorable Wilms' tumor, it was nonresponsive to chemotherapy macroscopically and microscopic cartilaginous degeneration made complete resection difficult. Hence, factor predicting no response to chemotherapy other than histology

Fig. 4 **a** total tumor thrombus extension. **b** right renal mass

need to be studied to prevent chemotherapy related complication including difficult resection intraoperatively or failure to resect tumor completely.

Conclusion

Factors predicting nonresponse to chemotherapy other than histology need to be studied to prevent chemotherapy related complication including difficult resection.

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