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Long-term physiologic and oncologic outcomes of inferior vena cava thrombosis in pediatric malignant abdominal tumors

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ABSTRACT

Background: The long-term physiologic and oncologic outcomes of treatment for inferior vena cava (IVC) thrombosis in children with malignant abdominal tumors are unclear.
Methods: We conducted a retrospective review of children with malignant IVC tumor thrombosis treated at our institution between January 1996 and December 2011. Extent of tumor thrombus was classified using the Hinman system. Disease stage, management, and oncologic and physiologic outcomes and complications were evaluated.
Results: We identified 15 patients (median age, 4.7 years): 12 with Wilms tumor, 2 with hepatoblastoma, and 1 with adrenocortical carcinoma. Neoadjuvant chemotherapy changed Hinman levels in 2 (13%) patients. IVC thrombus resection was complete in 6 (40%) patients, partial in 7 (47%) patients, and not performed in 1 (6.7%) patient. On follow-up imaging, 8 (53%) patients' IVCs were patent, 6 (40%) had residual thrombus, and 1 (6.7%) was surgically interrupted. Three (20%) patients had perioperative complications, and 2 (13%) experienced transient effects related to IVC occlusion.
Conclusions: Surgical management of tumor thrombus in the vena cava of children with solid abdominal tumors is challenging. Evidence on which to base strong treatment recommendations is lacking. Few long-term physiologic complications were observed.

The presence of tumor thrombus in the inferior vena cava (IVC) may complicate treatment planning of children with a variety of malignant abdominal tumors. Wilms tumor, rhabdoid tumor of the kidney, hepatoblastoma, hepatocellular carcinoma and adrenocortical carcinoma are the solid abdominal malignancies most often associated with IVC thrombosis [1–4]. Complete resection of the IVC thrombus directly affects tumor stage and the subsequent need for adjuvant therapy for these tumors [1–4]. The risks and benefits of surgical clearance of tumor thrombus are less clear.

Adherent inferior vena caval tumor thrombi have been treated with chemotherapy with or without radiation therapy either before or after surgical therapy. Surgical options for removing adherent tumor include stripping of the vessels intima with preservation of the cava, resection of the thrombus with part of the IVC wall, or resecting a portion of the IVC with or without reconstruction. These interventions may be associated with caval occlusion or narrowing. While some information on physiologic outcomes of adults treated for malignant IVC thrombosis exists [5–7] few reports address results in children [8].

In this study, we describe our experience with surgical management of malignant IVC thrombi in children with malignant abdominal tumors, and describe their long-term oncologic and physiologic outcomes.

1. Methods

A retrospective chart review was performed of patients who were managed for malignant abdominal tumors with IVC thrombi at St. Jude Children's Research Hospital between January 1996 and December 2011. The study was approved by the institutional review board. All pediatric patients with an IVC thrombus and primary liver, renal, or adrenocortical tumor were included in the study. Data on the type and stage of tumor, the site and extent of IVC thrombus, chemotherapy (neoadjuvant and adjuvant), radiation therapy (dose and site), and surgical management of the IVC thrombus were reviewed. The extent of the IVC thrombus was classified according to the Hinman system: level I, infrahepatic thrombus; level II, thrombus above the hepatic veins but below the diaphragm; and level III, thrombus at or above the level

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of the diaphragm [9]. Outcome variables assessed included patient and disease free survival, and any identifiable problem related to IVC obstruction.

All patients at St. Jude undergo active follow-up until death, or a disease free interval of 5 years. Patients free of disease for 5 years are enrolled in the St. Jude LIFE and After Completion of Therapy (ACT) Clinics and are then seen yearly until 10 years after diagnosis or 18 years of age, whichever is later. This comprehensive follow-up involves full clinical evaluations with laboratory and imaging studies when indicated.

Survival outcomes were analyzed for the 12 patients with Wilms tumors. Overall survival (OS) distributions were estimated by the Kaplan–Meier method and compared with the log-rank (Mantel–Cox) test. OS was defined as the time from diagnosis by biopsy to death caused by a disease. The nominal significance level was set at 0.05. Patients who died without experiencing an event at their date of death and patients who were still alive without experiencing an event at their last follow-up were censored in the estimates. SPSS version 16.0 (IBM Corp., New York, NY) was used for statistical analysis.

2. Results

2.1. Surgical management of IVC thrombus and related morbidity

Fifteen children (9 females/6 males) with malignant solid tumors of the abdomen with IVC thrombi were identified. The extent of tumor and resection performed are illustrated in Fig. 1. Tumor resection and thrombectomy were performed in the same sitting in 12 patients, in subsequent operations in 2 patients, and no thrombectomy was performed in 1 patient. Resection of visible IVC thrombus was judged to be complete in 6 patients and partial in 7 patients, and no resection was performed in 1 patient; the extent of thrombus resection was unknown in 1 patient. Two patients required partial caval resection and reconstruction because of adherent thrombus—a Gore-Tex® vascular patch was used in patient 12, and venoplasty was performed in patient 13. Patient 15 had large azygous collaterals, and had a segment of thrombosed cava excised without reconstruction. Cardiopulmonary bypass was employed in patients 6 and 8, and anticipatory aortocaval cannulation was performed in patient 14 without actual cardiopulmonary bypass. Patients 2 and 4 had Hinman level 3 tumors that were managed by clamping the lower portion of the right atrium during the thrombectomy and did not have cardiopulmonary bypass. IVC surgery was performed at our institutions in 9 patients, while 6 patients underwent surgery at other institutions before referral. No patient received long-term anticoagulation after IVC surgery. The median follow-up duration was 1.9 years (range: 0.6–15.6 years).

Perioperative complications occurred in 3 patients. Patient 5 had intraoperative hemodynamic decompensation requiring cardiopulmonary resuscitation. Patient 8 had postoperative dehiscence of a median sternotomy wound, which was reclosed. Patient 13 had a bile leak from segment 1 that required reexploration and a hepaticojejunostomy on postoperative day 7. None of these patients experienced long-term sequelae from these perioperative complications.

Five of six patients who had complete resection of their IVC thrombus had a patent IVC at follow-up (Table 1). Patient 15 had resection of the cava without reconstruction. Both patients who underwent caval resection and reconstruction (patients 12 and 13) remained patent. None of these patients received boost radiation to the vena cava, and none had subsequent venous complications or physiologic sequelae.

Three of the 7 patients who had partial resection of IVC thrombus had a patent IVC at follow-up and 4 had obstruction of the vena cava. The 6 patients with Wilms tumor and partial resection of IVC thrombus received between 9 and 30 Gy of additional radiation to the vena cava. Half of these patients maintained caval patency and half did not. Patient 11 did not have the extent of resection of IVC thrombus recorded and had a patent IVC on follow-up. Patient 10 had no attempt at thrombus resection and had an occluded vena cava.

Physiologic sequelae related to IVC occlusion occurred in 2 of the 7 patients who had a partial thrombus resection. Patient 9 had preoperative bilateral lower-limb deep venous thrombosis that resolved with anticoagulation with low molecular weight heparin. That patient died of widespread metastatic disease 1.9 years after resection. Patient 14 developed Budd–Chiari syndrome and veno-occlusive disease, which manifested as pleural effusions, persistent ascites, and lower extremity swelling that resolved after 10 months of therapy. This child was alive with widespread metastatic disease 2.1 years after resection.

2.2. Oncologic management and outcomes

2.2.1. Wilms tumor

Twelve patients had Wilms tumor. At diagnosis, 7 patients had a level I thrombus, 1 patient had a level II thrombus, and 4 patients had level III thrombus; one extended to the junction of the IVC and right atrium (patient 4) and three extended into the right atrium (patients 2, 6, and 14).

Three patients (4, 5, and 10) had unfavorable histology and all died of disease 0.6 to 2.1 years after resection. Nine patients had favorable histology. Two (patients 7 and 9) died of disease 1.9 and 2.2 years after resection. Patient 14 is alive with disease 2.1 years after nephrectomy with atrial and partial caval thrombectomy leaving some tumor in the retrohepatic cava, which was subsequently treated with a 30 Gy IVC boost. This patient's course has been complicated by flank, liver and lung recurrences, veno-occlusive disease, and Budd–Chiari physiology with ascites. Patients 2 and 11 were lost to follow-up 1.6 and 2.6 years after resection. Patient 11 was known to have a liver recurrence treated with radiation therapy before being lost to follow-up.

Four patients with favorable histology are alive with no evidence of disease 8.0 to 15.8 years after resection. Two had complete resection of the tumor thrombus and two had partial resection. Pathology at the time of resection showed 3 of the 4 had viable tumor in their thrombus at the time of resection. The two with partial thrombus resection had a subsequent boost of radiation to the cava, while the two with complete resection had standard radiation therapy for local stage. These 4 (patients 1, 3, 6, and 12) are on long-term follow-up in the ACT clinic.

Ten patients received preoperative chemotherapy, 2 patients (patients 1 and 5) with Hinman level I thrombus received upfront surgery. Interestingly, of the 4 patients with level III thrombus (patients 2, 4, 6, and 14), none had retraction of the thrombus to level II or below.

Adjuvant radiation therapy was used for Stage III (local) disease in 11 patients. The doses of radiation administered to the flank or abdomen ranged from 9 to 12 Gy. Three patients who had partial resection of tumor thrombus with viable tumor on histology received boosts to the vena cava of 9 to 30 Gy. No complications from radiation therapy were detected in our series.

Overall survival for the 12 patients with Wilms tumors was significantly associated with IVC patency on follow-up imaging ($P = 0.03$) and histologic type (favorable versus unfavorable histology, $P = 0.01$). OS was not associated with Hinman level, viability of tumor thrombus, and completeness of surgical thrombectomy, ($P = 0.39$, 0.70, and 0.98, respectively, log-rank test).

2.2.2. Hepatoblastoma

Patients 13 and 15 had stage IV hepatoblastoma. Biopsy and 4 courses of cisplatin, 5-flurouracil, vincristine and doxorubicin (C5VD) were administered before definitive surgery per treatment guidelines from AHEP 0731. In both cases, tumor thrombus was Hinman level 3, and in both cases the thrombus decreased in size and retracted to Hinman level 2. Hepatic resections were performed with vascular isolation of the liver using a Pringle maneuver, and clamping the cava above the tumor at the diaphragm, and below the tumor at or below the level of the renal veins without cardiopulmonary bypass. In case 13 the cava