Seminars in Pediatric Surgery 25 (2016) 395–403

Contents lists available at ScienceDirect

Seminars in Pediatric Surgery

journal homepage: www.elsevier.com/locate/sempedsurg

Complications in the surgical management of children with malignant solid tumors

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ARTICLE INFO

Keywords:
Pediatric cancer
Surgery
Complications
Neuroblastoma
Wilms tumor
Sarcoma

ABSTRACT

With improvement in the outcomes for children with cancer has come an increasing focus on minimizing the morbidity from therapeutic interventions, including surgical procedures, while continuing to have a high likelihood of cure. Thus, an appreciation for the potential complications of surgery, both acute and long term, is critical when considering the risks and benefits of any procedure performed on a child with cancer. Although not meant to be an exhaustive review, here we discuss the most common and significant surgical complications that may occur when performing diagnostic, therapeutic, or supportive procedures in children with the most common malignant solid tumors.

Significant improvement has been made in the outcome for children with cancer over the last 60 years with overall survival increasing from about 30% to currently over 80%.[1] Surgery plays a critical role in the management of pediatric patients with cancer, particularly those with solid tumors. In addition to achieving a good oncologic outcome, however, attention is increasingly being paid to the morbidity and complications, both acute and long term, associated with each of the various modalities used to affect cure, including surgery. As survival has improved, there is now greater opportunity to appreciate long-term complications of therapy.

Pediatric surgeons play a critical role in diagnosing, staging, and treating children with solid malignant tumors. Therefore, it is imperative for the pediatric surgeon, as a member of the multidisciplinary team involved in the care of these patients, to understand the indications for and implications of surgery in their treatment and the risks and benefits of any surgical procedure. Here we review the most common and significant surgical complications that can occur with different operations. Generic complications such as bleeding, infection, poor wound healing, and complications related to anesthesia will not be discussed in detail here.

Neuroblastoma resection

Neuroblastoma is a malignancy of the sympathetic nervous system and is a heterogeneous disease; tumors can spontaneously regress or mature or display an aggressive, therapy-resistant phenotype. Complete resection of a localized neuroblastoma with favorable biology offers definitive therapy with generally excellent outcome; although, the value of complete tumor removal may be overestimated because of the possibility that localized neuroblastomas may not require any therapy, including resection. The role of surgery is even less clear in the curative treatment of patients with high risk, metastatic neuroblastoma,[2] although a recent review of the Children's Oncology Group (COG) experience suggests that $\geq 90\%$ resection of the primary and regional disease is associated with significantly better event-free survival and a lower cumulative incidence of local progression.[3] However, overall survival in this study was not significantly impacted. Additionally, it has long been recognized that neuroblastoma resection, in part because of its frequently infiltrative growth pattern, can be associated with a high complication rate.[4–7] Thus, it is crucial that surgeons consider the heterogeneous nature of neuroblastoma and the molecular and biologic characteristics associated with good or bad prognoses as well as the potential complications associated with neuroblastoma resection when determining the role of surgery in any specific case.[8] An illustrative example is the very favorable overall outcome for infants with metastatic, single-copy *MYCN* disease, regardless of the extent of surgery.[9] Clearly, the excellent prognosis for these patients should not be jeopardized by overly aggressive surgery that may lead to significant morbidity or even mortality.

Vascular injury

Intra-abdominal neuroblastoma, particularly with unfavorable biology, has a propensity for encasing visceral vessels. As a

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http://dx.doi.org/10.1053/j.sempedsurg.2016.10.003
1055-8586/

consequence, up to 10% of patients will suffer an injury to a major vascular structure during attempts at surgical resection. A critical step for avoiding injury to these vessels is their identification before they pass through the tumor, most often at their take off from the aorta or vena cava. This should be done as early as possible in the course of an operation. The tumor is then removed piecemeal after freeing the circumference of the artery. It is very difficult to identify the artery by simply dissecting into the middle of the tumor and this approach should be avoided. Even with meticulous dissection, significant blood loss and resultant transfusion requirement is common after resection of high risk neuroblastoma.

Neurologic injury

Extension of neuroblastoma through neural foramina and into the spinal column is a fairly common occurrence, especially with paraspinal and thoracic primaries, occurring in 7–15% of cases with half being symptommatic.[10] In general, there is rarely an indication to remove the tumor extension surgically as the risks of resecting this residual disease appear to outweigh the benefits. Patients with favorable clinical characteristics and tumor biology have an excellent oncologic and neurologic prognosis despite leaving some gross residual disease in the neural foramina and spinal column. Patients with unfavorable clinical characteristics and tumor biology will receive intensive multimodality therapy which is a critical component of successful treatment. Complications of aggressive surgery can include the development of an intraspinal hematoma and cord compression or direct injury to nerves which may result in deficits including sciatic nerve palsy, urinary and fecal incontinence, neurogenic bladder, erectile dysfunction, leg weakness, or nerve root injury. Nevertheless, tumor extension into the neural foramen and spinal canal that causes acute neurologic deterioration may be most appropriately treated by emergent surgical resection via laminotomy.[10]

Ischemia of the cord can occur following resection of a paraspinal neuroblastoma, particularly inferiorly located posterior mediastinal tumors. This is due to injury to the artery of Adamkiewicz, an artery that arises off the aorta, typically at the level of 9–12th left posterior intercostal artery but whose origin can be variable, and which serves as the main blood supply to the spinal cord. Because of this, some authors have suggested the use of preoperative spinal angiography and intraoperative cord monitoring in certain circumstances, as they may guide the conduct of tumor resection, to avoid injury to this critical artery.[11]

Kidney loss

Every effort should be made to avoid nephrectomy when resecting a retroperitoneal neuroblastoma. Patients with favorable clinical characteristics and tumor biology generally have an excellent outcome regardless of the completeness of resection while patients with unfavorable clinical characteristics and tumor biology need intensive multimodality therapy for which normal renal function is required in order to receive the full recommended doses. Nevertheless, for this later group, some perform nephrectomy when it is required to achieve complete tumor resection, at reported rates of 5–10%.[12,13] The benefit of this, when considering the impact on renal function and ability to tolerate high dose chemotherapy is uncertain.

Because neuroblastoma often grows into the renal hilum encasing the renal vessels, kidney loss due to ischemia is not an uncommon occurrence, particularly in patients with high risk disease. This complication occurs due to injury to the renal vasculature rather than to the kidney itself. This can be due to inadvertent ligation and division of the renal artery or vein, injury to either of these vessels that cannot be successfully repaired, or trauma to the artery from torque that results in spasm and renal ischemia. The later may result in a "disappearing kidney," a term that refers to atrophy of a kidney likely due to vascular injury at the time of surgery. However, the consequence of this traumatic injury is generally not noted until later in a patient's clinical course, often months later, when follow-up imaging demonstrates a diminutive or completely absent kidney. The exact etiology for this complication is not well understood but is believed to involve spasm and/or intimal disruption of the renal artery due to excessive manipulation, particularly torque, on the vessel when trying to expose and resect lymphadenopathy from behind the renal vein. Thus, great care must be taken when removing tumor from around the renal vessels not to apply torque to the artery while retracting the tumor mass. Some advocate systemic renal dose dopamine or intramural lidocaine in an attempt to prevent or break the spasm of the artery.[14]

Extensive associated lymphadenopathy may also encase the ipsilateral ureter putting it at risk for injury during resection of extensive retroperitoneal disease. As mentioned previously when discussing avoidance of vascular injury, it is also important to identify the ureter before it passes through the involved lymph nodes. Additionally, preoperative placement of a ureteral stent may facilitate identification of the ureter and avoidance of injury.

Occasionally neuroblastoma may invade the kidney, potentially leading to the misdiagnosis of Wilms tumor at presentation.[15] Distinguishing these tumor types is critical as the surgical management for neuroblastoma and Wilms tumor differs significantly. The presence of constitutional symptoms, intratumoral calcification or vascular encasement on preoperative imaging should heighten suspicion for neuroblastoma. In addition, laboratory evaluation, including urinary catecholamines and radiographic studies, such as MIBG, should be completed prior to surgery when the etiology of an abdominal tumor is uncertain.

Chylous ascites/chylothorax

Postoperative chyle leak is a well-recognized complication of neuroblastoma surgery that results from disruption of either mediastinal or retroperitoneal lymphatic channels during tumor resection. Neuroblastoma often has an infiltrative growth pattern around major vessels where lymphatics are also residing making them susceptible to injury or disruption when performing a perivascular dissection. Nonsurgical treatment is effective for most patients with chyle leak. Management includes fasting to reduce lymph flow often requiring the use of total parental nutrition. Drainage via tube thoracostomy or paracentesis may be required to alleviate compressive symptoms. Most patients respond to conservative management within 1–2 months although some will require operative intervention for failure of conservative management. Surgical options include primary direct surgical repair, fibrin glue application, embolization or establishment of a peritoneovenous shunt. However, the exact duration that conservative therapy should be tried before surgical treatment is controversial as early ligation of the leakage site may be helpful in avoiding metabolic complications, delay in adjuvant therapy, and prolonged hospitalization.[16]

Diarrhea

After resection of advanced abdominal neuroblastoma children may have persistent diarrhea, perhaps resulting from disruption of the autonomic nerve supply to the gut during clearance of tumor from the major vessels of the retroperitoneum. In one series, 30% of patients had postoperative diarrhea.[17] Dissection around the superior mesenteric and celiac arteries was associated with a