Pediatric Interventional Oncology: Big Cases in Small People

An overview of the current state of interventional radiology in pediatric oncology.

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Cancer. Few words strike the fear and anxiety that cancer does. However, the field of oncology has undergone tremendous advances with respect to the medical, surgical, and radiation treatments that can now be offered. Perhaps the greatest strides have been made in the field of interventional oncology (IO), which is now firmly established as the fourth pillar of cancer care. In the past decade, there has been a profound expansion in this area, with a greater integration of interventional radiology (IR) in all aspects of the management of cancer patients.[1,2] IR occupies an increasingly prominent role in the multidisciplinary team caring for those affected by cancer, with the traditional diagnostic and interventional components of radiology blending more and more in order to optimize diagnosis, treatment, and follow-up.

Although this fourth pillar of care is firmly established in adult medicine, its value is only now beginning to be recognized in the pediatric setting. There is no doubt that adult IO serves as an important example for advances made in the field of pediatric IO, with efforts made throughout the world to improve the access and delivery to this important patient group. Integrated patient-centric delivery of care has long been recognized as a major strength of pediatric medicine; however, the evidence for the role of IO in pediatric care considerably lags behind adult medicine.[3,4] This may be due to many possible factors, including:

- The lack of a specific approval process for needed techniques, medications, and devices in the pediatric setting
- Protocol limitations created by large cooperative oncology groups or prospective clinical trials
- A lack of awareness of techniques (and benefits of techniques) accepted in adult practice
- Possible reluctance to introduce novel oncologic interventions due to resistance from pediatric oncologists and surgeons
- A lack of evidence-based medicine supporting the use of IO in the pediatric setting, as well as the inherent bias of the literature toward adult practice, due to the exclusion of pediatric patients in larger trials

Despite these challenges, many pediatric centers now offer this important service line. This article reviews the traditional roles of IO, including biopsy and supportive care, and discusses current and evolving locoregional treatment strategies, including potential treatments on the horizon.

BIOPSY

Image-guided biopsy has been recognized as a strength of pediatric IR. Due to patient-specific reasons, percutaneous biopsy is often performed using ultrasound guidance. Although it plays an important role, CT-guided biopsy is usually considered a second-line approach due to concerns associated with ionizing radiation in children. If CT guidance is required, "quick check" CT fluoroscopic techniques may be extremely beneficial in improving speed and accuracy, with optimization of scan parameters such as peak tube kilovoltage (kVp) and milliamperage (mA) allowing for a reduction in patient and staff exposure to ionizing radiation (Figure 1).

Due to the complexity of some of the clinical trials in which children with cancer are enrolled, fine-needle aspiration is rarely performed. Large-core biopsies

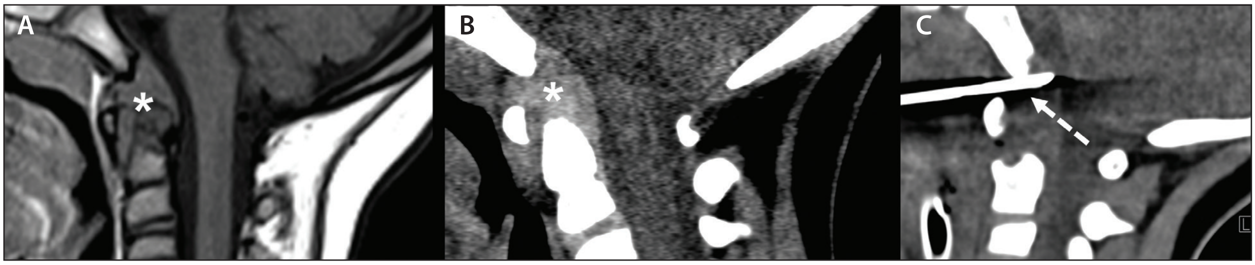

Figure 1. Sagittal T1-weighted MRI and CT images from a 4-year-old girl presenting with progressive painful stiffness of the upper neck, demonstrating an extradural mass centered at the clivus/C1 and extending to the mid/lower C2 (asterisk), with associated bony destruction of the clival tip (A, B). Transoral, 18-gauge core biopsy (arrow) performed using CT fluoroscopic guidance with a coaxial technique (C).

(often 18–14 gauge) are needed to allow for a range of immunohistochemical and genetic tests. This is especially important given the increasingly recognized benefit of personalized oncogenomics, which requires greater tissue volumes to be obtained. Therefore, unique approaches may be required, such as transvenous biopsies when a percutaneous approach is contraindicated (ie, transjugular liver biopsies in patients with graft-versus-host disease and associated coagulopathy) or localization of target lesions for subsequent surgical resection (ie, microcoil localization for video-assisted thoracoscopic surgery of removal of subpleural lung nodules).[5]

VENOUS AND ENTERIC ACCESS

Another important role that pediatric IR plays in the care of the cancer patient is establishing intermediate and longer-term vascular access. This is required for medication (including chemotherapy) administration and parenteral nutrition, as well as for repeated blood sampling. Although peripherally inserted central catheters play an important role, the placement of tunneled venous access devices or ports is well established. Active communication with the care team is required to determine the best type and location for central venous access.

The pediatric oncology patient may also require enteric access for nutrition supplementation. This situation may be due to luminal obstruction or swallowing impairment, which can occur in the setting of head and neck malignancy or upper gastroesophageal cancers, or increased metabolic and hydration demands, which is seen with many cancers including leukemia and solid tumors. Image-guided placement of feeding tubes may range from nasogastric or nasojejunal tube insertion to percutaneous image-guided placement of gastrostomies or gastrojejunostomies. All of these can be done with very low risk, in patients of all ages, ranging from neonates weighing a few kilograms to teenagers weighing ≥ 100 kg.

TRANSARTERIAL THERAPIES

Transarterial delivery of medications has been recognized as an effective treatment strategy, with the idea of increasing the local dose of medication while reducing systemic complications.[6] Intra-arterial administration of chemotherapeutic agents, such as melphalan in the setting of retinoblastoma, has been shown to be highly efficacious,[7] with use of additional targeted infusion strategies for malignancies affecting the neural axis.

In the setting of hypervascular disease requiring surgical resection, preoperative embolization may be appropriate.[8] This is typically performed via a transarterial approach. A variety of embolic agents can be used in this setting, including liquids (eg, medical-grade alcohol, n-butyl cyanoacrylate, or Onyx [Medtronic]), particles, Gelfoam (Pfizer, Inc.), or coils, and often a combination of these agents may be used. Occasionally, a transarterial approach may be augmented or replaced by percutaneous intralesional embolization or a transvenous approach.

Bland embolization can be used to control symptoms in the palliative setting or as a preoperative strategy for aiding in surgical resection (due to reducing operative blood loss, shortening surgical times, and potentially reducing the complexity of surgery) (Figure 2). Transcatheter arterial chemoembolization (TACE) is now increasingly performed, as it is highly beneficial in increasing the concentration of the chemotherapeutic delivered to the target tissue, with the embolization aspect of this procedure increasing the dwell time at the target tissue level while reducing the amount of drug entering the systemic circulation. In addition, the hypoxia and ischemia induced by TACE may further augment the chemotherapy dose achieved within the neoplastic tissue. TACE can be performed as an emulsion of the chemotherapeutic with an oil-based contrast medium or with drug-eluting beads. It is typically performed in tissues that have dual blood supply, with the liver being the main site. TACE has been performed in the pediatric setting, such as for hepato-

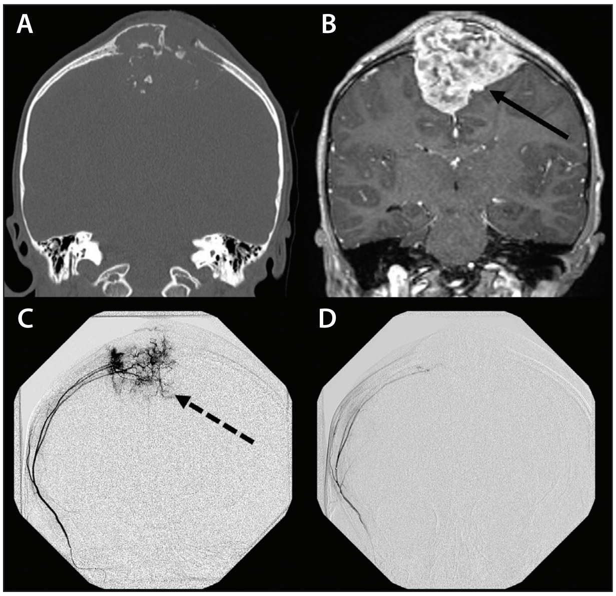

Figure 2. An enlarging painless mass at the vertex of the skull in a 16-year-old boy. Coronal reformatted CT (A) and coronal postgadolinium-enhanced T1-weighted MRI (B) demonstrate a destructive mass arising from the midline calvarium, representing a slow-growing osteosarcoma. Preoperative angiography in the right middle meningeal artery showing profound tumoral blush (C), and particulate embolization was performed (D). Additional tumor embolization was also performed (not shown).

blastoma[9,10] and hepatocellular carcinoma (Figure 3). Published literature also exists for its use in the setting of Wilms tumor, as well as selected lung tumors, due to the dual supply from the bronchial and pulmonary arteries.

An exciting area of transcatheter arterial therapeutics is radioembolization. This involves selective catheter placement and introduction of β radiation–emitting radioisotopes directly into the tumor mass by means of glass, albumin, or resin microspheres. Through incorporation of β radiation–emitting yttrium-90, targeted brachytherapy is possible. An increasing number of reports of its potential in the pediatric setting are now being published, which is not unexpected given the dramatic increase in its utilization for hepatic malignancies in adults.[11] This may be particularly important in those who do not have a chemotherapy-sensitive tumor or when toxicity limits have been reached from previous chemotherapy. Prior to its delivery, radioembolization requires appropriate patient workup and preparation, including arterial mapping studies, embolization of nontarget collaterals, and evaluation of pulmonary shunt fraction. In selected settings, as is sometimes done in the adult setting, there may be a role for preoperative portal vein embolization, a technique typically used to promote hypertrophy of the liver prior to partial hepatectomy.

ADVANCES IN LOCOREGIONAL ABLATIVE TECHNIQUES

Local tumor ablation offers another strategy for achieving tumor control (and, in some cases, the possibility of a cure). Multiple techniques currently exist for image-guided tumor ablation, with radiofrequency ablation (RFA) the most frequently used. There are multiple reports on the use of RFA in the pediatric setting in similar locations used to treat malignancies in the adult population.[12] This includes hepatic and renal malignancies, as well as malignancies involving the skeleton/spine and lungs.[13,14] RFA has also been used to treat malignant tumors in the soft tissues.

Cryoablation is increasing in popularity and offers a more predictable thermal injury, the potential for "sculpting" the ice ball through appropriate placement of additional ablation probes, and reduced lesional/local

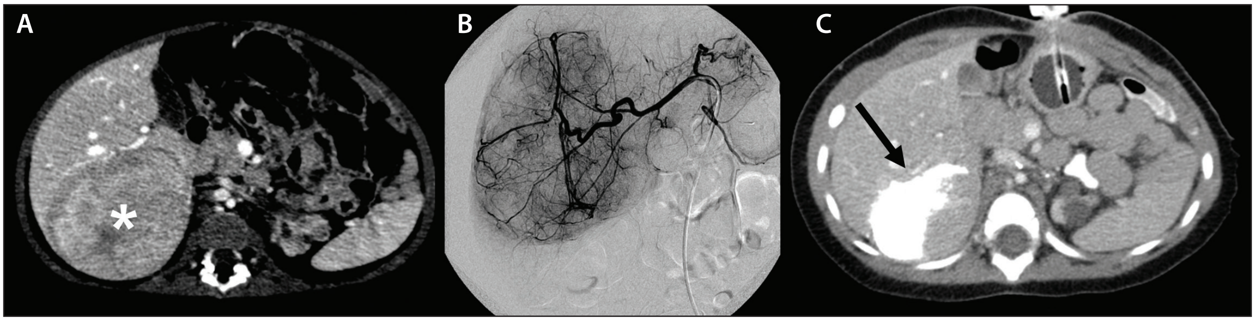

Figure 3. Contrast-enhanced CT demonstrating a rapidly growing, biopsy-proven hepatoblastoma in a 20-month-old girl with sensorineural hearing loss (asterisk) (A). Angiography of the hepatic arterial circulation showing marked hypervascularity associated with the tumor, with TACE performed using powdered cisplatin in lipiodol in order to reduce risk of further hearing loss (B). Post-TACE CT demonstrating distribution of chemoembolic (arrow) (C), with repeat CT 6 weeks after therapy showing a 75% reduction of the tumor prior to surgical resection (not shown).

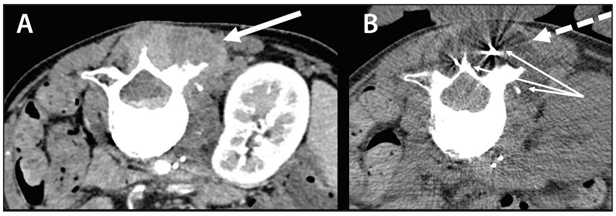

Figure 4. Contrast-enhanced CT from a 13-year-old boy with a metastatic Wilms tumor and progressively worsening back pain, demonstrating involvement of the L2 with epidural and paraspinal extension and impending skin breach (arrow) (A). CT-guided cryoablation was performed using multiple probes (thin arrows), with a sculpted ice ball well appreciated on monitoring CT (dashed arrow) (B). Marked relief in preprocedure pain was achieved, with maintained skin integrity.

tissue stimulation (Figure 4). Although cryoablation can be performed without the same degree of anesthetic support typically required for RFA, some of its disadvantages include longer ablation times, stiffer (and longer probes), and potential for cold-induced injury ("frostbite") to nontarget tissues.

PALLIATIVE MEASURES TO IMPROVE QUALITY OF LIFE

An important area of IR in the pediatric oncology patient is managing complications. Treatment in this setting is primarily targeted at relieving symptoms, alleviating pain, and addressing potentially life-threatening complications, such as massive hemoptysis, hematemesis, or pleural/peritoneal hemorrhage. These complications of malignancy, which may result directly from the cancer or secondary to cancer-directed care, are also meant to improve quality of life in the palliative setting. Obstruction of the biliary, urinary, or gastrointestinal tracts may be amenable to percutaneous drainage techniques, with the possibility of transluminal-directed therapies, such as stent placement. Combined procedures may sometimes be required in order to achieve the desired benefit, with tube change procedures (eg, biliary tubes or internal/external nephroureterostomy stents) that can be performed without significant inconvenience to the patient.

An uncommon but highly problematic complication of pediatric malignancy is the development of ascites or pleural effusions. Both can be very uncomfortable and may require frequent aspiration/drainage procedures as part of their management. Placement of tunneled drainage catheters, such as the Pleurx catheter (Becton, Dickinson and Company) for malignant pleural effusions, allows intermittent frequent drainage in the outpatient environment and may reduce the morbidity associated with these complications (ie, dyspnea, cough, and chest pain). IR may also play a role in performing pleurodesis. This can be accomplished via instillation of a sclerosing agent (typically talc) via a percutaneously placed thoracostomy tube once complete drainage of the effusion has been performed.

Pain is an extremely debilitating complication of cancer. The impact of pain on the patient, especially when inadequately controlled, can be profound. Although administration of opiates remains the mainstay of pain control, IR is assuming an increased role in the management of cancer pain. This includes percutaneous local anesthetic and/or corticosteroid administration, image-guided neurolysis/neural ablative procedures, and image-guided placement of infusion catheters or ports. In the setting of upper abdominal visceral malignancies, celiac ganglion/celiac axis blocks can be performed. When pain originates from osseous neoplastic involvement, cementoplasty with or without adjuvant thermal ablative techniques may have a role (Figure 5).

VENOUS THROMBOTIC/THROMBOEMBOLIC COMPLICATIONS

Malignancy is a widely recognized risk factor for the development of venous thrombosis. Pulmonary embolism is a highly morbid and potentially fatal complication of venous thrombosis, especially if the lower extremities and pelvic/inferior vena cava (IVC) circulation are involved. IVC filters can be placed quite easily in the pediatric setting, especially with the lower-profile delivery systems now

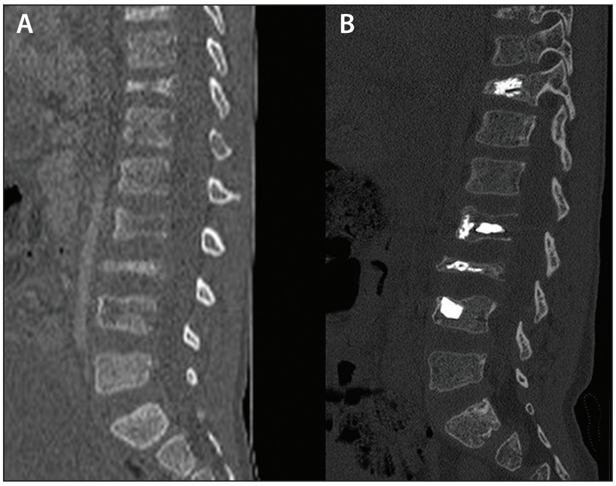

Figure 5. Sagittal reformatted CT demonstrating multiple pathologic compression fractures in a 6-year-old boy with palliative metastatic rhabdomyosarcoma (A). CT after fluoroscopic-guided cementoplasties (B) performed at the T11, L2, L3, and L4, as well as the T1, T6, T7, and T9 (not shown) for intractable back pain. Significant pain relief was noted after these procedures.

available. Indications for insertion of an IVC filter include (1) occurrence of a lower limb deep vein thrombosis in patients who have a contraindication to anticoagulation, (2) patients in whom an anticoagulation complication has occurred, and (3) patients who have multiple pulmonary emboli despite adequate anticoagulation.

Percutaneous treatment strategies directed at rapid thrombolysis/thrombectomy are also gaining popularity in the pediatric setting. Often, mechanical thrombectomy devices are used in conjunction with pharmacologic thrombolysis and may be even more important when there are contraindications to continuous anticoagulation. Rapid clearance of the target venous structures can be achieved in this manner.

FUTURE DIRECTIONS

Many promising advances are on the horizon for IO. Modality fusion image-guidance systems during ultrasound-guided procedures are becoming increasingly available and are able to project a needle or probe in real time onto a preexisting MRI or CT data set. Microwave and laser techniques may offer additional potential for locoregional therapy. Another technique with potential in the pediatric setting is irreversible electroporation. This is performed by delivering high-voltage, microsecond electrical pulses via probes placed percutaneously into the tumor, resulting in apoptosis of tumor cells through creation of permanent pores in the tumor cell membranes. This nonthermal ablative technique is fast and has the added benefit of avoiding the risk of thermal injury to nontarget tissues.[15]

High-intensity focused ultrasound offers a novel way of treating localized tumors.[16] This may technically be performed in any location penetrable by ultrasound and offers the potential to treat disease without need for probes or percutaneous access, as well as real-time monitoring of the ablation via MRI.

As techniques and approaches continue to evolve, nanomedicine may offer a less-invasive alternative to locoregional treatment. Genetic agents may be administered directly into the tumoral tissue, possibly using viral vectors or utilizing clustered, regularly interspaced palindromic repeat (also known as CRISPR) interference techniques. Through these strategies, specific aspects of the tumor, including immune response, oncogenic expression, susceptibility to chemotherapeutics, or its genetic potential, may be altered.

CONCLUSION

The field of pediatric IO is rapidly growing. Through continued collaboration with all those involved in pediatric cancer care (ie, surgery, oncology, general pediatrics, diagnostic radiology, and others), the recognition of this very important service continues to grow, as will the appreciation for the advantages it offers. With our ability to deliver the standard (as well as state-of-the-art) care, pediatric IO will continue to expand and improve by working with and learning from our counterparts in adult medicine. Organizations such as the Society for Pediatric Interventional Radiology (www.spir.org) may also be of value in expanding the network of those providing this important care as the fourth pillar of cancer treatment by facilitating communication and education. A greater acceptance and adoption of IO in the pediatric realm will undoubtedly occur, with its scope continuing to evolve and improve in the upcoming years. Through this, we can offer greater hope, comfort, and quality of life to children affected by cancer, as well as their caregivers and families. ■

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