Surgery of Bone and Soft Tissue Sarcomas in Children

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The role of surgery in the assessment and treatment of malignant bone and soft tissue tumors is two-fold. The first function is to sample the tumor (biopsy), which provides a diagnosis; and the second role of surgery is part of definitive local therapy to treat the sarcoma. In bone and soft tissue sarcomas, it is essential to complete all pre-operating staging studies prior to performing a biopsy. Typically this includes a CT scan of the chest, MRI of the lesion, and PET-CT. Staging studies such as MRI done after an operative procedure are difficult to interpret because the edema caused by the biopsy makes the tumor appear more extensive and it often masks the tumor mass itself.

For most pediatric tumors, open surgical biopsy is preferred over needle biopsy to obtain adequate amounts of tissue for diagnosis, biologic studies and frozen tissue for banking. The specimens should be sent from the operating room on a moistened saline sponge in a fresh state. About one cubic centimeter of viable tissue is required. Although needle biopsy may provide enough tissue for diagnosis, it may be difficult to obtain adequate tissue for all of the necessary studies by multiple passes with a needle. When needle or open biopsy is performed, it is important to make the approach in the line of the definitive surgical incision. Pre biopsy consultation should be made with the surgeon who will be performing the definitive surgical procedure. If a malignancy is suspected and you are not planning to do the definitive therapy, it is preferable that the patient be referred to a pediatric tumor center for staging studies and biopsy.

The most common malignant bone tumors in children are Ewing sarcoma and osteosarcoma. In most cases, the plain radiographs provide the best indication that the bone tumor is malignant. A poorly delineated transition zone from tumor to normal bone and an aggressive periosteal reaction with breaching of the cortical bone are worrisome signs of malignancy. In contrast, soft tissue sarcomas are difficult to characterize by pre-operative staging evaluations. Although soft tissue sarcomas are relatively rare in children compared to other benign lumps, deep sub-facial tumors greater than 5 cm. in size are best investigated by pre-operative imaging with MRI or at least an ultrasound prior to biopsy. It is always preferable to do an incisional biopsy rather than an excisional biopsy in order to avoid an “UPS” procedure (unplanned surgical excision).

Most pediatric malignant tumors are treated with neo-adjuvant chemotherapy which lasts about 12 weeks. After this time, the staging studies are repeated and definitive local therapy is performed. In some cases this will be surgery alone while in other patients, surgery is preceded or followed by radiotherapy.

The second role of surgery for most pediatric sarcomas is definitive local therapy. Ewing sarcoma and rhabdosarcoma can be treated by definitive radiotherapy alone but overall patient survival is improved when surgery is part of the treatment program. In most cases, the objective of surgery for sarcomas is to achieve a complete excision with negative pathologic margins. There are two parts to a definitive surgical procedure for malignant bone tumors. The first is complete removal of the tumor (the oncologic procedure) and the second part is the reconstructive procedure to maximize limb function.

There are three types of surgical oncologic procedures to remove malignant tumors. The first is a wide excision with clear pathologic margins (R0 resection). The plane of dissection is within normal tissue. The acceptable width (mm.) of normal tissue is controversial. The second type of surgery is a marginal excision.
Rotationplasty has become a very successful reconstructive technique especially in young children. Rotationplasty was first described in a patient with tuberculosis who was treated in 1927, but it only began to be used in the treatment of children with non-surgical tumors during the late 1970s. In this procedure, the limb segment containing the bone tumor is removed (usually the distal femur or a proximal tibia), the lower segment is rotated 180 degrees and reattached to the proximal femur. A split skin graft and foot ends at the level of the opposite knee functions as a knee joint. The patient becomes a functional below knee amputee.

Despite the unusual appearance of the limb, there are several advantages for the patient. Future growth can be accommodated by adjustments of the amputation level and exercise. The proximal tender (that can lead to urinary retention) may be more sensitive to changes than the distal tender (axonal degeneration). Vincristine is classified as a "vinca alkaloid" and arrests cell division by inhibiting "microtubule" and "vinca alkaloid" and arrests cell division by inhibiting tubulin polymerization. The peripheral nervous system is more susceptible to chemotherapy than the central nervous system. Vincristine is presently used in the treatment of hematological malignancies (leukemia, non-Hodgkin lymphoma) and solid tumors (Wilms tumor, malignant mesenchymal tumors). It induces peripheral neuropathy by binding on the intracellular tubulin of both the fast- and slow-conducting axons.

**Symptoms/Classification**

Vincristine used in the treatment of children with cancer impairs conduction in the entire peripheral nervous system, which may also affect the autonomic nervous system (approximately 30% of patients), resulting in orthostatic hypotension, peripheral neuropathy, paralytic ileus and bladder atony (that can lead to urinary retention). Recent studies report that there appears to be ethnic variation in the rate of vincristine induced neuropathy. There may be underlying genetic susceptibility in determining who develops this toxicity. Rarely (less than 1:4,000), a dose-related cumulative dose of unilateral or bilateral laryngeal paralysis may present as swallowing dysfunction (repetitive wet or dry coughing), airway symptoms (stridor and voice change), and may require tracheostomy, alternative feeding routes and/or mechanical ventilation.

Vincristine neuropathy can present as numbness, tingling sensation in a glove-like distribution of the hands and feet. Peripheral sensory loss and autonomic dysfunction may become progressively worse as dose accumulates. Reported symptoms may include orthostatic hypotension, airway symptoms (stridor and voice change, and may require tracheostomy, alternative feeding routes and/or mechanical ventilation). Caution must be used to avoid interactions with other drugs that the patient may be taking, including the patient’s chemotherapy regime.

For bone sarcomas, the second part of a definitive local control surgical procedure is limb reconstruction. In children, biological age is preferred. When choosing the best reconstruction for an individual child, the surgeon should consider the future mechanical function of the affected limb. Younger children may not only be prone to early mechanical failures and require revision or amputation. Final function depends on the extent of the limb segment replaced and the remaining muscles that are available to provide joint movement. When there is significant tumor reactive zone just outside the tumor, there is a chance of local recurrence. This chance of local recurrence increases if this toxicity relates to the fact that they are prone to many complications and eventually have to be replaced by a definitive adult type endoprosthesis. "Growing endoprostheses which are available for young children but there are significant drawbacks. These prostheses are very expensive (about $40,000 each); they are prone to many complications and eventually have to be replaced by a definitive adult type endoprosthesis. "Growing endoprostheses which are best done in selected tumor centers and should be considered experimental.

**Villin**

Villin is a brush border membrane protein that is present in a variety of human cells including absorptive enterocytes, neutrophils, hepatocytes, and smooth muscle cells. It has been shown to be a component of the firm adhesion complex. In vitro, villin is involved in the reorganization of actin filaments. It is not clear what role villin plays in vivo. However, the expression of villin in the apical membrane of absorptive enterocytes is increased in conditions of increased mucosal permeability such as inflammatory bowel disease and ulcerative colitis. It has been suggested that villin may play a role in the regulation of tight junctions.

**Histocompatibility antigens**

Histocompatibility antigens are a group of proteins that are present on the surface of all human cells. These proteins are involved in the immune response and play a role in the rejection of transplanted organs. The most important of these antigens are the human leukocyte antigens (HLA). There are two main classes of HLA antigens: class I and class II. Class I antigens are present on all nucleated cells and are involved in the presentation of small peptides to CD8 T cells. Class II antigens are present on antigen-presenting cells and are involved in the presentation of larger peptides to CD4 T cells. The HLA antigens are polymorphic, meaning that different individuals have different combinations of HLA antigens. This polymorphism is important in determining tissue compatibility and is the basis for tissue typing in organ transplantation.

**Therapeutic agents**

Several therapeutic agents are used in the treatment of acute lymphoblastic leukemia (ALL) such as vincristine, cyclophosphamide, and doxorubicin. Vincristine is a Vinca alkaloid that inhibits microtubule polymerization and arrests cell division by inhibiting tubulin polymerization. It is a microtubule inhibitor and has a broad spectrum of activity against a variety of tumor types. It is used in the treatment of hematological malignancies such as acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Vincristine is also used in the treatment of solid tumors such as soft tissue sarcomas, Burkitt lymphoma, and neuroblastoma. It is a vinca alkaloid and inhibits the polymerization of tubulin, which is required for the formation and maintenance of microtubules. This disruption of microtubules leads to cell death and is responsible for the antineoplastic activity of vincristine.
control and that children adapt by adopt-
ing “an in-born ability” to co-ordinate and co-activate muscle agonists and antag-
ons to decrease the degree of freedom with their available muscle, which results in a reduction of their svelvacy. This is an inefficient method to gain balance control and may decrease their ability to par-
ticipate in more challenging (e.g., sport-
ing) activities34.

Hartman et al. (2006) evaluated mo-
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From Hospital to Home: The Role of Occupational Therapy in Pediatric Oncology

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“Is this so what occupational therapy is?” A mother exclaims as I mould and shape a splint over a toddler’s arm. Given the excitement and satisfaction in her voice, I resist explaining that splinting is only a small part of what an occupational therapist (OT) does and may be the only beginning of the occupational therapy process. Looking back on the event however, this may have been the perfect starting point to describe some of the many other ways I also help children and families...­

Parents are not the only ones uncertain about what occupational therapy has to offer in a pediatric oncology setting. Members of the health care team may struggle to identify when to call upon the OT for assistance. This is not surprising. In pediatric oncology, the role of occupational therapy is vast and varied. While the oncology OT may be called upon to fabricate custom foot drop splints for the ankles or resting hand splints to reduce the risk of contractures in a child experiencing vincristine-induced peripheral neuropathy, the same therapist may also assess the swallowing function of this child. The OT may also consider: finding adaptive positioning and participation alternatives and adaptations to school activities as necessary and appropriate for the child. For an adolescent in elementary school, they may need close supervision on the playground at recess time for poor balance. They may even need to stay in for recess if the weather is bad and they are at increased risk for falls on slippery terrain. For an adolescent in high school, it may be recommended that the child be allowed to leave classes five minutes early to have more time to get to their next class and avoid having to navigate the busy, crowded hallways at the bell. They may also be assigned a buddy to help carry books and provide missed notes when leaving class early. The OT also assesses and advocates for these accommodations.

Following this example, it is clear that occupational therapy goes beyond poly-­

In addition to deficits in aerobic capacity, lower anaerobic capacity and coordination have also been identified in childhood ALL have also been found to have significantly higher levels of vigorous and moderate physical activity12. Survivors of childhood cancers should be encouraged to participate in regular physical activity and should avoid a sedentary lifestyle8.

The role of the physical therapist can be to provide direction in the design of individualized exercise and activity programs that target specific deficits and outcomes, in addition to providing para-­

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UPCOMING CONFERENCES

CARE OF THE ADOLESCENT WITH CANCER
TOO YOUNG, TOO OLD, WHERE DO I FIT IN?

Thursday, May 10, 2012 - Evening session
Friday, May 11, 2012 - Full day session
Chan Centre for Family Health Education, BC Children’s Hospital, Vancouver, BC

The Division of Oncology/Hematology/BMT, Department of Pediatrics, University of British Columbia presents a multidisciplinary conference on Care of the Adolescent with Cancer. This conference will include discussions on ethical considerations, strategies and interventions to improve the care for this population through the trajectory of illness and survivorship. We will hear from health care professionals with expertise in this field and learn from the adolescents themselves.

Agenda:
- Post Traumatic Stress Disorder in Adolescents with Chronic Illness
- Adolescent Brain Development
- Ethics and Decision-Making in Adolescent Care
- Sexuality and Fertility Preservation
- “Does the Journey Ever End…Through Our Eyes” – adolescents’ and parents’ perspective on recovery and challenges of survivorship
- “Let Me Help You Help Me Better” – adolescents’ insights on how to improve care to adolescents
- “A Funny Thing Happened to Me on the Way to Chemotherapy” – Dr. Dan Shapiro

For more information and to register, please go to the UBC Continuing Professional Development website http://www.ubccpd.ca/Events/CPD_Conferences/Pediatric_Oncology_Hematology_Education_Day.htm

FIFTH INTERNATIONAL NURSING CONFERENCE ON CHILD AND ADOLESCENT CANCER SURVIVORSHIP

June 6-7, 2012
Colonial Williamsburg Resort, Williamsburg, Virginia, USA

This conference is designed to meet the educational, research and networking needs of nurses and other health care professionals working with survivors of childhood and adolescent cancer. The conference provides an opportunity for international networking.

For more information visit the Children’s Hospital of Philadelphia website http://www.chop.edu/export/download/pdfs/articles/cme/adolescent-cancer-2012.pdf

15TH INTERNATIONAL SYMPOSIUM ON PEDIATRIC NEURO-ONCOLOGY (ISPNO)

June 24-27, 2012
Sheraton Centre Hotel, Toronto, ON

ISPNO has become the premier event in the paediatric neuro-oncology community. This symposium is a special meeting at which new information and results can be shared and new collaborations can be established for health care professionals involved in the care of children and adolescents with central nervous system tumours. The program will feature plenary and poster sessions, as well as an Education Day and a Family day.

For more information visit the ISPNO 2012 website http://www.ispno2012.com/home