

Complications of limb salvage surgery in childhood tumors and recommended solutions

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Abstract Bone and soft tissue malignancies are associated with serious diagnostic and therapeutic problems in every level of pubertal growth in children. Current treatment modality preferred in bone and soft tissue tumors is wide resection of tumor followed by the reconstruction of consequent defect by various methods. Chemotherapy and radiotherapy are applied for systemic effects to the patient pre- and post-operatively and for local effects that facilitate the surgical procedure. Mostly, it is very difficult to control problems following wide resection and reconstruction. In this study, our aim is to discuss the problems encountered in different resection and reconstruction approaches in childhood bone and soft tissue tumors, and the recommended solutions addressed to these problems. From 1990 to 2003, a total of 68 patients (38 female, 30 male) with a mean age of 13.1 (1.5–18) were included in the study. 85.3% of patients were diagnosed as osteosarcoma and the rest was Ewing's sarcoma. Seventy-five percent of patients had stage IIB disease. The lesions of 34 patients were detected to be in distal femur, 26 in proximal tibia and fibula, 4 in foot and ankle joint, and the remaining 4 in pelvis. As reconstructive surgery, 40 patients had modular prosthesis, vascularized fibular graft was performed in 13 patients, and 10 patients underwent arthrodesis with vascularized fibular graft. 20.6% of patients had shortened limb, infection was detected in 4 patients, laxity in 5, and

restricted motion in 4 as complication of prosthesis. With sacrificed physis, 13 patients had a mean value of 4.6 cm limb shortness. Limb salvage surgery has been considered as the gold standard treatment in orthopedic oncological surgery. More understanding of the biology of sarcoma, introduction of new effective chemotherapeutic agents, development of new techniques concerning the surgical resection, advances in diagnostic methods, and improvements in reconstructive surgery all make a major contribution to limb salvage surgery. Since some problems are still encountered, we offer a therapeutic algorithm for complications in the management of childhood tumors that we have encountered so far.

Keywords Childhood tumors · Tumor prosthesis

Introduction

Bone and soft tissue malignancies are associated with serious diagnostic and therapeutic problems in every level of pubertal growth in children. Approximately, 10% of newly diagnosed malignant tumors in children, adolescences, and adults are comprised of bone and soft tissue malignancies [1].

Current treatment modality preferred in bone and soft tissue tumors is wide resection of tumor followed by the reconstruction of consequent defect by various methods. Chemotherapy and radiotherapy are applied for systemic effects to the patient pre- and post-operatively and for local effects that facilitate the surgical procedure. The success rates achieved in each step improve the survival. In last three decades, 5-year disease-free survival has increased up to 60–70% [2]. However, this has led to complications due to either treatment methods applied or long-term use of reconstructions performed.

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Chemotherapy-induced side effects, primarily systemic, may result in serious problems. The frequency and type of secondary malignancies that may develop after treatment differs depending on administered chemotherapy or radiotherapy, or patient's genetic features. Malignancies secondary to chemotherapy occur within the first 5 years after the treatment regimen, usually in the form of acute non-lymphoid leukemia, especially due to the use of increasing doses of topoisomerase-II inhibitors, anthracyclines, or alkylating agents. The development of secondary solid tumors is thought to be associated primarily with radiotherapy or genetic predisposition, where alkylating agents have also role, though less frequently. The occurrence of secondary solid tumors increases year by year in direct proportion to the administered dose. Systemic growth and development retardation occurs during the treatment, yet the growth rate accelerates and reaches the normal limits after the cessation of chemotherapy, which is defined as "catch-up growth". Delayed side effects that might arise from radiotherapy may be short stature in relation to radiated area.

The complications which may be originated from the resection could be divided into two main groups as age-independent and age-dependent. Age-independent complications can further be grouped as biological and endoprosthetic etiology; the former including infection and non-union, and the latter laxity, infection, shortness, and restricted range of motion. Age-dependent complications can be categorized as three subgroups: physis loss, definite physis injury, and radiotherapy-induced injury. Physeal loss presents with shortness, partial loss of physis with deformity, and sequel of radiotherapy with deformity and pelvis asymmetry (Table 1).

Our experiences allow us to declare that although we try to do our best in controlling most problems following wide resection by required reconstruction procedures, we cannot prevent many other problems to occur.

In this retrospective study, based on our experience, we will discuss the problems encountered in different resection and reconstruction approaches in childhood bone and soft tissue tumors, and the recommended solutions addressed to these problems.

Patients and methods

Our study population is comprised of 68 patients applied to our clinic between 1990 and 2003, whose treatment was undertaken by us. With malign or benign aggressive lesion involving pelvis or lower limb, 30 patients were female and 38 patients were male (Table 2). Mean age was 13.1 (range 1.5–18). Seventy-five percentage of patients had stage IIB disease. Ten patients were diagnosed with Ewing's sarcoma and 58 of them with osteosarcoma (Table 3).

Table 1 Recommended solutions addressed to each problem

Age-independent		Age-dependent	
Problems and consequent solutions of biological reconstruction		Problems related to physical loss and consequent solutions	
Problems and consequent solutions of endoprosthetic reconstruction		Problems related to partial physical injury and consequent solutions	
Problems and consequent solutions of radiotherapy and consequent solutions		Problems related to radiotherapy and consequent solutions	
Solutions for deformity/shortness	Solutions for infection	Solutions for shortness	Solutions for deformity
Solutions for non-union	Solutions for loosening	Solutions for restricted ROM	Solutions for pelvic asymmetry
Solutions for infection	Stable osteosynthesis	Physical therapy + relaxation operations	Solutions for deformity
Allograft + polymethylmetacrylate (bone cement) with antibiotic	Prosthesis without cement	Prosthesis + growing stem	Solutions for deformity
Close follow-up	Allograft + polymethylmetacrylate (bone cement) with antibiotic	Growing endoprosthesis	Compensation for shortness
Elongation	Physical therapy + relaxation operations	Vascularized epiphyseal transfer (for proximal humerus)	Close follow-up
Temporary epiphysiodesis of joint	Prosthesis + growing stem	Prosthesis + growing stem	Elongation
Deformity correction	Prosthesis + growing stem	Prosthesis + growing stem	Temporary epiphysiodesis of joint
			Deformity correction

Table 2 The distribution of patients by gender

Gender	Number	Percentage (%)
Male	38	56
Female	30	44

Table 3 The distribution of tumors by diagnosis

Diagnosis	Number	Percentage (%)
Ewing's sarcoma	10	15
Osteosarcoma	58	85

Table 4 The distribution of tumors in the body parts

Affected part	Number	Percentage (%)
Distal femur	34	50
Proximal tibia and fibula	26	38
Foot and ankle joint	4	6
Pelvis	4	6

The lesions of 34 patients were detected to be in distal femur, 26 in proximal tibia and fibula, 4 in foot and ankle joint, and the remaining 4 in pelvis (Table 4).

Twenty-seven patients had single physal injury and 4 had double physal injury, whereas 13 patients experienced radiotherapy-induced physal injury. As reconstructive surgery, 40 patients had modular prosthesis, vascularized fibular graft was performed in 13 patients, and 10 patients underwent arthrodesis with vascularized fibular graft (Table 5).

Infection was detected in 4 patients, laxity in 5, restricted motion in 4, and shortened limb in 14 patients as complication of prosthesis (Table 6). The infectious agents isolated in the infected four patients were methicillin-

Table 5 Types of performed reconstructive surgery

Reconstruction type	Number	Percentage (%)
Modular tumor prosthesis	40	59
Vascularized fibular graft	13	19
Arthrodesis (with vascularized fibular graft)	10	15

Table 6 Complications of prosthesis

Endoprosthetic complications	Number	Percentage (%)
Infection	4	10
Prosthesis loosening	5	12.5
Restricted range of motion	4	10
Limb shortness	14	35

resistant *Staphylococcus aureus*, which was treated by teicoplanin and surgical debridement.

Limb shortness occurred in 13 patients with sacrificed physis, which had a mean value of 4.6 cm (range 1–12). Eleven patients developed orthopedic deformities of various anatomical directions.

Discussion

Limb salvage surgery has been considered as the gold standard treatment in orthopedic oncological surgery since publications by Swetnam [2] and by Kotz [3]. More understanding of the biology of sarcoma, introduction of new effective chemotherapeutic agents, development of new techniques concerning the surgical resection, advances in diagnostic methods, and improvements in reconstructive surgery all make a major contribution to limb salvage surgery in becoming the gold standard.

A limb sparing surgical approach to achieve success depends on the recognition of the anatomy of tumoral tissues by appropriate radiological methods, complete resection of tumor, biological destruction of tumor, conservation of surrounding healthy tissues, and reparation and restoration of the tissue remained after resection. Limb salvage surgery can be performed in a multidisciplinary approach that ensures all these factors to be perfectly applied. This approach should absolutely involve the cooperation of an orthopedic oncologist, a medical oncologist, a radiation oncologist, a pathologist, and radiologist specialized in bone and soft tissue tumors, a reconstructive surgeon and a physiotherapist.

After the acceptance of limb salvage surgery as gold standard, orthopedic oncologists started to make use of tumor resection prostheses, vascularized fibular grafts, intercalary allografts, rotationplasty techniques; chemotherapists used various chemotherapeutical agents; and so did radiotherapists by advanced radiotherapeutical devices. The utilization of these methods in the children that do naturally not complete their growth has led to a number of problems previously not observed: limb shortness, deformation, growth retardation, aseptic laxity, and infection in prostheses.

Torbert et al. [4], in their study comprised of 139 patients with bone and soft tissue sarcoma, reported 1 prosthesis malalignment, 2 patients with periprosthetic fracture, 2 patients with dislocation, aseptic loosening in six patients, mechanical failure in prostheses of 8 patients, and local tumor recurrence in another eight patients following endoprosthetic reconstruction, which had been applied to all study population.

Alan et al. based on their clinical experiences, described the problems that may be faced in long-term as local tumor recurrence, wound associated complication, and mechanical and biological reconstruction failure. It was reported

that when these problems emerged, delayed complications may develop in the form of re-hospitalization, occupational or educational absenteeism, social loss during recovery period, and problems in physical and psychological relationships, and in extremity functions [5].

Bernstein et al. reported that late stage prosthetic failure or infection might be observed and that the possibility of re-operation was present and that sometimes amputation might be necessary following the limb salvage surgical procedures. As non-surgical complications, they mentioned about that the growth potential of bone and soft tissue was observed to decrease in patients subsequent to applied radiotherapy, even causing radiation osteosarcoma, and that the probability of leukemia was 1–2% after the chemotherapy [6].

In their study consisting of modularly growing resection prostheses applied in childhood bone tumors, Neel et al. reported that growth differences after resection were acceptable. They also emphasized that these short-term results should be compared with long-term results [7–14].

Hurson stated that prostheses, allografts, vascularized free fibular grafts could be used in the reparation and/or restoration of the defects secondary to resection, yet only easily by socio-economically developed countries. On the other hand, the author added that it was more reasonable in the economical approach that the reparation and/or restoration of the defect to be performed by distraction–compression osteogenesis in developing countries [8].

Leow et al. and Ilic et al. [9] reported that limb salvage treatments were an effective and beneficial treatment modality in malignant bone and soft tissue sarcomas.

The rotationplasty, defined by Borrgreve in 1930 and Van Nes in 1950, and applied by Salzer et al. in 1981, still keeps its position as an alternative approach in distal femoral tumors. Rödl et al. suggested two important parameters in the treatment of orthopedic oncology, one of which was the tumor size and neurovascular involvement, and the other being the age of the patient. Based on these important parameters, they explained the fact that rotationplasty should be considered as an alternative to amputation in some distal femoral tumors that amputation seemed to be the mere option. They also stated that functional outcomes of rotationplasty were more superior compared to amputation [10].

Ramseier et al. observed two infections, 5 allograft fractures, 2 patients with local recurrences, four patients with local wound healing problem, two patients with arthritis, and no complication at all in 4 patients out of 19 patients in total, who were applied either osteoarticular or intercalary allografts. Five of these patients died of the disease itself, whereas the remaining 14 patients have continued to live for 11 years without any complications [11].

Bach et al., in their study consisting of 4 patients, reported that osteocutaneous fibular graft-facilitated fusion lasted for a mean duration of 5 months in patients undergone into limb

salvage surgery, and it played a significant role in the formation of adequate soft tissue coverage [12].

The study performed by Muscolo et al. showed a high possibility of the joint to remain healthy as intermediate and long-term results in cases where distal femoral allografts were used [13].

Ilic et al. reported that multiple factors such as age, diagnosis, anatomical location, stage of disease and of socio-economical origin may have impacts on the treatment success in pediatric orthopedic oncology and that the therapeutic algorithm cannot be easily established. They also declared that the targeted priorities, in order, were saving life, saving the limb, saving the function of the limb, equalizing both limbs, and restoring cosmetic appearance in musculoskeletal malignant tumors treated in a multidisciplinary approach [15].

The problems that we encountered in the patients of our study exhibited great similarities to that reported in the literature. In patients where the limbs were salvaged with tumor resection prosthesis, we observed four patients with infection, 5 patients with aseptic loosening, restricted motion in 4 patients, 14 patients with unequal limbs in length. The emergence of these inequalities in 14 patients out of 40 with tumor resection prosthesis clearly demonstrated us that shortness occurred in 1/3 of patients, which, in our opinion, was high.

Thirteen patients among those physeal and epiphyseal sacrifice was performed, had unequal extremity lengths, 11 of which were detected to be associated with multiplanar deformity. The number of patients where coincidence of bone loss and limb length inequality was present was found to be six.

We observed pelvic asymmetry and shortness in three of our radiotherapy applied cases, which we recommended compensation for shortness and a close follow-up.

Although limb salvage surgery is considered as the gold standard of orthopedic oncological treatment modalities, the increasing effectiveness of chemotherapy and radiotherapy in growing children offers high life expectancy, yet also causes many problems that should be overcome [16].

The complications which may be originated from the resection could be divided into two main groups as age-independent and age-dependent. Age-independent complications can further be grouped as biological and endoprosthetic etiology; the former including infection and non-union, and the latter loosening, infection, shortness, and restricted range of motion. Age-dependent complications can be categorized as three subgroups: physis loss, definite physis injury, and radiotherapy-induced injury. Physis loss presents with shortness, partial loss of physis with deformity, and sequel of radiotherapy with deformity and pelvis asymmetry.

The table presents the therapeutic algorithm and the solutions addressed to the complications that we have so far encountered.

Age-independent

A. Biological reconstruction

1. Infection: Allograft + polymethylmetacrilate (bone cement) with antibiotic
2. Non-union: Stable osteosynthesis
3. Deformity
 - a. Close follow-up
 - b. Temporary epiphysiodesis of the joint
 - c. Deformity correction
 - d. Elongation

B. Endoprosthetic reconstruction

1. Laxity: Prosthesis without cement
2. Infection: Allograft + polymethylmetacrilate (bone cement) with antibiotic
3. Shortness
 - a. Growing endoprosthesis
 - b. Prosthesis + growing stem
4. Restricted ROM

Age-dependent

A. Physeal loss (joint resection)

1. Shortness
 - a. Growing endoprosthesis
 - b. Prosthesis + growing stem
 - c. Vascularized epiphyseal transfer (for proximal humerus)

B. Partial physeal injury

1. Deformity
 - a. Close follow-up
 - b. Temporary epiphysiodesis of the joint
 - c. Deformity correction
 - d. Elongation

C. Sequel of radiotherapy

1. Deformity
 - a. Close follow-up
 - b. Temporary epiphysiodesis of the joint
 - c. Deformity correction
 - d. Elongation
2. Pelvic deformity
 - a. Compensation for Shortness and Follow-up

problems in these cases, it should be remembered that such complications secondary to limb salvage surgery may, in long-term, lead to serious problems once survival ensues in these growing children. Although these complications could be corrected by other surgical procedures, the emergence of new problems in still growing cases makes the addressed solutions more difficult to work.

In conclusion, taking probable complications subsequent to the limb salvage surgery into account, we consider the ideal solution to be the implants that ensure a normal or near-normal range of motion and equalization of lengths of both limbs with a single implant.

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Taken into consideration the treatment modalities that we applied into our study population and the consequent