BONE TRANSPLANTATION IN LIMB SAVING SURGERIES: THE PHILIPPINE EXPERIENCE

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ABSTRACT

Until the turn of the decade, Filipino patients afflicted with malignant and aggressive extremity tumors were almost uniformly treated with mutilating amputations. Limb-saving surgery only recently became an option locally – this resulting not only from a better comprehension of surgical oncologic principles but also from the development and refinement of reconstructive procedures following such surgeries. Foremost among the latter is the use of long bone transplants, otherwise known as large segment bone allografts.

Large-segment allografts are available from the Tissue and Bone Bank of the University of the Philippines -- the only bank of its kind in the country. All allografts are harvested from appropriate donors (both cadaveric and live), processed at the Bank, radiation-sterilized at the Philippine Nuclear Research Institute (PNRI), and finally brought back to and stored in a -80°C deep freezer at the Bank.

This paper presents our 4-year experience with large-segment allografts for extensive defects of limb salvage surgery in musculoskeletal tumors. All patients included in this presentation had: (1) malignant or aggressive extremity tumors; (2) surgery performed by the University of the Philippines-Musculoskeletal Tumor Unit (UP-MuST Unit); (3) follow-up of at least one year; and (4) available pre- and post-operative radiographs for review.

Over a period of 4 years (January 1993-January 1997), 63 patients with malignant or aggressive extremity tumors (who formerly would have been amputated) underwent limb salvage surgery by the UP-MuST Unit. Twenty (21) of these patients had reconstructions utilizing irradiated large-segment allografts and fulfilled the above criteria for inclusion in this review.

Tumors included osteosarcoma (6), giant cell tumors (12), and metastatic lesions (3). Ages ranged from 16-64 years; 14 males and 7 females. Bones involved were the femur (12), tibia (6), and humerus (3). Average length of the defects was 15 cm. Surgeries performed were segmental replacement (5), resection arthrodesis (12), hemicondylar allograft (3), and allograft-prosthesis-composite (1). Implants used were usually intramedullary nails or plates and screws, with or without bone cement.

Follow-up ranged from 16-60 months or until death. Sixteen (16) were alive with NED (no evidence of disease), 3 were dead (2 of disease, 1 of other causes), and 2

were AWED (alive with evidence of disease). Functional evaluation using the criteria of the International Society of Limb Salvage (ISOLS) was performed in 18 patients. There were 15 good to excellent results (83%) – many having returned to their previous work and recreation. The 3 poor results were due to infections in 2 cases, and a fracture (secondary to a fall) in 1 case.

Limb-saving surgery for Filipino patients with musculoskeletal tumors continues to be a challenge because of both tumor size and the size of the defect requiring reconstruction. Large-segment allografts from the UP-Tissue & Bone Bank, however, make this difficult surgery realizable in our setting; and offers to our patients a chance to save not only life but also limb.

Key words: Tumors, limb-salvage surgery, large-segment allografts, bone transplant, Philippines

INTRODUCTION

Limb salvage surgery for extremity tumors is an accepted alternative to ablations. Adequate margins with appropriate adjuvant treatment can provide survival rates equal to that of amputations. In the Philippines, however, options for reconstruction in limb salvage after bone tumor excision are limited not only by the size of the defects but also by the unavailability and unaffordability of tumor prostheses and implants.

Since its formation in 1993, the UP-Musculoskeletal Tumor Unit of the Philippine General Hospital (**UP-MuST Unit**) has performed limb salvage for approximately 25-30% of extremity tumors which in previous years would have been amputated. After tumor excision, bony reconstruction has utilized vascularized and non-vascularized autogenous grafts, chipped autografts with or without allografts, implants with bone cement, large segment allografts (bone transplants), or a combination of these procedures. For extensive tumor defects which cannot be bridged by chipped bone grafts we have utilized either the vascularized fibular graft or the large segment allografts or a combination of the two. This is a report of our initial four-year experience with large segment allografts in tumor reconstruction. Only those cases with at least twelve months follow-up will be included.

MATERIALS AND METHODS

During the period January 1993-December 1997, 63 cases of limb salvage surgery were performed by the UP-MuST Unit. Twenty-one (21) of these cases were reconstructed with bone transplant. All patients included had: (1) malignant or aggressive extremity tumors; (2) surgery performed by the UP-MuST Unit; (3) follow-up of at least one year; and (4) available pre- and post- operative radiographs for review.

All tumors were either malignant or aggressive bone lesions; these include twelve (12) cases of giant cell tumor (GCT), three (3) metastatic lesions, and six (6) osteosarcoma. Ages of the patients ranged from 16-64 years with fourteen males and females. All cases were first time cases, except for one (reconstruction

with a Kuntscher nail and bone cement done elsewhere which had failed; the patient was subsequently referred to the Unit).

Surgeries performed were resection arthrodesis (12), segmental replacement (5), allograft prosthesis-composite (1), and hemicondylar bloc allograft (3). The femur was involved in twelve (12) cases: eight of which were distal, three intercalary, and one proximal. The proximal tibia and humerus were affected in six (6) and three (3) cases respectively. Bone defects ranged from 3.5-21 cm, with a mean length of 15 cm.

All the allografts were obtained from the Department of Orthopedics Tissue and Bone Bank (the only Bank of its kind in the entire country) and all were radiation-sterilized at 2.5 megarads at the Philippine Nuclear Research Institute. Fourteen (14) of the allografts were fixed to host bone with plates and screws and in four (4) cases intramedullary nailing was used. Except for those cases fixed with intramedullary nails, all allografts were reinforced with bone cement. Due to the inadequate supply of large segment allografts (high demand, low supply), host bone matching could not be exact. In six cases, the allograft used was an entirely different bone e.g. tibia for femur, femur for humerus, etc.

RESULTS

Follow-up ranged from 16-60 months, all patients personally followed up by the author. Sixteen patients were alive with no evidence of disease (NED) and two were alive with evidence of disease (AWED). The latter two included a thyroid metastatic patient and a case of osteosarcoma in a 16-year-old boy who had lung metastasis 18 months after initial surgery. One patient had a local recurrence at 52 months but this patient underwent repeat excision and is presently alive with NED.

Three (3) patients have died, 2 of disease, and 1 of other causes. The 2 patients who have died of disease include one metastatic thyroid patient and one osteosarcoma patient; the third patient was a metastatic liver cancer patient who died of a myocardial infarct 10 months after shoulder surgery.

Time to union between host bone and allograft bone averaged approximately four to five months. Delayed union was noted in 2 patients – one patient had osteosarcoma; at time of death (nine months) there was radiologic union at the proximal allograft-host bone junction but still no union at the distal junction. The second patient had a GCT of the distal tibia reconstructed with a tibial transplant. She failed to follow-up until after 20 months during which time no union was noted at both allograft-host junctions. Bone grafting was done for her non-union.

There were 2 fractures, one who had fallen from the bed onto her reconstructed shoulder, and one patient, with parosteal osteosarcoma, whose allograft showed lysis prior to fracture at 10 months after surgery. The first patient refused further surgery, and the second patient benefited from her psuedoarthrosis, this giving her added motion at the shoulder.

There have been four cases of infection (3 cases of GCT and 1 case of osteosarcoma). The first was a patient with GCT in which reconstruction involved a combination of allograft and vascularized fibular graft; infection was noted shortly after surgery. Despite antibiotic beads and several debridements, the wound continued to discharge; infection settling only after the allograft was removed. The second patient was initially reconstructed with an osteoarticular distal femur. A draining sinus developed at 3 months, and during debridement, it was decided to fuse the knee (arthrodesis), after which infection was controlled. The last 2 patients both had poor soft tissue coverage, the third infecting at 9 months, the last at 4 months – both of whom eventually had amputations.

Of the eighteen patients still alive, functional evaluation was performed at latest follow-up using the modified Enneking functional evaluation protocol[5] adopted by the International Society of Limb Salvage (ISOLS). Evaluation showed good to excellent results in fifteen cases (83%) – many patients having returned to their former work and recreation. The 3 failures were 2 patients who had amputations for infected transplants; and the metastatic patient who refused surgery after her allograft fracture.

Four representative cases will be presented.

VC, 55 year old male was referred to the Tumor Clinic for GCT of the right proximal femur. After marginal excision of the lesion, a 14-cm defect was reconstructed with an allograft-prosthesis composite. Since there was no right femur available, a left proximal femur was used and reamed for proper fitting of a right hip prosthesis. A regular stem in lieu of a long-stem partial hip prosthesis was used because of the unavailability of the latter. Step-cuts were made between allograft and host bone to diminish rotation; and cerclage wires used to encircle these cuts. At four months, there were radiologic signs of allograft-host bone union. At twelve months, he had 90 degrees of active hip flexion 30-35 degrees internal rotation. At fifty-nine months, there are no signs of recurrence and patient is full weight bearing, occasionally using a crutch.

RL, 32 year old male, with GCT of a hemicondyle of the distal femur, refused resection arthrodesis despite the extremely thinned out articular surface. After meticulous curettage, an entire hemicondyle (without cartilage component) was shaped to fit the defect. This bloc allograft was then fixed to host bone with a condylar plate. At twelve months, he had full range of knee motion. At twenty-four months, he returned to active basketball against medical advice. At thirty months, he has returned to heavy labor carrying sacks of rice. At sixty months (5 years) follow up, patient is free of disease and using his leg fully.

RD, 32 year old male, was diagnosed as having periosteal osteosarcoma of the tibia. After appropriate workup, patient underwent wide excision of the lesion, leaving a 15 cm defect. An allograft tibia was prepared and transplanted onto the defect, fixed with a plate and screws. On latest follow up at 29 months (2-1/2 years), Pastor RD is free of disease, the transplant has fused, and he has returned to work on a full-time basis.

RM, 62 year old businessman, with liver cancer diagnosed around 1-1/2 years ago, developed metastasis to the right humerus. His reconstruction at another hospital had failed; the bone cement and implants to the right humerus. His reconstruction at another hospital had failed; the bone cement and implants giving way. Upon referral to our Unit, we subjected him to a reconstruction using a bone transplant; but since no available humerus was available, a femur was used together with bone cement and a plate and screws. Postoperatively, RM was able to use this hand for daily activities, except heavy lifting. He died of a myocardial infarct, however, at 10 months time.

DISCUSSION

At the UP-Musculoskeletal Tumor Unit of the Philippine General Hospital, approximately 25-30% of all aggressive and malignant primary bone tumor patients undergo limb salvage surgery. All such patients undergo both local and systemic work-up to provide the correct Enneking stage.[4] Appropriate adjuvant therapy, e.g., chemotherapy, is provided when necessary. All patients undergoing limb salvage surgery must meet these requirements.

All twenty-one patients reported in our series underwent appropriate work-up, after which they underwent marginal or wide excisions for limb saving surgeries. Bone defects after tumor removal were extensive averaging 15 cm. In the Philippines, options for reconstruction of such bone defects are limited. Late presentation of patients, whether a result of patient or physician ignorance, often result in large neglected tumors such as those of our patients, the excision of which leave defects autografts cannot bridge. Some patients have been treated previously and bone graft donor sites (e.g., fibulae) utilized. Tumor prostheses and other modular implants are unavailable and their costs prohibitive for the average patient.

In 1908, Dr. Eric Lexer from Germany first reported the clinical use of bone allografts or transplants in orthopedic surgery.[7] Like many techniques, support for its use was slow to come. In the 1970's, there was renewed interest in long bone allografts, spearheaded by Mankin et al. from Massachusetts General Hospital.[9] Replacement of excised bones of the extremities with large segment allografts has since then slowly gained popularity throughout the world. Large segment allografts have become an important alternative in tumor reconstruction.

Defects in all our twenty-one patients were adequately bridged by large segment allografts. Early and medium-term results of these patients are encouraging. Fifteen out of the eighteen still living patients were rated as having good to excellent functional results. This functional evaluation is a system which takes into account six factors; motion, pain, stability or deformity, strength, functional activities and emotional acceptance, and complications.[5] Those who have continued to follow-up for over two years have returned to their previous work or level of activity.

Complications of limb salvage surgery using large segment allografts include infections, fractures, and delayed or non-unions. Infections range from 12-

40%.[2,8,10] The majority of infections occur within one to four months postoperatively and infections are usually deep-seated and polymicrobial or gram positive in etiology. Dick and Strauch found wound and soft tissue complications to be the major predisposing risk factors[2] similar to 2 of our cases. Furthermore, tumor surgeries are usually extensive and require prolonged periods of time. Our infection rate of 19% compares well with that reported in literature.

Fractures, reported to be 10-25%[1,3], usually occur within the first four years. We have had two fractures (9.5%), both occurring in transplants which utilized fibular allografts. In both cases, because of technical difficulty, no bone cement was used to fill in the medullary canals. Wilkins and Brown report a slightly lower rate of fractures with cemented allografts in limb salvage procedures.[12]

Delayed unions on the other hand are often attributed to chemotherapy.[6] Interestingly, one of our cases with delayed union had been on adjuvant chemotherapy. The other case had been lost to follow-up for 20 months, and on return, it was noted the allograft-host bone junctions had a larger area of lysis.

As more limb salvage surgeries are performed, methods of reconstruction of extensive defects must be considered. Our case series shows very encouraging early to medium-term results with the use of large segment allografts. Due to certain limitations, allografts were often not matched or not used in a conventional way.[11] At latest follow-up, however, results have been good to excellent; and it would seem that large segment allografts are a most viable option in our setting.

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