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review

Limb salvage in soft tissue sarcomas

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In 2000, most patients with soft tissue sarcomas of the axial or appendicular skeleton can expect 'to walk away' from the surgery. This compares to just 20 years ago when a relatively high percentage of patients were treated with amputation. Now the treatment has changed to one of wide local excision with a 1 cm to 2 cm margin on normal tissues and an adventitial margin on critical structures such as nerves or vessels, followed or preceded by radiotherapy. With the use of adjuvant treatments in combination with reconstructive surgery, over 90% of patients with sarcomas of the soft tissues or bone may be rendered disease free locally. The only restriction to this approach is when tumor involves the major nerve to a limb or when microscopic, clear margins cannot be obtained at the time of surgery as both of these are best treated with an amputation.

Key words: soft tissue neoplasms; sarcoma surgery; extremities; neoplasms staging; survival rate

In 2000, most patients with soft tissue sarcomas of the axial or appendicular skeleton can expect 'to walk away' from the surgery. This compares to just 20 years ago when a relatively high percentage of patients were treated with amputation. Now the treatment has changed to one of wide local excision with a 1 cm to 2 cm margin on normal tissues and an adventitial margin on critical structures such as nerves or vessels, followed or preceded by radiotherapy. Unfortunately, this approach still results in 20 % local recurrence in the best centres around the world. In the most recent series, some from centres such as the Memorial Sloan-Kettering, we see the recurrence ranges from as low as 7 % all the way to 34 %.

We are most fortunate in our province in having a centre that supervises treatment of all cancers for a population of about 2 million people. In 1984 we established an interdisciplinary Sarcoma Group, including plastic surgeons, orthopedic surgeon, surgical oncologist, radiation oncologist, medical oncologist, and pathologists, to try to improve the results in these patients. We took advantage of the experience reported by Eilber out of Los Angeles who demonstrated a 4 % local recurrence rate in over 100 patients followed for 5 years using a preop chemotherapy and radiotherapy regime. Their morbidity rate, howev-

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er, was fairly high with a re-operation rate of 20 % and a fracture of the long bone in follow-up of 5 %.

In 1984, we began a prospective study to look at a modification of this regime, which I will report to you in the following series. This includes patients treated for soft tissue sarcoma, bony sarcoma, and pelvic sarcoma.

The first is a prospective, cohort trial of conservative surgery for soft tissue sarcomas. Our protocol administered the same amount of adriamycin as Eilber, usually by the intra-arterial route if there was a feeding vessel, at 30 mg/day continuous infusion for 3 days. Radiation followed immediately with 3 Gy for 10 days for a total of 30 Gy. This is followed by a surgical excision no sooner than 4 weeks after the completion of radiotherapy. For example, a 35-year-old woman presented with a large mass, which had been followed mistakenly for 8 months as a hematoma. A CT scan showed a large mass behind the femur, applied to the sciatic nerve. Biopsy demonstrated this to be a myxoid liposarcoma. She was treated with the intra-arterial infusion of the common iliac artery as described and radiotherapy. In the planning film prior to radiotherapy a lead wire shows a mass extending well past the greater trochanter of the hip but after therapy there was marked shrinkage of this tumor so it is difficult to see any extension. The tumor was excised taking a centimetre of normal tissue and preserving the sciatic nerve. On cross section, the tumor still had viable components that are typical of a myxoid liposarcoma but was one half the original size. She is alive now, 17 years after the surgery, with excellent cosmetic and functional result. This study reports all our patients up to 1992 so we have a minimum of a 3-year follow-up at which time 90 % of all local recurrences would be expected to have occurred. This is based on a population rather than a referral practice. We took all soft tissue limb and trunk sarcomas which were in the high-risk category of recurring, including the deep, large, high grade or recurrent tumors. Lesions that involved sciatic nerve or brachial plexus were excluded as the resection of the sciatic nerve results in a senseless and motionless limb. Patients with positive margins were offered amputation. We had 42 patients, ages 13-79, who were treated with this protocol. Two failed this protocol in that they had positive margins; one refused amputation and subsequently re-resected with a recurrence and is still free of disease. The follow-up ranged from 24 to 110 months with a mean of 5 years. This included 25 primary and 15 recurrent tumors that had failed previous attempts at surgery. The majority of these lesions are on the lower extremities, with 6 on the upper extremities, 2 on the abdominal wall, and 2 in the head and neck.

The TNM staging shown here with all but 4 patients being Stage II or greater with some being as advanced as Stage IV. The majority of these lesions are IIB and III Stages. The histologic tumor type varied among many cell types with the most common being synovial cell, leiomyosarcoma, liposarcoma, and malignant fibrohistiocytoma. Complication rate in these patients included problems with the adriamycin infusion in 10 %, wound infection, prolonged drainage in 12 %, re-operation in 2 %. Five percent had positive margins, and out of these, 1 ultimately required an amputation. The follow-up, now which was an average of 6 years since the study was completed, is 97 % local control for appendicular and 100 % for tumors on the trunk. The survival of these patients shows that only 40 % are alive at 10 years demonstrating the highly malignant potential of most of these lesions.

This protocol is unique in the literature in terms of its local control and the very low incidence and minimum of wound complications. These lesions, in our study, were all at high risk to recur as documented by the analysis from MD Anderson which showed that Stage II had a minimum of 14 % local recurrence increasing to 45 % in Stage IV.

Lesions larger than 5 cm had a 31 % incidence of local recurrence as well as this being shown for tumors with higher grade and for those having recurrences. We are still struggling, in approximately 30 %, with minor adriamycin rashes, and in 10 % significant complications. These, however, happened in the first few patients where we had intra-arterial thrombosis during infusion. It is absolutely critical that these patients be maintained on enough heparin to keep the prothrombin time well above 60 seconds. Tumors have been seen to shrink during the adriamycin infusion and these patients are hypercoagulable because of the massive procoagulant release of the dying tumor cells. We are still struggling with the problems of seroma in these large cavities and plastic surgical techniques with bringing in local muscle flaps have promised to improve this dilemma. As well, large tissue defects can now be covered with flaps which avoid the problems of wound breakdown.

We feel that this is a complex disease where the close cooperation between the surgeons and the radiotherapists is important for improving the result. We do not feel that this tumor should be approached by the surgeons who have not had special training in this area or in the absence of team support.

Overall survival of these patients with this dose of chemotherapy is unlikely to be affected. Now that local control has been accomplished in these tumors, the next and very pressing issue is to continue studying the use of adjuvant chemotherapy which to date has been disappointing in all but a few of the sarcomas such as Ewing's, osteosarcoma, and perhaps rhabdosarcoma.

In conclusion, this population-based, prospective study documents a superior approach for local control of soft tissue tumors.

We have now extended this same approach to management of sarcomas involving the bony appendicular and axial skeleton. To this day, the standard of care for these patients is, in fact, an amputation. However, with the neoadjuvant approach it may be that with the technical support for replacing bones, the same principles could apply. So along with our study of soft tissue sarcomas, we also began a parallel study for tumors involving the bone. In planning the surgery, MRI became a critical component to identify intramedullary extension of the tumor. This compares to the soft tissue tumors where CT scan alone is a very reasonable approach. Once again, our objective was to provide a microscopic clear margin with a 1 cm margin in all direction except for the bone being frequently a much more difficult task. An allograft or an alloplastic interposition graft was planned prior to the surgery. To demonstrate the approach, I am presenting 2 patients. The first one having Maffucci's Syndrome with multiple enchondromas, 2 of which had become chondrosarcoma. A total scapulectomy and removal of the proximal 2/3 of the humerus was planned and an alloplastic titanium insert was designed using the same engineering developments that have been pioneered for the space shuttle. The model of the scapula and humerus was created from the CT scan and the final constrained prosthesis designed for the surgery. The operative defect shows the arm only connected by a small skin bridge and the axillary nerves and vessels. The scapula and humerus were replaced by a prosthetic alloplastic scapula. The postoperative x-ray shows the prosthesis in place. The patient had full function of her lower arm.

The second patient is a young woman who presented with an expanding mass of the wrist with having failed a previous attempt at controlling a giant cell tumor. This tumor was locally infiltrative and destroyed the distal radius. She was treated with a preoperative radiotherapy and chemotherapy and taken to surgery 4 weeks later where the tumor was completely resected, preserving only the ten-

dons, nerves, and vessels. The resected portion was replaced by an allograft portion of radius plated in place and she has a fully functioning hand with no local recurrence 5 years later.

Our population of these patients now includes 10 patients with ages ranging from 17 to 73. Two patients were treated with shoulder replacements, 3 with replacement of pelvic bone, and 5 with lower femur replacements. Using TNM staging, they were at least Stage IIB. The pathology included 5 osteogenic sarcomas, 2 giant cell tumors, 1 chondrosarcoma, and 1 undifferentiated sarcoma. These patients all completed a metastatic work-up and for those patients with an osteogenic sarcoma or Ewing's sarcoma, preoperative systemic therapy was part of the management. All patients ended up with a functional limb but did require braces or walking aids for those having an internal hemipelvectomy and to date there has been no local recurrence. However, 1/3 of these patients developed systemic disease and ultimately succumbed. None of these patients had graft failure. One patient had a chronic infection requiring removal of the graft. During treatment approximately half of these patients had fractures of the treated bone during the time of radiotherapy but were treated with a brace until the time of surgery. This did not result in local recurrence with follow-up averaging 3 years. This experience contrasts to the analysis in the literature reported by Mankin where an above-knee amputation for osteosarcoma of the distal femur resulted in 8 % local recurrence and hip disarticulation 0 %. The survival was unchanged at 55 %. This confirms that the possibility of local recurrence does not change the propensity of the tumor to metastasize. This is an inherent property of the cell, which has taken place, as far as we can determine, many months before the initial presentation in the majority of patients. Therefore, our protocol of chemotherapy and radiation has reduced the requirements for amputations from 100 % to 11 %. One amputation was necessary in a patient with a tumor infiltrating the popliteal nerve. Fracture of the bone did not affect the subsequent therapy or local recurrence and in all these patients with reconstruction, a functional limb was retained. We currently are favoring alloplastic replacement despite the expense. However, in none of our allografts have we had a fracture although that is a well-documented, long-term complication of using this material.

In conclusion, neoadjuvant chemotherapy and radiotherapy for marginal resections of soft tissue and bony components of bone sarcomas can be done without compromising local control or long-term survival.

Finally, I will focus on a special area of experience in the management of the most difficult problem of these tumors involving the axial pelvic structure. This is particularly challenging because of the traffic of significant neural, vascular, and other organs within or surrounding this structure. However with the principles of limb salvage surgery, which we have determined both in soft tissues and appendicular skeleton, we felt that it was reasonable to apply them to tumors of the bony pelvis where the standard therapy would generally be a hemipelvectomy. Our series includes all patients with localized tumors whether they were primary or secondary. The patients had a full work-up with a bone scan, CT scan, and MRI of pelvis. The same adjuvant radiotherapy and chemotherapy protocol was used. These patients were approached with the same surgical principles of wide local excision when possible of 1cm to 2 cm. Reconstruction of the missing pelvic girdle was done either with a portion of allograft femur or an allograft pelvis. It was found that covering this bone was necessary with a myocutaneous flap to avoid the extrusion of the allograft through the skin over the iliac crest. For example, I present to you a 17-year-old male who had Ewing's sarcoma of the left

iliac bone, which extended up to the kidney. He was treated aggressively with multi-agent chemotherapy and radiotherapy and presented 9 months later for possible resection with a residual 8 cm mass on CT scan. There was a defect in his left iliac wing caused by the tumor and the MRI shows the initial extent of the mass. The patient was positioned in the lateral position for surgery where the entire iliac wing was resected from the sacral ala to just above the acetabulum. The pathology showed a few live cells in the hypocellular stroma. This is despite the fact that this tumor went from approximately 30 cm in length down to less than 8 cm. The defect was repaired with a portion of femur. The patient was alive 2 years later without evidence of recurrence. A second patient, a 27-year-old male who presented with a mass growing out of his pubis for 6 months. The x-ray shows a loss of the superior pubic ramis and the CT scan shows a large mass displacing the femoral nerve and vessels laterally. This extended into the pelvis pushing the bowel and bladder towards the contralateral side. The patient was radiated by placing an intra-abdominal prosthesis to protect the small bowel and post radiation the tumor had not particularly shrunk but had become cystic in nature. The entire ischium and pelvis were removed leaving the only connection to the axial skeleton, the femoral vessels and nerve and the sciatic nerve. An allograft pelvis was used to reconstruct. This was plated in place and he functioned with a cane because of weakness at his hip. He had normal function of his lower leg.

We had 7 patients with the following tumor characteristics, 5 being sarcoma and 2 being other carcinomas. In 3 patients, the iliac bone was resected, in 2 cases portions of the pubis, in 1 the ileum, and in 1 patient the sacrum was resected. Repair after the surgery required myocutaneous flaps in 4 of the patients and allograft bone in the defects of resection of the iliac crest and ischium. allograft bone was not used when the pubis alone was resected. In 1 patient there was a positive margin, in 1 patient there was allograft infection, and in 1 patient allograft disintegration which resulted in a subsequent hemipelvectomy. In those patients with preoperative radiotherapy as part of their planned treatment, there was no local recurrence but there was 1 patient who had systemic disease at a follow-up of 24 months. Those patients who had previously failed radiation had a higher local and systemic recurrence. In planning for these patients, the resection of the sciatic nerve would result in an insensate and functionless limb, which would render this type of surgery and reconstruction less useful. However, we have resected femoral nerve with patients being able to function extremely well even without a cane for their everyday activities. In 1 patient we have grafted the femoral nerve defect and had some rejuvenation of muscle occur.

In conclusion, pelvic girdle salvage surgery provides local control particularly with preoperative adjuvant radiotherapy and chemotherapy. Allograft replacements provide functional integrity for these patients so that they can mobilize with a minimum of walking aids.

In summary, with the use adjuvant treatments in combination with reconstructive surgery, over 90% of patients with sarcomas of the soft tissues or bone may be rendered disease free locally. The only restriction to this approach is when tumor involves the major nerve to a limb or when microscopic, clear margins cannot be obtained at the time of surgery as both of these are best treated with an amputation.