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S. M. Kumta · T. C. Chow · J. Griffith · C. K. Li
J. Kew · P. C. Leung

Classifying the location of osteosarcoma with reference to the epiphyseal plate helps determine the optimal skeletal resection in limb salvage procedures

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Abstract Between 1989 and 1996, 21 skeletally immature patients were treated for osteosarcoma of the extremity. Their average age was 12.6 years (range 9–16 years). We classified the location and extent of the lesion in bone on magnetic resonance imaging (MRI) with reference to the growth plate and joint margin into five subtypes. This classification served as a guide for the level of resection and the type of reconstruction required for a limb salvage procedure. All patients received neoadjuvant chemotherapy using a modified T10 protocol before the definitive operation. These patients were followed up for periods ranging from 11–86 months, with a mean of 35.5 months. Patients were assessed for (1) local tumour recurrence, (2) metastatic disease, (3) allograft complications and (4) extremity function and joint stability. Excellent function was retained in 2, good in 13 and fair function in 6 patients. The MRI classification proved useful for the resection and provides an insight into the possible functional outcomes.

S. M. Kumta (✉) · P. Cl. Leung
Department of Orthopaedics and Traumatology,
Prince of Wales Hospital, The Chinese University of Hong Kong,
Shatin, NT, Hong Kong
Fax: +852-26377889

T. C. Chow
Department of Anatomical & Cellular Pathology,
Prince of Wales Hospital, The Chinese University of Hong Kong,
Hong Kong

J. Griffith
Department of Radiology & Organ Imaging,
Prince of Wales Hospital, The Chinese University of Hong Kong,
Hong Kong

C. K. Li
Department of Paediatric Oncology, Prince of Wales Hospital,
The Chinese University of Hong Kong, Hong Kong

J. Kew
Department of Clinical Oncology, Prince of Wales Hospital,
The Chinese University of Hong Kong, Hong Kong

Introduction

In children and adolescents, limb salvage surgery is being increasingly accepted as the standard of care for most malignant neoplasms affecting the extremities. However, segmental bone loss following tumour resection presents reconstructive challenges similar to those in adults but with added complexity. The primary concern in young patients is to obtain a durable construct that addresses the problems of the future growth of the limb.

Metallic spacers and prosthesis, though suitable for adults, are of unproved benefit in children [4]. Concerns related to the optimal fixation to the host bone, the longevity of the implant and the potential complications have not been satisfactorily addressed. Biological reconstruction with allografts or autografts or a combination of both remains the best means to reconstruct large bone and osteoarticular defects in children [9]. In addition, there have been attempts to improve contiguous joint function by means of an intercalary resection preserving the entire or part of the articular surface. Such a resection was made possible by understanding the metaphyseal spread of tumour with reference to the adjacent epiphyseal plate [10]. In selected patients intraepiphyseal or even metaphyseal resections have been performed with oncologically adequate margins and with reasonable results [1, 2, 8]. These joint sparing resections provide superior joint function and congruity by retaining the patient's own joint cartilage and stabilizing structures, and in some the potential for continued axial growth.

We classified the degree of tumour extension with reference to the epiphyseal cartilage and the joint surface into five types, based on the preoperative magnetic resonance imaging (MRI) findings. This classification served to guide the resection margin and the surgical procedure in 21 skeletally immature patients with high-grade extremity osteosarcoma.

Table 1 Patient data (*NED* no evidence of disease, *DOD* died of disease, *DOC* died of complications, *AWD* alive with disease)

Patient	Sex/age (years)	Site	Extent of tumour	Reconstruction	Follow-up (months)	Function	Local recurrence	Survival data
WCK	M/9	Femur	Type I	Intercalary	11	Good	No	DOD
KSY	F/9	Femur	Type I	Intercalary	26	Good	No	NED
KCY	M/11	Femur	Type I	Intercalary	75	Good	No	NED
CHW	M/16	Femur	Type I	Intercalary	24	Good	No	NED
LCK	M/16	Femur	Type I	Intercalary	20	Good	No	NED
TCY	F/16	Tibia	Type I	Intercalary	64	Excellent	No	DOD
YCY	F/10	Femur	Type II	Intercalary	28	Good	No	AWD
WTP	M/10	Femur	Type II	Intercalary	30	Good	No	NED
BWY	F/11	Femur	Type II	Intercalary	60	Good	No	NED
AMW	M/16	Femur	Type III	Intercalary	62	Good	No	AWD
LWS	M/14	Tibia	Type III	Intercalary	61	Good	No	NED
SKW	M/10	Femur	Type IV	Osteoarticular	13	Good	No	DOC
TCW	M/9	Femur	Type IV	Osteoarticular	14	Fair	Yes	DOD
CHL	M/16	Femur	Type IV	Osteoarticular	27	Fair	No	DOD
PTM	M/14	Tibia	Type IV	Osteoarticular	36	Fair	Yes	DOD
PK	F/16	Tibia	Type IV	Osteoarticular	21	Fair	No	DOD
ISM	M/11	Femur	Type IV	Osteoarticular	86	Fair	No	NED
NWL	M/14	Radius	Type IV	Osteoarticular	30	Good	No	NED
WCT	M/13	Tibia	Type V	Arthrodesis	36	Good	No	DOD
YLP	F/13	Humerus	Type V	Arthrodesis	38	Excellent	No	NED
LYM	F/13	Tibia	Type V	Arthrodesis	18	Good	No	NED

Patients and methods

Between 1989 and 1996, 21 skeletally immature patients with osteosarcoma were treated with neo-adjuvant chemotherapy and limb salvage surgery. Their average age was 12.6 years (range 9–16 years). All patients were diagnosed with stage II B osteosarcoma in the extremity after a complete imaging work-up which comprised whole-body scintigraphy, thoracic computed tomography (CT) scan, and MRI of the affected limb followed by an open biopsy (Table 1). MRI included coronal and axial T1-weighted sequences prior to and following gadolinium enhancement together with pre-contrast sagittal T2-weighted and fat-suppressed coronal sequences. Particular attention was paid on MRI to the distance between tumour/peritumoral oedema and the physes or the joint surface. Based on the MRI findings, we classified the tumours into five types according to the location and extent of the lesion with reference to the growth plate and joint margin (Fig.1). Resection of the tumour with "wide" margins was performed after completion of two cycles of chemotherapy using a modified T10 protocol [11].

Tumor location

In type 1 lesions (n = 6), the tumour is located more than 2 cm from the epiphyseal cartilage (Fig. 1). In these patients the tumour was excised with retention of the physeal plate and a small portion of the adjacent metaphysis (Fig. 2 a). An intercalary allograft was used to reconstruct the defect (Fig. 2 b).

In type II lesions (n = 3), the tumour is located within 2 cm of the epiphyseal cartilage (Fig. 1). The tumour was excised, and the plane of resection was juxtaphyseal and passed either through or

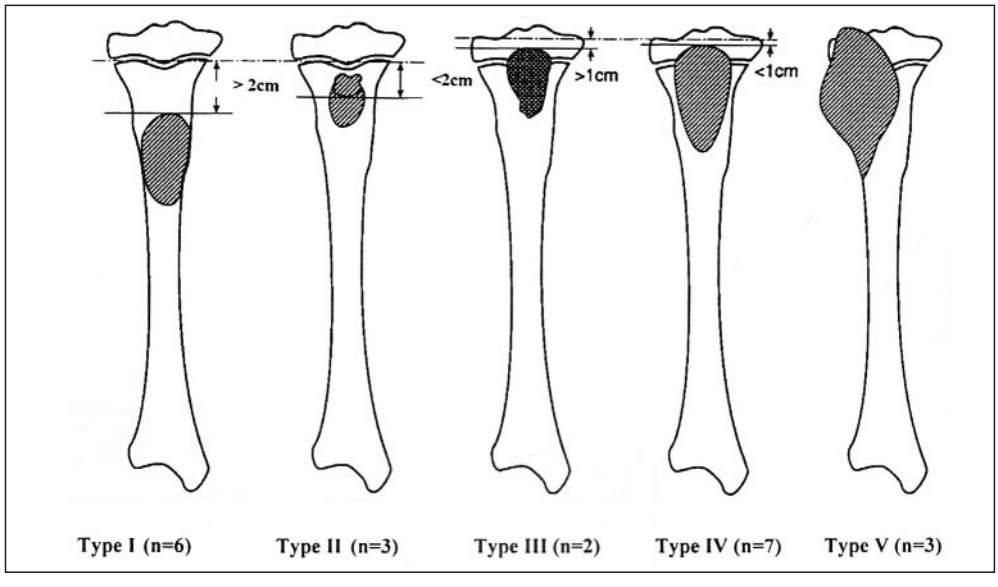

Fig. 1 Classification of the tumours according to their extent in relation to the epiphysis and the articular surface on magnetic resonance imaging (MRI)

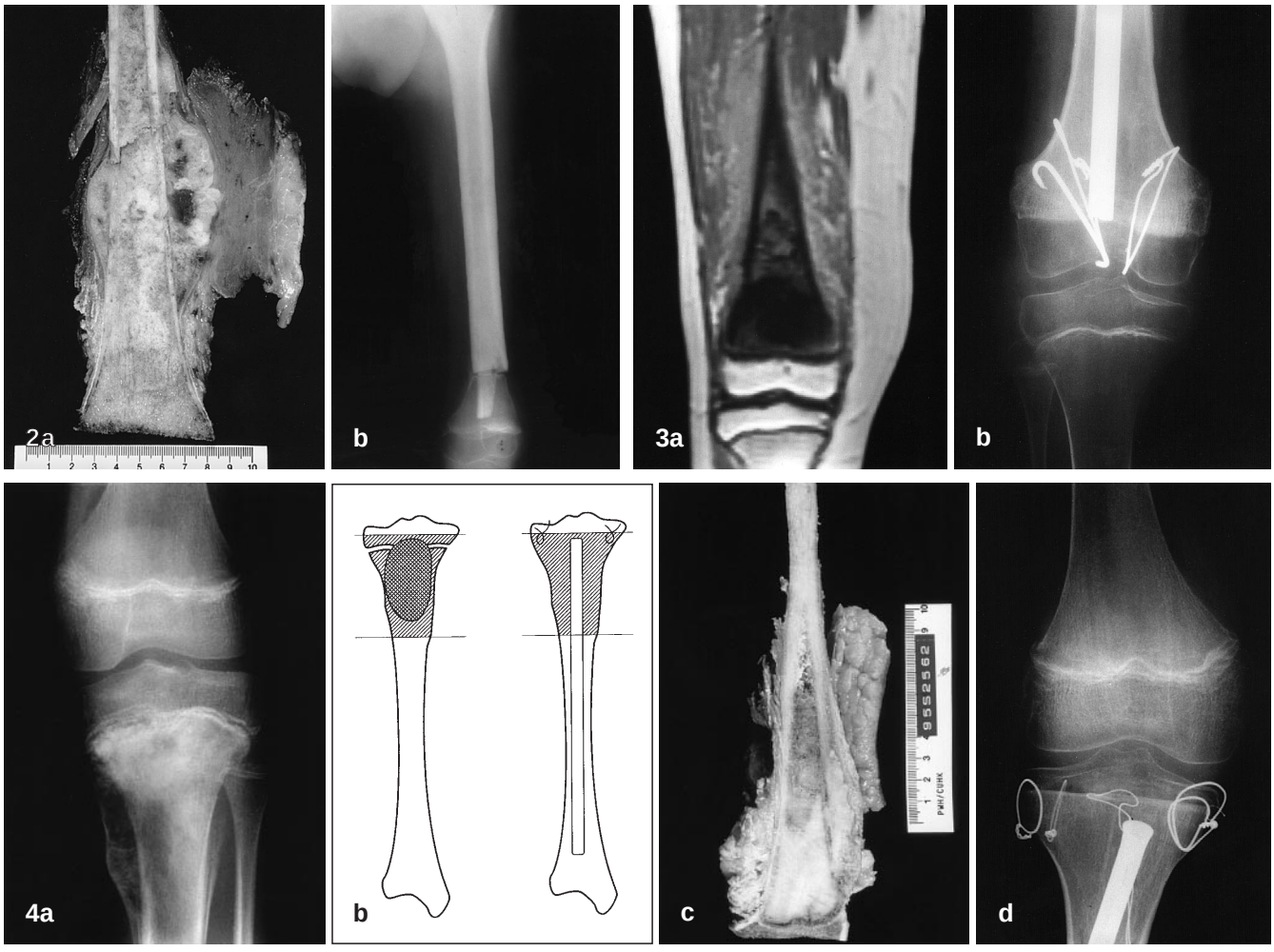

Fig. 2 **a** Intercalary excision of a femoral type I lesion. Resected specimen showing extent of tumour and its metadiaphyseal extent. **b** Femoral allograft reconstruction. The epiphysis and part of the metaphysis is spared

Fig. 3 **a** MRI of distal femur showing type II location of tumour (tumour just touches epiphyseal plate). **b** Radiograph showing intercalary reconstruction of the femur with an allograft. The resection is through the physes and the joint surface is preserved

Fig. 4 **a** Radiograph of tibial osteosarcoma type III location. **b** Type III lesion and extent of proposed intercalary resection. Resection plane is intra-epiphyseal. **c** Resected specimen of the tibia showing intra-epiphyseal plane of resection. The growth plate cartilage can be clearly seen. **d** Radiograph showing intercalary resection and reconstruction with an allograft. The thin proximal tibial fragment is secured to the allograft using wire loops

just beyond the epiphyseal cartilage, resulting in complete or partial ablation of the growth plate (Fig. 3a). An intercalary allograft was used to bridge the defect (Fig. 3b).

In type III lesions (n = 2), the tumour extends to or beyond the epiphyseal cartilage, but more than 1 cm of epiphyseal tissue is retained beyond the tumour (Fig. 1). An intercalary resection through the epiphysis with preservation of a thin layer of articular cartilage and subchondral bone was performed in these patients. The growth plate cartilage was included in the resection, and an intercalary allograft was used for reconstruction in these patients (Fig. 4).

In type IV lesions (n = 7), the tumour breaches the physes and extends to the subchondral region but does not breach the articular surface (Fig. 3). Less than 1 cm of epiphyseal tissue is preserved, and joint-sparing resection was not possible in view of the inadequate margin. An osteoarticular resection, in which the articular end of the affected bone is excised, was performed. The joint was reconstructed with an osteoarticular allograft in order to retain joint motion.

In type V lesions (n = 3), the tumour breaches the articular surface and involves the adjacent joint. Extraarticular resection and joint arthrodesis were performed in these patients.

All the specimens were histologically examined for assessment of tumour necrosis and adequacy of resection margins. Margins were considered adequate (“wide”) if there was a layer of normal tissue surrounding the tumour on histological sections. Adequate (“wide”) margins were attained in 19 of the 21 patients. In two patients (type II and type V), the margins were “marginal” at some areas of soft-tissue extension. The margins in bone were wide.

The follow-up period ranged from 11 to 86 months, with a mean of 35.5 months. Patients were assessed for (1) local tumour recurrence, (2) metastatic disease, (3) allograft complications and (4) extremity function and joint stability. Extremity function was assessed using a system of functional evaluation, while joint stability was assessed clinically [3].

Results

Local tumour recurrence

There were two local recurrences (Table 1 and 2). These occurred in patients with type IV and type V tumour loca-

Table 2 Type of lesion margins, recurrence and mortality

	Wide margins	Local recurrence	Marginal margin	Local recurrence	Deaths
Lesion					
Type I (n = 6)	6				2
Type II (n = 3)	3				
Type III (n = 2)	2				
Type IV (n = 7)	2	1	1	0	4 + 1 (DOC)
Type V (n = 3)	2	1	1	0	1

tion and were seen at 8 months and 24 months after the operation respectively. In both patients, adequate margins were achieved, but tumour necrosis following chemotherapy was less than 50%. In the two patients with "marginal margins", no local recurrences were observed. Both these patients had an excellent response to chemotherapy, with tumour necrosis in excess of 90 %.

Metastatic disease/survival

Eight patients (38%) died subsequently, including the two patients with local recurrence. Seven patients died of pulmonary metastases, and one of adriamycin toxicity 11 months after surgery. Mean time of death was 30 months after diagnosis. Kaplan-Meier survival analysis was done, and median survival was 42.5 months. The mortality in relation to location of disease is given in Table 2.

Allograft complications

There were seven allograft complications, (33%), consisting of delayed union (n = 2),fracture (n = 3) and infection (n = 2). Delayed union of the host allograft junction was treated successfully with cancellous bone grafting.

Allograft fracture was seen in three patients. In two patients the fracture occurred at the diaphyseal location and required salvage with a vascularised bone graft. One of these two patients developed major infection in the allograft, requiring repeated debridement and eventual salvage with another bone grafting procedure. One patient with a type II lesion underwent intercalary resection of the tumour in the proximal tibia. The proximal articular surface fractured 22 months after the operation. Arthrodesis of the knee was performed later with a good result.

Allograft-related infection was seen in two patients. The chronic discharging sinuses were treated with debridement and gentamicin bead implantation. The infections were controlled, and the extremity function remained unaffected.

Extremity function and joint stability

In type I, II and III lesions, excellent or good function was achieved in all 11 patients (Table 3). Mean articular range of motion was 68% (range 52%–89%) of the unaffected side.

Joint stability was preserved in all 11 patients. For type IV lesions, one of the patients had good extremity function, while the remaining six had fair extremity function. The mean articular motion retained was 43% of the unaffected side (range 34%–58%). Good joint stability was retained in one patient. In six patients the reconstructed joints were unstable and required the use of a permanent external brace for support. In type V lesions arthrodesis was performed. All patients had good extremity function and excellent stability across the fused joint. Limb length discrepancy was noted in all patients and ranged from 2–13 cm.

Discussion

Joint instability and incongruity are major problems with osteoarticular allografts in children. Bone allografts are almost always obtained from adult patients, and this results in a size mismatch when used in children. Progressive articular degeneration has been observed as early as 3 years after implantation [9]. Multi-directional joint instability persists despite ligamentous reconstruction, and these patients require permanent use of a supporting brace. Thus, intercalary resection results in superior joint and extremity function as articular stability is preserved. The problem of cartilage and joint degeneration that occurs with osteoarticular allografts is also avoided. Our classification of the location of the tumor with reference to the epiphyseal plate is a useful guide for planning the most appropriate resection.

There are, however, problems associated with the secure stabilization of the relatively short distal bone seg-

Table 3 Functional results

Lesion	Type of reconstruction	Range of joint motion (*compared to opposite normal side*)	Extremity function		
			Excellent	Good	Fair
Types I, II, III (n = 11)	Intercalary	68% Range 52%–89%	1	10	
Type IV (n = 7)	Osteoarticular allografts	43% Range 34%–58%		1	6
Type V (n = 3)	Allograft arthrodesis	Fused	1	2	

ments following intercalary resections for type II and type III cases. Conventional methods of skeletal stabilization need to be modified. The residual fragments bearing the articular end are so small that wire loops and Kirschner wires are the only suitable implants that could be used without damaging the articular surface. The joint therefore needs to be immobilized, and this mandatory immobilization required may offset some of the advantages offered by such limited resections.

Technically, wide resections as performed for patients of our series are perhaps best described as "limited" resections to distinguish them from marginal resections where the tumour extends to the resection boundary. Chemotherapy-induced tumour necrosis influences the chances of long-term survival as well as of local recurrence [5, 6]. The rate of local recurrence in this small series is 9.5% and appears to be unrelated to the margins. We have made no attempt to correlate the local recurrence rate and the degree of tumour necrosis as the numbers are too few for any meaningful statistical evaluation.

The relatively high rate of distant metastasis (38%), and thus the mortality, may be related to resistant tumour. The possibility of resistant disease and inefficacy of chemotherapy are important factors that may influence the choice of surgery. Our surgical practice tends to favour intercalary resection with its obvious functional advantages, and for that we have found this classification to be useful. Intercalary resections are possible in types I, II and III locations, while in types IV and V locations osteoarticular and extra-articular resections are required. In types I, II and III cases intercalary resections are technically possible, but achieving a conventionally "wide" margin may be technically difficult. In future, we may perhaps limit these "limited" resections to those patients in whom the response to chemotherapy has been unequivocally good (as judged by thallium scans [7] or serial MR) so that we minimize the risk of residual disease and local recurrence.

References

1. Canadell J, San Julian M, Forriol F, Cara JA (1995) Removal of metaphyseal bone tumours with preservation of the epiphysis. Proceedings of the 8th International Society of Limb Salvage Meeting; May 8–11, Florence, p 109
2. Capanna R, Manfrini M, Ceruso M, Bertoni F, Montanari N (1995) Intraepiphyseal resection in high grade bone sarcomas. Proceedings of the 8th International Society of Limb Salvage Meeting, May 8–11, Florence, p 108
3. Enneking WF (1987) A system for the functional evaluation of the management of musculoskeletal tumours. In: Enneking WF (ed) Limb salvage in musculoskeletal oncology. Bristol-Meyers Zimmer Symposium, New York, pp 5–19
4. Gebhardt MC, Jaffe KA, Mankin HJ (1989) Bone allografts for tumours and other reconstructions in children. In: Langlais F, Tomeno B (ed) Limb salvage: major reconstructions in oncologic and nontumoral conditions. Fifth International Symposium, St Malo, ISOLS-GETO, pp 561–572
5. Gherlinzoni F, Picci P, Bagci G, Gherlinzoni F, Picci P, Bagci G, Campanacci M (1992) Limb salvage versus amputation in osteosarcoma. Ann Oncol 3:23–27
6. Glasser DB, Lane JM, Huvos AG (1992) Survival, prognosis and therapeutic response in osteogenic sarcoma. Cancer 69: 698–708
7. Lin J, Leung WT, Ho KW, Ho KC, Kumta SM, Metreweli C, Johnson PJ (1995) Quantitative evaluation of thallium-201 uptake in predicting chemotherapeutic response of osteosarcoma. Eur J Nucl Med 22:553–555
8. Manfrini M, Bertoni F, Bacchini P, Bacci G, Picci P (1996) Osteosarcoma and growth plate: considerations on pathology. Proceedings of the 2nd Osteosarcoma Research Conference, Nov 19–22, Bologna, Italy, p 139
9. Mankin HJ, Springfield DS, Gebhardt MC, Tomford W (1992) Current status of allografting for bone tumours. Orthopaedics 15:1147–1154
10. Neel M, Bush C, Scarborough M, Enneking WF (1995) Transphyseal extension of osteosarcoma. Proceedings of the 8th International Society of Limb Salvage Meeting, May 8–11, Florence, p 107
11. Rosen G, Caparros B, Huvos AG, Kosloff C, Nirenberg A, Cacavio A, Marcove RC, Lane JM, Mehta B, Urban C (1982) Preoperative chemotherapy in osteogenic sarcoma: selection of post operative adjuvant chemotherapy based on the response of the primary tumour to pre-operative chemotherapy. Cancer 49: 1221–1230