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CASE REPORT

Successful management of a childhood osteosarcoma with epiphysiolysis and distraction osteogenesis

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ABSTRACT

In an 11-year-old boy with osteosarcoma in the proximal tibia (type III), 2 cycles of DIA chemotherapy (cisplatin, ifosfamide, doxorubicin) were administered preoperatively while epiphysiolysis was performed. Clinical response was determined to be complete by radiography and histopathology. Marginal excision was then performed with preservation of the proximal tibial epiphysis. Metaphyseal reconstruction was performed using distraction osteogenesis. Six cycles of DIA chemotherapy were administered postoperatively. Twenty months later, the patient had developed no complications and experienced full bone healing, with no limb discrepancy.

In selected adolescent patients with osteosarcoma, in whom the tumour is in full contact with the epiphysis, epiphyseal preservation by epiphysiolysis and reconstruction by distraction osteogenesis can provide an excellent outcome, resulting in a stable reconstruction that functionally restores the native limb.

KEY WORDS

Osteosarcoma, epiphysis preservation, epiphysiolysis, distraction osteogenesis, limb function, quality of life

1. INTRODUCTION

In malignant bone tumours affecting children and adolescents, 75% are located close to the growth plate[1]. In children, treatment of juxtaarticular osteosarcomas near the knee with epiphysis preservation and biologic reconstruction using distraction osteogenesis can yield excellent functional results[2]. However, if all the tumour is in full contact with the epiphysis (type III[3]), physeal distraction is contraindicated[3].

Here, we describe a case of osteosarcoma in the proximal tibia (type III) that was successfully managed with epiphysiolysis and distraction osteogenesis. Related papers are also reviewed.

2. OSTEOSARCOMA MANAGEMENT

An 11-year-old boy presented in 2012 with pain in his right knee during running. He was referred to our orthopedic department after a radiograph showed an abnormal shadow.

This patient's past medical history and family history included nothing of note. Physical examination revealed right knee edema and warmth. Serum phosphorus was 1.92 mmol/L (normal: 0.9–1.9 mmol/L), and serum alkaline phosphatase was 186 IU/L (normal: 45–125 mmol/L). Radiography revealed sclerotic changes and a periosteal reaction in the lateral part of the proximal tibia.

On magnetic resonance imaging (MRI), the lesion had homogeneous low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images, which demonstrated full contact between tumour and epiphysis. Angiography showed a tumour stain, and ^{99m}Tc scintigraphy demonstrated increased uptake in the proximal tibia.

A puncture biopsy was performed, and the tumour was histologically diagnosed as an osteosarcoma (Figure 1).

We administered 2 cycles of preoperative chemotherapy consisting of cisplatin 120 mg/m^2 (day 1), doxorubicin 30 mg/m^2 (days 1–3), and ifosfamide 2 g/m^2 (days 1–5)[4]. Consequently, the chief complaint of pain was relieved, and by angiography and ^{99m}Tc uptake, the tumour stain disappeared. Serum phosphorus and alkaline phosphatase concentrations declined to 1.06 mmol/L and 113 IU/L respectively. The tumour response was judged to be complete.

The surgical procedure consisted of two phases:

- In phase 1, two pins were inserted into the epiphysis and another two into the diaphysis 10 cm from the tumour. An external monolateral fixator with a 5-cm T-shaped piece for the epiphyseal pins, strong enough for achieving epiphysiolysis, was attached[5]. Distraction began in the operating room and was continued at a rate of 1–1.5 mm

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daily until 1–2 cm of distraction was achieved. Distraction was maintained for the next 15 days, with the patient's report of referred pain indicating rupture of the growth plate. Radiography showed disruption of the physis.

- In phase 2, a transepiphyseal resection was performed. *En bloc* resection of the tumour left a wide margin, but without exposing the metaphyseal surface of the physis (Figure 2). In the resulting surgical specimen, the histologic response to preoperative chemotherapy was classified as grade 4 (no viable cells)[6].

Reconstruction involved bone transport using distraction osteogenesis. The metaphyseal defect was 7 cm. A medial gastrocnemius flap was transferred anteriorly, covering the bone defect[7]. The patellar tendon then was reattached to the transferred gastrocnemius flap. A bone cylinder taken from the diaphysis was fixed using wires. Tibial alignment was not affected by the external fixation. Dressings were typically changed twice weekly. Active movement of the knee was initiated as bleeding and pain eased.

One week after the operation, the bone cylinder was applied to transport bone toward the residual epiphysis at a rate of 1 mm daily. Knee-motion exercises were started 3 weeks after the operation because the patellar tendon was reattached to the gastrocnemius flap. After 1 year, the external fixation was removed, and use of weight-bearing crutches was instituted. Six cycles of postoperative chemotherapy (same protocol as was used preoperatively) were given.

We evaluated the functional results and quality of life of this patient by physical examination, radiographs, and a questionnaire based on recommendations from the U.S. Musculoskeletal Tumor Society[8]. Follow-up studies included clinical examination and imaging with plain radiography, computed tomography, and MRI.

Follow-up at 1 month, 3 months, 6 months, 9 months, 12 months, and 20 months showed no local recurrence in the epiphyseal region, no infection, no limb length discrepancy, and no other complication. The Musculoskeletal Tumor Society questionnaire scores at those visits were 26, 28, 27, 29, 31, and 32 respectively (Figure 3). The quality-of-life scores were 3, 3, 4, 4, 5, and 5 respectively. After 20 months, lung imaging by computed tomography showed no metastasis, and radiography showed full bone union (Figure 4).

This patient is still being followed.

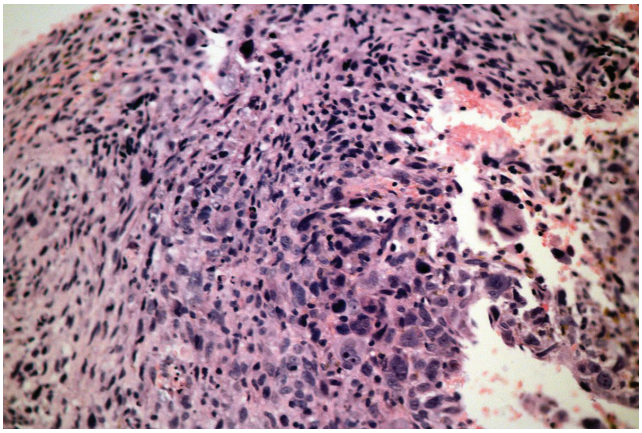


FIGURE 1 *Preoperative puncture biopsy led to a pathology diagnosis of osteosarcoma. Hematoxylin and eosin staining, 200× original magnification.*

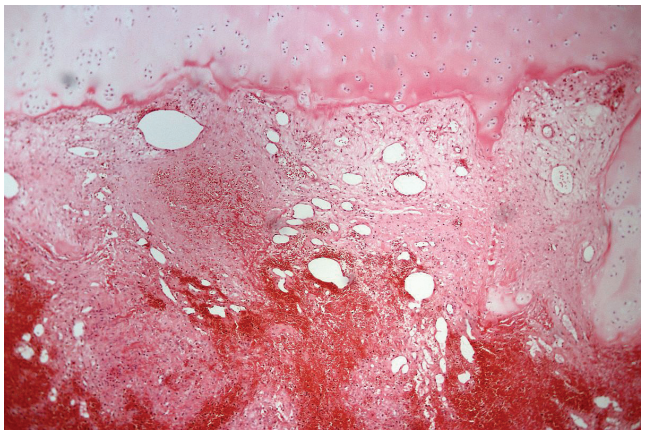


FIGURE 2 *The metaphysis showed hemorrhage between the epiphysis and physis, with no invasion by the tumour, which indicated that partial resection of the epiphysis could achieve safe margins. Hematoxylin and eosin staining, 40× original magnification.*

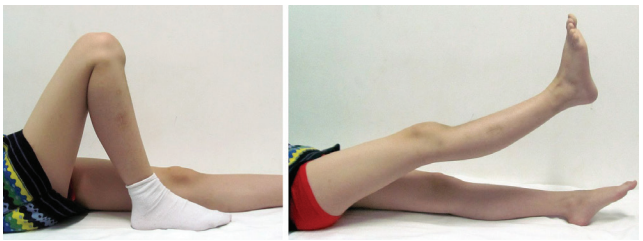


FIGURE 3 *At 20 months' follow-up, a functional knee exam showed nearly normal flection and extension. The Musculoskeletal Tumor Society questionnaire score was 32, and the quality-of-life score was 5.*

3. DISCUSSION

3.1 Physeal Distraction

In tumours of the extremities or axial skeleton, the indications for limb salvage are the potential to achieve optimal surgical margins, moderate (or less) soft-tissue extension, no compromise to neurovascular bundles, absence of metastasis (or metastases that are responsive to curative treatment), and a patient that is in good clinical condition, free of infection, and compliant to treatment[9]. The limb salvage procedure should not

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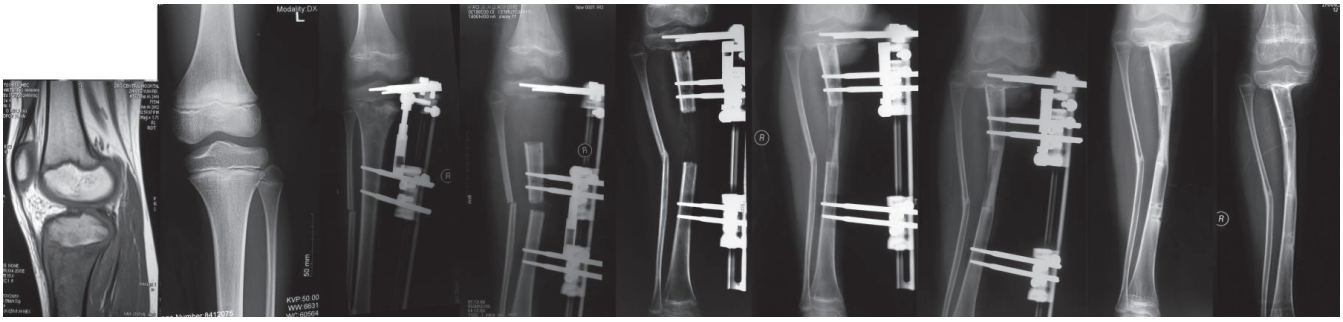


FIGURE 4 Preoperative imaging by magnetic resonance and radiography (left-most two panels). Imagining by radiography at 16 and 18 days and 10, 6, 9, 12, and 20 months after distraction (subsequent panels). Preoperatively, the tumour was in full contact with the epiphysis and was classified as type III[3]. At 20 months, full bone union is seen.

delay adjuvant therapy; the reconstruction should be permanent and not be associated with a large number of local complications requiring secondary procedures and frequent hospitalizations; and the resulting limb function should approach that obtained by amputation[10]. Optimal surgical margins around a malignant bone tumour are 3 cm of normal bone and 1 cm of normal soft tissue[11].

In most cases, especially those involving young patients, a 3–5 cm "safe" margin in osteosarcoma means loss of the adjacent joint when the tumour is in the metaphysis, usually leading to limb-length discrepancy. However, by definition, the wide margin is considered to be of a layer of normal tissue—as opposed to reactive or inflammatory tissue—surrounding the tumour. Thus, a safe margin in the context of a metaphyseal tumour can be obtained without sacrificing the epiphysis. As described by Cañadell and colleagues[5], physeal distraction in tumours that do not cross the growth plate provides a safe margin, while averting loss of the epiphysis. They believe that the growth cartilage itself provides a dependable margin of safety and that the 3-cm to 5-cm margin suggested by most authors is unnecessary. The absence of anastomoses between epiphyseal and metaphyseal vessels means that, in cases in which imaging determines that the epiphysis has not been affected by the tumour, it is possible to conserve the epiphysis and the joint while resecting the tumour[5]. This approach is made possible by physeal distraction according to Cañadell's technique[12]. In tumour surgery, physeal distraction allows for preservation of the epiphysis in the growing bone and can provide a safe margin of excision. It is not used for bone lengthening, but is the first part of a tumour resection that allows for separation of the epiphysis from the tumour-bearing metaphysis.

The indications for physeal distraction in pediatric bone sarcomas are a tumour location in the metaphysis, an open physis, and a tumour that has not transgressed the physis. If the tumour is in contact with part of the physis, physeal distraction can be tried. In evaluating physeal tumour involvement, MRI is the imaging method of choice, dividing tumours near the epiphysis into three types[3]. As described by San-Julian, if the entire physis is affected, the possibility of tumour cells passing the physis is great, and so physeal distraction is contraindicated[3]. Crucial factors are a positive response to chemotherapy, accurate preoperative assessment of tumour extension to the epiphysis by MRI, and appropriate reconstruction techniques. However, the imaging techniques currently in use, particularly MRI, can safely and accurately define tumour limits in patients who have a metaphyseal osteosarcoma growing toward the epiphysis in the knee joint. After their experience of 13 patients with a high-grade metaphyseal osteosarcoma, Muscolo *et al.*[13] concluded that preservation of the epiphysis in high-grade metaphyseal osteosarcoma at the knee is an alternative in carefully selected patients in which the tumours are fully in contact with the growth plate. The reason is that MRI showed a sensitivity of 100% in detecting epiphyseal extension of osteosarcoma[3], with only a few false positives having been reported[14]. Thus, MRI is a sensitive indicator of epiphyseal involvement by osteosarcoma, but its specificity is lower, sometimes overestimating the extent of the tumour.

Based on the foregoing considerations, we treated our patient (a defined type III[3]) with physeal distraction before partial preservation of the epiphysis[15].

3.2 Distraction Osteogenesis

An ideal reconstruction should demonstrate biologic affinity, resistance to infection, and sufficient biomechanical strength and durability. Reconstructive procedures include distraction osteogenesis[2], autoclaved autogenous bone supplemented with a vascularized fibular graft[16], and frozen allograft[13]. All of the relevant studies describe various complications, but no recurrences at the retained epiphysis.

Distraction osteogenesis, which was established by Ilizarov and Lediaev[17] in the 1960s, harnesses the bone's intrinsic regeneration potential by performing an osteotomy followed by bone distraction as a suitable approach to repairing large segmental bone defects. The advantages of the approach are the possibility to

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correct deformities[18], the small area of the associated soft-tissue defects, and immediate mobilization. Its disadvantages are the long duration of the external osteosynthesis materials, the frequency of pin-tract infection, and the pain accompanying transport[19].

Yokoyama *et al.*[16] used free vascularized fibular grafts to treat 4 patients with tibial bone defects and distraction osteogenesis to treat another 4. The mean defect length in the vascularized bone graft group was 7.3 cm; in the distraction group, it was 4.6 cm. The union rate of the distraction group was 100%; in the vascularized graft group, it was 75%. External fixation has been used safely and successfully during postoperative chemotherapy for fixation and distraction osteogenesis[20]. Postoperative chemotherapy for malignant bone tumours has been reported not to adversely affect the ability to achieve union or cause hypertrophy, and to have a minimal effect on distraction osteogenesis[20].

Distraction osteogenesis avoids some complications, but might lead to others that require appropriate management: for example, deep infection, leg-length discrepancy and deformity, and even fracture[21]. Fortunately, we encountered no such complications during our patient's treatment.

The critical conditions for the success of the technique are a lesion no more than 15 cm in length, the availability of at least 0.5 cm of subchondral bone and sufficient remaining metaphyseal cortex after excision of the tumour, and a good response to chemotherapy[2].

4. CONCLUSIONS

In selected adolescent patients with osteosarcoma in which the tumour is in full contact with the epiphysis, epiphyseal preservation by epiphysiolysis and reconstruction by distraction osteogenesis can provide an excellent outcome, resulting in a stable reconstruction that functionally restores the native limb.

5. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to declare.

6. REFERENCES

1. Mercuri M, Capanna R, Manfrini M, *et al.* The management of malignant bone tumors in children and adolescents. *Clin Orthop Relat Res* 1991;:156–68.
2. Tsuchiya H, Abdel–Wanis ME, Sakurakichi K, Yamashiro T, Tomita K. Osteosarcoma around the knee. Intraepiphyseal excision and biological reconstruction with distraction osteogenesis. *J Bone Joint Surg Br* 2002;84:1162–6.
3. San-Julian M, Aquerreta JD, Benito A, Canadell J. Indications for epiphyseal preservation in metaphyseal malignant bone tumors of children: relationship between image methods and histological findings. *J Pediatr Orthop* 1999;19:543–8.
4. Yu X, Xu M, Song R, Xu SF. Marginal resection for osteosarcoma with effective preoperative chemotherapy. *Orthop Surg* 2009;1:196–202.
5. Cañadell J, San-Julian M, Cara JA, Forriol F. Conservation of the epiphysis while removing metaphyseal bone tumours: epiphysiolysis before excision. In: Cañadell J, San-Julian M, eds. *Pediatric Bone Sarcomas: Epiphysiolysis Before Excision*. New York, NY: Springer; 2009: 101–8.
6. Rosen G, Caparros B, Huvos AG, *et al.* Preoperative chemotherapy for osteogenic sarcoma: selection of postoperative adjuvant chemotherapy based on the response of the primary tumor to preoperative chemotherapy. *Cancer* 1982;49:1221–30.
7. Malawer MM, Price WM. Gastrocnemius transposition flap in conjunction with limb-sparing surgery for primary bone sarcomas around the knee. *Plast Reconstr Surg* 1984;73:741–50.
8. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res* 1993;:241–6.
9. Mavrogenis AF, Coll–Mesa L, Gonzalez–Gaitan M, *et al.* Criteria and outcome of limb salvage surgery. *J BUON* 2011;16:617–26.
10. Simon MA. Limb salvage for osteosarcoma in the 1980s. *Clin Orthop Relat Res* 1991;:264–70.
11. Veth R, van Hoesel R, Pruszczynski M, Hoogenhout J, Schreuder B, Wobbes T. Limb salvage in musculoskeletal oncology. *Lancet Oncol* 2003;4:343–50.
12. Cañadell J, Forriol F, Cara JA. Removal of metaphyseal bone tumours with preservation of the epiphysis. Physeal distraction before excision. *J Bone Joint Surg Br* 1994;76:127–32.
13. Muscolo DL, Ayerza MA, Aponte–Tinao LA, Ranalletta M. Partial epiphyseal preservation and intercalary allograft reconstruction in high-grade metaphyseal osteosarcoma of the knee. *J Bone Joint Surg Am* 2004;86-A:2686–93.
14. Onikul E, Fletcher BD, Parham DM, Chen G. Accuracy of MR imaging for estimating intraosseous extent of osteosarcoma. *AJR Am J Roentgenol* 1996;167:1211–15.
15. Muscolo DL, Ayerza MA, Aponte–Tinao LA, Ranalletta M. Partial epiphyseal preservation and intercalary allograft reconstruction in high-grade metaphyseal osteosarcoma of the knee. *J Bone Joint Surg Am* 2005;87(suppl 1):226–36.
16. Yokoyama K, Itoman M, Nakamura K, Tsukamoto T, Saita Y, Aoki S. Free vascularized fibular graft vs. Ilizarov method for post-traumatic tibial bone defect. *J Reconstr Microsurg* 2001;17:17–25.
17. Ilizarov GA, Lediaev VI. Replacement of defects of long tubular bones by means of one of their fragments [Russian]. *Vestn Khir Im I I Grek* 1969;102:77–84.
18. Ozkan C, Dogramaci Y, Kalaci A, Gulsen M, Bayram H. Results of using Ilizarov distraction osteogenesis technique for the treatment of cubitus varus deformities in adults. *Arch Orthop Trauma Surg* 2010;130:489–95.
19. Brinker MR, O'Connor DP. Outcomes of tibial nonunion in older adults following treatment using the Ilizarov method. *J Orthop Trauma* 2007;21:634–42.

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20. Tsuchiya H, Shirai T, Morsy AF, *et al*. Safety of external fixation during post-operative chemotherapy. *J Bone Joint Surg Br* 2008;90:924–8.
21. Shirai T, Tsuchiya H, Yamamoto N, Sakurakichi K, Karita M, Tomita K. Successful management of complications from distraction osteogenesis after osteosarcoma resection: a case report. *J Orthop Sci* 2004;9:638–42.

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