Osteosarcoma around the knee

INTRAEPIPHYSEAL EXCISION AND BIOLOGICAL RECONSTRUCTION WITH DISTRACTION OSTEOGENESIS

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In 11 patients juxta-articular osteosarcoma around the knee was treated by intraepiphyseal excision of the tumour and reconstruction of the bone defect by distraction osteogenesis. Preoperative and postoperative chemotherapy was given to eight patients with high-grade tumours. The articular cartilage of the epiphysis and a maximum of healthy soft tissues were preserved. Distraction osteogenesis was then carried out.

The mean gain in length was 9.7 cm. Full function of the limb was preserved in all except one patient, with a mean follow-up of 53.8 months. Treatment of juxta-articular osteosarcomas around the knee with joint preservation and biological reconstruction using distraction osteogenesis can give excellent functional results.

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Limb-salvage surgery is increasingly being accepted as the standard care for most malignant neoplasms affecting the limbs.1 For juxta-articular tumours, the joint adjacent to the tumour is usually sacrificed and replaced by a prosthesis, allogenic osteoarticular graft, autoclaved autograft or a combination.2 A juxta-articular tumour around the knee represents a surgical challenge since no joint replacement can function as well as the normal knee.2,3 Reconstruction of the extensor mechanism about the prosthesis so close beneath the skin is demanding.2 Joint instability and incongruity are major problems with osteoarticular allografts in children. Multidirectional joint instability persists despite ligamentous reconstruction and these patients require a permanent supporting brace.1

The disadvantage of autoclaved bone is that it takes a long time for it to revascularise and incorporate into bone, and the bone itself is brittle.2 Furthermore, a high rate of complications including infection, bone resorption and fracture has been reported after the use of massive autoclaved allografts and autografts for limb-salvage surgery.4 Therefore, if the anatomical knee can be preserved while allowing for a safe surgical margin of excision, better long-term functional results should follow.2 Recently, there have been a few reports of intraepiphyseal excision for juxta-articular tumours around the knee in a limited number of patients in whom reconstruction depended on autoclaved bone, vascularised autografts or allografts.1-3 In 1997, we described a series of 19 patients with skeletal tumours treated by limb salvage using distraction osteogenesis.5 Our present study describes the long-term results of 11 patients with osteosarcoma around the knee which was treated by intraepiphyseal excision followed by reconstruction of the bone defect using distraction osteogenesis. We clarify the indications for this procedure, provide technical notes about the technique and report on the subsequent bone remodelling.

Patients and Methods

There were five men and six women with a mean age of 21.5 years (9 to 43). The site of the tumour was the distal femur in six patients and the proximal tibia in five. All were investigated by whole-body scintigraphy, CT of the thorax and affected limb, MRI and angiography of the affected limb, followed by an open biopsy. Histopathological examination of the biopsy tissue rated the tumour as high-grade in eight patients and low-grade in three. Preoperative chemotherapy was not used for patients with a low-grade tumour but was given to those with a high-grade tumour. The K2 chemotherapy protocol which consists of five courses of intra-arterial cisplatin, caffeine and doxorubicin at intervals of three weeks was used. Evidence of a good chemotherapeutic response consisted of sclerotic changes or good margination of the tumour observed on plain radiographs, marked shrinkage of any extension of the tumour into soft tissue demonstrated on MRI, the disappearance of 'tumour' vessels on angiography or the disappearance of the abnor-
mal accumulation on thallium 201 scintigrams. The response of the tumour was judged to be complete in seven patients and partial in one. On histological examination, the seven patients with a complete response demonstrated total necrosis of the tumour and the patient with a partial response showed necrosis greater than 90%.

Candidates for treatment by intraepiphyseal excision included those with at least 1 cm of the epiphysis which could be preserved after adequate excision of the tumour (group A) (Fig. 1a) and those who had an articular surface, with or without the subchondral bone and substantial metaphyseal cortex, preserved after adequate excision of the tumour (group B) (Fig. 1b). Two Ilizarov wires were inserted into the preserved epiphysis in group A.

Three methods were used for reconstruction: I, conventional bone transport (Fig. 2a); II, shortening-distraction (Fig. 2b); and III, bone transport after insertion of a bone cylinder obtained from the diaphysis combined with bone grafts to reconstruct the epiphyseal and metaphyseal bone defect (Fig. 2c). In methods I and III, bone grafting was carried out to the docking site after completion of bone transport and in method II it was concurrent with excision of the tumour (Fig. 2). Method II was used unless the soft tissues did not allow immediate shortening when method I was used. Method III was reserved for upper tibial tumours in order to facilitate attachment of the patellar tendon and the medial collateral ligament to the bone cylinder, and for tumours of the lower femur in group B. Intramedullary nailing was used at the initial procedure in patients operated on by method II. Delayed intramedullary nailing was carried out after completion of bone transport in methods I and III to allow removal of the external fixator and early weight-bearing. Gradual distraction started one to two weeks after the operation and was applied at a rate of 1 mm/day. The dressings were changed twice-weekly as a rule, but daily if needed.
there was much discharge. Antibiotics were prescribed only if pus was observed.

Weight-bearing with crutches and active movement of the knee were initiated as bleeding and pain eased or three weeks after operation if the patellar tendon had to be reattached and internally fixed. Chemotherapy was continued during the postoperative period for patients with high-grade tumours, using intravenous cisplatin and caffeine with doxorubicin and high-dose methotrexate combined with citrovorum factor and vincristine (three courses each).6

Evaluation of the results depended upon three criteria: the time for which external fixation was required, the external fixation index obtained by dividing the external fixation time by the length of bone regeneration, and the distraction index obtained by dividing the duration of the distraction by the length of bone regeneration.5 Function of the affected limb was assessed using the evaluation system devised by Enneking et al.8 Follow-up studies included clinical examination and imaging with plain radiography, CT, and MRI. Remodelling was considered to be complete when the bone regained its normal shape and thickness of the cortex.

Results

Table I gives details of the results. Excision of the tumour followed pattern A in nine patients and pattern B in two. All high-grade tumours were excised with narrow margins and all low-grade tumours with wide margins, confirmed both macroscopically and microscopically. There was no histological contamination by tumour cells at the stump of excised specimens although high-grade tumours were excised through reactive tissues at the juxta-articular end and around any soft-tissue extension. Marginal excision was intentional for patients with high-grade osteosarcomas to preserve a maximum of healthy tissues because preoperative chemotherapy had been judged to be effective.6 The Ilizarov ring fixator was applied in nine patients and the Orthofix external fixator in two. Reconstruction was by method I for four patients, method II for three patients and method III for four patients. Intramedullary nails were used in three patients. The duration of external fixation was 297 ± 131.7 days, the distraction index was 14.1 ± 4.4 days/cm and the external fixation index was 33 ± 15.7 days/cm. The mean length gained was 9.7 ± 3.7 cm. The limb function was rated as 100% normal in all except one patient (case 3) in whom it was judged to be 77% of normal. Ten patients showed a full range of knee movement, but one (case 3) was limited to 0° to 50° of flexion. No patient reported restriction of recreational activities. They were able to walk, run and jump. One patient (case 3) reported symptoms of instability of the knee but she can walk without an aid. Bone remodel-

Table I. Details of 11 patients who were treated by intraepiphyseal excision and biological reconstruction with distraction osteogenesis for osteosarcoma around the knee

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Gender</th>
<th>Site</th>
<th>Grade</th>
<th>Fixator</th>
<th>Pattern of excision</th>
<th>Reconstruction method</th>
<th>Lengthening (cm)</th>
<th>Fixator time (days)</th>
<th>External fixation index (days/cm)</th>
<th>Distraction index (days/cm)</th>
<th>Outcome*</th>
<th>Follow-up (mths)</th>
<th>Time to remodelling (mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>M</td>
<td>Proximal tibia</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>I</td>
<td>10.0</td>
<td>317</td>
<td>31.7</td>
<td>14.1</td>
<td>Death from hepatitis</td>
<td>49</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>F</td>
<td>Proximal tibia</td>
<td>High</td>
<td>Ilizarov</td>
<td>B</td>
<td>III</td>
<td>5.5</td>
<td>349</td>
<td>63.5</td>
<td>17.6</td>
<td>CDF</td>
<td>82</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>F</td>
<td>Distal femur</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>I</td>
<td>15.0</td>
<td>522</td>
<td>34.8</td>
<td>7.3</td>
<td>CDF</td>
<td>91</td>
<td>Not remodelled</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>M</td>
<td>Distal femur</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>III</td>
<td>15.0</td>
<td>238</td>
<td>15.9</td>
<td>14.9</td>
<td>DOD</td>
<td>13</td>
<td>12</td>
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<tr>
<td>5</td>
<td>20</td>
<td>M</td>
<td>Proximal tibia</td>
<td>Low</td>
<td>Ilizarov</td>
<td>A</td>
<td>II</td>
<td>5.5</td>
<td>174</td>
<td>31.6</td>
<td>12.5</td>
<td>CDF</td>
<td>69</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>F</td>
<td>Distal femur</td>
<td>Low</td>
<td>Orthofix</td>
<td>A</td>
<td>II</td>
<td>6.6</td>
<td>124</td>
<td>18.8</td>
<td>16.7</td>
<td>CDF</td>
<td>66</td>
<td>8</td>
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<tr>
<td>7</td>
<td>15</td>
<td>M</td>
<td>Proximal tibia</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>III</td>
<td>12.5</td>
<td>496</td>
<td>39.7</td>
<td>20.6</td>
<td>CDF</td>
<td>65</td>
<td>18</td>
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<tr>
<td>8</td>
<td>9</td>
<td>F</td>
<td>Distal femur</td>
<td>High</td>
<td>Orthofix</td>
<td>A</td>
<td>II</td>
<td>9.0</td>
<td>124</td>
<td>13.8</td>
<td>12.9</td>
<td>CDF</td>
<td>58</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>26</td>
<td>F</td>
<td>Distal femur</td>
<td>Low</td>
<td>Ilizarov</td>
<td>B</td>
<td>I</td>
<td>9.0</td>
<td>277</td>
<td>30.8</td>
<td>9.7</td>
<td>CDF</td>
<td>43</td>
<td>22</td>
</tr>
<tr>
<td>10</td>
<td>13</td>
<td>F</td>
<td>Proximal tibia</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>III</td>
<td>5.7</td>
<td>322</td>
<td>56.5</td>
<td>20.0</td>
<td>CDF</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>11</td>
<td>9</td>
<td>M</td>
<td>Distal femur</td>
<td>High</td>
<td>Ilizarov</td>
<td>A</td>
<td>I</td>
<td>12.6</td>
<td>324</td>
<td>25.7</td>
<td>8.8</td>
<td>CDF</td>
<td>25</td>
<td>20</td>
</tr>
</tbody>
</table>

*DOD, died of disease; CDF, continuously disease-free

Radiographs showing a) full remodelling of the juxta-articular bone to its normal shape in a nine-year-old girl (case 8) and b) insufficient remodelling in a 13-year-old girl (case 3).
ling to normal shape was observed in all except this patient (case 3), after a mean of 14.4 ± 6.6 months (Fig. 3). The time required for complete remodelling after reconstruction methods I, II and III was 22 ± 2, 7.3 ± 3.1 and 14 ± 3.7 months, respectively. At the end of follow-up one patient (case 4) with pulmonary metastases at presentation, died from the disease after 13 months and one (case 1) died from fulminant hepatitis 49 months after surgery. The remaining nine patients are still alive and free from disease after a mean of 58.9 months (25 to 91). The mean follow-up for the entire series was 53.8 months (13 to 91).

Table II lists seven complications encountered in six patients. These were managed efficiently and did not affect the final outcome. No local recurrences appeared during the follow-up period; three patients had shortening during the course of follow-up. Two (cases 3 and 7) lost 5 cm at five years and two years respectively, and both required lengthening by distraction osteogenesis. One patient (case 8) showed shortening of 2.5 cm which required a shoe-lift.

**Discussion**

Efficient chemotherapy has made long-term survival possible after excision of malignant limb tumours, especially osteosarcoma, and has helped to reduce the margin of surgical excision. Caffeine-potentiated chemotherapy is highly effective by virtue of its DNA-repair-inhibiting effects. Narrower excision associated with caffeine-potentiated chemotherapy has not led to an increased incidence of local recurrence.

Reconstruction after intraepiphyseal excision for juxta-articular tumours around the knee using autoclaved bone, vascularised autografts and allografts, requires prolonged immobilisation of the knee. Vascularised bone transfer has limitations in length and strength. The well-recognised high incidence of infection after the use of autoclaved autograft and allograft is a serious concern. Deep infection is likely to necessitate amputation. Moreover, postoperative chemotherapy delays the incorporation and union of allografts because of negative effects on healing and revascularisation. The ideal reconstruction which would drastically decrease the incidence of such complications, should have biological affinity, resistance to infection, sufficient biological strength and durability. Distraction osteogenesis is well known to regenerate living bone to sufficient strength and, being biological, it can be expected to remain permanent once it is formed. In our series, one patient had a deep infection but did not require amputation. Leg-length discrepancy was not a major problem in children and was managed by subsequent lengthening manoeuvres.

The effect of chemotherapy on bone regeneration by distraction osteogenesis is a matter of concern in the postoperative period. Jarka, Nicholas and Aronson, using radiological, histological and chemical tests, showed that methotrexate did not have a serious effect on distraction osteogenesis in rats. Subasi et al studied the effects of a chemotherapeutic regimen consisting of high-dose methotrexate and citrovorum factor rescue, doxorubicin, and a combination of bleomycin, cyclophosphamide and dactinomycin on distraction osteogenesis in a rabbit model. They observed that those chemotherapeutic agents had no significant negative effects on distraction osteogenesis. Our caffeine-potentiated chemotherapy protocol seems to have had no hazardous effect on bone regeneration by distraction osteogenesis. Nevertheless, distraction osteogenesis may potentiate the effects of chemotherapeutic agents. We have previously shown that chemotherapy decreases the regional blood flow to the area of the tumour, but with distraction osteogenesis the regional blood flow can be kept within the normal range, or higher.

Remodelling of the bone to its normal shape was accomplished in all but one knee, after a mean of 14.4 months. Although comparison between the results after the three different methods of reconstruction is unreliable because of the limited numbers and the many variables, it seems that method II has the advantage of a short external fixation time and quick bone remodelling. Intramedullary nailing was useful additionally to shorten the external fixation time. In our series, the shortest external fixation time and fastest bone remodelling were seen in two patients who had intramedullary nailing with method II. From our experience, it also seems that delay in bone remodelling was related either to insufficient bone grafting or inadequate weight-bearing.

The methods reported here appear to be the only procedures available at present which can preserve the natural joint in patients with juxta-articular osteosarcoma around the knee. The critical conditions for the success of this tech-

<table>
<thead>
<tr>
<th>Case</th>
<th>Complication</th>
<th>Treatment</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Pes equinus</td>
<td>Physiotherapy</td>
<td>Corrected</td>
</tr>
<tr>
<td>3</td>
<td>Fracture after frame removal</td>
<td>Casting</td>
<td>Healed</td>
</tr>
<tr>
<td>4</td>
<td>Superficial infection</td>
<td>Antibiotics and dressings</td>
<td>Cured</td>
</tr>
<tr>
<td>5</td>
<td>Peroneal nerve palsy</td>
<td>Tendon transfer</td>
<td>No limitation of athletic activities</td>
</tr>
<tr>
<td>7</td>
<td>Deep infection at docking site</td>
<td>Resection of infected segment, shortening, then lengthening</td>
<td>Cured</td>
</tr>
<tr>
<td>7</td>
<td>Delayed healing</td>
<td>Bone graft</td>
<td>Healed</td>
</tr>
<tr>
<td>11</td>
<td>Delayed union at docking site</td>
<td>Bone graft</td>
<td>Healed</td>
</tr>
</tbody>
</table>

Table II. Details of the complications and their management after intraepiphyseal excision and biological reconstruction with distraction osteogenesis for osteosarcoma around the knee
nique are a lesion of no more than 15 cm in length, with at least 0.5 cm of the subchondral bone and sufficient metaphyseal cortex retained after excision of the tumour with a good response to chemotherapy. The presence of lung metastases must be considered as a relative, but not absolute, contraindication to the use of this technique. It follows therefore that early detection of osteosarcoma should result in more patients being suitable for this technique.

No benefits have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References