Unicameral bone cysts
A COMPARISON OF INJECTION OF STEROID AND GRAFTING WITH AUTOLOGOUS BONE MARROW


From National Cancer Center and Seoul National University College of Medicine, Seoul, Korea

Open surgery is rarely justified for the initial treatment of a unicameral bone cyst, but there is some debate concerning the relative effectiveness of closed methods. This study compared the results of steroid injection with those of autologous bone marrow grafting for the treatment of unicameral bone cysts. Between 1990 and 2001, 30 patients were treated by steroid injection and 28 by grafting with autologous bone marrow. The overall success rates were 86.7% and 92.0%, respectively (p > 0.05). The success rate after the initial procedure was 23.3% in the steroid group and 52.0% in those receiving autologous bone marrow (p < 0.05), and the respective cumulative success rates after second injections were 63.3% and 80.0% (p > 0.05). The mean number of procedures required was 2.19 (1 to 5) and 1.57 (1 to 3) (p < 0.05), the mean interval to healing was 12.5 months (4 to 32) and 14.3 months (7 to 36) (p > 0.05), and the rate of recurrence after the initial procedure was 41.7% and 13.3% in the steroid and in the autologous bone marrow groups, respectively (p < 0.05).

Although the overall rates of success of both methods were similar, the steroid group had higher recurrence after a single procedure and required more injections to achieve healing.

Although a unicameral bone cyst is a benign lesion, it may cause repeated pathological fractures and skeletal deformities during growth because of its proximity to the physis. Following the recognition of unicameral bone cysts by Virchow in 1876, treatment was by operation without considering other forms of management. Surgical procedures have ranged from simple curettage with autologous bone graft or allograft to subperiosteal resection with internal fixation and grafting.

In 1974, Scaglietti described the percutaneous injection of methylprednisolone acetate as a treatment for unicameral bone cysts. Subsequently, many authors have reported high rates of success, ranging from 50% to 90%. However, usually several injections are needed, and a return to strenuous physical activities may require one to three years. Although the low associated morbidity and simplicity of corticosteroid injection have made it popular, its relatively low success rate has led to interest in other methods of treatment. In 1996, Lokic described the use of autologous marrow based on the results of a study by Wientroub et al in which autologous marrow aspirate was used to improve the osteogenic potential of bone grafts in children. The aim of treatment of unicameral bone cysts should be the prevention of repeated fractures and prolonged immobilisation. Aggressive open surgery is not justified, at least initially. Current concern focuses more on the comparative effectiveness of closed methods. Few reports have compared the osteogenic potentials of autologous bone marrow and steroid injection. This study compared the results of autologous bone marrow grafting with those of steroid injection for the initial treatment of unicameral bone cysts in terms of the overall rate of success, recurrence, the number of procedures required, and the time to healing.

Patients and Methods
Between 1990 and 2001, of 74 consecutive patients who were diagnosed as having unicameral bone cysts based on the characteristic radiological features, 58 were managed by steroid injection or by autologous marrow grafting. There were 42 boys (72.4%) and 16 girls (27.6%), with a mean age of 11.2 years (2 to 18). The mean follow-up was 4.7 years (2 to 15.5). The proximal metaphysis of the humerus was affected in 33 cases (56.9%), the distal humerus in one (1.7%), the proximal femur in 16 (27.6%), the distal femur in one (1.7%), the calcaneum in five (8.7%), the tibia in one (1.7%) and the radius in one (1.7%).
Malignant lesions such as Ewing’s sarcoma or osteosarcoma may show cystic features radiologically, so patients in whom an open biopsy was required to make the diagnosis were excluded from the study.

Before the paper by Lokiec et al in 1996 describing grafting with autologous marrow, we had treated 30 patients (21 boys and nine girls) by corticosteroid injection. Since 1997 we have used autologous marrow to treat 28 unicameral bone cysts in 21 boys and seven girls. Overall, 39 of our 58 patients (67.2%) had experienced more than one pathological fracture and had a persistent cyst. Pathological fractures were allowed to heal for four to six weeks before treatment with steroid or bone marrow. There were no statistical differences between the two groups with respect to demographics, the location and activity of the cyst, and a history of previous pathological fractures (Table I).

All procedures were performed by the senior author (SHL) under general anaesthesia and guided by fluoroscopy. Two spinal needles were inserted proximally and distally into each cavity. They were located at the thinnest accessible wall of the cyst, avoiding major neurovascular bundles. The contents of the cyst were aspirated and cystography was performed before irrigation with normal saline.

The doses of steroid were based on the patient’s body weight, and the amount of marrow used was determined by the size of the cyst, as measured on the radiographs, using the formula \[ \frac{\pi}{6} \times \text{length} \times \text{width} \times \text{height}. \] Between 60 mg and 250 mg of methylprednisolone and 12 ml to 50 ml of autologous marrow were injected. Autologous marrow was aspirated from the anterior iliac crest using an 11-gauge needle. In order to avoid injury to the iliac physis, the needle was inserted 1.5 cm below the crest. Multiple sites were punctured to obtain enough bone marrow, taking no more than 3 ml to 5 ml at each site. It has been recommended that the volume of marrow aspirated at each site should not exceed 10 ml, because the smaller the volume aspirated, the richer the count of colony-forming cells with less haemodilution.

Physical activity was restricted for four weeks in cases with a humeral lesion and for six weeks in those in the lower limb. Radiographs were taken three months after the procedure and repeated every three months until evidence of healing was observed. After a cyst had consolidated or had formed satisfactorily thick cortices, the radiographs were repeated annually. Radiological changes were evaluated according to the modified Neer classification used by others (Table III).

The procedure was considered successful if the cyst was completely healed or had healed with a radiological defect. When evidence of consolidation of the cyst or cortical thickening was absent six months after the initial procedure, or when recurrence occurred, an additional procedure was carried out.

The results of autologous bone marrow grafting were compared with those of steroid injection in terms of the overall success rate, recurrence, the number of procedures required, and the time to healing. Additional factors, including age, gender, previous fracture, and the location and activity of the cyst, were also assessed.

The chi-squared test was used to evaluate categorical variables and Student’s t-test for continuous variables. Three pathological fractures in the bone marrow group were excluded from the statistical analysis. A p-value of < 0.05 was considered significant.

### Results

#### Success rate and recurrences

The overall success rates for the steroid and bone marrow groups were 86.7% (26 of 30) and 92.0% (23 of 25), respectively. There was no statistical difference between the two groups. Seven cysts (23.3%) healed after one procedure and 12 patients (40%) showed a good response, but five required a second injection in the steroid group. The mean interval between the initial injection and recurrence was 11.2 months (4 to 26). A total of 13 patients (52%) in the bone marrow group healed after one procedure (p < 0.05), 15 patients (60%) showed a good response and only two recurred, one at five months and the other after 13 months. The cumulative success rates after the initial and second procedures were 63.3% in the steroid and 80.0% in the bone marrow group, which did not show a statistical difference (p > 0.05).

We compared patients in both groups who healed after the initial procedure with those who did not in terms of age, gender, location of the cyst, activity of the cyst and history of previous pathological fracture. None of these factors was found to affect the success rates of the procedures in either group (Table IV).

#### Mean number of procedures

A total of 30 patients received 74 steroid injections and 25 (3 were excluded due to pathological fractures) had 44 autologous bone marrow grafting procedures. The mean number of procedures was 2.47 (1 to 6) in the steroid group and 1.76 (1 to 4) in the
autologous bone marrow group \(p < 0.05\). The mean number of procedures that had been needed to heal cysts, excluding those which did not heal and eventually required an open procedure, was 2.19 (1 to 5) and 1.57 (1 to 3) in the steroid and bone marrow groups, respectively \(p < 0.05\).

**Time to healing.** We defined time to healing as the period required to achieve cortical thickening on the anteroposterior and lateral radiographs, as well as consolidation of the cyst (Table III). The mean time to healing was 12.5 months (4 to 32) in the steroid group and 14.3 months (7 to 36) in the bone marrow group. There was no statistically significant difference between the two.

**Pathological fracture.** Three fractures occurred within four weeks of autologous bone marrow grafting in patients who had ignored instructions about immobilisation. All healed after conservative treatment.

**Discussion**

Several theories have been proposed to explain the aetiology of unicameral bone cysts, including failure to resorb haematomas,\(^{16}\) low-grade form of osteomyelitis,\(^{17}\) a defect in remodelling,\(^{18}\) a true intra-osseous synovial cyst,\(^{19}\) the degenerative phase of a benign tumour,\(^{20,21}\) and venous obstruction.\(^{22}\) Of these theories, the one proposed by Cohen,\(^{22}\) that venous obstruction elevates intra-osseous pressure leading to cyst formation, is probably preferred. Komiya et al\(^{23}\) presumed that prostaglandin E\(_2\), interleukin-I\(_\beta\) and gelatinase in cyst fluid promote bone resorption, and surmised that trepanation of a cyst reduces the internal pressure, removes bone resorptive factors and promotes venous recirculation. Steroid injection might effectively inhibit the generation of these bone resorptive factors, but this in itself would not provide bone-forming potential. When venous recirculation is insufficient, a cyst cannot escape the osteoclastic pathway completely. However,

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**Table II. Details of the steroid injection and autologous bone marrow grafting groups**

<table>
<thead>
<tr>
<th></th>
<th>Steroid group ((n = 30))</th>
<th>Bone marrow group ((n = 28))</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>10.6 (3 to 13)</td>
<td>11.9 (2 to 18)</td>
<td>0.677</td>
</tr>
<tr>
<td>Male:female ratio</td>
<td>21:9</td>
<td>21:7</td>
<td>0.670</td>
</tr>
<tr>
<td>Previous fracture (%)</td>
<td>22 (73.3)</td>
<td>17 (60.7)</td>
<td>0.306</td>
</tr>
<tr>
<td>Number of active cysts (%)</td>
<td>8 (26.7)</td>
<td>13 (46.4)</td>
<td>0.118</td>
</tr>
<tr>
<td>Location (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humerus</td>
<td>20 (66.7)</td>
<td>14 (50.0)</td>
<td>0.272</td>
</tr>
<tr>
<td>Femur</td>
<td>6 (20.0)</td>
<td>11 (39.3)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>4 (13.3)</td>
<td>3 (10.7)</td>
<td></td>
</tr>
</tbody>
</table>

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**Table III. Modified Neer classification of radiological results**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healed</td>
<td>Cyst filled by new bone, with or without small radiolucent area(s) &lt; 1 cm in size</td>
</tr>
<tr>
<td>Healing with defects</td>
<td>Radiolucent area(s) &lt; 50% of the diameter of bone, with enough cortical thickness to prevent fracture</td>
</tr>
<tr>
<td>Persistent cyst</td>
<td>Radiolucent area &gt; 50% of diameter of the bone and with a thin cortical rim. No increase in the size of the cyst. Continued restriction of activity or repeated treatment is required</td>
</tr>
<tr>
<td>Recurrent cyst</td>
<td>Cyst reappeared in a previously obliterated area, or a residual radiolucent area has increased in size</td>
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</tbody>
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**Table IV. Comparison of successful results after failure of the initial procedure**

<table>
<thead>
<tr>
<th></th>
<th>Steroid group ((n = 30))</th>
<th>Bone marrow group ((n = 28^*))</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Male:female ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous fracture (Y:N)</td>
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<td></td>
<td></td>
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<tr>
<td>Active cyst:latent cyst</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humerus</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Femur</td>
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<td></td>
<td></td>
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<tr>
<td>Others</td>
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</tbody>
</table>

\(*3 cases with pathological fractures were excluded from statistical analysis*
grafting with autologous bone marrow might induce successful bone formation owing to its own osteogenic potential, reduce the internal pressure of the cyst and remove bone resorptive factors. This osteogenic potential may explain the lower rate of recurrence.

Although no preferred treatment for unicameral bone cysts has been established, most authors agree that open surgery cannot be justified as an initial approach. In the current study, the overall success rates in both the steroid (Fig. 1) and the autologous marrow (Fig. 2) groups were satisfactory after several procedures, but were less impressive after a single procedure, especially in the steroid group. Other studies have found that the healing response to steroid injection was unpredictable and usually incomplete. Scaglietti et al. found recurrence, or no response, after the initial injection in 32% of their patients. Capanna et al. thought that recurrence after steroid injection was associated with multiloculation, the size of the cyst and the age of the patient. They recommended that close radiological surveillance should be maintained in those with risk factors even after the cyst has consolidated. Several other studies also suggested that repeated steroid injections may be needed to achieve adequate consolidation.

Autologous bone marrow grafting of unicameral bone cysts was introduced by Lokie et al. in order to circumvent the repetition of steroid injections. Although grafting does not completely prevent recurrence, it has been reported that the healing rate after a single bone marrow graft is about 60%.

Recently, demineralised bone matrix has been used in the treatment of unicameral bone cysts and has provided excellent results, inducing bone formation by osteoconduction. A mixture of demineralised bone matrix and autologous bone marrow introduces osteoprogenitor cells as well as osteoconductivity and osteoinductivity.

Our study was a retrospective comparison of the two methods, and a prospective randomised controlled trial might be necessary to better assess differences between the two methods. The number of patients enrolled was small, and thus the statistical power of the study was relatively weak. A larger study would provide more information.

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

References


