Treatment of simple bone cysts of humerus by intramedullary decompression and drainage with elastic stable intramedullary nailing combined with intrallesional injections of steroids

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Abstract
Background: Simple bone cysts (SBCs) are common benign lytic bone lesions in children. This study focused on exploring a clinical treatment method, minimally invasive intramedullary decompression and drainage with elastic stable intramedullary nailing (ESIN) combined with intralesional injections of steroids, and evaluated its effectiveness, complications and morbidity through functional and radiographic outcomes. Methods: The postoperative recovery of 18 children who suffered from SBCs of humerus was evaluated (mean follow-up, 40 months) from January 2009 to December 2016. These patients (11 males, 7 females; 8 in the left, 10 in the right; mean age, 10.9 years old) were treated with minimally invasive intramedullary decompression and drainage with ESIN combined with intralesional injections of steroids. The diagnosis was based on not only pre-operative typical medical images (X-rays/CT/MRI) but also surgical findings and pathological diagnosis. Radiological and functional outcomes were evaluated according to Capanna and Musculoskeletal Tumor Society (MSTS) score. The interclass differences were analyzed by t-test. Results: According to Capanna and MSTS criteria, after treatment, 14 patients made full recoveries which was presented by all the cysts filled with bone tissue, and 4 patients made partially recoveries, which were presented by cystic spaces partially filled with low density bone. All the cysts responded to treatment method, and there was no cyst recurrence. All except 2 patients had good functional results. One of the two patients had irritation of the end of the nail and one patient had a valgus deformity. Conclusions: Treatment for SBCs of humerus by minimally invasive intramedullary decompression and drainage with ESIN combined with intrallesional injections of steroids is safe, effective and convenient. The clinical effect is satisfactory and worth popularizing.

Background
According to Virchow, simple bone cysts (SBCs), also called unicameral bone cysts (UBCs), are benign fluid-filled bone tumors, which commonly and typically locate in metaphysis of long bones in children [1]. SBCs are usually discovered in the presence of pathological fractures [2-4], and they are more common in long bones, especially in humerus and femur, and less common in tibia, fibula, radius, and ulna [5, 6]. The sex ratio of male to female patients with SBCs is approximately 2:1, indicating the
incidence of this disease may be related to gender [7]. In addition, many studies have raised other relevant hypotheses on its pathogenesis, including venous obstruction, and destructive factors like interleukin (IL)-1 and Prostaglandin (PG) [8, 9]. There is no specific and standard therapeutic schedule in terms of the treatment of SBCs, and surgical methods commonly used in clinical practice are total resection with bone grafting and subtotal resection with or without bone grafting [10, 11]. Those aggressive operations are extensive and complex, often with high complications as well as high recurrence [12]. In recent decades, new treatments have been developed, such as intralesional injections of steroids [13], intralesional injections of bone marrow [14], bone grafting with homologous cancellous bone chips [15], bone grafting with freeze-dried crushed cortical bone [16], and decompression with multiple drill holes [17]. Even though these new surgical treatments present promising short-term outcomes, most of them are likely to end up with partial recoveries [18], and the recrudescence and tenacity are still the biggest challenges [3].

Recently, with the rapid development of minimally invasive surgical techniques, great changes have taken place in the treatment of SBCs by percutaneous intramedullary decompression. Santori et al. was the first to report elastic nails in 1986 [19]. Then, elastic nails were used in the treatment of unicameral bone cyst in long bones by Roposch’s group [20]. When the elastic intramedullary nails were inserted between the medullary canal and the cyst cavity, continuous drainage and intracystic pressure decompression were carried out. Furthermore, elastic intramedullary nails could play a stable and supporting role, enabling early postoperative motion, preventing adjacent joint stiffness and promoting healing, particularly in the treatment of pathological fractures [21, 22]. However, it was reported that residual lesions were found in the patients with SBCs after treated of only by elastic stable intramedullary nailing (ESIN) [23, 24]. Various methods in the treatment of SBCs ended up with partial healing or residual lesions, thus there is a debate on whether to take conservative treatment or aggressive surgical treatment. However, as SBCs are typically located in metaphysis of long bones in juvenile children, who are eager to return to sports and activities, the minimally invasive and reliable fixed method seemed to be the optimal choice. To explore a better treatment, with a retrospective of SBCs' etiology, we found both venous
outflow obstruction and PG E2/IL-1β enzymes within the cyst fluid, which would cause bone
destruction [25]. Considering the validity of minimally invasive intramedullary decompression,
-drainage with ESIN, and steroids intralesional injection to these pathogenic factors, and there were no
related reports about a combined method before, we conducted the current research to assess the
safety and effectiveness of this combination therapy in the clinical practice.

Methods

This retrospective study was approved by the local ethics committee. From January 2009 to
December 2016, 18 children who had an SBC of the humerus were treated with intramedullary
der compression and drainage with ESIN combined with intralesional injections of steroids. The surgery-
indications of these patients included large and painful SBCs with or without pathological fracture.
Diagnosis information was obtained from orthopedic files, including preoperative/postoperative X-
rays, computed tomography (CT) and magnetic resonance imaging (MRI). Clinical data included
gender, age, symptoms, presence or absence of pathological fracture, surgical procedures, and
functional or radiological outcomes.

As well known, X-ray images of SBCs show that the medullary cavity is a central elliptical bright
shadow with no gravel-like densification point inside, which sometimes is segregated by bone
ridges, and cortical bone will expand and becomes thinner, but there is no periosteal reaction (except
pathological bones). Magnetic Resonance Imaging (MRI) always presents a low or intermediate signal
on T1-weighted images and a homogeneous high signal on T2 weighting. The cystic fluids extracted
by surgeon are tested for pathological examination, which can confirm the diagnosis of SBCs. In this
study, considering the diagnosis of simple bone cysts was clear based on related images, especially in
X-rays and MRI, no preoperative biopsy it was performed.

The demographic data of this study group are summarized in Table 1. 11 males and 7 females were
included in this study, and the mean follow-up period was 40 months (range, 19-65 months). Most of
the cysts were located in the metaphyseal, isolated diaphyseal or metaphyseal-diaphyseal regions of
the humerus. According to the standard proposed by Neer et al [26], the cysts were distinguished into
four grades, and the classification was based on the severity of the lesion. As a result, those cysts
were found active in 16 cases and inactive in 2 cases. Most of the patients were brought to the outpatient by their parents due to upper arm pain or accidental injury, or diagnosed pathological fracture in other institutions. A pathological fracture happened in 12 cases. Recurrence, partial healing and pathological fracture were all our surgical indications.

Surgical technique

After a review of related imaging studies, according to symptoms and physical signs, a conclusion that a benign tumor was the more likely diagnosis was drawn. Surgery was always performed under general anesthesia and radiographic control, and it started from an incisional penetration with a big syringe in the region of the bone cyst located under a C-arm X-ray. The order of the penetration was from the distal part of the cast to the proximal and the surgeon should try to avoid touching vital nerves and vessels in case of hurting any of them. The syringe was through minimally percutaneous penetration, trying to avoid open incision. If the cystic cavity was too large, two or three penetrative points were necessary. Then extracted the cyst liquid which was yellow and transparent, and hemorrhagic combined with pathological fractures. To help confirm the diagnosis at the same time, a pathological application was necessary. Afterwards, wash the cavity with normal saline and cause no further damage to the wall.

Titanium elastic intramedullary nailing (TEN) was applied, which meant to insert elastic intramedullary nails through windows cut on the lateral cortex of the distal of humerus. There were two operative approaches. One was to operate on the medial epicondyle of the humerus and ectepicondyle of humerus, and the other was to operate on the same side of the lateral of ectepicondyle of humerus. The surgeon should be careful not to cause any ulnar nerve injure. For the patients with pathological fractures, reduction should first be performed to reduce injury. The length of the nails was variably selected according to the patient's sex, age, and the bone length (confirmed on the basis of the preoperative images). The diameter of the nails was selected according to the criterion which said 2 nails would occupy 2/3 of the minimum diameter of the medullary cavity, and the longest one was not allowed to be beyond the epiphyseal plate line. In case of disturbing epiphyseal growth, the distal end
of the nails was left in a manner to avoid irritation of the surrounding soft issues. The procedure was under the guidance of a C-ram system. As the elastic intramedullary nail passed through the cyst, decompression and drainage were completed. Methylprednisolone acetate was injected into the cavity through previous percutaneous penetrative point at a variable dose according to the volume of the cavity. The volume of the methylprednisolone acetate was from 5 ml to 50 ml. Since the elastic intramedullary nail had passed through the bone cyst and the decompression was done, the internal drainage was accomplished.

**Postoperative patient management**

All the patients wore a sling after operation, the patient was checked every 2 days. On average, it took about 7-14 days for them to stay in hospital. Active finger and waist motion, and passive elbow and shoulder motion were allowed immediately after operation. Active elbow and passive shoulder motion were allowed 4 weeks after operation. Active shoulder motion was allowed 6-8 weeks after operation.

**Radiological and functional analysis**

Radiological and functional follow-ups were mostly taken in the orthopedic outpatient clinic, and patients' radiographs were evaluated at admission (preoperative), 1 week, 1 month, 2 months, 3 months, 6 months, 12 months and 24 months after the operation, as well as the last follow up. All the patients were asked to take an anteroposterior and lateral radiograph of the humerus.

Musculoskeletal Tumor Society (MSTS) criteria was used to assess the function [27] before and after the operation (Table 2). Using this scoring system, each patient’s emotion, function and pain were evaluated, besides, weight lifting for upper lesions, hand position and hand skills were also recorded. Treatment success was evaluated by Capanna criteria [28], which includes four grades, grade 1: complete healing, fully filled with bone; grade 2: partial healing with a small residual cystic area remains; grade3: partial healing with a large residual cystic area remains; grade 4: partial healing, with response (Table 3). In order to make statistical analysis easier, we made a slight revision of
Capanna criteria. As shown in Table 6, we defined grade 1 to be 4 points, grade 2 to be 3 points, grade 3 to be 2 points, and grade 4 to be 1 point. Preoperative and postoperative results of the last follow-up were recorded in Table 7.

Complications

Early or late complications were recorded, including wound problems, infection, refracture, deformity and nerve injury.

Statistical analysis

Statistics work was done with SPSS17.0 statistical software (USA). Paired t tests were used to compare the MSTS scores, the visual analog scale (VAS) scores and the Capanna scores separately before and after operation. And we defined $P < 0.05$ as statistically significant difference.

Results

Patients in this study were followed for 19 to 65 months with a mean of 40 months. The MSTS scores significantly increased from 3 months to 24 months after the operation, and the most obvious change happened within 3 months after the operation compared to the preoperative status ($P<0.05$). And there were no significant differences during the period from 24 months after operation to the last follow-up ($P>0.05$) (Figure 1-3). As shown in Table 7, the modified Capanna criteria scores showed that the complete healing happened in 14 cases (78%, 14/18), while partial healing was founded in 4 cases (22%, 4/18). The treatment regimen used in this study was effective in all cases. All patients had pain relief. The average VAS score on admission was $4.33 \pm 1.49$, which decreased to $0.33 \pm 0.48$ after operation, and there was a significant statistical difference with $P<0.05$. No nonunion occurred in all the combined pathological fracture patients who suffered from displaced fractures or microfractures. However, the healing time varies.

The function of the elbow and shoulder obtained complete recovery with the fixation of elastic intramedullary nails, and the average recovery time was found to be 9 weeks (range: 8-11weeks). Besides, the elbow and shoulder were allowed to exercise not long after operation, and no pain or
weakness occurred. Elastic intramedullary nails in most cases were removed within 1 to 2 years after operation. In only one case, the elastic intramedullary nails were manipulated under general anesthesia after the 7 months because of the patient's skin irritability induced by intramedullary nails loosening.

The complications of the surgical method were summarized in Table 5. There was one case of refracture caused by accident in 1 month after surgery, and the valgus deformity was showed by posteroanterior X-ray in Figure 4. However, the parents of this child refused a second surgery, and an "O" shaped cast fixation was done after reexamination in outpatient clinic. The child was treated with conservative treatment including the use of a sling for 4 weeks. At follow-up, although the radiographic result was not satisfactory, there was no functional and visual defects, and no nerve injury.

Discussion
Many researchers believed that SBCs did not require special treatment, and it could be resolved before the bone matured. However, spontaneous healing occurs only about 5-10% of all cases [29]. Besides, risk factors such as pain, refracture and deformity had baffled parents and doctors [30, 31]. The main goals when treating SBCs are tantamount to decrease the risk of pathological fracture, assist cyst healing and stop pain. So, exploring a safe, effective, minimally invasive treatment and quick recovery methods had always been the pursuit. Various treatments for SBCs have been development, but there is no agreement on the best strategy. Open surgical methods, including curettage and bone grafting were regarded as the most common procedures methods [32]. However, various complications, such as invasion, infection, wound problems (scars and keloids), growth plate damage, limb varus or valgus deformity, and shortening of limb deformities, limit their application.

With the rapid development of medicine, minimally invasive surgery to see a doctor has become the main form of surgery. Percutaneous and less invasive methods are widely promoted because of the advantages of lower infection rates, fewer wound problems, smaller scars, less anesthetic and fewer complications, making it easier for patients and their families to accept a surgery. The most common ones are percutaneous needle aspiration [33] and injection treatment of steroid or autologous bone
marrow [34, 35]. A study compared treatments in which the simple bone cysts were injected with bone marrow or steroid [36]. Two years after treatment, X-ray examination showed that successful healing of bone cysts was more common in children who had received steroid injections. But the difference is small. Steroid therapy has many advantages, such as its simplicity, low cost, high availability and lack of direct post-operative adverse effects, etc. However, one of the most common problems with steroid therapy in SBCs is its long duration.

Many researchers had demonstrated the application of ESIN in the treatment of SBCs [37, 38]. The intramedullary nails can make a balance between the pressure of the cyst and the medullary cavity, relieve the venous obstruction and improve the local blood circulation. Bumci [39] et al considered that a cut-through between the medullary canal and the cyst cavity could decrease the pressure, improve the microcirculation between them and stimulate bone formation. Besides, the curved and flatted nail tip can effectively damage the cystic wall, and make it easier for ossification and formation of an osteogenic microenvironment in the cystic cavity. Most importantly, elastic intramedullary nailing provides mechanical stability for the prevention or effective fixation of pathological fractures.

Through reviewing the etiology and pathology of the SBCs, the most commonly accepted hypotheses include elevated intraosseous pressure due to venous obstruction and bone destruction caused by PGE2 and IL-1β enzymes [40, 41]. On the basis of existing hypothesis, we can conclude a combination therapy that can not only achieve effective decompression but also inhibit the obstruction of PGE2 and IL-1β enzymes by applying both percutaneous needle aspiration and injection steroid. Moreover, to shorten the treatment duration and provide early mechanical stability for the SBCs with pathological fractures while promoting bone healing, we combined application of elastic intramedullary nails (ESIN) with those two methods. To our knowledge, no such treatment was reported previously. On the basis of the previous work, we combined elastic intramedullary nails with methylprednisolone acetate. In the 18 patients 100% complete or partial radiographic healing was achieved with no recurrence or adverse response, and no patient suffered a second surgery to eradicate the cyst. This fully demonstrated the advantages and development prospects of this
combination therapy. However, as one patient’s intramedullary nail had loosened and the patient developed skin irritability, an earlier removal surgery was manipulated under general anesthesia.

This study still had many limitations. Firstly, all SBCs of patients in this work were located in humerus but no other sites involved. Secondly, the study population was small and a large number of samples were necessary to draw more reliable conclusions. Thirdly, the amount of injections of steroids was not the same. Anyway, in our study, minimally invasive intramedullary decompression and drainage with ESIN and intralesional injections of steroids had achieved perfect results in the treatment of SBCs. In the future study, we should expand the sample size, optimize the dose of steroid, further explore the mechanism of this method in the treatment of SBCs and apply it in the treatment of other diseases.

Abbreviations

ESIN: Elastic stable intramedullary nailing; SBC: Simple bone cyst; UBC: Unicameral bone cyst; TEN: Titanium elastic intramedullary nailing; MSTS: Musculoskeletal Tumor Society; CT: Computed tomography; MRI: Magnetic resonance imaging; VAS: Visual analog scale; PGE2: Prostaglandin E2; IL-1: Interleukin-1.

Declarations

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Authors’ contributions: Tao Zhang made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; Guowei Cheng and Li Sun performed the experiments; Lei Deng have been involved in drafting the manuscript or revising it critically for important intellectual content; Xin Wang given final approval of the version to be published. Nan Bi agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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Availability of data and material

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics, consent and permissions

The Cangzhou hospital of integrated TCM-WM·Hebei Ethics Committee approved this study (Approval number: 2019030). Written informed consent was obtained from each subject.

Consent for publication

Written consent for publish from the participant (or legal parent or guardian for children) to report individual patient data.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Demographic data and general data for study

| ASE | Age | L or R | gender | fracture or not | stage | treatment | follow-up | radiographic healing |
|-----|-----|--------|--------|-----------------|-------|-----------|-----------|---------------------|
| 1   | 7   | L      | M      | Y               | active | S+EIMN    | 19        | grade 1             |
| 2   | 9   | R      | F      | Y               | active | S+EIMN    | 24        | grade 1             |
| 3   | 13  | R      | F      | N               | active | S+EIMN    | 28        | grade 1             |
| 4   | 11  | L      | M      | Y               | active | S+EIMN    | 37        | grade 1             |
| 5   | 14  | R      | M      | N               | active | S+EIMN    | 42        | grade 1             |
| 6   | 15  | R      | M      | Y               | inactive | S+EIMN    | 31        | grade 1             |
| 7   | 8   | L      | F      | Y               | active | S+EIMN    | 53        | grade 1             |
| 8   | 15  | L      | F      | Y               | active | S+EIMN    | 34        | grade 2             |
| 9   | 12  | R      | M      | N               | active | S+EIMN    | 48        | grade 1             |
| 10  | 7   | L      | M      | Y               | active | S+EIMN    | 60        | grade 1             |
| 11  | 9   | R      | M      | N               | active | S+EIMN    | 44        | grade 1             |
| 12  | 13  | L      | F      | Y               | active | S+EIMN    | 31        | grade 2             |
| 13  | 10  | R      | M      | Y               | active | S+EIMN    | 55        | grade 1             |
| 14  | 14  | L      | M      | Y               | active | S+EIMN    | 65        | grade 2             |
| 15  | 10  | L      | M      | Y               | active | S+EIMN    | 58        | grade 1             |
| 16  | 14  | R      | M      | N               | inactive | S+EIMN    | 39        | grade 2             |
| 17  | 9   | R      | F      | N               | active | S+EIMN    | 25        | grade 1             |
| 18  | 7   | R      | F      | Y               | active | S+EIMN    | 29        | grade 1             |

(N/A=not complications)

Table 2 MSTS (preoperation and postoperation)
| ASE | pre-3months | post 3 months | post 6 months | post 12 months | post 24 months | last follow-up |
|-----|-------------|---------------|---------------|----------------|----------------|---------------|
| 1   | 10          | 22            | 26            | 28             | 0              | 29            |
| 2   | 8           | 24            | 27            | 29             | 0              | 30            |
| 3   | 12          | 23            | 27            | 28             | 29             | 29            |
| 4   | 10          | 26            | 28            | 29             | 30             | 30            |
| 5   | 9           | 21            | 26            | 28             | 30             | 30            |
| 6   | 11          | 23            | 25            | 29             | 29             | 29            |
| 7   | 12          | 25            | 28            | 29             | 29             | 29            |
| 8   | 8           | 23            | 27            | 29             | 30             | 30            |
| 9   | 13          | 25            | 28            | 29             | 29             | 29            |
| 10  | 11          | 26            | 28            | 29             | 30             | 30            |
| 11  | 12          | 24            | 26            | 27             | 27             | 27            |
| 12  | 9           | 23            | 26            | 28             | 29             | 29            |
| 13  | 10          | 22            | 28            | 29             | 30             | 30            |
| 14  | 14          | 26            | 27            | 29             | 30             | 30            |
| 15  | 12          | 24            | 27            | 28             | 29             | 29            |
| 16  | 10          | 23            | 25            | 27             | 28             | 28            |
| 17  | 9           | 24            | 26            | 28             | 29             | 29            |
| 18  | 12          | 25            | 27            | 29             | 30             | 30            |

Table 3 Capanna criteria

| Classification | Clinical manifestation |
|----------------|------------------------|
| Grade 1        | Completely healing, fully filled with bone |
| Grade 2        | Partially healing, with a small residual cystic area remains |
| Grade 3        | Partially healing, with a large residual cystic area remains |
| Grade 4        | Partially healing, with response |

Table 4 MSTS ranking score

| MSTS ranking score | perfect: 23, above 23 | good: 15-22 | moderate: 8-14 | bad: 8, below 8 |

Table 5 complications

| complications    | cases |
|------------------|-------|
| wound            | 1     |
| infection        | 0     |
| refracture       | 0     |
| deformity        | 1     |
| nerve injury     | 0     |
| others           | 0     |

Table 6 modified Capanna criteria
Classification | Capanna ranking score
--- | ---
Grade1 | 4
Grade2 | 3
Grade3 | 2
Grade4 | 1

Table 7 Clinical detail of surgical groups

| Capanna | VAS | pre | post | pre | post |
|---|---|---|---|---|---|
| Average ± SD | 1±0 | 3.777±0.427 | 4.33±1.49 | 0.33±0.48 |

Figures
The scores of MSTS. The graph shows the preoperative and postoperative follow-up MSTS scores. Functional scores increased progressively until the end of postoperative 12 months, and then a plateau was reached and preserved throughout the rest of follow-up.
Radiographs of a 10-year-old boy who presented with pathological fracture of the left humerus. (a-b) Anteroposterior and lateral radiograph on admission. (c-e) MRI indicates a low signal on T1-weighted images and a homogeneous high signal on T2 weighting. (f-k)
After the operation of minimally invasive intramedullary decompression and drainage with ESIN combined with intralesional injections of steroids; At the interval points of postoperative 1 weeks, 2 months, 6 months, 9 months, 12 months, 14 months the lesion is significantly smaller and shows signs of healing gradually. At 14 months, Radiograph show complete cyst healing (Capanna grade 1 healing). (l-o) At 16 months, the bone cyst has resolved, and then the intramedullary nails are removed. (n-o) Radiographs show complete cyst healing (Capanna grade 1 healing) after second surgery.
Radiographs of an 11-year-old boy who presented with pathological fracture of the left humerus. (a-b) Anteroposterior and lateral radiograph on admission. (c-d) MRI indicates a low signal on T1-weighted images and a homogeneous high signal on T2 weighting. (e-f) Three-dimensional CT image reconstruction and a sagittal CT scanning show fracture of proximal humeral bone cyst. (g-l) After the operation of minimally invasive intramedullary decompression and drainage with ESIN combined with intralesional injections of steroids; At the interval points of postoperative 1 week, 2 months, 6 months, the lesion is significantly smaller and shows signs of healing gradually, the fracture gradually healed, Radiographs show complete cyst healing (Capanna grade 1 healing).
Radiographs of a 10-year-old boy who presented with pathological fracture of the right humerus. (a-b) Anteroposterior and lateral radiograph on admission. (c-d) MRI indicates a big bone cyst in humerus. (e-f) After the operation, postoperative 1 weeks Radiographs show a good position of the fixation. (g-h) At one month after surgery, an accident is happened, posteroanterior X-ray shows a valgus deformity and a secondary fracture in the cyst region. (i-j) An"O" shaped cast fixation was done after reduction in outpatient clinic, X-ray shows a valgus deformity. (k-n) At the interval points of postoperative 6 weeks, 2 months
Radiographs show a valgus deformity. (o-p) Radiographs show complete cyst healing while there is a valgus deformity, although the position of photograph was not satisfactory, there was no functional and visual defects.