Treatment of Unicameral Bone Cysts in Pediatric Patients With an Injectable Regenerative Graft: A Preliminary Report

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Background: Multiple treatment modalities exist for unicameral bone cysts (UBC), including steroid injection, autologous bone marrow injection, mechanical decompression, intramedullary fixation, curettage, and bone grafting. All have their own potential limitations such as high recurrence rates, cyst persistence, need for multiple procedures, and prolonged immobilization. A minimally invasive regimen consisting of curettage, decompression, and injection of a calcium sulfate-calcium phosphate ($CaSO_4$-$CaPO_4$) composite has been utilized at our institution in an attempt to obtain optimal results for the treatment of UBCs in the pediatric population.

Methods: We retrospectively evaluated 16 patients with pathologically confirmed UBC who were treated with curettage, decompression, and injection of a calcium sulfate-calcium phosphate composite between April 2006 and August 2010 at a single institution. The average age of the patients at time of surgical intervention was 9.4 years of age (range, 3 to 16 y). Average follow-up was 16 months (range, 6 to 36 mo). Radiographic healing, clinical outcomes, and complications were evaluated.

Results: Final follow-up radiographs demonstrated healing in 93.7% (15 of 16) of patients after a single procedure. Complete healing was observed in 14 of 16 patients and partially healed with a defect in 1 of 16 patients. One patient had a persistent cyst but did not wish to receive further treatment. All patients returned to full activities including sports on average at 3.1 months (range, 1 to 6 mo) and were asymptomatic on most recent follow-up. No postoperative complications, including refracture, were observed.

Conclusions: Curettage, decompression, and injection of a calcium sulfate-calcium phosphate composite for UBC in the pediatric population demonstrates encouraging results with low recurrence rates and complications compared with conventional methods.

Level of Evidence: Case series, Level of Evidence IV.

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None of the authors received financial support for this study.

The authors declare no conflict of interest.

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Key Words: unicameral bone cyst, calcium sulfate-calcium phosphate, curettage and grafting, intramedullary decompression

(*J Pediatr Orthop* 2013;33:254–261)

Unicameral bone cysts (UBC), also known as simple cysts or solitary bone cysts, are the most common benign intraosseous lesions found in children.[1] The incidence is about 1 per 10,000 children each year with a male predominance of 2:1.[2] Some lesions remain asymptomatic and resolve spontaneously after skeletal maturity, whereas others will enlarge causing symptoms or fracture secondary to minor trauma. Treatment is typically indicated if pain or a pathologic fracture exists, or when there is risk of an impending fracture because of cyst location and size.

Historical treatment of these lesions included open curettage and bone grafting with either autogenous or allogeneic bone. Initial success rates from open procedures demonstrated a high recurrence rate of up to 45% along with multiple complications.[3–7] Percutaneous injection of methylprednisolone acetate (MPA) has shown variable success rates ranging from 50% to 80% but at the expense of repeat injections and prolonged limitations of physical activities.[5,7–9] Outcomes after injection of autologous bone marrow aspirate have been similar to those after MPA injection.[10–13] Other injectable materials including dimineralized bone matrix, calcium sulfate, and calcium phosphate have been used but with mixed results.[14–22] Despite the extensive literature and numerous procedures proposed in the treatment of UBC, the optimal procedure, which balances outcomes with morbidity, remains to be defined.

After curettage of a UBC, the large remaining defect and small patient size often makes autogenous bone graft an impractical solution. This has prompted recent studies evaluating the effectiveness of injectable bone substitutes. Multiple investigators have utilized calcium sulfate ($CaSO_4$)-based bone graft substitutes both with and without demineralized bone matrix (DBM) for treatment of benign bone tumors.[15–20] These bone graft substitutes offer an osteoconductive scaffold to allow new bone formation and provide temporary osseous stability. They also avoid the morbidity associated with bone graft harvesting. Healing rates of 90% to 91% have been

demonstrated after treatment with percutaneous grafting with DBM and medical grade calcium sulfate pellets.[20,22] However, calcium sulfate is reabsorbed at a rate that exceeds bone growth, leaving the already vulnerable osseous structure at risk for fracture. Newer injectable materials, such as calcium sulfate-calcium phosphate composites, have been developed which demonstrate a more favorable resorption pattern. The purpose of this retrospective study was to evaluate the clinical results, complications, and radiographic healing rates obtained after curettage, decompression, and injection of calcium sulfate-calcium phosphate composite in the treatment of UBC in children.

METHODS

An Institutional Review Board approval was obtained before the start of the study. The authors and the institution did not receive any funding or financial support related to this research and declare no conflict of interest.

Sixteen children with UBC who were managed surgically with curettage, decompression, and a calcium sulfate-calcium phosphate ($CaSO_4$-$CaPO_4$) injectable composite (PRO-DENSE Injectable Graft; Wright Medical Technology Inc., Arlington, TN) between April 2006 and August 2010 at a single pediatric institution were retrospectively reviewed. The diagnosis was on the basis of characteristic radiographic features and later confirmed after histologic analysis of intraoperative biopsy specimen. Six months of postoperative follow-up was required for inclusion in the study.

Patient records were evaluated for patient age, sex, anatomic location of the cyst, cyst size as measured on anterioposterior radiographs, history of previous fracture, and the type of any previous treatments. Postoperative clinical notes and radiographs were reviewed to evaluate length of follow-up, radiographic evidence of cyst healing, time till return to full activities, postoperative fractures, cyst persistence or recurrence, the need for additional procedures, and associated complications (Table 1). At least 6 months of postoperative follow-up was required for inclusion in the study.

Radiographic healing was evaluated according to the modified Neer classification system (Table 2).[3,7,8] The cyst was classified as healed when it had filled with new bone, with or without small radiolucent area(s) of < 1 cm in size and the cortical margins had thickened (Fig. 1). It was classified as healed with residual defects when the majority of the cyst had filled in with bone, radiolucent areas were $< 50\%$ of the diameter of the bone, and the cortical margins had thickened enough to prevent fracture. A persistent cyst was when radiolucent area involved $> 50\%$ of the diameter of the bone and there was no cortical thickening. A cyst was considered recurrent when it had initially healed but subsequently reappeared in a previously obliterated area or if a residual radiolucent area began to increase in size.

Surgical Technique

All patients were given a general anesthetic for the procedure. The cyst was localized with fluoroscopy and the boundaries were marked. A small 2- to 3-cm incision was made over the midportion of the cyst corresponding to the area with thinnest cortical wall. The skin and subcutaneous tissues were then divided. Overlying myofascial tissue that corresponded to the cyst location was carefully incised and muscular fibers were bluntly spread to expose the periosteum overlying the cyst. An H-shaped incision approximately 1.5 cm in length was made in the periosteum creating medial and lateral flaps that were elevated to expose the underlying bone cortex. A small hi-speed burr (4 or 5 mm) or small curette was used to trephine a cortical window approximately 6 to 8 mm in diameter. The fluid filling the cyst was aspirated and the tissue lining the cyst wall was removed and both were sent for pathologic study. Extensive curettage was used in an attempt to completely remove the cyst lining; however, care was taken to avoid the physis during this portion of the procedure when appropriate. The cystic void was then injected with saline to determine its volume. The superior and/or inferior margins of the cyst were then penetrated with trochar needles to allow ingress of marrow elements into the cystic cavity (Fig. 2). If the cyst location was near the physis, then only unidirectional decompression was performed. Adequate decompression was verified with fluoroscopy. The predetermined volume of PRO-DENSE was then injected into the cavity with the use of the 2 trochars supplied with the kit, 1 in the superior aspect of the cyst and 1 in the inferior aspect. Injection was given in an alternate manner to allow for gradual displacement of any blood in the cavity. Standard curing time for the material after injection is 20 to 30 minutes with maximal strength obtained at approximately 24 hours. Adequate filling of the cyst was confirmed with the use of an image intensifier (Fig. 3). An additional small amount of PRO-DENSE was used to form a plug for the cortical window. The periosteal flaps were then repaired and overlying soft tissues were closed in a standard layered manner. Patients with upper extremity lesions (humerus and clavicle) were immobilized in a sling, whereas those with lower extremity lesions (femur and calcaneus) were made nonweight bearing. Protected immobilization continued until there was adequate evidence of radiographic and clinical healing.

RESULTS

Sixteen patients with pathologically confirmed UBCs were treated with curettage, decompression and were injected with $CaSO_4$-$CaPO_4$ composite. The average age of the patients at time of surgical treatment was 9.4 years of age (range, 3 to 16 y). Nine of 11 boys and 4 of 5 girls demonstrated open physes on radiographs and thus, skeletal immaturity was demonstrated at the time of the index procedure. Average follow-up was 16 months (range, 6 to 36 mo). The femur was the most affected location (n = 7), followed by the humerus (n = 6), calcaneus (n = 1), fibula (n = 1), and clavicle (n = 1). Eight patients presented initially with a pathologic fracture, whereas the remaining 8 patients presented with pain and

TABLE 1. Patient Data

Patient Number	Sex	Age	Open Physis	Cyst Size*	Pathologic Fracture Before Treatment	Previous Treatments	Length of Follow-up (mo)	Radiographic Outcome	Clinical Resolution	Time Until Return to Activities (mo)
1	F	14	No	20.4	No	Curettage + osteoset pellets	31	Healed	Complete	4
2	M	4	Yes	9.8	Yes	No	36	Healed	Complete	3
3	M	5	Yes	9	Yes	No	9	Healed	Complete	3
4	M	8	Yes	11.3	Yes	Curettage + osteoset pellets	12	Healed	Complete	4
5	M	5	Yes	7	No	No	6	Healed	Complete	4
6	F	5	Yes	10	Yes	No	23	Healed	Complete	3
7	M	11	Yes	4.2	No	No	19	Healed	Complete	3
8	F	8	Yes	15.1	No	No	9	Healed	Complete	6
9	M	16	No	20.8	No	No	14	Healed with defect	Complete	3
10	M	13	Yes	4.7	No	No	24	Healed	Complete	3
11	F	6	Yes	7.8	Yes	No	12	Persistence	Complete	3
12	F	10	Yes	16.2	Yes	No	8	Healed	Complete	2
13	M	16	No	28.5	No	Curettage + osteoset pellets	14	Healed	Complete	3
14	M	13	Yes	5.6	Yes	No	9	Healed	Complete	1
15	M	12	Yes	2	No	Curettage + autogenous bone graft	18	Healed	Complete	3
16	M	5	Yes	15.3	No	No	12	Healed	Complete	3

*Cyst Size—based on anterioposterior radiographs (height × width) (cm^2).

presumed microfracture. Four patients had received previous alternative treatments of their UBCs that were unsuccessful. These treatments included open curettage and autogenous bone grafting (n = 1), and percutaneous curettage and grafting with calcium sulfate pellets (Osteoset) (n = 3).

After curettage, decompression, and injection of a $CaSO_4$-$CaPO_4$ composite, evaluation of radiographs from the latest postoperative visit demonstrated radiographic healing in 93.7% (15 of 16) of patients after a single procedure (Fig. 4). Complete healing was obtained in 14 patients, healed with defects in 1 patient and cyst persistence (6.3%) in 1 patient. The patient with cyst persistence was asymptomatic on the most recent postoperative visit and did not wish to undergo any further treatment (Fig. 5). All patients were fully functional and pain free at the time of last follow-up. Return to full activities including sports occurred at an average of 3.1 months (range, 1 to 6 mo) postoperatively. No patients experienced infection or fracture postoperatively.

DISCUSSION

UBC are a common entity encountered in pediatric orthopaedics. UBCs have been shown to contain elevated levels of prostaglandins and interleukins within the cyst which stimulate osteoclast resorption of bone, causing weakening and thinning of the local cortical structure.[23,24] Certain lesions will remain asymptomatic and resolve spontaneously. Broms[25] observed healing in 6 of 8 patients with conservative treatment. Conversely, Neer et al[3] reported that 38 of 41 children with UBCs who were treated conservatively eventually required surgical treatment, suggesting early surgical intervention to help prevent deformity or fracture and to expedite return to activities. Most authors agree that treatment is warranted when pain or a pathologic fracture exists, the cyst is enlarging or persistent, or at risk of an impending fracture.

The optimal treatment modality for UBCs continues to be a source of debate. Curettage and bone grafting has lost favor because of the high recurrence rates and associated complications. Neer et al[3] observed a 27% recurrence and reoperation rate in a series of 93 humerus or femoral cysts. Campanacci et al,[7] in a series involving 178 simple bone cysts, observed a recurrence rate of 33% and a limb length discrepancy in 14% of patients. Spence et al[6] treated 177 UBCs with curettage and freeze-dried cancellous bone grafting and observed recurrence in 45% of their patients. Lower recurrence rates have been reported only after subtotal resection, but

TABLE 2. Classification of Radiographic Healing

Classification	Description
Healed	Cyst filled with new bone, with or without small radiolucent area(s) < 1 cm in size, and thickened cortical margins
Healed with defects	Radiolucent areas < 50% of the diameter of the bone, and the cortical margins had thickened enough to prevent fracture
Persistent cyst	Radiolucent area > 50% of diameter of the bone and no cortical thickening. No increase in the size of the cyst
Recurrent cyst	Cyst reappearance in a previously obliterated area, or a residual radiolucent area has increased in size

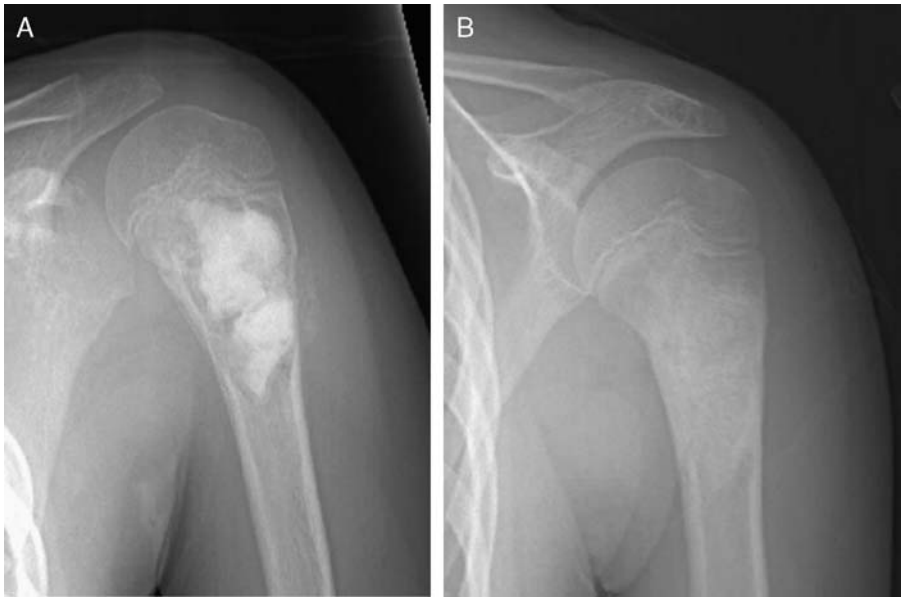

FIGURE 1. An 8-year-old girl after treatment with percutaneous curettage, decompression, and $CaSO_4$-$CaPO_4$ injection. A, Radiograph at 1 month postoperatively showing partial resorption of substrate. B, Radiograph at 9 months postoperatively demonstrating complete healing and reossification of the cyst.

these procedures tend to be more destructive and carry an increased risk of complications.[26,27]

Injection of MPA has been advocated as a treatment method for UBC. High recurrence rates, prolonged immobilization, and multiple injections have been associated with this treatment modality.[7–9] Other complications include pathologic fractures during treatment, leg length discrepancy, and proximal femoral epiphyseal necrosis. In a series of 163 patients, 76% of patients required subsequent injections, an average of 3 to 4 times during a period of 12 to 20 months.[9] In a study involving 90 patients treated with MPA injection, Capanna et al[8] reported a recurrence rate of 13.5% and an overall failure rate of 20%. In a similar study, Campanacci et al[7] treated 141 children with MPA injections and observed complete healing in only 50% of patients and a 15% recurrence. Autologous bone marrow injection has also been advocated to circumvent the multiple injections required with

FIGURE 2. A, Intraoperative radiographs of a proximal femur, illustrating proximal cystic penetration with a trochar needle. B, Distal penetration allowing ingress of marrow elements into the cystic cavity.

FIGURE 3. Fluoroscopic image of a proximal humerus demonstrating complete filling of the cystic defect after injection with $CaSO_4$-$CaPO_4$ substrate.

steroid injections. However, multiple injections were frequently required and the recurrence rates were similar to those obtained after MPA injection. Yandow et al,[10] in a series of 12 simple bone cysts obtained complete healing in only 67% of cases and 42% of patients required multiple injections. Chang et al[13] observed a 57% recurrence rate after the first injection and a 63% after the second injection. Wright et al,[28] in a randomized clinical trial, compared MPA and bone marrow aspirate injections in a series of 77 patients and demonstrated a 43% and 23% success rate, respectively, for these procedures.

The theory of obstructed intramedullary venous circulation has been widely accepted as the most likely etiology associated with UBC formation.[29] Chigira et al[30] reported increased internal pressure of UBCs and lower PO_2 of cyst fluid when compared with normal bone marrow, suggesting venous outflow obstruction as the cause of simple bone cysts. After drilling multiple cortical holes using Kirschner wires, they observed complete healing in 4 of 7 patients.[31] This theory was further supported by the work of Bumci and Vlahovic,[32] in which success rates of 97.4% were obtained after simple breaching of the cortical intramedullary margins of the cyst. However, simple decompression fails to address the associated cortical weakness and large osseous void. Newer studies have combined cystic decompression with internal fixation, so as to provide some stability until cystic healing can occur. De Sanctis and Andreacchio[33] evaluated 47 patients and reported a 0% recurrence rate (66% completely healed and 34% healed with residual defect) after endomedullary nail placement, although 25% of patients required a subsequent surgery for nail removal. Roposch et al,[34] in a similar study, reported a 94% success rate (complete healing or healed with residual defect) in a series of 32 patients after flexible intramedullary nailing of UBCs in long bones. However, 28% of their patients required an exchange nailing and mean hospital stay was 7 days.

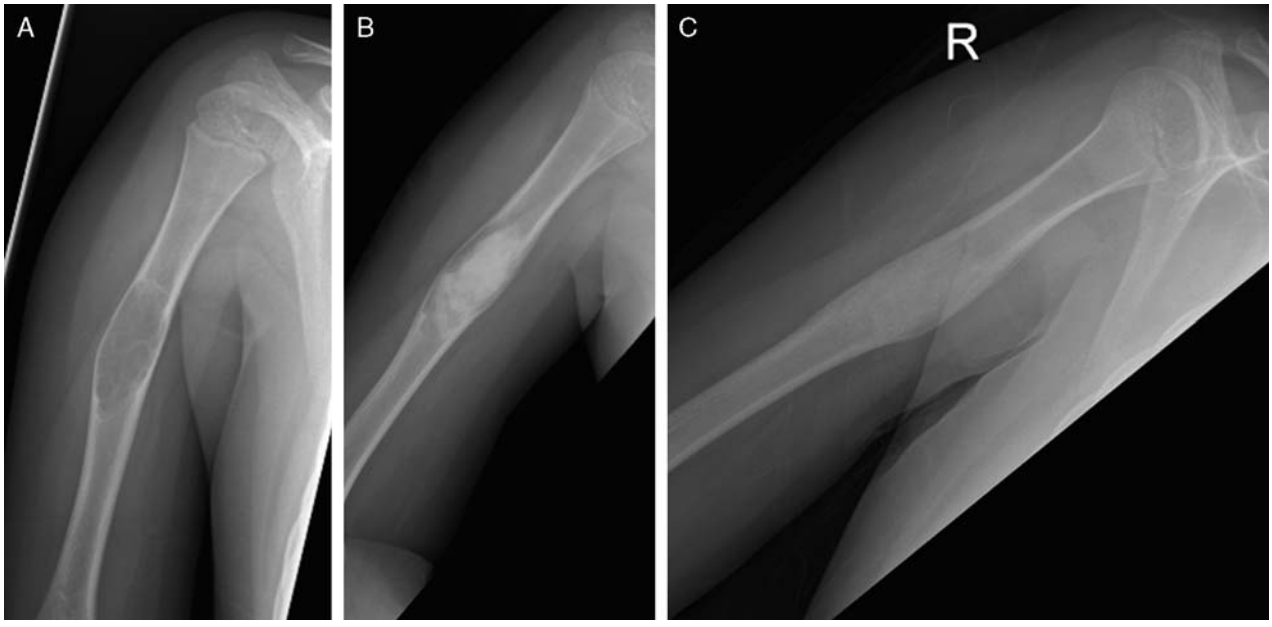

FIGURE 4. An 8-year-old boy with a mid diaphyseal humeral unicameral bone cysts. This patient had failed 2 previous surgical procedures with curettage and grafting with calcium sulfate pellets. A, Preoperative radiograph (24 mo after last surgical procedure). Radiographs at (B) 1 month, and (C) 9 months after treatment with curettage, decompression, and $CaSO_4$-$CaPO_4$ injection, demonstrating healing and reossification of the cyst.

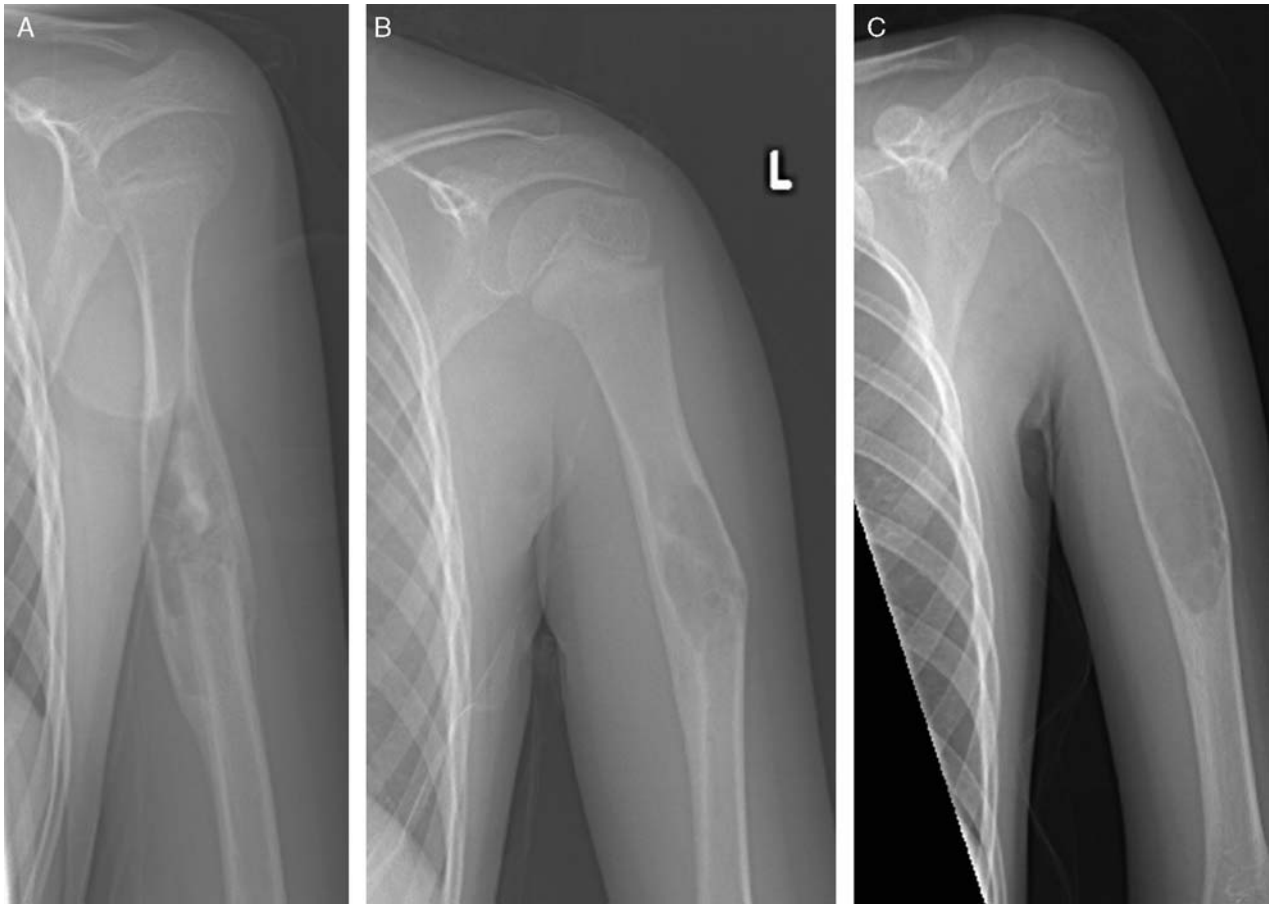

FIGURE 5. A 6-year-old girl with persistence of her unicameral bone cyst. A, Radiograph 1 month posteoperatively showing resorption of substrate along with some residual central radiolucency. B. Radiograph at 3 months shows partial healing, mainly involving the peripheral rim and cortex. C, Twelve-month follow-up radiograph demonstrating radioluceny involving >50% of the bone diameter and minimal cortical thickening, consistence with cyst persistence.

Recent studies have focused on disruption and decompression of the cyst wall in combination with injectable bone graft substitutes. Killian et al[21] reported on 11 patients after percutaneous cystic disruption and injection of DBM by a large bore needle. Complete healing occurred in 2 patients, partial healing in 7 patients, and 2 patients had persistence of their cyst. Kanellopoulos et al[35] treated 19 patients with UBCs using percutaneous reaming and injection of DBM and autologous bone marrow. Radiographic improvement was observed in all patients, although 2 patients required repeated intervention. Multiple studies have investigated the effectiveness of $CaSO_4$ bone graft substitutes for treatment of benign osseous lesions.[15–20] Wilkins[20] treated 11 UBCs with percutaneous grafting with DBM and medical grade calcium sulfate pellets and observed healing in 90% of patients after a single treatment. Dormans et al[22] demonstrated a 91% complete healing rate after percutaneous decompression, curettage, and grafting with medical grade calcium sulfate pellets in a series involving 24 patients. Three patients (12%) had cyst persistence after the initial procedure, 2 of who underwent a repeat procedure. Importantly, $CaSO_4$ graft resorption will exceed that of bone growth and result in an inadequately filled bone defect that could potentially fracture if not properly immobilized or protected.

Recently, an injectable calcium sulfate-calcium phosphate ($CaSO_4$-$CaPO_4$) composite graft became available for nonweight bearing bone defect applications. This material was shown to produce a significantly higher area fraction of new bone formation and compressive strength at 13 weeks than traditional $CaSO_4$ pellets in a canine proximal humerus model.[36] The amount and strength of the restored bone were also improved when compared with autograft treated defects.[37] The material is exothermic during application but never generates heat greater than body temperature. $CaSO_4$-$CaPO_4$ is a porous substrate that allows for direct communication with the cellular contents of the marrow canal and demonstrates a multiphase bone resorption pattern.[36] Initially, the faster resorbing $CaSO_4$ matrix is replaced by bone, whereas the slower resorbing $CaPO_4$ scaffold remains. Eventually, the $CaPO_4$ scaffold will be replaced with bone as well. This combination offers a slower resorption profile which is less

susceptible to environmental effects or potential fracture than traditional $CaSO_4$ grafts, although offering faster resorption when compared with traditional $CaPO_4$ grafts.

To date, there have been no published studies evaluating the outcomes associated with injection of a $CaSO_4$-$CaPO_4$ composite in the treatment of UBCs in pediatric patients. Our study is the first to assess clinical and radiographic outcomes of UBC in a pediatric population after curettage, decompression, and injection of a $CaSO_4$-$CaPO_4$ composite. In our series involving 16 patients, radiographic healing was achieved in 93.7% (15 of 16) of patients after a single procedure. Return to full activities including sports, occurred at an average of 3.1 months (range, 1 to 6 mo) postoperatively. The 1 patient with cyst persistence was completely asymptomatic and did not wish to undergo any further treatment. Clinically, all patients were pain free and fully functional on the latest follow-up. No fractures occurred after treatment was initiated nor were there any associated postoperative complications.

Our study is not without limitations. It is a retrospective study and involves a small cohort (n = 16). Moreover, there is no formal control group for comparison. Longer follow-up would be beneficial to ensure that there is no late cyst recurrence, although the vast majority of cysts that demonstrate healing at 6 months will remain healed. We therefore report on the preliminary results utilizing this technique. A larger multicenter prospective study comparing $CaSO_4$-$CaPO_4$ injection with other traditional methods would be useful.

We have described a novel minimally invasive technique of curettage, decompression, and injection of a $CaSO_4$-$CaPO_4$ composite for the treatment of UBC in the pediatric population. This technique demonstrated a high radiographic healing rate superior or at least equivalent to the other treatment methods offered for UBCs. It is done as a single procedure and avoids the expenses associated with multiple operating room trips and the potential complications associated with anesthesia. It also utilizes the healing benefits of intramedullary decompression and curettage but with minimal patient morbidity. The $CaSO_4$-$CaPO_4$ substrate used serves as a potent osteoconductive scaffold and offers improved structural support until complete filling of the bone defect can occur. This avoids the need for supplementary internal fixation and the subsequent surgery to remove the implants. We therefore conclude that the treatment of UBC in pediatric patients with curettage, decompression, and injection of a $CaSO_4$-$CaPO_4$ composite is a safe and cost-effective treatment with a low recurrence and complication rate when compared with conventional methods.

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